Neuregulin (NRG)-1 is implicated in the preservation of left ventricular performance in pathophysiological conditions. This study analysed the effects of NRG-1 treatment in an animal model of pulmonary arterial hypertension (PAH) and right ventricular (RV) failure.

Male Wistar rats (180-200g) received monocrotaline (MCT, 60mg/kg, sc) or vehicle. After 14 days, these animals were randomly assigned to receive treatment with NRG-1 (40μg/kg/day, ip) or vehicle. The study resulted in 4 groups: CTRL (n=10); CTRL+NRG (n=10); MCT (n=10); MCT+NRG (n=10). Echocardiography, RV invasive hemodynamics and sample collection for morphometric, histologic and molecular studies were performed 25-28 days after MCT administration. Only significant results (p<0.05) are reported. MCT group developed PAH, as shown by increased RV maximum pressure (MCT vs CTRL: 63±3 vs 34±3mmHg) and by decreased cardiac output (MCT vs CTRL: 34±6 vs 65±5ml/min), which were both attenuated in the MCT-NRG group (53±3mmHg and 52±2ml/min). Echocardiographic evaluation showed increased RV dimensions and tricuspid regurgitation in the MCT group (MCT vs CTRL: 5.5±0.19 vs 5.0±0.08 mm and 2.3±0.01 vs 0.61±0.06 m/sec). Pulmonary regurgitation, decreased pulmonary flow velocity and acceleration time were also observed in the MCT group (0.80±0.27 vs 0.00±0.00 m/sec, 0.76±0.07 vs 1.12±0.03 m/sec, 17.97±2.29 vs 25.86±1.46 ms, respectively). MCT-NRG animals revealed improvements in all parameters (4.89±0.20 mm, 0.62±0.17 m/sec, 0.00±0.00 m/sec, 0.98±0.02 m/sec and 28.15±1.86 ms, respectively). MCT group animals developed RV hypertrophy (RV weight/tibia length MCT vs CTRL: 0.70±0.05 vs 0.46±0.03 g/cm, respectively). MCT-NRG animals developed RV hypertrophy (RV weight/tibia length MCT vs CTRL: 0.65±0.02 vs 0.56±0.00 g/cm) and pulmonary congestion (lung weight/tibia length MCT vs CTRL: 0.70±0.03 vs 0.45±0.03 g/cm). MCT group revealed significantly higher protein expression of Col1A1 in FOXO3a-/- fibroblasts compared to WT mice (P<0.001). This study aimed to test the hypothesis that up-regulation of SMP30 inhibits cardiac hypertrophy and remodeling.

**Results:**
- After 2 weeks, weight was significantly lower in MCT-TG mice than in WT mice (P<0.01).
- Echocardiography revealed that calculated left ventricular (LV) mass and E/e' were lower in SMP30-TG mice than in WT mice (P<0.01 and P<0.05, respectively), suggesting that diastolic function was preserved in SMP30-TG mice. Histological analysis showed that the degree of cardiac fibrosis was lower in SMP30-TG mice than in WT mice (P<0.05). Dihydromethidium staining demonstrated that generation of reactive oxygen species was reduced in SMP30-TG mice compared with WT mice (P<0.05). Furthermore, the numbers of senescence-associated β-galactosidase-positive cardiac myocytes and myofibroblasts were also significantly reduced in SMP30-TG mice compared to WT mice (P<0.05). In addition, p21 mRNA levels were significantly suppressed in SMP30-TG mice compared to WT mice (P<0.01).

**Conclusions:** This study demonstrated that cardiac specific overexpression of SMP30 inhibits Ang II-induced cardiac hypertrophy and remodeling. These findings suggest that SMP30 has a cardioprotective role with anti-oxidative and anti-aging effects.
Osteoglycin deficiency leads to maladaptive 
remodeling and severe cardiac hypertrophy in a 
mouse model of cardiac hypertrophy

Osteoglycin (Ogn), a small leucine rich proteoglycan, is a potent 
regulator of collagen fibrillogenesis. We could recently demonstrate its important 
role in the initiation of cardiac hypertrophy. However, the contribution of 
Ogn in cardiac hypertrophy is still unknown. Therefore, the aim of this study was 
to investigate the influence of Ogn on remodeling processes and cardiac function 
in pressure-overload hypertension.

Background: Osteoglycin (Ogn), a small leucine rich proteoglycan, is a potent 
regulator of collagen fibrillogenesis. We could recently demonstrate its important 
role in the initiation of cardiac hypertrophy. However, the contribution of 
Ogn in cardiac hypertrophy is still unknown. Therefore, the aim of this study was 
to investigate the influence of Ogn on remodeling processes and cardiac function 
in pressure-overload hypertrophy.

Methods: Left ventricular (LV) pressure overload was induced by subtotal trans- 
verse aortic constriction (TAC) in wildtype mice (WT, n=16) and Ogn knockout 
mice (OgnKO, n=16). Sham-operated mice (n=16 per group) served as controls. 
After 8 weeks, systolic and diastolic parameters were assessed by high-resolution 
echocardiography followed by heart excision. Parameters typically associated with 
hypertrophy were determined by quantitative real-time PCR (qRT-PCR), and 
gelatinoxytic activity of matrix metalloproteinases (MMP) was detected byzymog- 
raphy. Morphological analysis was performed with immunohistochemical staining. 
In an additional subset of WT mice, Western blot analyses were performed to 
determine the contribution of Ogn amount.

Results: In WT mice, a transient decrease of Ogn protein amount was evident 
2 days after TAC. All animals developed a cardiac hypertrophy with a reduced 
LV function after TAC. In OgnKO mice, echocardiography revealed a severely im- 
paired systolic LV function 3 weeks after TAC (LV ejection fraction 24±3.2% vs. 
47±3.2%, p<0.001, control 64.5±5.3%; cardiac output 8.8±0.8 ml/min vs. 
12.4±0.5 ml/min, p=0.05, control 15.1±1.4 ml/min). Furthermore, OgnKO mice had 
a profound diastolic dysfunction with a significantly increased E/E' ratio and an 
increased E' ratio. In addition, OgnKO mice exhibited a significant LV dilatation 
in comparison to WT mice (LV inner diameter 5.2±0.1 mm vs. 3.8±0.1 mm, 
p<0.001) and an increased heart weight (heart weight/tibia length 12.6±0.8 
mg/mm vs. 9.2±0.5 mg/mm, p=0.05). OgnKO mice had an increased fibrosis 
(relative total collagen content 10.2±6.0 mg/mm vs. 9.2±0.5 mg/mm, p=0.05). The mRNA 
expression of osteopontin, connective tissue growth factor and insulin-like growth 
factor was increased in both groups after TAC. However, the expression and ac- 

Conclusions: Inhibition of nuclear translocation of calcineurin significantly de- 
creased myocardial hypertrophy. It appears that calcineurin acts as an intranu- 
clear Ca2+ sensor which translates intranuclear Ca2+ rises into increased NFAT 
mediated transcription.

In conclusion, we found that Ca2+ perinuclear stores suffer from progressive loss 
after TAC, as well as in severely failing human hearts (EF<35%), similar changes of 
CaTs also occurred in the cytoplasm. In control CMs, electron microscopy and 
staining of perinuclear Ca stores revealed a nuclear envelope and its invagina- 
tions transversing the nucleus, containing nuclear pore complexes (NPC) and 
SERCA pump. A significant increase in number of invaginations per nucleus was 
observed during physiological growth, while in TAC CMs, the number of invagi- 
nations per nucleus progressively decreased. Immunostaining of Ca regulatory 
proteins showed that CMs from TAC hearts contain less RyRs and more IP3Rs 
as compared to control hearts, suggesting a shift in Ca signaling from rhythmic 
CaTs to local IP3 induced Ca fluxes. It appears in the regions surrounding the nucleus. 
Similar changes were also observed in failing human myocardium.

In conclusion, we found that Ca perinuclear stores suffer from progressive loss 
of tubular invaginations which may contribute to the slower upstroke (absence of 
NPC in the nuclear lumens) and decay (absence of SERCA pump) of electrically 
stimulated CaTs, resulting in build-up of basal Ca2+ within a range of stimula- 
tion frequencies. Together with the accumulation of IP3Rs in the perinuclear region, 
I may alter both, local and global Ca handeling and induce dysreg- 
ulation of gene transcription.

ANTITHROMBOTIC THERAPY: KEEP ON LEARNING

Low TAFI levels increase the risk of hemorrhagic complications during long-term warfarin therapy

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Thrombin activatable fibrinolysis inhibitor (TAFI) is a component of fibrinolysis, 
which acts by inhibiting the assembly of fibrinolytic factors on the fibrin surface.

Purpose: To determine associations between TAFI levels and hemorrhagic comp- 
ications during long-term warfarin therapy in pts with venous thromboembolism (VTE).

Methods: Ninety eight pts (70 men) in the age 18-76 (mean 54±14 years with VTE and/or pulmonary embolism were included in the study. Pts 
received unfractured or low molecular weight heparin for at least 5 days fol- 
lowed by long-term warfarin therapy (international normalized ratio (INR) 2.0-3.0).

TAFI levels were measured once during warfarin therapy by a chromogenic as- 
say with reagent kits “STA STACHROM TAFI” (Diagnostica Stago).

Results: In all VTE pts, median of TAFI levels was 106 (interquartile range 90- 
133) %. Twenty four pts had low TAFI levels (<90%), and 74 pts had high TAFI 
levels (≥90%). We found no associations between the carriage of CYP2C9 and 
VKORC1 genetic polymorphisms and TAFI levels. The frequency of hemorrhagic 
complications during 18 months of warfarin therapy was 22% in pts with low TAFI 
levels and 26% in pts with high TAFI levels (p=0.8). Further, pts with hemorrhagic 
complications had significantly higher frequency of spontaneous bleedings (80% vs 21%, 
p<0.028) and bleedings in a target INR (100% vs 27%, p=0.018). Cox propor- 
tional hazard model showed that in VTE pts with hemorrhagic complications 
and TAFI levels <90%, the hazard risk of spontaneous bleedings was 4.16 (95% CI 
1.34-16.65; p=0.04), and the hazard risk of bleedings in a target INR (2.0-3.0) 
was 3.06 (95% CI 1.35-7.24; p=0.018) compared in VTE pts with hemorrhagic 
complications and TAFI levels ≥90%.

Conclusion: In VTE pts with hemorrhagic complications during long-term war- 
farin therapy, TAFI levels <90% increase the risk of spontaneous bleedings and 
bleedings in a target INR (2.0-3.0).
The effect of doubling the dose of ASA versus Impact of omeprazole (OME), esomeprazole (ESO) +/− The distribution of risk alleles for clopidogrel response concentrations of inflammatory markers in patients with T2DM and HTPR. was observed in comparison to group 1 \[\text{OR} \ 4.15; \ 95\% \ CI: \ 1.34 – 12.82; \ p=0.013\].

Results:

Conclusions: Not only severe, but moderate CKD contributes to MBE. The ability to predict MBE in patients with AF on anticoagulation could be improved by recognition of moderate CKD as a contributing factor for MBE.

The effect of doubling the dose of ASA versus switching to clopidogrel on inflammatory markers in patients with type 2 diabetes with high-on-treatment platelet reactivity: the AVOCADO study

Materials and methods:

Background: Low-grade inflammation and high platelet reactivity play pivotal role in atherothrombotic complications of diabetes. We determined the effects of doubling the dose of acetylsalicylic acid (ASA) or switching to clopidogrel on inflammatory markers concentrations in patients with type 2 diabetes (T2DM) and high-on-treatment platelet reactivity (HTPR).

Methods and materials:

Results:

Conclusions: Doubling the dose of ASA or switching to clopidogrel reduced concentrations of inflammatory markers in patients with T2DM and HTPR.

2022

Impact of omeprazole (OME), esomeprazole (ESO) +/- acetylsalicylic acid (ASA) and lansoprazole (LAN) on the pharmacodynamics (PD) and pharmacokinetics (PK) of clopidogrel in healthy volunteers

Methods: Both studies enrolled healthy volunteers. In study #34 (106 volunteers), the effect of OME, ESO or LAN on the PD of clopidogrel was assessed by maximum inhibition of platelet aggregation (mIPA) and change in platelet reactivity index (PRI, using VASP) on Days 2, 6, 15 and 30 relative to baseline. The effect on the PK of clopidogrel was assessed by means of systemic exposure (AUC and Cmax) of the active metabolite (AMC) after a loading dose (300mg; Day 1) and during maintenance dosing (75mg/day) on Days 5, 14 and 29. In study #10 (80 volunteers), the effect of ESO 20mg + a ESO 81mg on the PD of clopidogrel (75mg/day) was assessed by mIPA after 9 days relative to baseline. Systemic exposure of AMC (AUC and Cmax) was assessed on Day 9.

Results:

Conclusions: All PPIs tested decreased the effect of clopidogrel and decreased systemic exposure to the active metabolite. However, the antiplatelet effect was not different when esomeprazole was administered in a fixed combination with ASA together with clopidogrel versus clopidogrel alone, even though systemic exposure to the active metabolite was decreased.

2024

An open-label, phase 1 study to evaluate the effects of hepatic impairment on edoxaban pharmacokinetics

Purpose: Edoxaban is an oral, direct factor Xa inhibitor under investigation for prevention of stroke in AF and the secondary prevention of VTE. Changes in hepatic function may affect edoxaban exposure due to altered metabolism, albeit edoxaban is primarily excreted unchanged. This study assessed edoxaban pharmacokinetics (PK) in subjects with hepatic impairment (HI) compared with matched healthy subjects (HS).

Methods: Adults (18-65 years) with mild (Child-Pugh Grade A) or moderate (mod) (Child-Pugh Grade B) HI were matched with HS by age, gender, and weight (4 cohorts of 8 subjects). Subjects received a single oral dose of edoxaban 15 mg. Serial blood and urine samples were collected for up to 72 h. The primary objective was to compare edoxaban PK: area under the curve (AUC), maximum concentration (Cmax), and elimination half-life (t1/2), in HI vs HS. Secondary objectives were safety, PK for M-4 (edoxaban metabolite), and pharmacodynamics.

Results: 33 subjects were enrolled and 32 completed. AUC decreased by 4.2% and 4.8% in subjects with mild or mod HI, respectively, vs HS (Table 1). Cmax decreased by 10% and 32% in subjects with mild or mod HI, respectively, vs HS (Table 1). Median t1/2 decreased by 13% and 21% in subjects with mild or mod HI vs HS, respectively. AUC for M-4 increased 28% for mod HI and did not change for mod HI vs HS. A subject with mod HI vomited after dosing and was replaced; no other AEs were reported.

2025

The distribution of risk alleles for clopidogrel response in Czech patients with coronary stenting

Methods: By means of lineukaryotic CKD stage 3, 4, and 5 group were compared to no/mild CKD group (P<0.001). Multivariate analysis showed CKD stage 3 (HR, 3.65; P=0.005), stage 4 (HR, 6.06; P=0.018), and stage 5 (HR, 6.01; P=0.012) were all independent predictors of MBE. The area under the curve of modified HAS-BLED score was superior to original HAS-BLED score for predicting MBE (0.70 vs 0.65, P=0.026).

Results:

Conclusions: The results of this study suggest that hepatic impairment had a minimal effect on the PK of edoxaban and its metabolite, M-4.
Association of arterial stiffness with various markers of inflammation and hemostasis: results from the population-based Gutenberg Health study

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Purpose: There are numerous studies, demonstrating an independent association between elevated concentrations of inflammatory biomarkers and increased arterial stiffness (AS). However, all of these studies were based on the measurement of inflammatory markers and left future research on the role of non-invasive pulse wave analysis using stiffness index (SI) as still missing.

Methods: Data from 10,000 participants of the population-based Gutenberg Health study, stratified for age, gender and residence were used. All data were collected according to standard operating procedures with detailed quality control using computer-assisted personal interview data, laboratory measurements and clinical examinations. AS was determined by PulseTrace 2000 (Cardinal Health) in 8,060 subjects (4,226 men (M)/3,834 women (W); age range 35–74 yrs.) due to clinical examinations. AS was determined by PulseTrace 2000 (Cardinal Health) in 8,060 subjects (4,226 men (M)/3,834 women (W); age range 35–74 yrs.) due to clinical examinations. CRP, WBCC, albumin, fibrinogen and WBV were significantly and independently associated with SI in a fully adjusted model in males, whereas hematocrit remained independently associated with AS in both genders. Further, IL-1RA, fibrinogen, hematocrit and WBV in both genders and IL-18 in men and albumin in women were associated with AS (all per 1-SD increase in biomarker concentration). However, after further adjustment for CV risk factors, only hematocrit remained independently associated with AS in both genders. Further, IL-1RA was independently associated with SI in a fully adjusted model in males, whereas WBCC, albumin, fibrinogen and WBV were significantly and independently associated with SI after multivariable adjustment in females.

Conclusion: We found gender-specific differences with regard to the association of AS with markers of inflammation and hemostasis. Further studies are needed to understand the underlying mechanism for these associations.

Association of circulating endothelial microparticles with cardiovascular risk factors in the Framingham Heart Study

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Purpose: Circulating microparticles are shed membrane vesicles released during cell apoptosis and/or activation. It has been suggested that circulating enothelial microparticles (EMPs) are increased in individuals with a high burden of cardiovascular risk factors. Nonetheless, prior studies have been limited to small, highly-selected samples of risk studies. We examined the association of circulating EMPs with cardiovascular risk factors in a large, community-based sample.

Methods: We studied 915 individuals without history of cardiovascular disease from the Framingham Heart Study Offspring Study (9–16 yrs., 55% women). Circulating CD144+, CD62e+ and CD31+CD41- EMPs were analyzed using flow cytometry methods.

Results: The Table 1 displays the age- and sex-adj usted correlations between CD144+, CD62e+, and CD31+CD41- EMPs and individual cardiovascular risk factors. In multivariable analyses adjusted for all risk factors simultaneously, the associations between CD144+ (p=0.003) and CD31+CD41- EMPs (p<0.0001) with triglycerides remained significant. In the subset of individuals without diabetes (n=901), CD144+ and CD62e+ EMPs were both associated with the presence of metabolic syndrome (p<0.05). CD31+CD41- EMPs had the strongest associations with the Framingham risk score (p=0.01).

Conclusion: In a large community-based sample, circulating EMP levels are associated with the presence of cardiovascular risk factors, particularly dyslipidemia. These data underscore the potential influence of high-risk metabolic profiles on endothelial integrity.

Abstract 2035 – Table 1

<table>
<thead>
<tr>
<th></th>
<th>Age and Sex-Adjusted Partial Correlation Coefficient (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>F</td>
</tr>
<tr>
<td>Sex</td>
<td>F</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>0.12 (0.005)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.06 (0.001)</td>
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<tr>
<td>Total HDL cholesterol</td>
<td>0.13 (0.003)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>0.02 (0.61)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.05 (0.70)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.00 (0.68)</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.00 (0.68)</td>
</tr>
</tbody>
</table>

CD144+EMP     -0.05 (0.16) -0.08 (0.02)  0.00 (0.92) 0.00 (0.92)  0.17 (0.001) 0.15 (0.001) 0.02 (0.45)
CD62e+EMP     0.03 (0.43) -0.06 (0.10)  0.09 (0.03)  0.00 (0.92)  0.13 (0.003) 0.03 (0.33) 0.01 (0.85) 0.05 (0.70) 0.05 (0.70) 0.05 (0.70) 0.05 (0.70) 0.17 (0.001) 0.15 (0.001) 0.22 (0.001) 0.04 (0.91) 0.02 (0.65)

Conclusion: The Table 1 displays the age- and sex-adjusted correlations between CD144+, CD62e+, and CD31+CD41- EMPs and individual cardiovascular risk factors. In multivariable analyses adjusted for all risk factors simultaneously, the associations between CD144+ (p=0.003) and CD31+CD41- EMPs (p<0.0001) with triglycerides remained significant. In the subset of individuals without diabetes (n=901), CD144+ and CD62e+ EMPs were both associated with the presence of metabolic syndrome (p<0.05). CD31+CD41- EMPs had the strongest associations with the Framingham risk score (p=0.01).

Conclusion: In a large community-based sample, circulating EMP levels are associated with the presence of cardiovascular risk factors, particularly dyslipidemia. These data underscore the potential influence of high-risk metabolic profiles on endothelial integrity.
Molecular lipidomics analysis reveals marked differences in lipid composition of high-density lipoprotein (HDL) in patients with coronary artery disease and healthy subjects.

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Background: Nardilysin (NRDc) is a zinc peptidase of the M16 family. We identified NRDc as a specific binding partner of HB-EGF, and demonstrated that NRDc endocytosis regulates multiple membrane proteins such as TNF-α and neuregulin1. We also demonstrated that NRDc regulates axonal maturation in vivo through modulation of neuregulin1 shedding. On the other hand, we have recently established a high sensitive ELISA system for NRDc and reported that serum NRDc is increased in gastric cancer patients. In this report, we showed the growth-promoting effect of NRDc through the activation of TNF-α shedding. While these results suggest the important roles of NRDc in inflammatory diseases, pathophysiological roles of NRDc in cardiovascular diseases remain unclear.

Results: Among 80 consecutive patients admitted to our department, the serum concentration of NRDc in patients with cardiovascular diseases, and investigated the expression pattern of NRDc in acute coronary syndrome (ACS). Levels of serum NRDc were available at all time points.

Conclusions: We have identified altered levels of circulating miR-133a, 122, 92a and 126 levels showed no correlation with TnT. There was no association between any of the studied miRs and serum CRP levels. The differences noted were not explained by changes in renal or liver function.

Conclusions: We have identified altered levels of circulating miRs in ACS. These miRs show similar changes in acute coronary syndromes and may offer significant prognostic information in patients undergoing cardiac surgery.

IMPROVING OUTCOME AFTER ACUTE MYOCARDIAL INFARCTION?


Background: Primary percutaneous coronary intervention (PPCI) has resulted in shorter hospital stays with discharge at 48 hours in low-risk patients possible. We investigated whether in low risk patients stratified to 48 hour discharge, 48 hour discharge would be feasible

Methods: An observational study involving 2,980 patients who underwent PPCI from 2004-2011. Patients with TIMI 3 flow, ST segment resolution, good or moderate left ventricular function, and no dysrhythmia post-PPCI were discharged at 48 hours.

Results: Among 80 consecutive patients admitted to our department, the serum concentration of NRDc in patients with cardiovascular diseases, and investigated the expression pattern of NRDc in acute coronary syndrome (ACS).

Conclusions: We have identified altered levels of circulating miRs in ACS. These miRs show similar changes in acute coronary syndromes and may offer significant prognostic information in patients undergoing cardiac surgery.
A meta analysis on primary PCI for unprotected left main disease in acute myocardial infarction patients


Purpose: Limited data is available on outcomes after primary percutaneous coronary intervention (PCI) in patients presenting with unprotected left main coronary artery (ULMCA) related acute myocardial infarction (AMI). Therefore, we performed a meta-analysis to evaluate 30-day mortality in this patient group.

Methods: Medical literature databases were searched to identify studies reporting on PCI for ULMCA related AMI. The primary endpoint was 30-day mortality. Binary outcomes from individual studies were combined with the Mantel–Haenzel or inverse variance fixed-effect models. Furthermore, average estimated 30-day mortality was calculated as Relative Risk.

Results: 13 retrospective studies were included, comprising 979 patients, of whom 253 (26%) presented in cardiogenic shock or inverse variance fixed-effect models. Furthermore, average estimated 30-day mortality was calculated as Relative Risk.

Conclusions: In this large meta-analysis of patients treated with primary PCI for ULMCA related AMI, 30-day mortality in patients presenting with shock is much higher than in patients presenting without. The estimated all cause mortality may serve as benchmark for future reference.

Predictors of 1-year mortality in patients with contemporary optimised guideline-adherent secondary prevention therapy after acute myocardial infarction: results from the OMEGA Study

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Background: Independent predictors of mortality after acute myocardial infarction (AMI) are well characterized. However, these risk factors are based on data almost exclusively derived from older studies without consistent use of reperfusion therapy, statins, clopidogrel etc. We therefore sought to investigate predictors of 1-year mortality in survivors of AMI treated with contemporary guideline-adherent therapy.

Methods and Results: We conducted a retrospective analysis of 3,604 patients surviving acute STElevation and non STElevation myocardial infarction (STEMI and NSTEMI) who were enrolled in the prospective, randomized, double-blind, controlled OMEGA trial with 104 German centers. The primary objective of the OMEGA study was to determine the effect of highly purified omega-3 fatty acid ethyl-ester-90 on the rate of sudden cardiac death in patients surviving AMI and receiving current guideline-adherent treatment within 1 year of follow-up. 86.1% of the patients received early reperfusion therapy. At discharge 94.1% of the patients received beta-blocker, 93.3% ACE inhibitor/sartans, 94.2% statins, 95.2% aspirin, and 88.4% clopidogrel. Death at 1 year occurred in 158 patients (4.3%). The multivariate logistic regression analysis revealed the following independent predictors of 1-year mortality in decreasing order of importance: ejection fraction < 40% (odds ratio [OR] 2.24, 95%-confidence interval [CI] 1.50-3.36), age > 70 years (OR 2.19, 95%-CI 1.43-3.34), creatinine > 2 mg/dl (OR 2.08, 95%-CI 1.91-4.30), peripheral arterial disease (OR 1.97, 95%-CI 1.19-3.25), heart rate > 85/min. (OR 1.91, 95%-CI 1.29-2.83), prior stroke/transient ischemic attack (OR 1.90, 95%-CI 1.09-3.29), chronic obstructive pulmonary disease (OR 1.81, 95%-CI 1.04-3.16) and HDL-cholesterol < 40 mg/dl (OR 1.73, 95%-CI 1.13-2.63).

Conclusion: In patients surviving AMI and treated with contemporary guideline-adherent therapy 1-year mortality was low. Nevertheless, ejection fraction < 40%, older age and chronic renal insufficiency were the strongest predictors of long-term mortality supporting the findings from previous studies.

Patient education after acute myocardial infarction: cardiologists should do a better job. The FAST-MI 2010 registry

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Background: A shorter time delay between onset of symptoms and first call to medical attention would be expected in patients with a history of ischemic heart disease (HD), compared with patients not known to have HD, either because they have already experienced an AMI or because their GPs/cardiologists would have educated them to recognize symptoms of AMI.

Aim: To determine whether time to first call for a STEMI differed between patients with and without history of coronary artery disease.

Methods: FAST-MI 2010 is a nationwide French registry that included 4169 patients with AMI at the end of 2010 in 213 centres. These comprised 2364 STEMI patients. Factors correlated with time to first call were assessed, with a specific emphasis on previous history of HD (HD+ n=382), compared with patients without history of HD (HD– n=1862).

Results: Time from onset to first call (TOFC) was 245±453 min (median 75 min) in HD+ patients vs 246±431 min (median 75 min) in HD– patients (P<0.95). TOFC was ≤ 60 minutes in 48% of HD+ patients and in 47% of HD– patients (P=0.77). TOFC was ≤ 120 minutes in 66% and 63%, respectively (P=0.33). Only few factors were significantly related to a shorter TOFC: greater chest pain intensity (P<0.001), diurnal onset of symptoms from 7:00 am to 11:00 pm (P<0.001), syncope/cardiac arrest as initial symptom (P<0.001), anterior location of MI (P<0.004), higher Killip class on admission (P=0.02), and not living alone (P=0.03). With the only exception of chronic treatment with aspirin (P=0.03), none of the medications used before onset of AMI was associated with a shorter TOFC.

Conclusions: Patients with a history of HD do not call earlier than AMI-naive patients when they are confronted with symptoms of AMI. Cardiologists should spend more time to educate their coronary patients to recognize symptoms of AMI.

Long-term trimetazidine modified release therapy improves prognosis in post-myocardial infarction patients with angiina pectoris and heart failure

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Aim: Several preliminary trials and meta-analysis showed that trimetazidine (TMZ) reduces mortality in patients (pts) with coronary artery disease (CAD) and heart failure. However, long-term effects of TMZ on the prognosis of post-myocardial infarction (post-MI) pts remain unclear. The aim of our study was to determine long-term effects of TMZ 35 mg modified release (MR) on all-cause mortality in post-MI pts with stable angina and heart failure.

Methods: 120 post-MI pts (mean age 58.4±2.2) with stable angina (mean CCS functional class: 2.4±0.1) and heart failure (mean NYHA functional class: 2.5±0.1) were included in this long-term, prospective, randomized clinical trial.
Pts were randomized into two groups – the group of active therapy (TMZ MR on top of standard post-MI therapy after discharge from hospital, continued for the next 6 years, n=61) and the control group (standard therapy without TMZ MR, n=59).

Results: Baseline characteristics were the same in the two groups of post-MI pts. Six-year survival in post-MI pts receiving TMZ MR was 84% vs. 65% in the Control group, p<0.05. Over the 6 year follow-up, long term TMZ MR therapy was characterized by a significant reduction of all-cause mortality (RR 0.51; 95% CI 0.25 – 0.92, p<0.05) (Figure 1), as well as major cardiovascular events (cardiac death, nonfatal myocardial infarction, acute stroke, need for coronary revascularization, hospitalization for unstable angina or heart failure) (RR 0.61; 95% CI 0.35 – 0.97, p<0.05).

Figure 1: Six year survival in patients treated with or without trimetazidine on top of standard therapy

Conclusions: Long-term trimetazidine modified release therapy is associated with a significant reduction in mortality in post-MI pts with angina and heart failure. Large-scale randomized clinical trials are needed to further confirm this data.

2053 Prognostic value of microRNA-150 after acute myocardial infarction

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Purpose: Prediction of left ventricular (LV) remodelling after acute myocardial infarction (AMI) is a challenging task. We hypothesized that circulating microRNAs (miRNAs) may predict LV remodelling after AMI.

Methods: This study enrolled 90 patients with first AMI. 60 patients characterized by echocardiography pre-discharge and at 6-months follow-up were used as test cohort and 30 patients characterized by magnetic resonance imaging at 4-months follow-up were used as validation cohort. Longitudinal changes in LV volume at discharge were measured by microarrays and quantitative PCR. Potential predictors of remodelling were isolated using a systems-based approach.

Results: Microarrays identified 160 miRNAs in the blood of patients of the test cohort. 74 miRNAs were differentially expressed between patients with increased end-diastolic volume between discharge and follow-up (ΔEDV >0) and patients with decreased EDV (ΔEDV ≤0). Analysis of a network of interactions between miRNAs and genes known to regulate remodelling revealed strong associations between miR-150 and remodelling. Indeed, in the validation cohort, patients without remodelling had elevated levels of miR-150 (2-fold, P=0.03). On multivariate analysis, miR-150 and N terminal pro-brain natriuretic peptide (Nt pro-BNP) were significant predictors of ΔEDV (P=0.007 and P=0.04, respectively). Receiver-operating characteristic (ROC) curves confirmed that miR-150 outperformed Nt pro-BNP to predict remodelling (area under the ROC curve (AUC) of 0.74 and 0.60, P=0.02). In addition, we observed a significant association (P=0.001) between miR-150 and the change of ejection fraction between discharge and follow-up (ΔEF). miR-150 predicted ∆EF with an AUC of 0.87 whereas Nt pro-BNP provided an AUC of 0.67.

Conclusion: Low circulating levels of miR-150 are associated with the development of LV remodelling after AMI and may be used as prognostic biomarker.

2082 High-density lipoprotein cholesterol level is associated with fibrous-cap thickness in patients with acute coronary syndrome

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Purpose: While low high-density lipoprotein cholesterol (HDL-C) level has been reported as an independent risk factor for coronary heart disease, few studies addressed a relationship between HDL-C levels and morphological features of vulnerable plaques. The aim of this study was to determine the association between HDL-C and fibrous-cap thickness in patients with acute coronary syndrome (ACS).

Methods: We enrolled 211 patients with ACS who underwent optical coherence tomography (OCT) prior to percutaneous coronary intervention. Patients were divided into a TCFA group (n=102) and a non-TCFA group (n=109) according to the OCT findings of the culprit lesion. TCFA was defined as a plaque with lipid content ≥2 quadrant and the thinnest part of the fibrous cap measuring <70 μm.

Results: There were no differences in patient’s characteristics between the two groups except for HDL-C levels, low-density lipoprotein cholesterol (LDL-C) levels, LDL-C/HDL-C ratio, and high-sensitive C-reactive protein (hs-CRP) levels. Multivariate logistic regression analysis demonstrated that HDL-C levels (odds ratio [OR] 0.97, 95% confidence interval [CI] 0.920 to 0.975, P<0.001) and LDL-C levels (OR: 1.011, 95% CI: 1.001 to 1.021, P=0.031) were independent predictors of TCFA. Furthermore, HDL-C levels (β coefficient: 0.340, P<0.001), LDL-C levels (β coefficient: -0.139, P<0.005), and current smoking (β coefficient: 0.178, P=0.007) were independent contributors for fibrous-cap thickness.

Conclusions: Our results suggest that HDL-C is independently related to not only the presence of TCFA but also fibrous-cap thickness in patients with ACS. HDL-C would contribute to cap thickening, resulting in plaque stabilization.

2083 Optical coherence tomography analysis of clinical and subclinical plaque rupture

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Background: Coronary plaque ruptures occur not only in acute coronary syndrome (ACS) patients but also in non-ACS patients. There is a great interest in the reason why some plaque ruptures lead to ACS and others do not. We used optical coherence tomography (OCT) to identify anatomic features that lead to the development of culprit lesions causing ACS after plaque rupture.

Methods: We assessed 102 plaque ruptures by OCT and compared lesion morphologies between symptomatic and silent coronary artery plaque ruptures in unstable angina pectoris (UAP) (n=67) and silent plaque rupture in stable angina pectoris (SAP) (n=35).

Results: In the cross-sectional view, rupture was observed at plaque shoulder in 67% of UAP and 71% of SAP (p=0.660). In the longitudinal view, plaque rupture was located proximally to the minimal lumen area (MLA) site in 49% of UAP and 57% of SAP (p=0.449). Distance between the rupture site and the MLA was significantly shorter in UAP compared to SAP (p<0.001). Maximum ruptured cavity area was significantly greater in UAP compared with SAP (1.57±0.54 mm² vs. 1.30±0.72 mm², P=0.092). Lumen area at rupture site (3.00±0.86 mm² vs. 3.45±1.18 mm², p=0.030) and MLA (2.69±0.80 mm² vs. 3.12±1.14 mm², p=0.029) was significantly smaller in UAP compared with SAP. The frequency of lipid-rich plaque (84% vs. 63%, P=0.019) and intracoronary thrombus (94% vs. 3%, P<0.001) was significantly higher in UAP compared with SAP.

Conclusions: The present OCT study found 4 risk factors linking ruptured plaques to acute coronary syndromes: greater degree of plaque rupture, smaller lumen, lipid-rich plaque, and evidence of intracoronary thrombus. It is conceivable that the greater degree of plaque rupture in the lipid-rich plaque provokes more increased thrombus formation and the smaller lumen requires less thrombus to precipitate an acute coronary event.

2084 Histopathological findings of thrombus in patients with acute coronary syndrome undergoing manual thrombus aspiration and frequency-domain optical coherence tomography efficacy evaluation

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Background and Purpose: Thrombus aspiration (TA) has been shown to be fea...
sible and useful in STEMI and NSTEMI. Aim of the present study was to correlate the actual size of the material obtained by TA with the amount of thrombus removal calculated by frequency domain OCT in patients with acute coronary syndrome undergoing TA. Furthermore the athero-thrombotic material retrieved by TA was analyzed by histopathology.

Methods: Twenty consecutive patients (mean age 60 ± 13 yrs; 16 male) with ACS (13 STEMI, 7 NSTEMI) undergoing urgent coronary angioplasty were enrolled. FD-OCT assessment of culprit/thrombotic lesion was performed before and after TA. Intracoronary thrombus was assessed by using a score based on the number of the involved quadrants on the cross-sectional FD-OCT images and the longitudinal extension of the thrombus itself. The score was calculated as the sum of each cross-section score. The OCT thrombus removal score was calculated as pre-TA thrombus score minus post-TA thrombus score. This differential score was matched with the planimetry measured surface area of the actual aspirated material. The athero-thrombotic material retrieved by TA was also analyzed by histopathology.

Results: In 17 patients TA retrieved atherothrombotic material. The mean value of basal thrombus score was 91.6 ± 31.6, and decreased to 46.7 ± 27.2 post TA. Planimetric mean value of the aspirated material surface area was 7.5 ± 5.2 mm², and it correlated well with the OCT calculated thrombus removal score (r = 0.54).

Histologic analysis of the retrieved material was performed in 12 patients (in 3 patients no material was aspirated by TA and in 5 patients the material was of insufficient quality for histological analysis); the following components were found: inflammatory cells in 50% of 2 patients; lipid pool in 20%; fresh thrombus in 10%; organized thrombus in 30%; platelet in 3 patients; erythrocyte in 50%.

Conclusions: This OCT study showed that: 1) the thrombus score derived by OCT measurement is well correlated to the planimetry measured surface area of the actual aspirated material; 2) tissue components such as cholesterol debris and inflammatory cells can be retrieved during manual aspiration.

On-site 3-dimensional optical coherence tomography assessment of coronary wire re-crossing position during bifurcation stenting

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Purpose: In a bifurcation intervention, the coronary wire re-crossing through an appropriate cell of the jailing strut is important before kissing balloon post-dilation. Three-dimensional optical coherence tomography (3D-OCT) is useful to assess the re-crossing position of the wire. We developed novel off-line software for 3D stent imaging and tested a feasibility of 3D-OCT assessment of the wire re-crossing position passing to the jailed side branch in the interventional suite.

Methods: Twelve bifurcation lesions were assessed so far. After stent implantation on main vessel across the side branch, an additional coronary wire passed through the jailing strut. Fourier-domain OCT images (IULMIEN, LightLab Imaging Inc.) were obtained to check the wire re-crossing position. 3D-OCT image reconstructions were done using the off-line workstation. The entire 3D reconstructions were recorded and the wire positions were confirmed.

Results: The entire times including data transfer and 3D reconstruction were approximately 10 min. Locations of target bifurcation were left main 6, RCA 1, LAD 2 and LCx 2. Single stent procedure was 9 (BES 5, EES 3, ZES 1) and the remaining 3 cases were treated with the culotte stenting (BES 2, EES 1). The wire re-crossing position was clearly visualized in ten cases. Two cases could not be assessed due to the wire artefact and the severe motion artefact. A representative case which treated with a bolus stenting and tagged across the LCx was shown in Figure 1. The wire re-crossing position was changed the first attempt (A) to more appropriate position (B) according to 3D-OCT findings during procedure.

Conclusions: 3D-OCT guidance of the wire re-crossing the jailed side branch is feasible in the interventional suite and may improve stenting bifurcation.

The lipid contents of culprit plaque may have a correlation of myonecrosis after elective PCI. Optical coherence tomography can predict myocardial injury after elective PCI.
The Ratio between the lateral and septal Ea-velocities of the mitral annulus is significantly reduced in restrictive pericarditis in comparison to restrictive cardiomyopathy


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Introduction: Tissue Doppler Imaging has been proposed for the differentiation between constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM). Recently, the ratio between the lateral and septal early diastolic velocities (E') of the mitral annulus (MA) has been proposed as additional tool for this differentiation.

Methods: We studied 54 patients (pts) with heart failure of either proven pericardial (CP) or myocardial origin (RCM; biopsy proven cardiac amyloidosis). We studied the ratio E' between the lateral MA (13.7±2.4 cm/s) and septal MA (11.4±2.4 cm/s) on tissue harmonic imaging (SHIM). To avoid misinterpretation of false positive results, we included all pts with reduced ratio of E'lateral/E'septal in CP (1.2±0.3) versus RCM (1.6±0.3).

Results: Out of the 54 pts (mean age: 57±13 years) 27 had CP and 27 RCM. The thickness of the interventricular septum (IVSD) was significantly increased in pts with RCM (16.4±4 mm vs. 12.2±2 mm, p<0.001). S' assessed by TDI was significantly higher in pts with CP (septal MA: 7.1±2.4 cm/s vs. 4.2±1.6 cm/s, p<0.001; lateral MA: 6.8±2.2 cm/s vs. 4.4±1.9 cm/s, p<0.001), but there was no significant difference of the ratio of S' Lateral/S' septal between CP (1.5±0.3) and RCM (1.1±0.2; p=0.24). Pts with CP showed a higher E' both on the septal and lateral side of the MA (13.7±5.4 cm/s vs. 4.3±1.8 cm/s, and 11.4±4.2 cm/s vs. 4.9±2.0 cm/s, resp. p<0.001). The ratio of E' lateral/E'septal was significantly reduced in CP (0.9±0.3) versus RCM (1.2±0.3; p<0.01).

Conclusion: TDI analysis of MA motion demonstrated decreased systolic and diastolic velocities in pts with RCM as well a reduced ratio of E' lateral/E'septal in CP which could be very helpful for the differentiation between RCM and CP. The reduced ratio of E' lateral/E'septal in CP could be caused by pericardial calcifications at the lateral mitral annulus, which might have an effect on these velocities.

Is the acute myopericarditis a benign pericarditic syndrome?


Acute pericarditis represents a clinical syndrome of benign course. Cardiac troponin I levels has been considered a marker of poor prognostic in this setting. Acute pericarditis represents a clinical syndrome of benign course. Cardiac troponin I levels has been considered a marker of poor prognostic in this setting.

Methods: From July 2004 to December 2011, 103 consecutive pts with AM were included in this study. Demographic and clinical data, ECG and echocardiographic parameters as well as development of complications [arrhythmias, left ventricular dysfunction (LVD), acute heart failure (AHF), cardiac tamponade, pericardial effusions, pericardial constriction and mortality] were collected in every patient.

Results: Mean age was 33±14 years, 87.4% were males. Mean follow-up was 72±14 months. Thirty three pts (32%) developed complications during hospitalization: Eighteen pts (17%) developed LVD, 4 pts (3.8%) developed AHF, 12 pts (11.6%) presented mild pericardial effusions and 17 (16.5%) had arrhythmias. At admission, the following clinical parameters were associated with complications: Heart rate >90 bpm [Relative Risk of 1.44, IC 95% (0.91-2.27), p<0.05], systolic blood pressure ≤120 mmHg [RR of 1.94 IC 95% (1.55-2.36), p<0.001], pericardial friction rub (RR: 6.7, 95%CI (3.7-12.6), p<0.001). Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008), Troponin I ≥0.03 ng/ml (IC 95% (1.48-3.93), p=0.008). Independent predictors of complications are shown in the table. No patient with LVEF ≥50% developed AHF, severe pericardial effusion or cardiac tamponade during hospitalization.

Independent predictors of complications

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin I ≥0.03 ng/ml</td>
<td>13.52 (5.31-34.51)</td>
<td>0.014</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>1.33 (0.60-3.00)</td>
<td>0.362</td>
</tr>
<tr>
<td>FE ≥50%</td>
<td>2.38 (1.42-4.25)</td>
<td>0.002</td>
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Conclusions: Elevated Troponin I level is a predictor of complications during hospitalization, but is not associated with complications on long-term follow-up. Patients with normal left ventricular function (EF ≥50%) at the time of admission have a good clinical prognosis and can be managed on an out-patient basis.

Incidence rate of primary cardiac tumors: a population study

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Purpose: Incidence of primary cardiac tumors (CT) is not known. Literature data come from autopsic studies or echocardiographic registries. It’s known an incidence of 1/1000 autopic and 1/5000 echocardiographic study but no data are available about the real number of new cases per year in the general population. Purpose of our study was to provide incidence of CT in a geographically defined Tuscany community.

Methods: We prospectively evaluated a consecutive population of 39 cases of primary cardiac tumor in a period of 14 years. The study population included inhabitants of Grosseto’s county in the south of Tuscany (Italy). The mean inhabitants number in the period was 219,861. Our Cardiology Department is the referral center of the county. Since 1998 all cases of suspected cardiac mass has been evaluated in our Department with basal echocardiogram, transesophaqgeal echo (TE) and/or cardiac magnetic resonance (CMR).

Results: In the period 1998-2011 we found 39 new cases of primary CT. All diagnosis were confirmed by surgeon or by multimodal imaging when surgery was not indicated. Benign CT were 32 (87%) and malignant CT 5 (13%). We found 18 myxomas (41%), 6 lipomas (15%) 5 fibroelastomas (13%), 2 Inffomas (5%), 2 haemangiomas (5%), 2 sarcomas (2%), 3 rhabdomyas (8%) and 1 pericardial haemangioepirctomatous. Excluding 3 cases of neonatal rhabdomyas, mean age was 64 years for benign CT and 62 for malignant ones. Surgery was performed in 31 cases. Cumulative 1 year mortality 8% and 100% for malignant CT. Incidence rate of primary CT was 1,26/100.000 inhabitants/year. Incidence of benign CT 1,00/100.000/year, referring only to myxomas we found an incidence of 0.8/100,000/year.

Conclusions: As far as we know, this is the first population study assessing the incidence rate of primary CT, a rare pathology which should be expected in 1,26 new cases per 100,000 inhabitants per year.

The value of left ventricular global longitudinal strain assessed by three-dimensional strain imaging in the early detection of anthracycline-mediated cardiotoxicity

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Background: Anthracines are important anticancer drugs, but their use is limited by acute and chronic cardiotoxicity. Current approaches to surveillance are often inadequate to detect myocardial disease. Strain imaging might detect earlier myocardial dysfunction. Speckle analysis of three-dimensional (3D) echocardiography improves information on left ventricle (LV) segmental and global deformation by avoiding loss of speckles as it is the case in monoplane bidimensional-strain analysis. We assessed whether early 3D-strain analysis could predict later anthracycline-induced cardiotoxicity.

Methods: Echocardiography, Troponin T (NTnT) and National pro-B-type natriuretic peptide (NtproBNP) were performed in 59 patients (51±10 years) before, at 12 and 36 weeks after anthracycline treatment. LV global longitudinal strain (3DGLS), radial (3DGRS) and circumferential (3DGC) strain were assessed before and at 12 weeks after anthracycline treatment by 3D-strain analysis, and relative changes ( predications were performed for all layers for 3DGLS and 3DGRS). The results of our study suggest that 3DGLS can be a good predictor of future development of anthracycline-induced cardiotoxicity.
High dose allopurinol reduces left ventricular hypertrophy and improves endothelial function in patients with chronic stable angina

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Purpose: Left ventricular hypertrophy (LVH) and endothelial dysfunction are associated with a poorer prognosis in patients with ischemic heart disease. Oxidative stress is believed to play a pathophysiological role in the development of both LVH and endothelial dysfunction. Xanthine oxidase is an enzyme that results in the production of superoxide radicals. Hence we hypothesised that allopurinol, a xanthine oxidase inhibitor, may help reduce LVH and endothelial dysfunction in ischemic heart disease patients.

Methods: A randomised, double blind, placebo controlled, parallel study was undertaken of 66 patients with ischemic heart disease and left ventricular hypertrophy over a 9 month follow-up period. Patients received 100mg/day of allopurinol or placebo for 2 weeks, which was uptitrated to 300mg for 1 month. This was then increased to 600mg daily for 7 months. Cardiac magnetic resonance assessed left ventricular mass index (LVMI). Endothelial function was assessed using flow-mediated dilation (FMD) of brachial artery whilst arterial stiffness was measured using pulse wave analysis (PWA) and pulse wave velocity (PWV).

Results: 55 patients completed the study (27 active, 28 placebo). Mean age 65±7 years, mean office BP 135/77 (±10/7) mmHg. Allopurinol significantly reduced LVH (Δ LVM: -2.2 ± 2.8% placebo vs -5.2 ± 2.9% allopurinol; p<0.001), and pulse wave analysis (Δ PWV: -2.8 ± 5.1% placebo vs +1.0 ± 7.3% placebo; p<0.023). There was no significant effect on pulse wave velocity.

Conclusions: This study demonstrates that allopurinol can reduce LVH and endothelial dysfunction in chronic stable angina patients with left ventricular hypertrophy. This raises the possibility that allopurinol might reduce future cardiovascular events in these patients.

Exploring left ventricular function: from 2D to 3D strain

Normal ranges of left ventricular global longitudinal strain: a meta-analysis of 2484 subjects

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Purpose: The definition of normal values of Global Longitudinal Strain (GLS) of the LV is critical important to the clinical application of this modality. We aimed to determine normal range of left ventricular (LV) 3D strain in a larger healthy population and 2) investigate the effect of aging on strain gradient among different vendors.

Methods: We searched MEDLINE, EMBASE and the Cochrane Library database through August 2011 for with key terms “Speckle Tracking” and “left ventricle” and “echocardiography” and relevant phrases. Studies were included if the article reported the normal range of left ventricular strain by 3-dimensional speckle tracking analysis in healthy subjects.

Results: A total of 2484 subjects from 25 studies. Normal strain was -19.7% [95%CI: -20.2 to -19.1]. The source of variation was sought between studies using meta-regression. Age, gender, frame rate and vendors used were associated with variance in the GLS value.

Conclusions: The normal range -19.7%. Variation between studies likely reflects unmeasured differences between groups, but vendor does not appear to be a contributor to variation in GLS.

Determination of normal range of left ventricular strain: a meta-analysis of 2484 subjects

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Purpose: Normal range of left ventricular (LV) 3D strain in a large healthy population and 2) investigate the effect of aging on strain gradient among different vendors.

Methods: We searched MEDLINE, EMBASE and the Cochrane Library database through August 2011 for with key terms “Speckle Tracking” and “left ventricle” and “echocardiography” and relevant phrases. Studies were included if the article reported the normal range of left ventricular strain by 3-dimensional speckle tracking analysis in healthy subjects.

Results: A total of 2484 subjects from 25 studies. Normal strain was -19.7% [95%CI: -20.2 to -19.1]. The source of variation was sought between studies using meta-regression. Age, gender, frame rate and vendors used were associated with variance in the GLS value.

Conclusions: The normal range -19.7%. Variation between studies likely reflects unmeasured differences between groups, but vendor does not appear to be a contributor to variation in GLS.
Intra-observer variability for 3D strain was lower for AT and GLS than all other 3D strains were significantly correlated. GRS values were lower in 3D than in 2D (21.29 vs 25.6, p < 0.05). 2D and 3D strains were significantly correlated (r = 0.56; GRS r = 0.56 and GRs (r = 0.33). 2D and 3D LVEF were also significantly correlated (r = 0.79, p < 0.01). Correlations between strain parameters and LVEF are listed in Table 1. Our study points out a relatively poor correspondence of deformation indices between 2D and 3D modes. LVEF was optimally correlated with GCS and AT. Our study points out a relatively poor correspondence of deformation indices between 2D and 3D modes. LVEF was optimally correlated with GCS and AT.
NSE-values of 93 μg/L and 110 μg/L, respectively) regained adequate consciousness (CPC-score of 1 and physiological SSEE).

Conclusions: SSEEs are suitable to predict neurological outcome in OHCA-patients with VT. In contrast, NSE is unsuitable for this purpose. Our data support the more reliable algorithm for clinical practice, favoring the assessment of SSEEs in clinical decision making.

P2141 Emergency coronary angiography and interventions in comatosed patients resuscitated after out-of-hospital cardiac arrest treated with mild therapeutic hypothermia and aggressive antithrombotic therapy

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Purpose: In many patients (pts) resuscitated (ROSC) after out-of-hospital cardiac arrest (OHCA) due to ventricular fibrillation (VF) early coronary angiography (Angio) and interventions (PCI) improve outcomes. Furthermore, mild therapeutic hypothermia (TH) improves neuro-protection and outcomes of these pts. However, TH has several haematologic and coagulative side effects, increases the risk of bleeding and can interfere with the effectiveness of antithrombotic drugs routinely used during PCI.

Methods: Observational prospective analysis of all pts with ROSC after OHCA admitted alive to the Emergency Room (ER) of a tertiary center from March 27, 2004 to January 31, 2012 treated with TH and undergoing early Angio and PCI.

Results: During the study period 104 (42.4%) out of 245 pts with ROSC after OHCA admitted alive to ER were treated with TH -4 hours from symptom onset (mean age: 62±14 years, males:70%, shockable rhythm: 73%; interval OHCA-ROSC ≤20 min: 70%; 66 pts. (83.5%) underwent Angio and 33 (31.7%) a PCI (>6 hours from OHCA). Baseline characteristics of pts undergoing PCI were similar to those of pts without PCI, although most of the former had ST elevation myocardial infarction at the first EKG after ROSC and less comorbidities. Fifteen percent of pts undergoing PCI were in cardiogenic shock and 18% had an intrar- tialex stent being implanted. In 36% of pts PCI was performed through the radial approach. Multivessel PCI was performed in 30.3%, target vessel was the left anterior descending in 33%. In 91% of pts a post-PCI TIMI 3 flow was achieved and in 88% an early reflow was implanted in 88%. All pts received unfractionated heparin (70 U/kg bolus, 300 mg aspirin and 300 mg loading dose ciloprodil (9%), 600 mg loading dose) post-PCI; abciximab was infused in 45.4%. We observed only one major bleeding (gastric) in a subject treated with abciximab (5 red blood cell packs transfused) who afterward survived. In PCI treated pts hemoglobin, hematocrit, red blood cell and platelet counts showed minimal reduction during TH similar to those observed in pts. without PCI. No stent thrombosis occurred. The in-hospital crude mortality of pts with PCI was 21% (vs 28% without PCI – p=NS) and 61% of PCI treated survivors were discharged with a favorable neurological outcome (vs. 43% vs- p=0.06).

Conclusions: Emergency Angio and PCI in combination with TH and aggressive antithrombotic therapy are feasible and safe in pts. resuscitated after OHCA due to VF. Thus, a mature ST-segment elevation myocardial infarction network can be further developed to include a TH protocol for resuscitated OHCA pts.

P2142 Door to implantation time of percutaneous circulatory support systems predicts mortality in patients with out-of-hospital cardiac arrest


Background: Cardiopulmonary resuscitation (CPR) is associated with low success rates and high variability in survival outcomes especially in patients with out of hospital cardiac arrest (OHCA). When conventional CPR has failed, extracor- poreal life support (ECLS) systems can be implanted under ongoing resuscitation to provide hemodynamic stabilization. The implantation of ECLS may be considered when time without blood flow is short and the condition leading to the cardiac arrest can be considered to be reversible. Consequently, the routine use of ECLS systems is still under discussion.

Therefore, the aim of the present study was to identify predictors of mortality in patients with OHCA undergoing ECLS implantation.

Methods: 29 patients (observation period January 2010 – December 2011) with witnessed OHCA, who received CPR according to the current guidelines were included in this analysis. All patients were directly admitted to the cath lab and a femoro-femoral veno-arterial ECLS was set up by a team of interventional cardiologist, anesthesiologist and perfusionist in case of absence of spontaneous circulation (SHO). Heparin (10-12.5 mg/kg) was given in 35 pts (31%) and a shockable rhythm (VT/VT/VT) was found in 70 pts (62%). Coronary angiography was performed in 65 pts (57.5%), showing significant lesions in 44 (68%) with successful PCI in 40 (61%). Mild therapeutic hypothermia (MTH) was initiated in 71 pts (62%) with a median

cant longer in the non-survivor group compared to survivors (42.5 minutes (IQ 28.0-56.5) vs. 25.0 minutes (IQ 21.0-30.0); P=0.01). There was no difference in ECLS treatment duration between the two groups (survivors: 4 days (IQR 1.5-7.5); non-survivors 6.5 days (IQR 1.0-8.6); P=0.69). Kaplan-Meier survival analysis (Log Rank 6.29; P=0.012) and Cox regression analysis (HR 4.25; 95% CI 1.21-14.9; p=0.024) revealed that the difference in 30 day mortality is restricted to door to ECLS implantaion time less than 30 minutes.

Conclusion: Our data demonstrate that the door to ECLS implantation time less than 30 minutes improve 30 day mortality in patients with OHCA.

P2143 Which is the most effective algorithm for the management of the out of hospital cardiac arrest: a network meta-analysis

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Purpose: The optimal therapeutic algorithm for the management of patients with out of hospital cardiac arrest is not well-defined, since direct comparisons between therapeutic algorithms is limited. The aim of this study was to estimate the relative effectiveness of emergency medical services (EMS) algorithms in the management of patients with out of hospital cardiac arrest (OHCA) and to identify all controlled trials published in English that compared EMS therapeutic interventions in patients with OHCA. Interventions were grouped a priori into 6 different types of interventions. Prognostic parameters (age, gender, CPR initiated by bystander, time to EMS access, time on scene) and geographical parameters (density) were evaluated for each intervention. In combining direct and indirect evidence, IRO (for each intervention) was the most commonly used intervention, which was the basic life support with automated external defibrillator (BLS-D) provided by emergency medical technicians (EMTs) and paramedics, and was used as the reference intervention.

Results: We identified 14 controlled trials (18,718 patients) that described 6 direct comparisons of different interventions. The most optimal intervention was the therapeutic algorithm based on the initial care of patients with out of hospital cardiac arrest by non health professionals using external automated external defibrillator upon the arrival of the EMS (ORp 2.714, 0.302-24.415). Advanced life support (ALS) applied by physician, increases two folds the probability of survival at hospital discharge compared to BLS-D provided by EMTs and/or paramedics (ORp 2.173, 0.379-12.461). Sub-analysis revealed that the presence compared to the absence of physician at ALS team increases 70% the probability of survival at hospital discharge (ORp 1.703, 0.514-5.247).

Conclusions: The network meta-analysis revealed that the therapeutic algorithm based on the initial care of patients with out of hospital cardiac arrest by non health professionals using external automated external defibrillator upon the arrival of the EMS (ORp 2.714, 0.302-24.415). Advanced life support (ALS) applied by physician, increases two folds the probability of survival at hospital discharge compared to BLS-D provided by EMTs and/or paramedics (ORp 2.173, 0.379-12.461). Sub-analysis revealed that the presence compared to the absence of physician at ALS team increases 70% the probability of survival at hospital discharge (ORp 1.703, 0.514-5.247).

P2144 Prognostic factors in out of hospital cardiac arrest: a new score (DAANS) to guide the optimal management?

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Introduction: Cardiac arrest (CA) is a complex pathology with a poor survival rate despite advances in resuscitation strategies. After an out of hospital cardiac arrest (OHCA), the survival rate to hospital discharge remains catastrophic (< 1%).

Purpose: The aim of our study was to identify predictors of survival in patients presenting out of hospital cardiac arrest with no early recovery.

Patients and Methods: Between 2007 and Aug 2011 (4 years), 3,438 patients (pts) victims of OHCA were collected. After excluding obvious extra-cardiac causes, 113 patients were included. All of these achieved ROSC before mechanical ventilation and had normal or non-significant lesions on the ECG. All ECG recordings were reinterpreted by a cardiologist in retrospective analysis.

Results: Our population included 71% men, mean aged 58.7±15 years. Twelve pts (10.6%) had diabetes, 42 (37%) hypertension and 51 (45%) were smokers. Initial chest pain was found in 32 pts (28%). The median no flow duration was 3 min (0-40 min), and the CA to ROSC median delay was 25 min (2-95 min). CPR was immediately initiated in 63 pts (56%). Adrenaline bolus (2-6 mg) was given in 35 pts (31%) and a shockable rhythm (VT/VT/VT) was found in 70 pts (62%). Coronary angiography was performed in 65 pts (57.5%), showing significant lesions in 44 (68%) with successful PCI in 40 (61%). Mild therapeutic hypothermia (MTH) was initiated in 71 pts (62%) with a median
Does primary coronary angioplasty improve outcome in patients victims of out of hospital cardiac arrest?

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Introduction: Patients presenting with out of hospital cardiac arrest (OHCA) and no evidence of extra-cardiac cause have dreadful short-term outcome. Coronary angiography and mild therapeutic hypothermia (MTH) are now integrated in specific guidelines.

Methods and population: The purpose of our retrospective observational study is to evaluate the role of primary coronary angioplasty (PCI) on the survival of victims of OHCA with no immediate hemodynamic recovery.

Results: A total of 187 patients (Pts), requiring prehospital mechanical ventilation, were hospitalized in our center between January 2007 and August 2011. Among those, 113 had no evidence of extra-cardiac cause of cardiac arrest and represented our study group. Mean age was 58.7 ± 1.5 years and 80 (71%) were men. CPR was initiated in 63 cases (56%) and no flow period was 4.9 ± 6.9 min (0-40). Adrenaline was used in 50 Pts (80%) and defibrillation required in 70 (82%). Total duration of cardiac arrest to recovery was 28.5 ± 4.5 h in Pts without angiography (p=0.05).

Conclusions: The place of coronary angiography and angioplasty in the treatment of OHCA should be discussed for each patient but seems to improve survival only in specific subset of patients with ST-elevation and with duration of no-flow >10min.

Coronary angiography after out-of-hospital cardiac arrest: is a simple ECG a reliable tool to choose between urgent or delayed study?

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Background: In comatose patients resuscitated (ROSC) after out-of-hospital cardiac arrest (OHCA) the ECG is not considered a reliable tool to predict acute coronary-artery occlusion. Thus, immediate coronary angiography (CA) has been suggested for diagnostic and therapeutic purposes. However, CA could delay therapeutic hypothermia (TH), when indicated, and has other logistics drawbacks. Therefore, the aim of the study was to evaluate in survivors of OHCA the reliability of ECG to triage to immediate or delayed CA and interventions.

Methods: Observational prospective analysis of patients with ROSC after OHCA admitted alive to the Emergency Room (ER) of a tertiary center from March 27, 2004 to January 31, 2012 treated with TH and undergoing early CA and PCI.

Results: We analysed 76 pts patients with ROSC after OHCA, admitted alive to our ER during the study period that underwent early CA (mean age: 64.14 years, males: 67%, shockable rhythm: 80%, interval OHCA-ROSC 11 min ± 8min, interval ROSC-CA 56 min ± 32 min) with at least 2 consecutive ECGs post ROSC available (10 pts have been excluded due to insufficient data), 66 pts fulfilled the study criteria. The mean time between ROSC and the first ECG was 12 min. 26 pts (41%) meet the ECG criteria for ST elevated myocardial infarction (STEMI, Group A), 22 pts (32%) for subendocardial ischemia (Group B), and in 18 (27%) pts, the ECG was not positive. There were no ECG signs of ischemia (Group C). In the Group A at early CA 21 pts (81%) had acute coronary occlusion and 5 pts subocclusion of one vessel. All these pts underwent successful PCI. The mean max Troponin I value was 28 ng/ml. As opposed in the Group B and in the Group C, no one patient had severe coronary occlusion at CA, but 7 pts in Group B underwent immediate PCI due to the presence of a severe stenosis (70-90%). Notably, only 1 case in the Group B and 10 min and no elevated Troponin I, but the aetiology of OHCA in these cases was myocarditis and hypertrophic cardiomyopathy, respectively. The in-hospital crude mortality of patients was 20% in Group A, 15% in Group B and 22% in Group C; 60% of survivors were discharged with a good neurological outcome.

Conclusions: Our preliminary data suggest that a simple ECG after ROSC in OHCA survivors could be a good predictor for acute coronary occlusion. Therefore, STElevation cases could be triage to immediate CA and possible intervention, while in the absence of STElevation criteria CA could be delayed. These findings, if confirmed by adequately sized studies, could simplify the triage of ROSC pts after OHCA to CA.

Clinical relevance of operative coronary artery disease among patients resuscitated from out-of-hospital cardiac arrest

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Introduction: Coronary occlusion is the leading cause of cardiac arrest. However, the timing of coronary angiography in patients (pts) with out-of-hospital cardiac arrest (OHCA) is still controversial. Aim of this study were: 1) to investigate the influence of operative coronary artery disease (ObCAD) on survival, sudden unexpected death and post-ROSC ECG pattern (ST-segment elevation and other ECG patterns) and 2) to determine the in-hospital outcome of these pts in relation to treatment modality.

Methods: Clinical characteristics of resuscitated OHCA pts referred to our CathLab in the period 2008-2010 were retrospectively reviewed. Initial arrest rhythm (ROSC) was obtained; 2) to evaluate the relation between post-ROSC electrocardiogram (ECG) and ObCAD and 3) to determine the in-hospital outcome of these pts in relation to treatment modality.

Results: A total of 47 pts (65 ± 11 years, 34 male) were included in the study. The presenting rhythm was ventricular fibrillation/ventricular tachycardia in 39 (79%) pts. On post-ROSC ECG, ST-elevation was present in 20 (43%) pts. ObCAD was observed in 39 (83%) pts, in 19 (40%) pts with ST-elevation on post-ROSC ECG, and 20 (74%) pts with different ECG patterns (6-9ms). Successful PCI was performed in 19 (40%) pts, in 13 (65%) pts with ST-elevation on post-ROSC ECG and in 6 (22%) pts without ST-elevation. The hospital survival rate with good neurologic recovery (CPC score ≤2) was 60%, 44% among pts with ObCAD treated conservatively, 67% among pts with ObCAD treated with PCI and 75% among pts without ObCAD.

Conclusions: ObCAD is present in most OHCA pts without obvious extra-cardiac etiology. No relation is present between post-ROSC ECG and ObCAD, indicating that ST-elevation cannot be used as a selection criterion for emergent coronary angiography in patients with OHCA. In-hospital outcome is worse among OHCA pts with ObCAD treated conservatively. These findings support use of emergent coronary angiography and subsequent PCI when appropriate, in all pts with OHCA and no obvious extra-cardiac etiology independently from post-ROSC ECG, this approach may improve the outcome of these pts.

Outcomes of Percutaneous Coronary Intervention for stable Coronary Artery Disease compared with Acute Coronary Syndromes

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Context: The SYNTAX-score (SX-score) predicts procedural risk and annual rates of major adverse cardiovascular events (MACE) among patients undergoing

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percutaneous coronary intervention (PCI). The SX-score may, beyond the clinical presentation, assist in decision making regarding the prognosis of therapeutic interventions.

**Objective:** To categorize the risk of major adverse cardiac events (MACE) among patients with stable coronary artery disease (CAD) as compared to patients with acute coronary syndromes (ACS) using angiographic criteria.

**Design, Setting and Patients:** Patient-level data from the SIRTAX (N=10,121), LEADERS (n=1707) and RESOLUTE (n=2292) contemporary all-comers coronary stent trials were pooled. Analysis was performed on a cohort of 4,208 patients (84%) treated with drug-eluting stents who were clinically followed up for 2 years and had calculated SX-scores.

**Intervention(s):** Patients were stratified according to their clinical presentation and/or SX-score: Acute coronary syndrome (ACS, n= 2,607), stable low-risk (SLR, n= 583) and stable high-risk (SHR, n= 1,014) separated by the lowest tertile SX-score (Sx-score=II) among stable patients.

**Main Outcome Measure(s):** Event rates of MACE (a composite of cardiac death, non-fatal MI and ischemia-driven TVR) and stent thrombosis at 2 years.

**Results:** Rates of MACE were higher among SHR than ACS (OR 1.36; 95% CI 1.10-1.67, p=0.005) and adjusted for stent type at 2 years. The difference was largely driven by a higher rate of peri-procedural MI among females in the SHR group [I]. There were no differences between SHR and ACS patients in terms of all-cause and cardiac mortality as well as definite and definite/probable stent thrombosis.

**Conclusions:** The majority of patients undergoing PCI for stable CAD (Sx-score > 8) in routine clinical practice have a higher risk of MACE than ACS patients. It remains to be determined whether they would benefit from more intensive antiplatelet therapy.

**P2149 Ten-year follow-up survival of the medicine, angiology, or surgery study (MASS II): randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease in women**

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**Purpose:** Coronary artery disease (CAD) is the leading cause of death in women. The proposed treatments, percutaneous coronary intervention (PCI), medical treatment (MT) or coronary artery bypass graft (CABG), are similar to those made for men. However, in women with multivessel stable CAD and normal left ventricular (LV) function, the best treatment is unknown.

**Methods:** Prospective study with 10 years of follow-up randomized 188 women with chronic stable CAD to MT (N = 63; 33%), PCI (N = 68; 37%) or CABG (N = 56; 30%). CAD was defined by the presence of angina pectoris CCS class II and III, positive stress test, LV ejection fraction < 40% and ≥ 2 coronary lesions > 70%. The primary end points were the incidence of total mortality, Q-wave MI, or refractory angina that required revascularization. All data were analyzed according to the intention-to-treat principle.

**Results:** Patients treated with PCI and MT had more primary events than CABG and, respectively, of 34%, 44% and 22% (p=0.003) (Figure). The 10-year survival rates were 72% with CABG, 72% with PCI, and 56% with MT (p=0.156). Relative to the composite end point, Cox regression analysis showed a higher incidence of primary events in MT than in CABG (HR=2.38 (95%CI: 1.40 to 4.05); p=0.001), lower incidence in PCI than in MT (HR=0.60 (95%CI: 0.38 to 0.95); p=0.031) but no differences between CABG and PCI (HR=1.42 (95%CI: 0.83 to 2.45); p=0.203). To death, a protective effect of PCI compared to MT (HR=0.44 (95%CI: 0.21 to 0.90); p=0.025) was observed but not between PCI and CABG or MT and CABG.

**Conclusion:** Women with multivessel CAD and normal LV function, CABG and PCI were associated with fewer primary events and PCI with lower mortality.

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**P2150 Outcome of patients with ST-elevation myocardial infarction and multivessel coronary disease is dependent of management strategy**

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**Background:** Half of patients with ST-elevation myocardial infarction (STEMI) have multivessel coronary disease (MVD). Few contradictory data regarding their optimal treatment are available. We compared all management strategies available in these patients (pts), based on our registry, in order to define their clinical outcome.

**Methods:** Of 863 consecutive STEMI patients, 403 (47%) had MVD. 4 different strategies were compared: group I (5%) - pts with simultaneous treatment of non-infarct related arteries (1-stage PCI); group II (44%) - pts with scheduled PCI of non-infarct related arteries (2-stages PCI); group III (42%) - pts with medical management; and group IV (9%) - pts referred for CABG. Primary outcome was MACE, defined as: death, myocardial infarction, stroke, and driven angioplasty repeat revascularization at 30 days and one year.

**Results:** There were no differences in baseline characteristics between the four groups, apart from cardiogenic shock (higher in group I), and age (lower in group II). At 30 days, MACE was significantly lower in group II and III, by comparison with the other two groups (p<0.01) (Table). At one year, MACE was significantly lower in group II than in the other groups (p=0.02); mortality and myocardial infarction were also lower in group II and III (p<0.01). LAD lesions and an LV ejection fraction less than 30% were the main independent predictors of 1 year mortality (R²=0.51; p<0.03).

<table>
<thead>
<tr>
<th>Event</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>14.8</td>
<td>3.4</td>
<td>3.6</td>
<td>8.1</td>
</tr>
<tr>
<td>Death</td>
<td>9.8</td>
<td>1.7</td>
<td>1.8</td>
<td>2.7</td>
</tr>
<tr>
<td>MI</td>
<td>5.0</td>
<td>1.7</td>
<td>1.8</td>
<td>5.4</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.6</td>
<td>0.5</td>
<td>0.5</td>
<td>2.7</td>
</tr>
<tr>
<td>Revascularization (%)</td>
<td>0.2</td>
<td>0.8</td>
<td>1.8</td>
<td>2.7</td>
</tr>
</tbody>
</table>

**Conclusions:** Two-stages PCI is associated with the lowest MACE at 30 days and 1 year, and also with the lowest mortality and myocardial infarction. Based on our data, simultaneous treatment of non-infarct related arteries during primary PCI should be avoided.

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**P2151 Plaques with increased lipid core and thin fibrous cap occur in coronary artery regions with low endothelial shear stress: a 3D optical coherence tomography pilot study in human**

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**Purpose:** Animal studies have shown that low endothelial shear stress (ESS) leads to high-risk plaque development. The association of low ESS with high-risk plaque characteristics has not been investigated in man. We applied a new integrated imaging and functional assessment of the human coronary arteries to test the hypothesis that low ESS is associated with increased lipid core and thin fibros cap.

**Methods:** Five culprit coronary arteries from 5 acute coronary syndrome patients were 3D reconstructed with geometrically correct 3D OCT, a novel imaging methodology that combines optical coherence tomography (OCT) and bilinear angiography. The reconstructed arteries were divided into 3-mm-long subsegments and ESS was calculated in each subsegment using computational fluid dynam-
Low endothelial shear stress predicts the progression of coronary artery disease with increasing plaque eccentricity: an in vivo natural history study of atherosclerosis in humans

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Purpose: Atherosclerotic plaques progress in a highly individual manner. Plaque eccentricity has been associated with a rupture-prone phenotype and adverse coronary events in humans. Endothelial shear stress (ESS) critically determines plaque growth and low ESS leads to high-risk lesions. However, the factors responsible for rapid disease progression with increasing plaque eccentricity have not been studied. We investigated in vivo the effect of local hemodynamic and plaque characteristics on progressive luminal narrowing with increasing plaque eccentricity in humans.

Methods: Three-dimensional coronary artery reconstruction using angiographic and intravascular ultrasound data was performed in 374 patients at baseline (BL) and 6-10 months later (FU) to assess plaque natural history as part of the PRE-DICTION Trial. A total of 874 coronary arteries were divided into consecutive 3-mm segments. We identified 408 BL discrete luminal narrowings with a throat in the middle surrounded by gradual narrowing proximal and distal to the throat. Local BL ESS was assessed by computational fluid dynamics. The eccentricity index (EI) at BL and FU was computed as the ratio of max to min plaque thickness at the throat. Mixed-effects logistic regression was used to investigate the effect of BL variables on the combined endpoint of substantial worsening of luminal narrowing (decrease in lumen area > 1.8 mm² or > 20%) with an increase in plaque EI.

Results: Lumen worsening with an increase in plaque EI was evident in 73 luminal narrowings (18%). Independent predictors of worsening lumen narrowing with plaque EI increase were low BL ESS (<1 Pa) distal to the throat (odds ratio [OR] = 2.2 [95% CI: 1.3-3.7]; p=0.003) and large BL plaque burden (>51%) at the throat (OR=1.7 [95% CI: 1.0-2.8]; p=0.051). The incidence of worsening lumen narrowing with increasing plaque eccentricity was 30% in the presence of both predictors versus 15% in luminal narrowings without this combination of characteristics (OR=2.4 [95% CI: 1.4-4.3]; p<0.002).

Conclusions: Low local ESS independently predicts areas with rapidly progressive luminal narrowing and increasing plaque eccentricity. Coronary regions manifesting an abrupt anatomic change, i.e., at highest risk to cause an adverse event, can be identified early by assessment of ESS and plaque burden.

Low endothelial shear stress predicts the progression of coronary artery disease with increasing plaque eccentricity: an in vivo natural history study of atherosclerosis in humans

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The relationship between the location of coronary plaques and their factors of plaque vulnerability evaluated by optical coherence tomography color-coded mapping

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Purpose: We investigated coronary arteries with optical coherence tomography (OCT) to assess the distribution of lipid pools and the several factors which contribute to coronary plaque vulnerability and elucidated ordinary location of vulnerable plaques.

Methods: Eighty-one coronary plaques in 16 left anterior descending coronary arteries (LADs) of 16 patients were evaluated with OCT at every 0.225mm. Plaque components were analyzed by 10-degree intervals in every slice and classified into fibrous, lipid, calcification or thrombus. Also the location of thin fibrous caps (the thickness of the caps <65 micrometers), clusters of macrophages, vasa vasorum and cholesterol crystals were investigated at the same time. The results were visualized in the OCT color-coded maps.

Results: The largest lipid areas were seen in proximal side of the 1st diagonal branches. Spread of the lipid areas were positively correlated with the distance from the 1st diagonal branches in proximal and distal side (proximal side: p<0.0001, r=0.67, distal side: p<0.0001, r=0.68), but this tendency was not found around 2nd diagonal branches or septal branches. The majority of thin fibrous caps were seen between 10mm distal and proximal from the 1st diagonal branches (66%; 1048±157ROIs). Macrophages gathered around distal of the area where the branches met the LADs. The average number of macrophages around the 1st major septal branches was smaller than that around the septal branch (5.5 ROIs/mm and 14.3 ROIs/mm respectively: p=0.0005).

Conclusion: High-risk plaques with increased lipid core and thin fibrous caps develop in coronary regions with low ESS. Calculation of local ESS in combination with fibrous cap thickness and lipid content derived from OCT may facilitate the early identification and prompt treatment of high-risk plaques.

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Effect of intensive vs. moderate lipid-lowering therapy with atorvastatin on the stabilization of atherosclerosis in acute coronary syndromes: serial optical coherence tomography analysis

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Purpose: Recent clinical trials have demonstrated that intensive lipid-lowering therapy (iliatins could prevent recurrent cardiac events after acute coronary syndromes (ACS). Optical coherence tomography (OCT) is capable of estimating fibrous cap thickness (FCT) of coronary atherosclerotic plaques, which might be associated with plaque instability. This study was a prospective, randomized, open-label, dual-center study to compare the effect of intensive vs. moderate statin therapy on OCT by using OCT.

Methods: A total of 56 ACS patients with dyslipidemia (low-density lipoprotein cholesterol (LDL-C) levels >100 mg/dL) were enrolled in this study. After percutaneous coronary intervention (PCI), the patients were randomly assigned to two groups: intensive statin therapy (atorvastatin 20 mg/day, n=27) or moderate statin therapy (atorvastatin 5 mg/day, n=29). OCT was performed to measure FCT in non-culprit intermediate lesions at baseline and 12-month follow-up. Serum profiles of LDL-C, high density lipoprotein cholesterol (HDL-C), high sensitive C-reactive protein (hs-CRP), malondialdehyde LDL (MDA-LDL) and metalloproteinase 9 (MMP-9) were measured before PCI and at 12-month follow-up.

Results: Serum LDL cholesterol levels were significantly decreased in patients with intensive statin therapy (132.7±28.2 to 70.5±13.4 mg/dL, -45.4±13.0%) compared with moderate statin therapy (129.3±31.3 to 84.9±23.8 mg/dL, -32.9±23.8%) (p<0.001). The change of FCT had a significant negative correlation with the changes in LDL-C (r = -0.49, p < 0.001) and MDA-LDL (r = -0.32, p = 0.03), while there was no correlation between the changes of FCT and HDL-C (r = 0.06, p = 0.682). Furthermore, the change in FCT showed a negative correlation with the changes in hs-CRP (r = -0.30, p = 0.027) and MMP-9 (r = -0.57, p < 0.001).

Conclusion: This OCT study suggests that the intensive lipid-lowering therapy with atorvastatin might be more helpful to stabilize coronary atherosclerotic plaques through the thinning of the fibrous-caps in comparison with the treatment with 5 mg/day of atorvastatin.

P2154

Spontaneous Coronary Artery Dissection in patients with Acute Coronary Syndrome

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Background: Spontaneous coronary artery dissection (SCAD) found typically in young females without classical coronary risk factors is thought to be a very rare cause of acute coronary syndrome (ACS). While previous angiographic studies have reported that SCAD is only observed in 0.07% to 1.1% of patients with coronary artery disease, the real prevalence of SCAD in ACS subjects has been unclear due to the nature of coronary angiography. The aim of this study was to
use optical coherence tomography (OCT) to investigate the prevalence of SCAD in ACS.

Methods: This study consisted of 241 consecutive patients with ACS who underwent OCT to explore the entire culprit artery. Patients presenting severe constrictive heart failure, cardiogenic shock, unsuitable lesions for OCT imaging, and TIMI grade 0 or 1 after thrombectomy were excluded. All OCT images were analyzed by two expert OCT readers who were blind to the clinical data. The OCT criterion for SCAD was a separation of the different layers of the artery wall with the creation of a false lumen. Plaque rupture in OCT was diagnosed when plaque shoulders disappeared, and a fibrous cap with a cavity formation in continuity with the lipid core. Based on OCT findings, patients were assigned to three groups: 1) SCAD, 2) plaque rupture (PR), and 3) non-SCAD/non-rupture group.

Results: OCT revealed 11 (4.6%) SCADs and 117 (48.5%) plaque ruptures in ACS subjects. The percentage of females versus males was greater in the SCAD group (SCAD: 63.6% vs. PR: 17.1% vs. non-SCAD/non-rupture: 20.4%, P<0.001) while no difference was observed in age (SCAD: 66.4±13.7, vs. PR: 66.3±11.4 vs. non-SCAD/non-rupture: 66.1±10.3, P=0.99). The prevalence of dyslipidemia (SCAD: 27.3% vs. PR: 60.7% vs. non-SCAD/non-rupture: 67.2%, P=0.029) and smoking (SCAD: 9.1% vs. PR: 56.4% vs. non-SCAD/non-rupture: 56.6%, P=0.009) were different among the three groups.

Conclusions: SCAD is no rare cause of ACS, especially in female patients without dyslipidemia or smoking.

VASCULAR INFLAMMATION: SIGNALS AND MEDIATORS

2191 SIRT1 inhibits proliferation of smooth muscle cells and neointimal lesion formation by deacetylation of STAT3

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Purpose: Proliferation of vascular smooth muscle cells (VSMCs) is a hallmark of vascular-proliferative diseases. In this study, we tested the hypothesis that SIRT1, a class III histone deacetylase, modulates VSMC proliferation and neointima formation following vascular injury.

Methods: Using adenoviral vectors, the wild type form (pAd-SIRT1-WT) or a deacetylase-dead mutant (pAd-SIRT1-H535A) of SIRT1 were over-expressed in human VSMCs. Knockdown of SIRT1 was achieved with BrdU incorporation and expression analyses were based on cDNA-microarrays, qPCR, and immunoblotting. Wire injury of the femoral artery was performed on C57BL/6 mice with local application of pAd-SIRT1-WT, pAd-SIRT1-H535A, or pAd-control via a thermosensitive plasmonic gel. Vessels were harvested at 3 weeks after injury for morphometric analysis, immunohistochemistry, and qPCR (β).

Results: SIRT1 expression was significantly down-regulated in proliferating VSMCs and during the proliferative response of neointima formation in mice. Over-expression of wild-type SIRT1 but not the inactive mutant significantly reduced proliferation and migration of VSMCs, whereas knockdown of SIRT1 further enhanced the proliferative response. A gene microarray analysis identified STAT3 dependent target genes to be strongly regulated in response to changes in SIRT1 expression levels and SIRT1 activity. Using immunoprecipitation analyses, we could observe a direct interaction of SIRT1 with the transcription factor STAT3. Mechanistically, deacetylation of STAT3 by SIRT1 significantly prevented transcription of cyclinD1 and survivin. Following vascular injury in mice, neointima formation during the proliferative response of VSMCs during neointima formation, indicating that the effects of SIRT1 were dependent on its deacetylase activity.

Conclusion: Increased SIRT1 activity inhibits VSMC proliferation by deacetylation of STAT3 and thus impeding transcription of cyclinD1 and survivin. Therefore, activation of SIRT1 holds promise among the three groups.

2192 Activation of SIRT1 by resveratrol maintains a contractile phenotype and prevents proliferation in vascular smooth muscle cells

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Purpose: De-differentiation and the subsequent proliferation of vascular smooth muscle cells (VSMCs) are pivotal steps in the progression of atherosclerosis and neointima formation. Resveratrol is a grape polyphenol and a potent activator of a class III histone deacetylase, modulates VSMC proliferation and during the proliferative response of neointima formation in mice. Following vascular injury in SIRT1 largely reproduced the effects of resveratrol on VSMCs, indicating that activation of SIRT1 by resveratrol represents a key mechanism for maintaining a differentiated and quiescent VSMC phenotype.

Conclusion: Activation of SIRT1 by resveratrol induces a contractile phenotype in VSMCs and prevents proliferation in response to stimuli occurring during vascular proliferative diseases. Therefore, activating SIRT1 reflects an interesting therapeutic strategy to prevent the development of atherosclerosis or neointima formation.

2193 Genetic deficiency of CD40 aggravates adipose tissue inflammation in mice by increasing inflammatory cell recruitment

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Background: Infiltration of immune cells, such as T-cell subsets, is a hallmark of adipose tissue inflammation and the metabolic syndrome. T-cell function potentially depends on co-stimulatory pathways, such as the CD40L-CD40 dyad. CD40 deficiency increased accumulation of inflammatory cells in adipose tissue particularly of adipose tissue M1 macrophages and CD8+ T-cells. Gene expression analysis revealed upregulation of ~350 genes in visceral fat pads of CD40/-/- mice, including pro-inflammatory gene sets, such as matrix-metalloproteinases, chemokines, and macrophage and T-cell signaling adapters. Moreover, CD40 deficient mice developed aggravated systemic and peripheral insulin resistance as shown by euglycemic-hyperinsulinemic clamp analysis. Also, CD40/-/- mice had increased levels of low density lipoproteins (LDL) and accumulated cholesterol in the liver. Additionally, histological analysis revealed signs of worsened liver steatosis, such as increased vacuole formation and Oil-red-O-specific lipid deposition in the liver. Adipokine deficiencies, such as adiponectin, a-actinin, vimentin, tubulin, alpha-actinin, vimentin, and troponymin. In contrast, the largest cluster of the 11 significantly down-regulated proteins accounted for proteins controlling cellular metabolism and energy regulation, including pyruvate kinase isoenzymes, fructose-bisphosphate aldolase A, 3-hydroxyisobutyryl-CoA hydrolase, pyruvate dehydrogenase and Galectin-1. In VSMCs transfected with specific SIRT1-sRNA, the effects of resveratrol on inhibiting VSMC proliferation were significantly reduced. Moreover, over-expression of SIRT1 largely reproduced the effects of resveratrol on VSMCs, indicating that activation of SIRT1 by resveratrol represents a key mechanism for maintaining a differentiated and quiescent VSMC phenotype.

Conclusion: Activation of SIRT1 by resveratrol induces a contractile phenotype in VSMCs and prevents proliferation in response to stimuli occurring during vascular proliferative diseases. Therefore, activating SIRT1 reflects an interesting therapeutic strategy to prevent the development of atherosclerosis or neointima formation.

2194 Ang-2 induced pericyte dropout and increase in vascular permeability is abolished by PDGF-B transfection

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The Ang-Tie2-System is a key regulator in endothelial quiescence. Ang-2 leads to detachment of pericytes increasing vessel permeability (Hammer 2004), as does deletion of PDGF-receptor retention motif, which reduces PDGF-function (Nysens 2006). Here we analysed the role of Ang-2 in endothelial and pericyte restricted chronic overexpression of Ang-2 on vascular integrity, myocardial morphology and function and the effect of an AAV mediated PDGF-B transfection in this scenario.
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Methods: Two lines of Ang-2 overexpressing mice were established (expression driven by either Tie-2 or a-MHC promoter) and analyzed. These overexpressing mice were compared to control mice (Ang-2 on vs. Control, MHC-Ang-2 on vs. Control). At 12 weeks of age, the Ang-2 on mice were transcardially flushed using a lactating adenovirus encoding for PDKG-B (rAav-PDGFB-B, 5×1012 PFU). Mice underwent echocardiography, vascular leakage of 4kD-TRITC-dextran following i.v. injection was assessed using a MPLS microscope, at 24 weeks of age, organs were harvested for histological analysis.

Results: Ang-2 overexpressing mice displayed a cardiac dilatation at 12 wks age/LV-EDD: Ang-2 on: 0.33±0.01cm, Control: 0.30±0.01cm (p<0.05). Whileuntreated Ang-2 mice showed a further 15% LV dilatation at 24 wks, rAav-PDGFB-B treatment prevented this Ang-2 induced dilatation (rAav-PDGFB-B 6.8%). In addition, an increased heart weight/body weight ratio (twelve Ang-2 mice; 0.8±0.15, Control: 5.2±1.2 ng/kg) was abolished in rAav-PDGFB treated animals (rAav-PDGFB-B 4.9±0.5 mg/kg). Meanwhile, MHC-Ang-2 on mice showed no changes in weight and/or size. Furthermore Ang-2 on mice displayed a significant loss of intravascular fluorescence (f) 5min after TRITC injection compared to controls (Ang-2 on: delta f 52±6%; Control: delta f 37±4%), which was abolished after treatment with PDKG-B (rAav-PDGFB-B 34±6%). Histological analysis of heart sections demonstrated a significant decrease in pericytes density in Ang-2 on mice (Ang-2 on: 8±1.9 pericytes/HPF) which again was restored after PDGFB-B transduction (15±2.8 pericytes/HPF).

Conclusion: Prolonged endothelial Ang-2 overexpression increases vascular permeability and induces progressive LV dilatation. The progressive dilatation and hypertrophy is antagonized by increased PDGFB-B levels. Our results indicate that Ang-2 induced microcirculatory pericyte loss causes systemic cardiovascular alterations (vessel leakiness, cardiac hypertrophy), unless increased PDGFB-B levels enhance pericytes recruitment.

2195 Tissue factor disulfide mutation causes a bleeding phenotype with gender specific organ pathology and lethality

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Tissue factor (TF), the key initiator of coagulation, is expressed in sub-endothelial tissue, particularly in heart, lung and brain. The extracellular allostERIC disulfide bond Cys186-Cys209 of human TF shows high evolutionary conservation. In vitro experiments suggest that TF pro-coagulant activity depends on the intact Cys186-Cys209 disulfide bond. To investigate the role of this allostERIC disulfide bond in vivo, we generated a C213G mutant TF mouse by replacing Cys213 of the corresponding disulfide Cys190-Cys213 in murine TF. Only 17% of the offspring from heterozygous breeding pairs was homozygous for C213G TF at birth, while the distribution of genotypes was still normal on or after day 14. Rac1 activation by different PI3K isoform specific inhibitors or a specific Akt inhibitor did not abrogate TF induced barrier stabilisation effect at cell periphery. Inhibition of Rac1 abolished antiangiogenic effect on actin reorganisation and barrier stabilisation. Moreover, Rac1 activation was accompanied by an activation of PI3K/Akt and MEK/ERK pathway. Inhibition of MEK/ERK by different PI3K isoform specific inhibitors or a specific Akt inhibitor did not abrogate the major protective effect against thrombin-induced hyperpermeability. Inhibition of MEK/ERK pathway by specific pharmacological inhibitors potentialized cAMP-mediated antiangiogenic barrier stabilisation. On the other hand chronic activation of cAMP signalling (24 hrs) induced endothelial cell proliferation and migration (wound assay) which was completely blocked by a specific PI3K and weakly by PI3K, PIK3, or PI3K inhibitors. The angiogenic response of cAMP signalling was also blocked by MEK/ERK inhibitors U0126 and PD98059.

Conclusion: cAMP signalling stabilises the endothelial barrier via PI3K/Akt-independent activation of Rac1 and promotes angiogenesis via PI3K-dependent activation of MEK/ERK pathway. The findings of present study point potential targets for therapeutic angiogenesis.

RENAL ASPECTS AND RESISTANT HYPERTENSION

2201 Glomerular hyperfiltration and microalbuminuria in the early stage of hypertension: results of the HARVEST study

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Purpose: We did a prospective study to investigate the relationship between changes in glomerular filtration rate (GFR) over time and development of microalbuminuria in the early stage of hypertension.

Methods: We assessed 535 young-to-middle-age hypertensive subjects from the HARVEST study never treated for hypertension. Creatinine clearance at entry was ≥60 ml/min/1.73m2 in all. Albumin excretion rate (AER), creatinine clearance, and ambulatory blood pressure were measured at entry and at follow-up end. Subjects were then divided into 4 groups on the basis of GFR changes from baseline to the end: 1) Nor-Nor, n=396; 2) Nor-Hyp, n=31; 3) Hyp-Hyp, n=61; 4) Hyp-Nor, n=47.

Results: During a 8.5 year follow-up, 52 subjects developed microalbuminuria (GFR < 60 ml/min/1.73m2, progression of GFR progressively increased across the 4 groups and was 5.6% in Nor-Nor, 9.6% in Nor-Hyp, 16.4% in Hyp-Hyp, and 36.2% in Hyp-Nor (p<0.001). This association held true in a multivariable logistic regression in which several confounders, ambulatory blood pressure, and other renal function parameters were taken into account (p<0.001). In particular, hypertensives whose GFR decreased to normal at study end (Hyp-Nor) had an adjusted odds ratio of 9.2 (95%CI 4.1-20.4) for development of microalbuminuria compared to subjects with normal GFR throughout the study (Nor-Nor). These data show that glomerular hyperfiltration is the main mechanism of microalbuminuria development in young-to-middle-age subjects in the early stage of hypertension and support the hypothesis for a parabolic association between GFR and AER in this clinical setting. Early intervention with antihypertensive therapy should be considered in subjects with glomerular hyperfiltration before GFR declines to lower values.
Enhanced circulating endothelial apoptotic microparticle and endothelial progenitor cell ratio is associated with subsequent decline in glomerular filtration rate in hypertensive patients

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Purpose: Recent study showed that levels of endothelial progenitor cells (EPCs) reflecting vascular repair capacity decreased in hypertensive patients with nephropathy. However, whether decreased circulating EPC levels and increased endothelial apoptotic microparticles are related to subsequent decline in glomerular filtration rate (GFR) in hypertensive patients remains unknown.

Methods: Flow cytometry was used to assess circulating EPC levels (defined as CD34+/KDR+ and endothelial apoptotic microparticle (defined as CD31+/annexin V+) in peripheral blood samples. Estimated GFR was calculated by use of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, and the annual rate of decline of estimated GFR (ΔeGFR) was determined as the difference between the follow-up and baseline eGFR values, with this value divided by the time interval in years.

Results: Totally, 92 hypertensive subjects with serum creatinine <2.5 mg/dl were enrolled in the study. During follow-up (28.9±7.4 months), mean ΔeGFR was -0.79±0.44 mL/min. This was significantly correlated with CD31+/annexin V+ to EPC ratio (R=-0.319, p=0.003) and albumin excretion rate (R=-0.539, p=0.001). All study subjects were then divided into 4 groups according to the CD31+/annexin V+ to EPC ratio: group 1, ≤0.5 (n=24); group 2, 0.5-2.0 (n=18); group 2, 2.0-10 (n=18); group 4, >10 (n=22). There was a positive association between the degree of CD31+/annexin V+ to EPC ratio and the decline in GFR (mean ΔeGFR: 0.24±3.84 vs. 0.06±3.56 vs. 0.64±2.59 vs. 2.74±5.04 mL/min, p=0.046). By multivariate analysis, increased CD31+/annexin V+ to EPC ratio was an independent predictor of ΔeGFR (R=0.430, adjusted R square 0.141, p=0.013).

Conclusion: Our current data showed that hypertensive patients with enhanced CD31+/annexin V+ to EPC ratio and AER were associated with subsequent decline in GFR. These findings suggest increased endothelial damage and impaired vascular repair capacity may contribute to subsequent renal function deterioration in hypertensive patients.

Levels of soluble receptor for advanced glycation end-products are related with arterial stiffening, albuminuria and glomerular filtration rate in essential hypertensive subjects

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Purpose: To investigate the interrelationships of the soluble receptor for advanced glycation end-products (sRAGE) with urinary albumin excretion, expressed as the albumin to creatinine ratio (ACR), estimated glomerular filtration rate (eGFR) and arterial stiffness in essential hypertensives.

Method: Our population consisted of 320 newly diagnosed untreated non-diabetic patients with stage I to II essential hypertension [156 men, mean age 52 years, blood pressure (BP)=145±93 mmHg]. In all participants, ACR values were determined as the mean of two non-consecutive morning spot urine samples, and albumin excretion rate (AER) was calculated as the mean of two non-consecutive morning spot urine samples. ACR values (n=156) had greater body mass index (29.7±4.5 vs. 27.1±2.5 kg/m2, p=0.05) and 24-h systolic BP (139±16 vs. 121±10 mmHg, p=0.046). By multivariate analysis, increased CD31+/annexin V+ to EPC ratio (r=-0.319, p=0.003) and albumin excretion rate (r=-0.539, p=0.001) were the independent predictors of ΔeGFR (R=0.430, adjusted R square 0.141, p=0.013).

Conclusion: Our current data showed that hypertensive patients with enhanced CD31+/annexin V+ to EPC ratio and AER were associated with subsequent decline in GFR. These findings suggest increased endothelial damage and impaired vascular repair capacity may contribute to subsequent renal function deterioration in hypertensive patients.

Prevalence and main features of resistant hypertension in central and eastern Europe: the BP-CARE Study

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Purpose: Few information is available on the main features of resistant hypertension (RH) in Central and Eastern Europe. The Blood Pressure (BP) control rate and Cardiovascular Risk profile (BP-CARE) study allowed us to assess the prevalence and correlates of RH (2007 ESH/ESC guidelines).

Methods: The study was conducted in 1312 treated hypertensives in 9 Central and Eastern Europe countries.

Results: 423 patients were apparent RH, of which 168 pseudo-resistant (non-compliant or white-coat). True resistant hypertensive (TRH) were thus 255 (19.4%) with clinic BP (mean ± SD of 3 measurements) values amounting to 157±4.7/91±8.1±10 mmHg despite the daily use of 5±0.7 drugs. The corre-lation of no ABPM 24-hour values were 149.2±17.9±7.5±10 mmHg. Compared to controlled (C) (n=368, 28.1%) and uncontrolled hypertensive patients (U) (n=521, 39.7%) TRH were slightly older (TRH:61.2±11 vs C:58.3±10 and U:56.3±12 yrs) with a greater prevalence of females, while smoking habit was superimposable. They showed a higher rate of previous cardiovascular events and a very high cardiovascular risk profile. The TRH patients also displayed values of body mass index and waist circumference greater than C and U (TRH:29.9±4.5 vs C:27.9±4.5 and U:28.9±4.4 kg/m², and TRH:99.9±14 vs C:97.8±14 and U:97.6±13 cm, P<0.01), with a higher prevalence of visceral obesity. In TRH there was a tendency of total cholesterol, triglycerides and glucose to be greater than in C. Estimated glomerular filtration rate (eGFR) was significantly lower (TRH:70.7±13 vs C:79.9±21 vs U:76.7±23 mL/min/1.73m², P<0.01). At the multivariate analysis the variables more closely related to TRH were age (P<0.004, P<0.01), body mass index (P<0.011, P<0.01) and eGFR (P<0.004, P<0.005).

Conclusions: The present study provides evidence that the prevalence of TRH in Central and Eastern European countries is superimposable to that of western Europe and USA. It also shows 1) the very high cardiovascular risk profile of TRH and 2) the high association of this condition with overweight, obesity, diabetes, renal failure and a history of previous cardiovascular events.

Frequency of obstructive sleep apnea, secondary forms of arterial hypertension and drug adherence in patients with resistant hypertension - RESIST-POL study

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Purpose: To evaluate in patients with resistant arterial hypertension enrolled in the RESIST-POL study the frequency of obstructive sleep apnea (OSA), renal artery stenosis (RAS), primary hyperaldosteronism (PHA), pheochromocytoma, Cushing syndrome (CS) and conditions related to hypertension resistance.

Methods: We investigated 204 patients (123M, 81F, mean age 48.4, range 19-65 yrs) with resistant hypertension (clinical BP >140/90 and ambulatory daytime mean BP >125/85 mmHg staying on 3 antihypertensive drugs including diuretic), with eGFR >60 mL/min/1.73 m². All patients underwent thorough examination including: polysomnography, renal artery, adrenal and renal CT scan and hormonal evaluations for PHA, pheochromocytoma and CS. Oral glucose tolerance test (OGTT) was performed to exclude undiagnosed diabetes. Excessive sodium ingestion was defined based on urinary sodium excretion >200 mmol/24h. Insomnia and depression were diagnosed based on questionnaires. In 36 patients urinary albumin creatinine ratio (UACR) and albumin excretion rate (AER) were measured and the only responsible for resistant hypertension serum antihypertensive drugs levels were assessed. Patients in whom the serum level of at least one drug was below the limit of quantification of the assay were classified as non-adherent.

Results: Mild, moderate and severe OSA occurred in respectively 55 (27.0%), 38 (18.6%) and 54 (26.5%) patients. Secondary forms of hypertension were diagnosed in 49 patients (24.0%), the most frequent were PHA (15.7%) and RAS (5.5%). On OGTT previously undiagnosed diabetes was found in 14.2% of patients. Excessive sodium ingestion was found in 33.3% of patients. Depression and insomnia were found in 36.8% and 33.6% of patients respectively. A multivariate analysis nighttime BP levels were independently correlated with the presence of PHA, RAS and metabolic syndrome. However daytime BP levels were independently related only to PHA. 31 of 36 patients in whom serum antihypertensive drugs levels were assessed were classified as non-adherent (86.1%).

Conclusions: Non-adherence of patients to medical therapy was frequent in patients with resistant hypertension. In patients with resistant hypertension OSA is the most frequently diagnosed clinical condition followed by PHA and RAS.
Renal aspects and resistant hypertension / Predicting diabetic risk beyond high sugar

2206 Blood pressure (clinic, home, 24-h) profiles and clinical
correlates in resistant hypertension: data from the
PAMELA Study
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PREDICTING DIABETIC RISK BEYOND HIGH SUGAR
2211 Hypoglycemia and cardiovascular risk in diabetic and
non-diabetic outpatients at risk of or with
atherothrombosis in the REACH registry
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creased risk for the composite endpoint (adj. HR Q1 vs Q2 1.18 [1.04-1.32];
p=0.008), with similar trends for non-fatal MI (adj. HR 1.45; p=0.05), non-fatal
stroke (adj. HR 1.25; p=0.02), and bleeding (adj. HR 1.53; p=0.07), but not nonCV death (adj. HR 1.10; p=0.3), or heart failure (adj. HR 1.09; p=0.3). There was
no difference in the comparative CV risk of hypoglycemia in pts w/ and w/out DM
and pts w/ and w/out prior CVD.
Conclusion: In REACH, there was a U-shaped curve observed relating outpt
glycemia and risk for incident and recurrent CV events. Whether there is a pathophysiologic relationship between relative hypoglycemia and longitudinal CV ischemia requires further study, in particular whether there is an optimal lower
threshold for fasting glucose.

2212 The effect of visit-to-visit variability in blood pressure
on stroke and coronary events in 5213 patients with
diabetes: pooled analyses of TNT, IDEAL, and CARDS
trials
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Purpose: It has been suggested that visit-to-visit variability in systolic blood pressure (SBP) predicts cardiovascular (CV) risk independently of mean SBP in patients with hypertension and other CV risk factors. The aim of this analysis was
to determine the association between visit-to-visit variability in BP and the risk of
CV events in patients with diabetes and whether these parameters contributed
to the differences in clinical benefit observed with different statin treatment regimens.
Methods: Mean values of BP parameters from the 5213 patients with diabetes
in the TNT, IDEAL, and CARDS trials were calculated and analyzed to determine
the risk of CV events in relation to visit-to-visit variability in BP and evaluate any
impact of these BP parameters on the treatment effect.
Results: Visit-to-visit variability in SBP and diastolic BP (DBP) were significant
risk factors for stroke and coronary events after adjusting for treatment (Table)
and/or other BP parameters (data not presented). The treatment effect (atorvastatin 80mg [ATV 80] vs ATV 10 in TNT; ATV 80 vs simvastatin 20-40mg in IDEAL;
ATV 10 vs placebo in CARDS) for reducing risk of stroke (HR 0.67, 95% CI 0.50–
0.90) and coronary events (HR 0.83, 95% CI 0.70–0.98) was not affected by
adjustment for SBP or DBP variability or other BP parameters.
Table 1. Effect of visit-to-visit BP variability
Model

SBP
HR* (95% CI)

4

1

DBP
χ2

P

11.991
12.035
11.810
14.963

0.0005
0.0005
0.0006
0.0001

1.123
1.161
1.124
1.203

20.967
26.173
28.297
21.782

<0.0001
<0.0001
<0.0001
<0.0001

1.207
1.234
1.206
1.248

χ2

P

(0.984, 1.281)
(1.022, 1.318)
(0.986, 1.282)
(1.066, 1.358)

2.966
5.273
3.053
8.923

0.0850
0.0217
0.0806
0.0028

(1.120, 1.301)
(1.149, 1.325)
(1.120, 1.299)
(1.164, 1.337)

24.196
33.153
24.317
39.235

<0.0001
<0.0001
<0.0001
<0.0001

HR* (95% CI)

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I. Raz 5 , D.L. Bhatt 6 . 1 Harvard Medical School, Brigham and Women’s
Hospital, TIMI Study Group, Boston, United States of America; 2 Inserm U698
- AP-HP and University Paris Diderot-Paris 7, Paris, France; 3 University of
Michigan, Division of Cardiology, Ann Arbor, United States of America; 4 Tokai
University School of Medicine, Isehara, Japan; 5 Hadassah-Hebrew University
Medical Center, Jerusalem, Israel; 6 Harvard Medical School, Brigham and
Women’s Hospital, VA Boston Healthcare System, Boston, United States of
America

Stroke (N=5213)
SD
1.235 (1.096, 1.391)
CV
1.243 (1.099, 1.405)
VIM 1.243 (1.098, 1.407)
ASV 1.250 (1.116, 1.399)
Coronary Events (N=5213)
SD
1.185 (1.102, 1.274)
CV
1.213 (1.126, 1.306)
VIM 1.224 (1.136, 1.318)
ASV 1.181 (1.101, 1.267)

Purpose: Severe hypoglycemic events increase CV risk in type 2 diabetes mellitus (DM) patients (pts) but also correlate with non-CV events. Whether modest
hypoglycemia increases CV risk in DM and non-DM outpts at risk of or with (w/)
atherothrombosis has not been reported.
Methods: Fasting blood glucose (FBG) was measured at baseline in the international outpt REACH Registry (n=45,227) and divided into quintiles. We evaluated
the magnitude of risk of hypoglycemia on CV events, independent of traditional
CV risk factors (RF), subclinical atherothrombosis, prior CV ischemia, and therapy.
Results: Among the 36,682 eligible REACH pts, baseline FBG ranged from 4.411.7 mmol/L; Q1 [median 4.7, IQR 4.4-4.9], Q2 [5.3, IQR 5.2-5.5], Q3 [6.0, IQR
5.8-6.2], Q4 [7.1, IQR 6.8-7.6], and Q5 [9.9, IQR 8.8-11.7]). The 4-yr risk of CV
death/MI/stroke was lowest among pts in Q2 and increased in all other glycemic
groups (figure). As compared w/ Q2, pts w/ relative hypoglycemia (Q1) had in-

*HR for 1 SD increase of variability in BP; SD = Standard deviation; CV = Coefficient of variation;
VIM = variability independent of mean; ASV = average successive variability.

Conclusion: Higher visit-to-visit variability in SBP or DBP is associated with significantly increased CV risk. The clinical benefit seen with ATV 80 in TNT and
IDEAL or ATV 10 in CARDS in reducing the risk of CV events is not mediated
through reduction in BP or BP variability.

2213 Effect of preoperative HbA1c level on long-term
cardiovascular outcomes after coronary
revascularization therapy in patients with diabetes
mellitus
N. Ehara 1 , Y. Furukawa 1 , M. Kinoshita 1 , T. Kitai 1 , S. Kaji 1 ,
A. Yamamuro 1 , T. Tani 1 , T. Kita 1 , T. Morimoto 2 , T. Kimura 3 on
behalf of CREDO-Kyoto Registry Cohort-2 Investigators. 1 Kobe City Medical
Center General Hospital, Kobe, Japan; 2 Kinki University, Osaka, Japan;
3 Kyoto University Graduate School of Medicine, Department of Cardiovascular
Medicine, Kyoto, Japan
Purpose: To evaluate the association between preoperative hemoglobin A1c
(HbA1c) level and cardiovascular outcomes in diabetic patients undergoing coronary revascularization.
Methods: CREDO-Kyoto cohort-2 is a multi-center registry enrolling consecutive patients undergoing first coronary revascularization in 2005-7 in Japan. This
study included 7935 patients whose HbA1c value at the index hospitalization was
available: non diabetes mellitus (DM); n=4760, DM with HbA1c≤6.8% (quartile1:
Q1); n=802, 6.9%≤HbA1c≤7.6% (Q2); n=805, 7.7%≤HbA1c≤8.7% (Q3); n=805,

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/339/430794 by guest on 04 November 2018

Purpose: Very few are the studies investigating the prevalence and main features
of resistant hypertension (RH) based on clinic, home and blood pressure (BP). In
the PAMELA study these issues were evaluated by analyzing the data collected
in the treated hypertensive patients.
Methods: In 399 treated hypertensives we evaluated the prevalence, the main
features and the relationships of RH (ESH/ESC 2007 Guidelines) with anagraphic, anthropometric and metabolic variables. The evaluation included 24-hour
BP variability and target organ damage. This was done by assessing clinic, home
and ambulatory BP monitoring (ABPM) values. The data were compared with
those obtained in treated controlled hypertensives (C).
Results: 48 (12.0%) were RH. Compared with C (n=84,21.1%) they were
slightly but significantly older (63.6±8 vs 60.1±10, mean±SD, P<0.05) with
greater clinic BP (average of 3 measurements) values (159.4±20/93.0±7mmHg
vs 127.6±8/80.5±6.1 mmHg, P<0.01). A similar trend was detectable for
home BP (146.1±20/83.4±9 mmHg vs 127.7±16/79±10, P<0.02) and ABPM
(128.9±13/76.4±7 vs 117.2±9/71.9±6, P<0.001). Clinic, home and 24-hour
heart rate were superimposable in the 2 groups. 24-hour systolic and diastolic
BP variability values were significantly greater in RH than in C(standard deviation 17.5±5/13.3±4 vs 14.0±3/12.1±2 mmHg, P<0.05). RH displayed a body
mass index similar to C (28.1±4 vs 27.4±4 kg/m2 ) but a significantly greater waist
circumference (92.9±11 vs 88.6±11 cm, P<0.05), with a greater prevalence of
visceral body fat depot. Cholesterol, triglycerides and glucose values were similar
in the 2 groups. Left ventricular mass index was significantly higher in RH than in
C (104±23 vs 94.3±19 g/m2 and 51.2±12 vs 45.5±10 gr/h2.7, P<0.02).
Conclusions: Thus in a mediterranean population the prevalence of RH is not different from that seen in central and north Europe. In addition they show that also
home and ABPM values are elevated, thereby increasing the overall risk profile of
the patients. This elevation is associated with an increase in BP variability, which
may contribute to the greater prevalence of cardiac structural alterations detected
in RH.

359


Hazard Ratios for AD and CE

<table>
<thead>
<tr>
<th>Non DM</th>
<th>DM</th>
<th>Non DM</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>HR</td>
<td>Q1</td>
<td>Q2</td>
</tr>
<tr>
<td></td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>0.03</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Conclusions: U-shape relationships were observed between preoperative HbA1c level and cardiovascular outcomes in diabetic patients undergoing first coronary revascularization.

Incidence of hypoglycemia in the elderly with type 2 diabetes in clinical practice - insights from DiaRegis

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Background: RCT have demonstrated that intensive glucose control is associated with a higher rate of hypoglycemia. Little is known about the incidence of hypoglycemia in elderly patients with type 2 diabetes in clinical practice.

Methods: DiaRegis is a German prospective registry including patients with type 2 diabetes being treated with oral mono- or oral dual anti-diabetic combination therapy in 2009/2010. We examined differences in co-morbidity and the incidence of hypoglycemia in diabetic outpatients <90 years (young, n=1268) with those ≥70 years (elderly, n=1997).

Results: Elderly patients had a later diabetes onset and a better glucose control than young patients and more often cardiovascular disease. Elderly patients more often received sulfonylureas (SU, 34.8 vs. 22.0%; p=0.001), while metformin and newer oral drugs (gliazones, DPP-4-inhibitors) were used less frequently. Hypoglycemia within 12 months prior to enrollment was more frequent in the elderly (12.7 vs. 9.1%; p=0.001). History of hypoglycemia (hypo) led investigators to discontinue SU in the elderly (12.7 vs. 9.1%; p=0.001).

Conclusions: Elderly patients have a distinct risk profile and higher incidence of hypoglycemia which may reasonably be attributed to the increased use of sulfonylureas. This was associated with a higher risk for incident morbidity in the following 6 months.

Prediction of cardiovascular events in a European high-risk population by an easily measured metabolic index

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Purpose: Hyperglycemia enhances the risk of cardiovascular events (CVE), while high-density lipoprotein cholesterol (HDLc) is protective. We applied a cardiometabolic risk index (CMRI) based on HDLc and fasting glucose (FG) adjusting for age, identifying patients at high risk of future fatal and non-fatal CVE in a European high-risk population. The properties of the CMRI as a predictor of CVE and all-cause mortality have previously been established in a European population with known coronary artery disease (European Heart Survey on Diabetes and the Heart) and a multi-ethnic US population (NHANES III).

Methods: IMPROVE is a European, multicenter, longitudinal cohort study, which enrolled individuals aged 54 to 80 years with at least 3 CVE risk factors and no history of CVE from 7 centers in Finland, Sweden, Netherlands, France, and Italy. The individuals were followed for 3 years regarding fatal and non-fatal CVE. The impact of risk factors on CVE was analyzed using crude and adjusted Cox regression.

Results: HDLc (mmol/L; median and interquartile range) was 1.3 (1.1–1.6) in women and 1.1 (0.9–1.3) in men, while FG was 5.7 (4.8–6.0) and 6.2 (5.2–6.6). According to the CMRI, 9% of individuals out of 3325 were at high risk, and 190 actually had a CVE. FG was borderline related to CVE (HR: 95%CI: 1.08; 1.00–1.16; p=0.050) whereas HDLc was protective (0.47; 0.30–0.73; p=0.001). The CMRI was related to CVE both in crude analysis (1.98; 1.31–2.99; p=0.001) (see Figure), after adjustment for sex and age (1.70; 1.11–2.61; p=0.014), and after further adjustment for other established CVE risk factors (1.59; 1.04–2.44; p=0.034).

Psoriasis is associated with increased risk of incident diabetes mellitus: A Danish nationwide cohort study

U. Khalid1, P.R. Hansen1, G. Gislason2, S.L. Kristensen1, J. Lindhardt1, L. Skov2, C. Torp-Pedersen2, O. Ahlehoff3, 1Gentofte Hospital - Copenhagen University Hospital, Department of Cardiology, Hellerup, Denmark; 2Gentofte Hospital - Copenhagen University Hospital, Hellerup, Denmark

Purpose: Psoriasis is associated with increased risk of cardiovascular events and increased prevalence of cardiovascular risk factors. Diabetes mellitus (DM) is a major contributor to cardiovascular morbidity and may be associated with psoriasis but nationwide prospective data has not been reported previously.

Methods: The study comprised the Danish population aged > 10 on Jan 1, 1997 followed until incident DM, death or Dec 31, 2009. Patients with a history of DM and/or psoriasis at baseline (n=96,551) were excluded. Data on comorbidity, concomitant medication, and socioeconomic status was linked on an individual level. Incident DM events per 1000 observational years were calculated. Rate ratios (RRs) with 95% confidence intervals (CIs) were estimated by Poisson regression.

Results: A total of 4,614,807 subjects were eligible for analyses with a maximum follow-up of 13 years. In the study period 52,613 patients received the psoriasis diagnosis including 6,784 patients with severe psoriasis. Patients with psoriasis...
had increased risk of incident DM. Rates of incident DM were 12.6 (CI 12.5-12.6) and 16.5 (16.1-16.9) for the reference population and patients with psoriasis, respectively. The risk of incident DM was increased in all patients with psoriasis (overall RR 1.96, 1.50-1.63) with RR 1.49 (1.43-1.56) and RR 2.13 (1.91-2.37) for mild and severe psoriasis, respectively.

**Conclusion:** In this nationwide cohort psoriasis was associated with increased risk of incident DM. The results add to accumulating evidence that psoriasis is associated with increased risk of cardio-metabolic disease and underline the importance of screening for these risk factors in patients with psoriasis.

### HEART FAILURE WITH PRESERVED EJECTION FRACTION: NEW INSIGHTS?

**2249**

High systolic blood pressure and increased rate of rise of blood pressure in mid-life predict impaired diastolic function in the elderly (The MRC NSHD)

A.K. Ghosh1, T.D. Trippel1, H.D. Duengen2, G. G eb r i c h 3, B. P i e s k e 4, R. Wachter5, T.D. Buchholz6, D. Pellerin3, J. Deanfield4, D. K u h 1, J . M a y e t 2, R . J . H a r d y 1. 1MRC Epidemiology Unit, University of Cambridge, Cambridge, United Kingdom; 2Department of Epidemiology, University of Leipzig, Leipzig, Germany; 3Department of Biostatistics, University of Cambridge, Cambridge, United Kingdom; 4The Heart Hospital, University College London Hospital Trust, London, United Kingdom; 5University of Cambridge, Institute of Child Health, Vascular Physiology Unit, London, United Kingdom

**Background:** Increased systolic blood pressure (SBP) and hypertension are associated with worse diastolic function in cross-sectional studies. However, the long-term effects of raised SBP in mid-life on diastolic function in later life are unknown.

**Methods:** Our study is a birth cohort of British men and women born in March 1946. 1700 participants (48% male) underwent echocardiography at age 60-64y. SBP at age 43y and 53y was used to assess diastolic function. The relationship between SBP at ages 36, 43, 53, 60-64 years and E/e’ was analysed using linear regression models (adjusted for sex, clinic attended and age). Estimates of the effect of SBP in mid-life were then further adjusted for confounders. The relationship between rate of change in SBP over 3 time periods (36-43y, 43-53y and 53y-current) and E/e’ was also analysed.

**Results:** Elevated SBP throughout mid-life predicted impaired diastolic function at age 60-64y (Table 1). Effects were independent of current SBP, and in case of SBP at age 53y, also independent of other confounders (current BMI, diabetes or treatment for hypertension). Greater rate of change in SBP in all 3 time periods also predicted poorer E/e’ at age 60-64y. This effect for the latter 2 time periods ([43-53y, coefficient 0.23, 95% CI: 0.11 to 0.36, p value <0.001] and [53y-current, coefficient 0.28, 95% CI: 0.16 to 0.40, p value <0.001]) was independent of confounders. Associations remained significant when those who were hypertensive (SBP>140 mmHg) and those on treatment for hypertension were excluded.

Table 1. Relationship between SBP at age 43 and diastolic function at age 60-64y

<table>
<thead>
<tr>
<th>Model 1</th>
<th>Sex, age and clinic adjusted</th>
<th>Model 1 adjusted for current SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current SBP</td>
<td>p value</td>
<td>Current SBP</td>
</tr>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>SBP at age 43y</td>
<td>0.004 (0.518-0.008)</td>
<td>&gt;0.001</td>
</tr>
<tr>
<td>SBP at age 53y</td>
<td>0.024 (0.198 to 0.020)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP at age 64y</td>
<td>0.016 (0.100 to 0.026)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusions:** Elevated SBP from 36y predicts poorer diastolic function (E/e’) at age 60-64y, independent of current SBP. This effect may be mediated by relatively accelerated increases in SBP in mid-life, with changes in SBP in the fourth decade appearing particularly influential. Patients with high normal SBP and/or marked rises in SBP in mid-life may need early intervention to prevent future diastolic dysfunction.

**2250**

Incremental prognostic value of isolated diastolic dysfunction in healthy patients: beyond framingham risk score

W. Aljauwari, M.C. Alraies, C. Halley, V. Menon, L. Rodriguez, R.A. Grimm, J.D. Thomas, W.A. Jaber. Cleveland Clinic, Department of Cardiovascular Medicine, Cleveland, United States of America

**Context:** There are limited data evaluating prognostic value of diastolic dysfunction (DD) in a healthy cohort.

**Objective:** To evaluate the incremental prognostic value of DD in healthy adults beyond Framingham risk score.

**Methods:** We identified participants without cardiovascular risk factors or co-morbidities who underwent baseline echocardiogram between 1996 and 2005 and had normal left ventricular ejection fraction. Diastolic function was labelled as normal or abnormal. Cox proportional hazard model (CPH) and net reclassification index (NRI) were performed to evaluate the association of DD with all-cause death, and the incremental prognostic value of DD beyond Framingham risk score.

**Results:** The cohort consisted on 1039 patients, mean age (SD) 47.9 (15.7) years, 73% female. 693 (66.7%) patients had normal diastolic function, and 346 (33.3%) had DD (227 were stage 1). After a mean follow-up time (SD) of 2.8 (1.2) years, 41 (3.9%) patients died. The mortality rate among patients with normal and abnormal diastolic function were 1.4% (2/993) versus 9.0% (31/346), respectively (log rank P < 0.001). After adjusting for age, gender, and race, DD remained an independent predictor of all-cause mortality with hazard ratio (95% CI) 3.07 (1.30;7.24) (p=0.011). Re-running the CPH model and adjusting for Framingham risk score and race, DD was also an independent predictor of mortality with hazard ratio (95% CI) 2.96 (1.26;6.90) (p=0.013), and resulted in NRI of 15.8% (p=0.047).

**Conclusions:** In healthy outpatients with no cardiovascular risk factors or co-morbidities and with normal LVEF, isolated diastolic dysfunction was associated with 3 fold increase in risk of death and had incremental prognostic value beyond Framingham risk score with net reclassification index of 15.8%.

**2252**

Peripheral endothelial dysfunction in heart failure with preserved ejection fraction: a link with the development of pulmonary hypertension


**Purpose:** Pulmonary hypertension (PH) is highly prevalent and often severe in heart failure with preserved ejection fraction (HFpEF). Peripheral endothelial dysfunction has been described in patients with HFpEF, as well as in patients with primary PH. The purpose of this study was to determine if the presence of peripheral endothelial dysfunction is associated with PH in patients with HFpEF.

**Methods:** Measurements of peripheral endothelium-dependent and endothelium-independent vasoreactivity using brachial artery flow-mediated vasodilation (FMD) and nitroglycerin-mediated dilation of the brachial artery were performed in 21 patients with HFpEF and 21 hypertensive control subjects without heart failure. Patients showing pulmonary artery systolic pressure (PASP) > 35 mmHg on echocardiogram were proposed to undergo a right heart catheterization.

**Results:** Compared to controls, patients with HFpEF had impaired peripheral endothelial function (FMD 0.105±0.03mm in HFpEF vs 0.29±0.04mm in controls, p=0.002). There were no differences in nitroglycerin mediated dilation. PH was present in 16 (75%) HFpEF patients and 13 of them underwent a right heart catheterization. Their PASP was 74.15±24 mmHg, PAPD 27.7±11 mmHg, pulmonary capillary wedge pressure 18.4±5 mmHg, cardiac Index 2.7±0.1 L/min/m², pulmonary vascular resistance (PVR) 6.3±4 Wood Units. Subsequent analysis of the association between FMD and PVR disclosed an inverse correlation (r = -0.69, p<0.009), showing that the less the brachial artery dilated in response to flow, the higher the PVR was.

**Conclusions:** In patients with HFpEF, there is a significant correlation between peripheral endothelial dysfunction and pulmonary vascular resistance. FMD might be a useful clinical tool for noninvasive estimation of pulmonary vasoreactivity and PH in patients with HFpEF.

**2253**

Effects of physical exercise training on adipokine expression in diastolic heart failure: results from Ex-DHF-P

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**Purpose:** In heart failure (HF) early recognition of metabolic changes is vital for optimal adjustment of medical therapy and has high prognostic relevance for affected patients. A pilot study on exercise training showed significant beneficial effects on morbidity in diastolic HF (Ex-DHF-P). We investigated the analonic and
The ageing process of the heart: Reduced systolic function and preserved ejection fraction - The MONICA/KORA Study

J. Stritzel1, C. Moeller1, A. Luchner2, A. Doering3, H.W. Herse4, H. Schunkert1

Background: Heart failure with normal ejection fraction (HFNEF) is a common disease especially in older individuals and strongly related to left ventricular hypertrophy and diastolic dysfunction. Once admitted to hospital prognosis of HFNEF patients is impaired. This may indicate that HFNEF could be a precursor of heart failure with reduced EF. Therefore we evaluated left ventricular systolic function in individuals with mild diastolic dysfunction in a large population-based sample.

Methods: Subjects (918 men and women, aged 35 to 84 years) who originated from隔壁 and agedistriiated random sample of German residents of the Augsburg area (MONICA F3) were examined by standardized echocardiography. Individuals presented with signs or symptoms of heart failure were excluded for further evaluation. Left ventricular (LV) ejection fraction was determined by the Simpson method in the 4-chamber view. Tissue Doppler derived myocardial tissue velocities as well as Doppler-derived transmural in-flow velocities were used to evaluate systolic contractility (S) and diastolic function (e'/em-ratio). Quantiles of e'/em-ratio were calculated and evaluated for differences in LV systolic function.

Results: Individuals in the first quartile (e'/em<7.8) presented with normal EF (63.2%[CI-95%: 62.3, 64.4]) and normal systolic longitudinal contractility (S: 8.3cms[8.2, 8.5]). In comparison, with increasing diastolic dysfunction (2nd-4th quartile; e'/em: 7.8-9.3,9.3-11.1; >11.1) there was a highly significant increase in left ventricular ejection fraction detectable (66.7% [65.7, 67.8], p<0.001; 66.2% [65.8, 67.3], p<0.001; 66.2% [65.8, 67.3], p<0.001). In contrast, when comparing the same groups, a significant decrease in systolic longitudinal contractility (8.1cms[8.0, 8.3], p<0.001; 7.9cms[7.8, 8.1], p<0.001; 7.6cms[7.4, 7.7], p<0.001) was observed.

Conclusions: In the general population we found decreasing systolic longitudinal contractility in asymptomatic individuals with early stages of diastolic dysfunction. These findings may indicate that both systolic and diastolic heart failure are two faces of the same coin. Consequently, the development of heart failure seems to be a continuous process starting with early diastolic dysfunction and ultimately leading to severe systolic dysfunction.

The ageing process of the heart: Reduced systolic function and preserved ejection fraction - The MONICA/KORA Study

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Conclusions: In the general population we found decreasing systolic longitudinal contractility in asymptomatic individuals with early stages of diastolic dysfunction. These findings may indicate that both systolic and diastolic heart failure are two faces of the same coin. Consequently, the development of heart failure seems to be a continuous process starting with early diastolic dysfunction and ultimately leading to severe systolic dysfunction.
distances, less Ca43 lateralization and reduced brp and osteopontin serum concentration.

**Conclusion:** CathA-inhibition prevents the development of functional and arrhythmogenic remodeling in the atrium independent of improved ventricular function or blood pressure in a rat model for T2D. These data suggest a causal relationship between atrial CathA-activity and atrial structural and functional remodeling in Zucker diabetic fatty-rats.

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**Aliskiren, a direct renin inhibitor, suppresses the atrial structural remodeling and fibrotic gene expressions in the canine atrial fibrillation model**

A. Satoh, S. Niwano, H. Niwano, J. Okawa, J. Kishihara, Y. Aoyama, Y. Komatsu, Y. Kitasato

**Background:** We have documented suppressive effect of aliskiren, a direct renin inhibitor, on the electrophysiological changes in the canine atrial fibrillation (AF) model. In the present study, we analyzed the effect of aliskiren on the tissue fibrosis and fibrotic gene expressions to investigate the molecular mechanisms on the atrial remodeling in the AF model.

**Methods:** Continuous atrial rapid stimulation was delivered with implantable stimulator (29 dogs). They were divided into 2 groups with and without aliskiren (30mg/kg/day, n=12, and pacing control, n=12). In each group, 6/12 dogs were put down after 6 week atrial pacing and the remaining 4/12 dogs were put down at week 12 after the change of additions around the time course. At the end of the protocol, the left atrial dimension was measured by the echocardiogram and atrial tissue was sampled for the histological staining and analysis of the mRNA expressions of fibrotic genes, i.e., monocyte chemotactic protein-1 (MCP1), fibronectin 1(FN1), transforming growth factor-β (TGF-β) and collagen type 3 (COL3), using the RT-PCR. These mRNA expressions were also evaluated in 4 sham dogs for data comparison.

**Results:** The pacing control group exhibited enlargement of the left atrial dimension and interstitial fibrosis and these changes were more advanced along the time course. In contrast, in the aliskiren group, left atrial enlargement was not observed, and the area of tissue fibrosis was less in comparison with the pacing control (p<0.05). In the 3 week protocol, expressions of MCP1 and FN1 were up-regulated in the pacing control group in comparison with sham group, but these up-regulations were suppressed in aliskiren group. In the 6 week protocol, these suppressive effects of aliskiren on MCP1 and FN1 up-regulations became significant. In contrast, COL3 exhibited significant up-regulation in the pacing control group, which was insignificant in the 3 week protocol, and this up-regulation was suppressed by aliskiren. Throughout the protocol, TGF-β did not exhibit any significant changes in any groups and any time points.

**Conclusions:** In the canine AF model, tissue fibrosis and fibrotic gene up-regulations were observed in the pacing control group and these changes were suppressed by aliskiren. This effect of aliskiren was considered to appear through suppression of MCP1 and FN1 in relatively earlier phase of the atrial remodeling and it resulted in later suppression of COL3 up-regulation. Its effect of TGF-β may not play a main role at least in this AF model.

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**Reversed transmural activation-repolarization gradient in Brugada syndrome exacerbated by increased cholinergic tone**

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Heterogeneities in conduction and repolarisation in the RVOT are thought to cause the typical ECG and ventricular arrhythmia in Brugada syndrome (BrS). Previous studies have reported prolonged or abbreviated activation-repolarisation intervals (ARIs) in RVOT epicardium (epi) compared with endocardium (endo). Increased cholinergic tone has been seen to enhance ST elevation and increase VT susceptibility. We recorded RVOT epi and endo ARIs simultaneously and assessed the effect of 6 mins of continuous atrial pacing at 250 bpm in 7 BrS and 7 control patients were studied. A non-contact mapping array was deployed in the RVOT and a great cardiac vein multipolar catheter recorded epicardial signals. 400 msec restitution curves were constructed before and after endrophonium (Edr) administration. Multilevel modelling was used to analyse the data.

In control patients (fig.1) there was a minimal mean transmural gradient (TMG) (3.4ms, 95%CI: 6.80,0.02, p<0.05), with endo ARIs marginally shorter than epi ARIs. In BrS patients (fig.2), there was a significantly larger mean TMG (20.5ms, 95%CI: 25.5,15.5, p<0.001), with epi ARIs shorter than endo ARIs. Post Edr, control TMG increased to 16ms (95%CI: 19.6,12.6, p<0.001) due to epi ARI prolongation and BrS TMG increased to 29.7ms (95%CI: 35.3,24.1, p<0.001) due to endo ARI prolongation. The TMG increases between both groups were not significantly different. There is a significant ARI TMG in BrS compared with epi to endo TMG in normal hearts. These gradients are exacerbated by increased cholinergic tone with preferential endo ARI prolongation in BrS indicating an increased heterogeneity between the 2 sites. It suggests the main cholinergic effects in BrS are exerted on the endo possibly combined with conduction delay exacerbating transmural repolarisation differences.

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**Mean duration of AF episodes in the PASCAL (Proxysmal Atrial Fibrillation Study with Continuous Atrial Fibrillation Logging) study are reduced by treatment with higher dose of lubodaron**

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**Purpose:** Studies of PAF utilizing continuous pacemaker monitoring (CPM), including TRENDS and ASSERT, have indicated that stroke risk correlates with duration of AF episodes. Increased risk has been demonstrated with episodes of 24 hours, 5.5 hours and more recently 6 mins. An efficacious anti-arrhythmic drug (AAD) should reduce the number and the duration of AF episodes. We sought to examine this effect of the drug in a blinded randomized placebo controlled prospective clinical trial.
Methods: PASCAL was a CPM study in 72 PAF patients at 44 centers in 4 countries. Following 1 month baseline evaluation free of AAD, patients with an AF burden (AFB) of 3% - 70% were randomized to receive either placebo (n=18), 200 mg (n=21), 400 mg (n=18) or 600 mg (n=15) biduradone po BID for 3 months in a parallel group study. The 1° EP was reduction in AFB from baseline and key 2° EPs were mean and median duration of AF episodes. All data was analyzed on an ITT basis.

Results: The 1°EP of PASCAL showed a 54% (p=0.01) and 74% (p=0.001) reduction in AFB with 400 mg and 600 mg biduradone, respectively. The results of the AF duration EPs are shown in the table. Despite marked variability in duration of AF episodes at baseline and on placebo, the mean duration of AF episodes on 400 mg and 600 mg biduradone, were 1.2 and 0.7 hours, respectively (p<0.01). The median duration of AF episodes on 600 mg was only 6 min. There was also a marked reduction in the variability on drug such that he longest episode of AF recorded during 3 months of treatment in any of the 25 patients on the two higher doses was 4.6 hours, compared to 221 hours at baseline off AAD or 218 hours on placebo.

Conclusion: The PASCAL study confirms that effective doses of biduradone, 400 mg and 600 mg, when given po BID for 3 months markedly shorten the duration of AF episodes. This suggests the drug achieved the goal of successful entrainment of the atria in PAF.

ADVANCES IN THE MANAGEMENT OF CARDIOMYOPATHIES

2293 Yield of genetic testing in 418 index patients with dilated cardiomyopathy; overview of 10 years experience


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Purpose: Idiopathic Dilated Cardiomyopathy (DCM) is thought to be familial in up to 50% of cases. Genetic analysis of DCM is costly and time-consuming because multiple DCM related genes have been identified, most of them accounting for only a minority of cases. The purpose of this study is to describe the yield of genetic analysis in DCM patients.

Methods: Clinical data from cardiological and neurological evaluation, family history, and results of genetic analyses in 418 index patients with idiopathic DCM (224 familial DCM, 173 sporadic DCM, and 21 DCM with associated neuromuscular disease) were collected from four cardiogenetics outpatient clinics in the Netherlands. We assessed the prevalence of identified mutations in DCM related genes and their clinical expression.

Results: Thirty-five (putative) pathogenic mutations were identified in 82 of the 418 DCM index patients (20% in the total group, 25% in familial DCM, 8% in sporadic DCM, and 62% in DCM with associated neuromuscular disease). Most prevalent were a PLN founder mutation (43 index patients) and 16 different LMNA mutations (19 index patients), with specific clinical expression in the majority of cases. Other mutations were found in the genes: MYH7, DES, TNNI3, TPM1, DMPK, SCNSA, SCGB, and TNN3. Only one patient was double heterozygous. After a median follow-up of 40 months (interquartile range: 13 to 90 months), combined death from any cause, heart transplantation, and malignant ventricular arrhythmias of successfully genotyped patients was worse compared to DCM patients without a known genetic cause (HR 2.0, 95% CI: 1.4-3.0). This seems to be mainly due to the arrhythmogenic phenotypes of LMNA and PLN mutation carriers.

Conclusions: Extensive genetic analysis in a large and well-defined DCM cohort provides insight in the prevalence of mutated genes and in genotype-phenotype associations. The yield of genetic analysis is high (62%) in DCM with associated neuromuscular disease, moderate (25%) in familial DCM, and low (8%) in sporadic DCM. We recommend genetic analysis in familial DCM and in DCM with associated neuromuscular disease. For sporadic DCM, specific clinical characteristics (like gene-specific characteristics and sudden cardiac death in relatives) can be used to select cases for DNA analysis. The results of this study form a solid base to develop next generation sequencing for DCM. This new technique will provide high-throughput, rapid and affordable genetic analysis for DCM.

2294 A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy: a proof of concept study

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Purpose: Risk stratification in patients with Hypertrophic Cardiomyopathy (HCM) is currently based on a relative crude summation of a few selected clinical risk factors. The aim of this study was to develop and externally validate a novel clinical risk prediction model to provide absolute, individualised probabilities for sudden cardiac death (SCD), which can be used in routine clinical practice to advise HCM patients on ICD therapy.

Methods: The model was developed by applying Cox proportional hazards method to retrospectively collected data from 1634 consecutively patients evaluated at The Hospital. A backward elimination strategy with a 20% significance level was used. The final model included the following baseline variables: age, maximal wall thickness (WT), left ventricular end-diastolic diameter, maximum left ventricular outflow tract gradient (LVOTG), left atrial diameter (LAD), family history of SCD (FHSCD), non-sustained ventricular tachycardia (NSVT), permanent/persistent atrial fibrillation and unexplained syncope. The model was externally validated by examining calibration and discrimination in a geographically distinct cohort of 456 consecutively evaluated patients from an Institute of Cardiology.

Results: The total study cohort consisted of 2099 HCM patients with 15199 patient-years of follow-up. The SCD events during follow-up were: 82 actual SCD, 17 resuscitated SCD and 35 appropriate ICD shocks. The overall annual rate of SCD was 0.9% (95% CI 0.7–1.0), with a 92% (95% CI 90.1-93.3) 10-year cumulative survival.

The model was developed in the London cohort: the final model estimating the risk of SCD at 5 years was: 1 – 0.9992exp(1.4854 + Age in years*0.0017612 + NSVT*0.846575 + log(WT) in mm*0.7823579 + LAD in mm*0.0143461 + syncope*0.6363927 + FHSCD*0.517554 + LVOTG in mmHg*0.0027697). For example a 20 year old patient with unexplained syncope, MWT of 23mm, no FHSCD or NSVT, LAD 44mm, and maximum LVOTG of 24mmHg has a 5-year risk of SCD of 6.7%.

The model was validated in the Bologna cohort, and the calibration (the agreement between the observed and predicted probabilities) of the model was 82% and Harrell’s c for discrimination (the ability of the model to distinguish high risk from low risk patients) was 78%.

Conclusions: The proposed clinical risk prediction model provides individualised, absolute risk estimates for SCD which can be used to help managing the risk of SCD in clinical practice. A larger multicentre study will help improve on the accuracy of the estimates.

2295 Prognostic role of high-sensitivity cardiac troponin T in hypertrophic 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, the role of in the prediction of cardiovascular events in hypertrophic cardiomyopathy (HCM) is unclear. The aim was to determine whether hs-cTnT can be a reliable prognostic marker of adverse events in HCM.

Methods: We performed clinical evaluation including measurements of hs-cTnT in 183 consecutive patients with HCM.

Results: Of 183 HCM patients, 99 (54%) showed high hs-cTnT values (> 0.014 ng/ml). During a mean follow-up period of 4.1±2.0 years, 32 of the 99 patients (32.3%) in the high hs-cTnT group but only 6 of 84 (7.1%) patients with normal hs-cTnT values suffered from cardiovascular events: cardiovascular deaths (All 9 patients with HCM related deaths were in the high hs-cTnT group), unplanned heart failure admissions, sustained ventricular tachycardia, embolic events, and progression to New York Heart Association functional class III or IV status; hazard ratio (HR): 5.1, p = 0.001. High hs-cTnT value remained an independent predictor of these cardiovascular events after multivariable analysis (HR: 3.2, p = 0.012). Furthermore, in the high hs-cTnT group, overall risk increased with the hs-cTnT values (HR: 1.243±0.015 ng/ml increase, p = 0.002).

Conclusions: Serum concentration of hs-cTnT considered to reflect myocardial injury is a useful prognostic predictor in HCM patients.
2296 Hereditary transthyretin-related amyloidosis with exclusively cardiac phenotype: disease profile and differential diagnosis with hypertrophic cardiomyopathy and senile systemic amyloidosis

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Purpose: In a cohort of patients with hereditary transthyretin (TTR)-related amyloidosis (ATTR), we assessed prevalence, genetic and disease profile of cases with an exclusively cardiac phenotype (i.e. without neurological involvement), highlighting possible hints for differential diagnosis with hypertrophic cardiomyopathy (HCM) and Senile Systemic Amyloidosis (SSA).

Methods: We compared the clinical, ECG and echocardiographic characteristics of patients with ATTR and an exclusively cardiac phenotype at diagnosis with those of 30 age-matched gender matched patients with sarcornic HCM and of 30 patients with biopsy-proven SSA.

Results: Among 166 patients diagnosed with ATTR between 1990 and 2010 at three large Italian Centres with coordinated amyloidosis network, 31 (17%) showed an exclusively cardiac phenotype at presentation due to ile68leu (n=23, 74%) or other 7 different TTR mutations. Their main clinical, ECG and echocardiographic findings and those of HCM and SSA patients are reported in the Table.

<table>
<thead>
<tr>
<th>Age, years (median [IQR])</th>
<th>ATTR (n=31)</th>
<th>SSA (n=30)</th>
<th>HCM (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, n (%)</td>
<td>29 (94)</td>
<td>28 (93)</td>
<td>26 (87)</td>
</tr>
<tr>
<td>LV systolic wall thickness, mm (median [IQR])</td>
<td>11 (30)</td>
<td>10 (30)</td>
<td>8 (30)</td>
</tr>
<tr>
<td>LV hypertrophy on ECG, n (%)</td>
<td>2 (7)</td>
<td>3 (10)</td>
<td>17 (57)</td>
</tr>
<tr>
<td>Diastolic interventricular septum thickness, mm (median [IQR])</td>
<td>16 (18–20)</td>
<td>16 (18–22)</td>
<td>19 (17–22)</td>
</tr>
<tr>
<td>Diastolic LV posterior wall thickness, mm (median [IQR])</td>
<td>16 (15–18)</td>
<td>17 (14–19)</td>
<td>14 (13–15)</td>
</tr>
<tr>
<td>LV ejection fraction, % (median [IQR])</td>
<td>45 [56–51]</td>
<td>50 [55–58]</td>
<td>68 [67–76]</td>
</tr>
<tr>
<td>LV end-diastolic diameter, mm (median [IQR])</td>
<td>49 [44–51]</td>
<td>47 [43–50]</td>
<td>44 [40–47]</td>
</tr>
</tbody>
</table>

Conclusions: ATTR (which can be mistaken for HCM or SSA) should always be considered in subjects older than 60 years with unexplained left ventricular (LV) hypertrophy, even in the absence of overt neurological manifestations. While a careful interpretation of ECG and echocardiogram can direct towards the right diagnosis between ATTR and SSA, it is based solely on molecular genetics.

2297 Device therapy in noncompaction cardiomyopathy - data from the German noncompaction registry (ALKK)

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Noncompaction cardiomyopathy (NCCM) is considered a genetic cardiomyopathy showing a high prevalence of heart failure, arrhythmias and thrombembolic events. The AHA/ACC/HRS Guidelines concerning device-based therapy recommend ICD-implantation (impl) in NCCM as a IIa (C) indication. We therefore investigated the impact of device therapy on clinical outcomes of pts with NCCM.

Methods: The German ALKK registry was initiated in 2006. By February 1st, 2012 233 pts were enrolled (median 156, 75 women, age 18 to 87 yrs, mean 56.2 yrs). The pts were followed in 6 mths intervals looking for deterioration of clinical status, LV function, and reaprashof therapy. Device based therapy (ICD, CRT-D, pacemaker systems) and implantable loop recorder devices (ILR) were analysed, separating the pts into a group with severely reduced LV function (group A, EF≤35, n=89) and into a group with normal to moderately reduced LV function (group B, EF > 35%, n=144).

Results: 13 cardiac deaths occurred during follow up. 5 of them were sudden cardiac deaths (SCD). All SCD occurred in group A, 2 of them prior to scheduled ICD-impl. In 2 cases aborted SCD occurred as initial symptom in asymptomatic pts with only mildly reduced LV function, one of them with LBBB. 51 pts (group A, 18 group B) received an ICD system (34 single chamber systems, 8 dual chamber systems and 9 CRT-D) or a pacemaker. Adequate device therapy was observed in 5 of 24 pts with primary preventive indication in group A, while there was no adequate shock therapy in group B with primary prevention. 3 of the 51 pts with ICD-impl (all group B) encountered device-related complications (1 pt with atrial fibrillation, 1 pt with and 3 pts with the ICD electrode in the coronary sinus, 2 pts with inappropriate shock therapy). 11 pts (4 of group B) required a pacemaker for AV block or sick sinus syndrome. In 2 pts of group B an ILR was implanted after syncope, but to date no arrhythmia was detected.

Summary: Device therapy is frequently used in pts with NCCM. ICD therapy prevents sudden cardiac deaths in pts with severely reduced LV function in primary prevention and should be chosen particularly in cases with pacemaker indication. Primary preventive implantation in pts with NCCM and LVEF < 35% should be performed with caution, e.g. in pts with additional risk factors. CRT implantation can successfull be performed in NCCM pts with LBBB and severely reduced LV function. Pacemaker therapy is recommended according to the actual guide lines. ILR impl could be a diagnostic alternative in pts with NCCM and preserved LV function to choose the adequate device.

2298 Pregnancy in women with arrhythmogenic right ventricular cardiomyopathy

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Objectives: To assess the morbidity and mortality in pregnant women affected by Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC).

Background: The risk associated with pregnancy in women with ARVC is an important and increasingly frequent clinical issue for which systematic data have not been reported so far.

Methods: The study cohort included 27 women affected by ARVC with one or more live births, for a total of 47 live births. Maternal mortality and morbidity related to ARVC during pregnancy was evaluated with a follow-up programme, consisting of personal and family history, 12-lead ECG, signal-averaged ECG, 24-h AECG monitoring, Holter and two-dimensional and Doppler echocardiogram within three years of the pregnancy. The symptoms considered were dyspnea, asthma and palpitations. Moreover in 18 patients clinical and instrumental findings detected at the time of the first and the second pregnancy were compared. Finally, data of 13 nulliparous ARVC patients (mean age 32.3±5.9yrs) were correlated to those of 10 multiparous patients with the same age (34.9±3.3yrs).

Results: No pregnancy-related death occurred. In the 27 patients evaluated within close proximity of their pregnancy, 4 (14%) showed a worsening of arrhythmias during pregnancy. They were all characterized by having a severe form of the disease. One patient experienced a sustained ventricular tachycardia 50 after delivery. None patient complained of a worsening of symptoms. In the 18 patients who had more than one pregnancy, the comparison between the first and the second pregnancy demonstrated a worsening of symptoms (P=0.05) and of arrhythmias (P=0.03) after the second delivery. Similarly, the comparison between nuliparous and multiparous ARVC patients demonstrated after the second pregnancy a significant dilatation of Right Ventricular Outflow Tract (RVOT 21mm/m2 p=0.03) as well as a worsening of symptoms (P=0.05) and arrhythmias (p=0.03).

Conclusions: Maternal mortality is not increased in patients with ARVC compared with the general population. During gestation a worsening of arrhythmic pattern is more common in subjects with a severe form of the disease. The presence of a second pregnancy seems to be associated with a worsening of clinical and instrumental features of patients. Pre-conception planning and risk assessment are essential.

UNUSUAL FACES OF ISCHAEMIA

2303 Changes in left ventricular twist during dobutamine stress echocardiography in patients with myocardial infarction: association with left ventricular reverse remodeling

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Purpose: Left ventricular (LV) twist, an emerging marker of global LV function, has not been evaluated during stress echocardiography (DSE) in patients following ST segment elevation myocardial infarction (STEMI). We therefore aimed to: 1) describe the changes in LV twist at each stage of DSE in this group of patients and 2) to investigate whether the increment in LV twist during DSE could predict follow-up LV reverse remodeling, a known predictor of favorable long-term outcome.

Methods: Consecutive patients admitted with first STEMI undergoing primary percutaneous coronary intervention and standard protocol DSE at 3 months follow-up were selected. DSE studies positive for ischemia (defined as new or worsening regional wall motion abnormalities) or for sustained arrhythmias were excluded. LV twist – defined as the net difference (in degrees) of the apical and basal rotation at isochronal time points – was calculated at each stage using speckle tracking analysis. In addition, baseline (within 48 hours) and 6-month follow-up 20 DSE studies with LV reverse remodeling were defined as a >10% decrease in LV end-systolic volume (ESV).

Results: In total, 82 patients (mean age 61, 85% male, mean LVEF 49%, median troponin T 3.02 ug/L) had complete DSE studies with adequate short-axis image
quality. Patterns of response of LV twist to dobutamine included those with a pro-
gressive increase through each stage (n=18), those with an increase at either low
peak-dose (n=53) and those with no significant increase (n=11). The increase in
LV twist from rest to peak-stress was significantly related to the reduction in
LVEFSV from baseline to 6 months follow-up (p<0.001, r=0.4). Overall LV reverse
remodeling occurred in 28 (34%) patients, who showed significantly higher peak-
stress global LV twist (5.95 vs. 7.77 °, p=0.01) and more frequently displayed the
pattern of progressive increase of LV twist to dobutamine through each stage as
compared to patients without LV reverse remodeling (p=0.005).

Conclusions: Significant increments in LV twist at one or more stages of DSE
occurred in the majority of patients 3 months post-STEMI. Both peak-stress LV
twist and the pattern of progressive increase in LV twist at each stage of DSE
were associated with LV reverse remodeling at follow-up. This finding suggests
a novel, clinical use for LV twist as a marker of contractile reserve in patients
following STEMI.

Methods and Results: We followed 718 patients for a median of 16 months after
high-dose dipryidamole contrast SE for evaluation of known or suspected CAD.
The ability of WM, CFR-LAD and MP to predict cardiac events was studied in
multivariable models and risk recategorisation analysis. Fifty cardiac events oc-
curred (annualized event-rate 6.0%). Abnormal SE was detected as a reversible
WM abnormality in 18%, as reversible MP defect in 27% and as CFR-LAD-2 in
38%. A normal MP stress test was the most reassuring result for patients, with a
1-year hard event-rate of 1.2%. The C-index of outcomes prediction based on
clinical data was improved with MP (p<0.001), WM/CFR-LAD (p=0.003) or MP
(p=0.003) on top of clinical and WM data. Net risk reclassification was improved
by adding MP (p<0.001) or CFR-LAD (NRI p=0.001) on top of clinical and WM
data. The model including clinical data, WM/CFR-LAD and MP performed better
than without MP (p=0.012).

Figure 1. Total cardiac 1-year event rate

Conclusions: Contrast SE allowed prognostication in patients with known or sus-
ppected CAD, whatever the parameter assessed. The multivariparametric assessment
of WM, CFR-LAD and MP during dipryidamole stress testing is feasible and the
addition of CFR-LAD and MP assessment to WM analysis and clinical data im-
proves the predictive value of SE.

Eplerenone improves cardiac sympathetic nerve activity in patients with first acute anterior myocardial infarction


Purpose: In EPHEMUS study, eplerenone, a selective aldosterone blocker, signi-
ficantly reduces morbidity and mortality when given in patients who have left
ventricular dysfunction and heart failure after acute myocardial infarction (AMI).
However, effects of Eplerenone on cardiac sympathetic nerve activity (CSNA) as
evaluated by 123I-metaodobenzylguanidine (MIBG) scintigraphy have not been
determined for patients with AMI.

Methods: We studied 20 patients with their first anterior AMI. All patients were
studied with angiotensin converting enzyme inhibitors or Angiotensin II recep-
tor blockers. Beta blockers and statins were administered unless there were
contraindications. 10 patients were randomized to receive oral eplerenone (25-
mg/day) and the other 10 patients received a placebo. The delayed heart-
tracers were analyzed using dynamic cardiac SPECT. CSNA was measured using
radioactive markers, and heart rate and blood pressure were recorded during
stress tests. The results were compared between the two groups.

Results: At baseline, TDS, H/M ratio, WR, LVEDV, LVEFSV, and LVEVF were simi-
lar in both groups. After 6 months, TDS decreased significantly in both groups.
In placebo group, WR [40.5±2.8 to 38.9±4.2 (p=0.22)] and H/M ratio [2.23±0.40
to 2.36±0.43 (p=0.14)] did not significantly change. In contrast, WR decreased
significantly from 43.6±7.0 to 39.2±8.7 (p<0.009) and H/M ratio improved signif-
icantly from 2.05±0.37 to 2.36±0.43 (p=0.007) in eplerenone group.

Conclusion: The addition of eplerenone to optimal medical therapy is beneficial
for CSNA in patients with anterior AMI.

Effect of gastric bypass on vasomotor function of the coronary circulation in morbid obese individuals
without cardiovascular diseases

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Nuclear Medicine, Geneva, Switzerland

Aims: We aimed to evaluate the effect of gastric-bypass on coronary vasomotor function in morbid obese individuals (MOB) without other cardiovascular risk
factors (RFs) and without known coronary artery disease (CAD), in a longitudinal 12
months follow-up study.

Methods: Myocardial blood flow (MBF) responses to cold pressor test (CPT),
mostly representative of endothelial-dependent function, and pharmacoletic va-
sodilation, as index of predominantly endothelial-independent vasodilation, were
measured with $^{13}$N-ammonia PET/CT in 12 MOB (BMI, Body Mass Index >40) at baseline (B-MOB) and 12 months after gastric-bypass intervention (FU-MOB).

Results: After gastric bypass, BMI and fat percentage significantly decreased in FU-MOB as compared to B-MOB (30.8 (27.3, 34.7) versus 44.8 (43.3, 48.2), p = 0.0001 and 29.1 (24.1, 30.4) versus 46 (40.4, 48.9), p = 0.0001, respectively). The hyperemic-related change in MBF during CPT from rest (±MBF) was significantly reduced in MOB as compared to a group of age-matched controls with normal body weight [0.03 (−0.08, 0.15) versus 0.26 (0.02, 0.39) ml/min/g, p = 0.0001]. Hyperemic MBFs were also lower in MOB than in normal (2.10 (1.40, 2.35) vs. 2.28 (1.87, 2.65) ml/min/g, p = 0.048). When compared with B-MOB, the endothelium-related change in MBF (±MBF) to CPT significantly increased in FU-MOB [0.03 (−0.08, 0.15) in MOB vs. 0.34 (0.18, 0.41) in FU-MOB, p = 0.002] reaching similar values as in normal individuals (p = 0.625). Hyperemic MBFs also increased after gastric-bypass intervention without reaching statistical significance [2.40 (2.04, 3.13) in FU-MOB vs. 2.10 (1.40, 2.35) ml/min/g in MOB, p = 0.081]. No significant association was observed between the degree of weight loss and the improvement in coronary circulatory function, suggesting that increases in body weight may disproportionately affect the function of coronary circulation.

Conclusion: Gastric-bypass induced a significant reduction in BMI and fat content in morbid obese individuals, which was associated with a marked improvement in coronary circulatory dysfunction. Whether the observed weight-loss induced improvement in coronary circulatory dysfunction also translates into an improved cardiovascular outcome, remains to be investigated.

2308 Effect of spinal cord stimulation on myocardial flow reserve in patients with severe angina pectoris

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Purpose: Spinal cord stimulation (SCS) relieves angina pectoris in patients with ischemic heart disease, but mechanisms of this effect remain incompletely understood. The electrophysiological basis of AF is not understood. Acetylcholine from the vagus nerve binds to muscarinic receptors causing dissociation of CaM kinase II and phosphorylation of HCN5. This increases the ratio of HCN5 and L-type calcium current and thereby the excitability towards AF induction and the occurrence of atrial fibrillation.

Methods: In vivo studies were performed in RGS 4 KO and wild type (WT) mice. Electrophysiological studies (EPS) were undertaken in 8-week old anaesthetised mice with a 1.1F catheter inserted into the right atrium via the right internal jugular vein. ECG and EP parameters were recorded. AF induction was attempted with burst pacing for 25 seconds and repeated after injection of 0.5mg/kg carbachol. Telemetry probes were inserted intra-abdominally into 12-week old mice. After a two-week recovery period, EPS were recorded in conscious mice for 48 hours and studied for AF and atrial ectopics (AE). An ECG post carbachol injection was analysed. Heart rate variability (HRV) was measured from 12 to 2pm, when murine vagal tone is highest.

Results: ECG and EP parameters were comparable. RGS 4 KO mice developed AF (76.9 vs 38.5%, P<0.04). Mean duration of AF for WT was 70.2±28.9 (1.9 to 770) versus 222.6±164.9 (1.9 to 2867.4, P=0.69) seconds for RGS 4 KO mice. Although this did not reach significance, there was a trend to a longer duration of AF in RGS 4 KO mice. Carbachol did not increase AF in KO or WT (P>0.28), although a trend was apparent. Conscious RGS 4 KO mice were tachycardic (634±3.52 vs 562±6.36 bpm, P<0.001), and had an enhanced bradycardic response to carbachol (288±2.37 vs 524±3.24 bpm, P<0.02). ECG and HRV parameters of WT and RGS 4 KO mice without and with carbachol were comparable (P>0.05). Carbachol-treated RGS 4 KO mice had disrupted HRV (P=0.008) compared to RGS 4 KO mice alone. This was not seen with WT treated with carbachol (P>0.05). Carbachol-treated RGS 4 KO mice had several pauses, 2 of which were for more than 30s. Neither AE nor AF were totally abolished in mice treated with carbachol. Without carbachol, no AE or AF was seen in RGS 4 KO or WT mice. Conclusions: This is the first report of AF and HRV in the RGS 4 KO mouse in vivo. These are tachycardic, have an enhanced bradycardic response to carbachol and disrupted HRV. This signifies altered sympathovagal balance. Mechanistic studies are underway to understand the electrophysiological basis of AF in the RGS 4 KO mouse. RGS 4 is a potential therapeutic target in the treatment of AF.
Clinical significance of bundle branch block in patients with atrial fibrillation: From the Fushimi AF Registry

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Purpose: Atrial fibrillation (AF) increases the risks of stroke and death, and the prevalence of AF is increasing significantly (0.7-0.8% of total population in Japan). The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients living in Fushimi-ku, Kyoto, which is a typical urban district of Japan with a population of 283,000; rough estimate of 2,200 AF patients. At present, we have enrolled 3,015 Japanese AF patients from March 2011 to February 2012. We aimed to investigate the clinical significance of bundle branch block (BBB) in AF patients.

Methods: We analyzed 12-lead electrocardiograms during AF at rest obtained from 1,830 Fushimi AF Registry patients (males 59.1%; 74.7 ± 10.7 years). We evaluated the presence of BBB, a metabolic effect, and the possibility of rate-dependent change. CHADS2 score was greater in AF patients with BBB compared with those without BBB (right: 2.24 vs. 2.12; p < 0.05, left: 2.51 vs. 2.11; p < 0.05) and chronic obstructive pulmonary disease (9.3% vs. 4.3%; p < 0.01). In contrast, AF patients with BBB were also older (76.7 ± 4.4; p < 0.01) and more likely to have diabetes (28.3% vs. 21.8%; p < 0.17), peripheral artery disease (PAD) (8.0% vs. 3.9%; p < 0.02), and chronic obstructive pulmonary disease (9.3% vs. 4.3%; p < 0.01) and chronic kidney disease (35.8% vs. 20.6%; p < 0.01).

Conclusion: BBB was more prevalent in patients with AF than those without AF. The presence of BBB may be related with co-existing cardiac diseases or metabolic abnormalities that lead to atherosclerosis.

Results: In this patient population, 27 patients had no recurrence after initial AF ablation and remaining 16 patients had a recurrence. The value of pRR–50 and SNN2 after ablation were significantly smaller in patients without recurrence than in patients with recurrence (Table 3). The value of 50% for SNN2 was not identified as a cut-off value to distinguish between the two subgroups.

Conclusion: The degree of parasympathetic denervation was a significant correlation with the extent of the ablated FP area. The parasympathetic denervation was also a predictor of successful AF ablation.

The correlation between the extent of fat pad modification during ablation of atrial fibrillation and the degree of parasympathetic denervation: LGE-MRI analysis

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Background: Parasympathetic denervation by affecting epicardial ganglionated-plexi (GP) is inevitable during pulmonary vein antrum isolation (PVAI) for patients with atrial fibrillation (AF). GP is known to reside within epicardial fat pads (FPs).

Objectives: We retrospectively investigated 43 patients who underwent LGE-MRI 3 months after ablation in order to assess the extent of scar created by ablation. FPs in well-known GP areas were segmented from T2 weighted MRI and processed to as-113MGB scintigraphy.

Methods: 12-lead ECGs were recorded, and after successful catheter ablation, the H/M ratio was measured on 4 hours delayed images after the injection of the tracer to assess the presence of a scar. The presence of 3 parameters was 100% predictive of spontaneous conversion (33%) while 86% of patients with any of those did not convert to SR within 18 hr (18/21), p < 0.001.

Conclusion: In line with previous observations of an association between low AF and efficacy of interventions for AF, a low AF was predictive of spontaneous conversion to SR in unsupervised patients with recent-onset AF. Along with clinical predictors such as first-ever AF episode and IHDF history, AF can be used for identification of patients prone to convert spontaneously if proven in prospective studies that are warranted by our findings.

Cardiac sympathetic innervation predicts initiation of rapid atrial fibrillation in patients with supraventricular tachycardia

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Purpose: Supraventricular tachycardia (SVT) acts as a trigger for atrial fibrillation (AF), which can be a potentially life-threatening arrhythmia when it conducts rapidly through the accessory pathway (AP). However, the noninvasive test currently plays little role in evaluating SVT.

The purpose of our study was to investigate whether cardiac sympathetic nervous system (SNS) activity is associated with the initiation of rapid AF in SVT patients. We hypothesized that low AF was predictive of spontaneous conversion to SR in unsupervised patients with recent-onset AF. Along with clinical predictors such as first-ever AF episode and IHDF history, AF can be used for identification of patients prone to convert spontaneously if proven in prospective studies that are warranted by our findings.

Methods: 368 Atrial fibrillation: underlying mechanisms

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P2320

Figure 1
Electrocardiographic phenotypes associated with genetic polymorphisms on chromosome 4q25 rs2200733, 16q22 ZFHX3, or 1q21 KCNN3 in Korean patients with non-valvular atrial fibrillation

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Background: Recently, GWAS revealed several genomes related with atrial fibrillation (AF), such as genetic variants on chromosomes 4q25 PITX2, 16q22 ZFHX3, or 1q21 KCNN3. We hypothesized that the patients with those genetic backgrounds are affected by co-factorial diseases, such as hypertension or heart failure in in Korean patients with non-valvular AF.

Methods and Results: We evaluated and compared the allelic frequencies of genetic polymorphisms of chromosome 4q25 rs200733, 16q22 ZFHX3, or 1q21 KCNN3 in 552 patients with non-valvular AF (57.6±11 years old, male 77%) who underwent catheter ablation and 523 sex-matched healthy control by direct DNA sequencing and SNaPshot™ assay. We compared P wave characteristics of 12 lead electrocardiography (ECG) between genetic variants and non-variants.

Results: 1. The 4q25 rs200733 (OR 2.935, 95% CI 2.152-4.03, p<0.001), the 16q22 ZFHX3 rs1006261 (OR 2.371, 95% CI 1.735-3.245, p<0.001), and the 1q21 KCNN3 rs1373633 variants were significantly prevalent in patients with AF than in control group 2. The 4q25 rs200733 variants were related with long PR interval than in non-variants (185.6±1.6 vs. 173.0±3.5 ms, p<0.001). 3. The 1q21 KCNN3 rs1373633 variants showed significantly longer P wave duration in V1 (69.7±3.5 vs. 60.7±1.1 ms, p<0.001) and low P wave amplitude in lead I (0.087±0.005 mV vs. 0.113±0.004 mV, p>0.05) than in non-variants. 4. The 1q21 KCNN3 rs1373633 variants showed significantly longer P wave duration in V1 (69.7±3.5 vs. 60.7±1.1 ms, p<0.001) and low P wave amplitude in lead I (0.087±0.005 mV vs. 0.113±0.004 mV, p>0.05) than in non-variants.

Conclusions: Genetic polymorphisms on chromosome 4q25 rs200733, 16q22 ZFHX3, or 1q21 KCNN3 are associated with longer P wave duration in V1 and low P wave amplitude in lead I, which might be related to its disease duration. Also, beta-alanine might play a role in its maintenance.
P2325
Frameshift mutation in sarcomeric gene causes recessive familial early onset lone atrial fibrillation
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Purpose: Familial clustering of atrial fibrillation (AF) is well recognized, particularly clearly onset lone AF. Several genes, mostly related to ion channels and gap junctions, have been linked to familial AF, including potassium channel KCNJ2, SCN5A, JQ58, and NPPA. AF also commonly occurs in other congenital cardiac diseases, both structural diseases like hypertrophic cardiomyopathy and skeletal myopathies, and primary electrical disorders like long-QT syndrome and Brugada syndrome. Recent genome-wide association scans have found common sequence variants at several sites, including PITX2 and ZFHX3 that are associated with AF. The purpose of this study is to identify sequence variants associated with early-onset AF, defined as having been diagnosed with AF before 60 years of age.
Methods: A genome-wide association scan for early-onset AF was performed based on imputed data over 20 million sequence variants identified through sequencing the whole genomes of 1176 Icelanders into 60,000 Icelanders and their relatives.
Results: The scan identified rare (0.7% allele frequency) single basepair deletions in the FLNC gene. A common variant in the FLNC gene was found to be associated with AF through a recessive mode of inheritance. Seven homozygous carriers of the deletion were identified in Iceland, all with early-onset lone AF (the youngest at age 14, the oldest at age 56). No excess heterozygous carriers was observed among middle-aged AF cases. The three affected carriers have been identified with personal medical records and all have been confirmed as affected by the current criteria. The presence of the sequence variant in the sarcomere gene MYH6 associating with heart rate and sick sinus syndrome and the example presented here are novel findings that shed further light on the important interplay between conduction and contractility of the cardiac muscle.
Conclusion: It is well established that structural heart disease is a major risk factor for AF (and other conduction disturbances) and arrhythmias are commonly seen in cardiomyopathies caused by mutations in sarcomeric genes. However, our recent discoveries of amino acid mutations in the sarcomere gene MYH6 associating with heart rate and sick sinus syndrome and the example presented here are novel findings that shed further light on the important interplay between conduction and contractility of the cardiac muscle.

P2326
LV dysfunction caused by persistent atrial fibrillation was associated with high reactive oxidative metabolites in coronary sinus vein
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Purpose: Oxidative stress (OS) plays critical roles in the pathogenesis of atrial fibrillation (AF). However, precise mechanisms of OS associated with the onset and persistence of AF and the source of them remain unclear. The purpose of this study was to reveal the source of OS by measuring derivative of reactive oxidative metabolites (dROM) in atrium, coronary sinus (CS) and peripheral vein (CV) in patients with AF and to estimate the relationship between OS and LV dysfunction.
Methods: Patients who underwent radiofrequency catheter ablation (RFCA) for AF in Shinshu Univ Hospital from 2007 to 2011 were enrolled (64±1.1±2 yrs, 63male, paroxysmal AF (pAF): n=37, persistent AF (psAF): n=29). We obtained blood sample from CV and left (LA) and right atrium (RA) and CS at RFCA to evaluate dROM. Brain natriuretic peptide (BNP) was also measured.
Results: There were no difference of dROM level among LA, CV and RA (±SEM) in pAF group. Furthermore, there was a strongly correlation between dROM in Cs and BNP. These findings indicated that left ventricular dysfunction caused by persistent AF was associated with high dROM level, and the improvement of LV dysfunction after RFCA resulted in the reduction of dROM and BNP level.
Conclusion: dROM in CS was high compared with the other sites, especially in psAF group. Furthermore, there was a strongly correlation between dROM in Cs and BNP. These findings indicated that left ventricular dysfunction caused by persistent AF was associated with high dROM level, and the improvement of LV dysfunction after RFCA resulted in the reduction of dROM and BNP level.

P2327
Pioglitazone prevents diabetes-related atrial fibrillation susceptibility in alloxan-induced diabetic rabbits
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Purpose: In the present study, we investigated the effects caused by pioglitazone, a peroxisome proliferator-activated receptor (PPAR)-γ activator, on atrial structural remodeling and electrical remodeling in alloxan-induced diabetic rabbits.
Methods: 24 rabbits were divided into three groups: normal control group (CN group), diabetic group (DM group) and diabetic pioglitazone treatment group (DPG group, 4mg/day/kg). After 8-week treatment, whole-cell patch-clamp technique was used to measure action potential duration (APD) and atrial ion currents (ICaL and INa). Isolated Langendorff perfused rabbit hearts were used to evaluate atrial electrophysiological parameters. Atrial collagen volume fraction (CVF) was calculated by Sirius-Red (SR) staining for pathological examination.
Results: Compared with DM group, CVF was decreased in DPG group (P<0.01). Patch-clamp studies demonstrated APD90 and APD50 of left atrial myocyte were shortened (P<0.05), and the densities of ICaL were reduced (7.58±0.57 vs. 9.60±3.59 pA/pF, P<0.01) and the densities of INa were increased (-103.25±6.98 vs. -76.90±12.53 pA/pF, P<0.01) in DPG rabbits. Electrophysiological studies showed IACT was shortened (29.50±1.69 vs. 37.91±6.81 ms, P<0.05), AERP was decreased (18.50±8.18 vs. 30.37±8.33, P<0.01) in DPG group. Inducibility of AF in DPG group was significantly less than DM group (2/8 vs. 6/8 of animals, P<0.05). Protein expression of ERK1/2 was no significant difference between DPG group and DM group (P>0.05), but protein expressions of NF-kB p50/p65, TLR4, TGF-β were increased (1.69 vs. 37.91±6.81 ms, P<0.05), AERP was decreased (18.50±8.18 vs. 30.37±8.33, P<0.01) in DPG group. Inducibility of AF in DPG group was significantly less than DM group (2/8 vs. 6/8 of animals, P<0.05). Protein expression of ERK1/2 was no significant difference between DPG group and DM group (P>0.05), but protein expressions of NF-kB p50/p65, TLR4, TGF-β, HSP70 and p-ERK1/2 were significantly decreased in DPG group (P<0.05).
Conclusions: Pioglitazone inhibited DM-related arrhythmogenic atrial remodeling and vulnerability to AF. PPAR-γ activators could become novel upstream therapy drugs for DM-related AF.
Gastroesophageal regurgitation disease and atrial fibrillation

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Background: Gastroesophageal reflux disease (GERD), the most common gastroesophageal disorder, and AF remains undetermined. Therefore, we aim to investigate the association of GERD and the development of AF.

Methods: Patients with GERD were identified from the 1,000,000 sampling cohort dataset from the Taiwan National Health Insurance database. The study cohort comprised 29,688 newly diagnosed GERD adult patients; 29,597 randomly selected, gender-, and comorbidities-matched subjects comprised the comparison cohort. Cox proportional hazard regressions were performed to adjust for the increased risk of AF (hazard ratio, 9.39; 95% confidence interval, 1.06 – 1.61, p = 0.013).

Conclusion: GERD is independently associated with an increased risk of future AF development.

Atrial fibrillation: underlying mechanisms

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Background: Atrial interstitial fibrosis was increased in diabetic rabbits (6.20 ± 0.64% vs. 5.60 ± 0.43%, p < 0.01). The underlying mechanism of atrial fibrillation (AF) and diabetes mellitus (DM) is not understood. The purpose of our study was to investigate the effects of hyperglycemia on atrial interstitial fibrosis, ion remodeling and vulnerability to AF in diabetic rabbits.

Methods: Twenty rabbits were assigned to an alloxan-induced diabetic group (n=10) and control group (n=10). Atrial collagen volume fraction (CVF) was calculated using Sirius-Red (SR) staining. Whole-cell patch-clamp technique was used to measure action potential duration (APD) and atrial ion currents (INa and ICaL). Isolated Langendorff-perfused rabbit hearts were used to evaluate atrial electrophysiological parameters. RT-PCR was applied to assess atrial mRNA expression of tumor necrosis factor-alpha (TNF-α) and Toll-like receptor 4 (TLR4).

Results: Atrial interstitial fibrosis in diabetic rabbits was increased (6.20 ± 0.64% vs. 5.60 ± 0.43%, p < 0.01). Patch-clamp studies demonstrated APD90 and APD50 of left atrial myocyte were prolonged in diabetic rabbits (p < 0.05). The densities of INa were reduced and the densities of ICaL were increased in diabetic rabbits (p < 0.01). Electrophysiological studies showed IACT was prolonged (37.91 ± 8.1 ms vs. 27.43 ± 6.13 ms, p < 0.01). AERP was increased (30.37 ± 8.33 ms vs. 14.70 ± 5.16 ms, p < 0.01). In diabetic rabbits, inducibility of AF was significantly higher than controls (9/10 vs. 1/10 of animals, p < 0.05). TNF-α and TLR4 mRNA expression were increased in diabetic group (p < 0.01).

Conclusions: Our study suggests that hyperglycemia contributes to atrial interstitial fibrosis, ion remodeling and vulnerability to AF in diabetic rabbits, which result in atrial structural remodeling and electrical remodeling for the development of AF.
Advanced atrial tissue fibrosis quantified using LGE-MRI predicts trans-episphageal echo abnormalities in patients with atrial fibrillation

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Introduction: Atrial fibrillation (AF) leads to spontaneous echo contrast (SEC) and thrombus formation commonly seen in the left atrial appendage (LAA) on trans-esophageal echocardiography (TEE). We studied the association of atrial fibrosis with TEE abnormalities and hypothesized that advanced atrial fibrosis increased the risk.

Methods: This study included patients undergoing TEE prior to catheter ablation. Baseline characteristics including the CHADS2 score, anti-coagulation status and valve disease were collected. Late-gadolinium enhanced cardiac MRI (LGE-MRI) was obtained in all patients and quantification of atrial tissue fibrosis was obtained. Patients were staged as follows: Utah Stage atrial tissue fibrosis (<5%), Stage II (5-20%), Stage III (20-35%) and Stage IV (>35%).

Results: 178 patients were included and atrheurpeic INR was present in 111 (62.4%). LAA thrombus was found in 11 patients (6.2%) while left atrial SEC was identified in 18 patients (10.1%). TEE abnormalities were significantly more prevalent in Utah stages III and IV compared to Utah stages I and II: 6 of 56 patients (10.7%) versus 31 of 122 patients (25.3%), p<0.05 for LAA thrombus and 9 of 55 patients (16.4%) vs 9 of 118 patients (7.6%); p<0.05 for LA-SEC. Logistic regression analysis showed that atrial fibrosis (Odds Ratio 2.7; p=0.03) and CHADS2 score (Odds Ratio 4.9; p=0.02) were significant multivariate predictors of LAA SEC. For LA-SEC, atrial fibrosis (OR 2.2; p=0.01) was the only significant predictor.

Conclusions: Atrial tissue fibrosis is an independent predictor of both LAA thrombus and SEC on TEE. It provides incremental risk stratification to the commonly used CHADS2 score.

Pro-inflammatory activity of epicardial adipose tissue may affects the occurrence of atrial fibrillation

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Background: Epicardial adipose tissue (EAT) inflammatory capacity was shown to correlate with coronary vessels’ narrowings in stable and unstable coronary artery disease. It has been also shown, that maximal standardized uptake value (SUV) of 18-fluorodeoxyglucose (FDG) detected by positron emission tomography is proportional to macrophage density. EAT contains abundant ganglionated plexi contributing to the occurrence of atrial fibrillation (AF). Accordingly, we examined EAT inflammatory activity using FDG-PET/CT in patients with AF and in controls.

Methods: 21 consecutive patients with confirmed history of AF underwent FDG-PET/CT. Patients were measured in supine position and then in right rood of left atrium (LAF), right ventricle (RVF), atrioventricular groove (AGF), and left main artery (LMF). Additionally SUV was measured in subcutaneous fat (SF), visceral thoracic fat (VS). Similar measurements of SUV were taken in a group of healthy volunteers matched for age and BMI (n=15). In the group of AF patients, associations of SUV with gender, age, body mass index (BMI), serum glucose, were further analyzed.

Results: EAT SUV in all locations was significantly greater in FA patients than in the control group (LAF: 1.21 vs 0.60, p<0.0001; RVF: 0.75 vs 0.40, p<0.0001; AGF: 1.46 vs 0.66, p<0.0001; LMF 1.41 vs 0.69, p<0.0001, respectively). In addition, LAF, RVF, AGF, and LMF was significantly greater than SUV in SF and VS for both FA and controls (SC-0.33; VS-0.58; LAF: 1.21; RVF: 0.75; AGF 1.46; LMF: 1.41; p<0.001). EAT SUV was not related to gender, age, BMI, or serum glucose.

Conclusions: 1. Inflammatory activity of EAT reflected by SUV is higher in FA patients, than in non-FA controls; 2. Inflammatory activity of EAT adjacent to left atrium, right ventricle, atrioventricular groove, and left main artery is greater than in subcutaneous or visceral thoracic tissue. In conclusion, the greater pro-inflammatory activity of EAT in patients with FA compared to healthy controls may contribute to the occurrence of AF.

Lymphomunonuclear infiltration and elevated fibrosis extent in the left ventricular myocardium are associated with history of atrial fibrillation regardless of cardiovascular co-morbidities

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Background: Chronic inflammation in the left myocardium was shown to contribute to development of atrial fibrillation in patients with atrial fibrillation (AF). However, it is not clear whether the inflammatory reaction extends on the left ventricle (LV). We aimed at assessing the extent of fibrosis and lymphomunonuclear infiltration in human LV myocardium and explore its association with AF.

Methods: Medical records from consecutive autopsies were checked for presence of AF. Heart specimens from 30 patients died from cardiovascular causes (men 12, y 17 men) were collected in three equal groups: no AF, paroxysmal and permanent AF. Tissue samples were taken from LV and stained with Masson’s trichrome. Immunohistochemistry was performed using antibodies against CD3- and CD45-antigens and quantified as number of antigen-positive cells per 1 mm2.

Results: The groups were similar in regard to age and comorbidities expressed as CHADS2 and CHA2DS2-VASc scores (Table). Fibrosis extent, CD3+ and CD45+ cell counts were elevated in AF patients regardless of AF clinical type. Inflammation was increased in both CD3+ and CD45-antigens and quantified as number of antigen-positive cells per 1 mm2.

Conclusions: The effect of AF on neural and inflammatory activity in the myocardium is more obvious when AF is paroxysmal or permanent. Further studies are needed to explore the mechanisms underlying the inflammation in the myocardium in patients with AF, which may affects the occurrence of atrial fibrillation.

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Atrial fibrillation: risk factors and epidemiology

**P2337**

**Determination of the left atrial fibrosis cut-off value associated with a maintenance of atrial fibrillation after successful mitral valve surgery**


Atrial fibrillation (AF) is a common arrhythmia in patients with mitral valve disease. Mitral valve surgery often promotes restoration of sinus rhythm (SR) in patients with AF, however there are some patients who do not maintain SR even after surgery. Left atrial remodeling is involved in atrial fibrillation development and maintenance. The purpose of this study was to determine a cut-off value of histological parameters which identify patients at higher risk of atrial fibrillation recurrence after mitral valve surgery.

**Methods:** 101 consecutive patients (76 female, 25 male, aged 23 to 71 years (mean 52)) with mitral valve disease who underwent mitral valve surgery were enrolled in the study. Specimens of the left atrial wall were obtained during the operation. The extent of fibrosis, myocyte diameter, intensity of inflammatory infiltrates, degree of myocytolysis and capillary density were determined. The heart rhythm was evaluated in 12 months observation. A receiver-operating characteristic (ROC) curve was designed to identify a cut-off value of left atrial fibrosis that best predicted the atrial fibrillation maintenance after 12 months follow-up. The study respected the principles outlined in the Declaration of Helsinki and was approved by the local Ethics Committee. All subjects signed an informed written consent.

**Results:** 14 patients had mitral stenosis, 12 mitral insufficiency, 61 combined mitral valve disease and 14 mitral and aortic valve disease. Preoperatively 36 patients were in sinus rhythm, 65 were in long-term persistent atrial fibrillation. 8 patients died before 12-month-follow-up, 3 patients were lost to follow-up. Re-mapping 29 patients were divided into two groups: according to the heart rhythm: group I - SR (50 patients), group II - AF (40 patients). In the multivariate analysis only fibrosis was independent predictors for persistence of AF 12 months after procedure (p=0.008) and myocyte diameter, intensity of inflammatory infiltrates, degree of myocytolysis and capillary density did not reach statistical significance. According to the ROC curve cut-off value of 34.06% for fibrosis (p=0.002) predicted the atrial fibrillation maintenance after 12 months follow-up.

**Conclusions:** Our results suggested that a cut-off value for left atrial fibrosis identified patients at higher risk of atrial fibrillation recurrence after mitral valve surgery is 34.06%.

**ATRIAL FIBRILLATION: RISK FACTORS AND EPIDEMIOLOGY**

**P2339**

**Subclinical atrial fibrillation: a missing link in the etiology of cryptogenic ischemic stroke?**

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Atrial fibrillation (AF) is an important risk factor for ischemic stroke. In many patients AF is paroxysmal and asymptomatic but paroxysmal and permanent AF are both associated with a risk of stroke. Finding AF after an ischemic cerebrovascular event could change the therapeutic approach as oral anticoagulants would be recommended to reduce the risk of stroke recurrence. A recent study by Mayhew et al. showed poor sensitivity for detection of paroxysmal AF (PAF) if the duration of ECG monitoring to detect PAF is still unknown.

**Study:** We hypothesized that subclinical PAF may be an under-recognized mechanism for cryptogenic ischemic stroke. The aim of this study was to evaluate if prolonged ECG monitoring by an implantable subcutaneous Holter and remote transmission finds episodes of PAF in patients with non-lacunar cryptogenic ischemic stroke.

We prospectively evaluated patients affected by cryptogenic ischemic stroke who had sinus rhythm on 12-lead ECG on admission, no evidence of PAF in a 24 h ECG recording and were referred for transcranial Doppler ultrasound and/or neuromaging data.

**Results:** Forty two patients (pts) have been included in the study. Mean age was 65±13 years and 50% were male. Other cardiovascular risk factors were: hypertension (57%), dyslipidemia (36%), diabetes (14%) and smoking habit (40%). The mean CHA2DS2-Vasc Score was 2 (IQR: 1,25-3,75). Twelve pts (29%) were previously treated with anticoagulant agent treatment.

The mean monitoring duration was 153±127 days (IQR: 57-236). PAF (lasting more than 30 s) was detected in 7 pts (17%). The first PAF episode was detected after 186±82 days of remote monitoring and, in 6 pts (8%) the PAF was detected with a monitoring duration over 10 days. The PAF episodes were asymptomatic in 6 pts (86%), mainly at night in 3pts (43%), shorter than 10 min in 4pts (57%) and the heart rate was below 100 bpm in 2pts (29%).

**Conclusions:** In patients with ischemic cryptogenic stroke long ECG monitoring by an implantable subcutaneous Holter and remote transmission detects a significant risk of asymptomatic PAF. The actual pathological relevance of this finding is still unknown, so that wider controlled studies may be appropriate.

**P2339**

**The Distribution of First-detected Atrial Fibrillation Patients without Structural Heart Diseases in view of Major Symptom Classification**

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**Background:** Although first-detected AF is important for intervening the disease, the clinical significance, characteristics and prognosis of this type of AF patients remain unclear in Japan, and have never been reported from the view of symptoms. Symptom of the arrhythmia is one of the determinants of therapeutic strategy, but is difficult to evaluate objectively. The Canadian Cardiovascular Society Severity in Atrial Fibrillation (CCS-SAF) scale is a simple scale classification to measure AF-related symptoms and may be practical for clinical use. More recently, a similar scale classification was proposed by the European Heart Rhythm Association (EHRA) classification.

**Methods:** The purpose of this study was to describe patient characteristics and clinical outcomes in relation to the symptom classifications in untreated first-detected AF patients in Japan. Out of 15,227 patients registered in a single urban hospital from 2004-2010, 2,259 patients were diagnosed as AF, and 427 of them were first-detected. In order to focus on the symptoms related specifically to AF, 289 patients with structurally normal heart were selected as the study population.

**Results:** A total of 289 patients with first-detected AF without structural heart diseases were distributed according to the both of classifications. The prevalence of paroxysmal AF, which only 5% was classified as the most symptomatic class. Female was more prevalent and age was higher in the most symptomatic class. In both of classifications, no category-associated difference was observed in the prevalence of co-morbidities, except for heart failure. Consequently, CHA2DS2 score was significantly higher in the most symptomatic class. During the follow-up period of the present study (506±530 days), the incidence rates of mortality, and hospitalization of CHF and stroke in patients with the most symptomatic class were 11.8%, 35.3%, and 11.8%, respectively, which were extremely higher than those in patients with the other classes. On the other hand, no apparent differences in the backgrounds and prognosis were observed in other classes.

**Conclusions:** This is the first report describing backgrounds and characteristics of patients without structural heart disease in view of both the CCS-SAF classification and the EHRA classification. Our observation would provide the basic information to understand the significance of AF-related symptoms in the clinical practice.

**P2340**

**All-cause mortality over time in patients with incident atrial fibrillation as primary and secondary diagnoses**

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**Purpose:** To determine the difference in subsequent all-cause mortality in patients hospitalized with incident atrial fibrillation (AF) as the primary or a secondary diagnosis.

**Methods:** 272,186 patients were hospitalized in Sweden with incident AF during the period between 1995 and 2008. From these, we selected patients younger than 85 years at admission who were free of an AF diagnosis 1987-1995, increasing the likeliness that AF was truly incident. Each patient was matched for age and gender with two persons, without an AF diagnosis, selected from the National Population Registry. Analyses were performed by linking data with those from the National Cause of Death Registry.

**Results:** 119,631 (45% women) patients were identified with AF as primary and 152,555 (43% women) as secondary diagnosis. Patients with AF as a secondary diagnosis were significantly older than those with a primary diagnosis, 75±9 vs 69±12 years, p<0.00. Women were older than men in both groups, but the difference was greater in patients with a primary diagnosis, 72±6 vs 70±10.2 years vs 66±1±13 years, p<0.001. The actual and relative risks of all-cause mortality were increased in both groups compared to controls, but significantly more so when AF was a secondary diagnosis, p<0.001. When patients were subdivided into three age groups, <65, 65-74 and 75-85 years at admission, this pattern remained in all age categories (p<0.001).

**Conclusion:** AF as a primary diagnosis was associated with a lower risk, compared to controls, that AF as a secondary diagnosis. This pattern persisted throughout the 14 year follow-up period. The relative risk of all-cause mortality was higher in women than in men, especially in the youngest female subgroup with secondary AF. In patients with primary AF, the gender difference was smaller.
Phenotypes associated with genetic polymorphisms in 4q25 rs2207033, 16q22 ZFHX3, or 1q21 KCN3N in Korean patients with non-valvular atrial fibrillation

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Background: Recently, GWAS revealed several genomes related with atrial fibrillation (AF), such as genetic variants on chromosomes 4q25 PITX2, 16q22 ZFHX3, or 1q21 KCN3N. We hypothesized that the patients with those genetic background are less affected by co-morbid factors, such as hypertension or heart failure in Korean patients with non-valvular AF.

Methods: We evaluated and compared the allelic frequencies of genetic polymorphisms of chromosome 4q22 rs2207033, 16q22 ZFHX3, or 1q21 KCN3N in 552 patients with non-valvular AF (57±11 years old, male 77.7%, 373 paroxysmal AF [PAF], 179 persistent AF [PeAF] who underwent catheter ablation and 523 sex-matched healthy control by direct DNA sequencing and SNaPshot™ assay.

Results: 1. The 4q22 rs2207033 (OR 2.935, 95% CI 2.152-4.003, p<.001), the 16q22 ZFHX3 rs1062261 (2.371, 95% CI 1.733-3.245, p<.001), and the 1q21 KCN3N rs14376333 (OR 1.533, 95% CI 1.073-1.989, p=.004) genotypes were significantly prevalent in patients with AF than in control group. 2. The prevalence of 4q22 rs2207033 was significantly higher in non-persistent patients than in persistent patients (93.5% vs. 88.5%, p<.001). 3. The prevalence of KCN3 rs13376333 was significantly higher in patients with body mass index (BMI) >24.5 m2/kg than those with BMI >24.5 m2/kg (8.0% vs. 2.6%, p=.0016).

Conclusion: Genetic polymorphisms on chromosome 4q22 rs2207033, 16q22 rs1062261, and 1q21 rs14376333 were associated with non-valvar AF in Korean patients. The variants of rs2207033 and rs13376333 were negatively associated with high BMI, and high AF occurrence.

Risk of new-onset atrial fibrillation in patients undergoing hemodialysis

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Introduction: Atrial fibrillation (AF) is one of the strongest risk factors for ischemic stroke. Recently, some studies reported the higher prevalence of AF in patients with end-stage renal disease (ESRD) than in the general population. However, most of these studies come from Western databases, the data in Asian population was still lacking.

Methods: We conducted a population-based cohort study by using National Health Insurance database in Taiwan. A total of 69,610 patients were enrolled into our study, including 34,829 patients in the hemodialysis (HD) cohort and 34,781 patients in the comparison cohort. The covariate variables were matched in the study, including 34,829 patients in the HD cohort and 34,781 patients in the comparison cohort. The covariate variables were matched in the study, including 34,829 patients in the HD cohort and 34,781 patients in the comparison cohort.

Results: During an average of 3.18±2.06 years' follow-up period, a total of 1,645 cases of new-onset AF were observed. The log-rank test showed that the occurrence rate of new-onset AF in the HD cohort was significantly higher than the control cohort (HD cohort vs control cohort = 1.166 [3.20%] vs 0.798 [1.38%], p<.0001). After adjusting for age, gender, hypertension, diabetes mellitus, hyperlipidemia and coronary artery disease, HD was found to be independently associated with an increased risk of AF occurrence (hazard ratio, 3.71; 95% confidence interval, 3.33-4.14; p<.0001).

Conclusion: Patients with ESRD who received HD were associated with an increased AF occurrence. Patients with ESRD who received HD were associated with an increased AF occurrence.

Fragmented QRS predicts postoperative atrial fibrillation (AF) in patients undergoing isolated coronary artery bypass graft surgery with no history of AF

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Background: Fragmented QRS has been associated with increased morbidity and mortality, sudden cardiac death and recurrent cardiovascular events (CVEs). The predictive role of IQRs was not studied for post-operative atrial fibrillation (POAF) which is a frequent and serious complication in patients undergoing isolated coronary artery bypass graft (CABG) surgery.

Methods: We included and followed two eligible patients who underwent isolated CABG surgery were enrolled consecutively. The patients were divided in two groups with post-op AF and non-AF. POAF was defined as any episode of AF within the hospital course after CABG surgery.

Results: POAF occurred in 62 of 272 patients (22.8%). Patients with POAF were generally older (p<.001) and female (p<.006), with hypertension (p<.008), lower hemoglobin levels (p<.011), chronic obstructive lung disease (COPD, p<.003), prolonged QRS time (p<.004), lower left ventricular EF (p<.001) and higher EUROSCORE (p<.001) compared to patients with non-AF. In addition, the patients with POAF had prolonged stay in the cardiac surgery intensive care unit (ICU) (p<.001) and extended in-hospital care (p<.001). New-onset POAF was significantly related to the presence and number of IQRs. In multivariate analysis with logistic regression, age (p=0.038), female gender (p=0.078), left main coronary artery involvement (p=0.026) and the presence of IQRs (p<.001) were independent predictors of POAF. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and the diagnostic accuracy (DA) of presence of IQRs on pre-op ECG to predict POAF were 66%, 76%, 45%, 88% and 74%, respectively.

Table 1. Multivariate analysis using the logistic regression method for POAF

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>OR value</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>0.038</td>
<td>1.052 (1.003-1.094)</td>
</tr>
<tr>
<td>LMCA involvement</td>
<td>0.026</td>
<td>3.958 (1.176-12.65)</td>
</tr>
<tr>
<td>IQRs, +</td>
<td>0.001</td>
<td>6.531 (4.39-17.488)</td>
</tr>
<tr>
<td>Number of IQRs, +</td>
<td>0.003</td>
<td>1.476 (1.140-1.910)</td>
</tr>
<tr>
<td>EUROSCORE, +</td>
<td>0.052</td>
<td>1.076 (0.837-1.367)</td>
</tr>
</tbody>
</table>

Conclusion: In our study, we found that new-onset POAF was significantly related to the presence and number of IQRs in patients undergoing CABG surgery. In addition, IQRs on pre-op surface ECG had high predictive values for new-onset POAF.

Is the high prevalence of atrial fibrillation in end stage renal disease related to the hemodialysis procedure itself?

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Introduction: Atrial fibrillation (AF) is common in patients with end stage renal disease (ESRD) and is associated with an increased risk of complications such as stroke. Pathophysiology might be related to common risk factors of both AF and ESRD. However it could also be related to dialysis-specific factors such as volume overload or electrolyte shifts during hemodialysis (HD). The aim of this study was to investigate a possible relationship of AF with the dialysis procedure.

Methods: All patients currently enrolled in the ICD-2 trial implanted with an ICD were included. All days submitted by the home-monitoring were analyzed for the onset of AF. All patients were on dialysis treatment for 3 days a week. The days of dialysis treatment were recodend as day 1, 3 and 5. The relationship between AF and dialysis procedure was subsequently assessed.

Results: A total of 49 patients met the inclusion criteria, with a follow-up of 28±17 months. (79% male, 70±7 years old). Fourteen patients suffered from at least 1 episode of AF during follow up (11 HD, 3 peritoneal dialysis (PD) patients). Characteristics of AF patients did not differ from the total group. A total of 372 AF episodes in the HD group and 40 in the PD group were monitored. AF onset was seen significantly more on the days of dialysis (1-3-5) in HD patients (p<0.001) (Graph). In PD patients there is no such relationship.

Figure 1: Conclusion: It seems that there is a clear relationship with the onset of paroxysmal AF and the dialysis procedure. These findings may early detection of AF, especially around dialysis, possible, which could influence therapy choices and thereby AF-related complications such as stroke.

Resting and exercise heart rate as predictors of incident atrial fibrillation in healthy middle-aged men

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There is sparse evidence about the importance of heart rate (HR) as a poten-
Hypertension is the most common modifiable risk factor in patients with atrial fibrillation. Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia. It is a disease of the elderly and it is common in patients (pts) with structural heart disease. Hypertension (HT), heart failure, and valvular heart disease are recognized predisposing factors to AF. Objectives: To evaluate predisposing factors for development of AF in our hospital settings.

Methods: From June 2000 to January 2012, 3343 consecutive pts with AF were studied during echocardiographic check-up. According to the transthoracic echocardiography, pts were divided into groups based on dominant underlying heart diseases. Electrocardiographically documented AF was subdivided into two groups: transitory and chronic. Binary logistic regression was used to investigate relationship of gender, age, hypertension, diabetes and underlying heart diseases with the type of AF.

Results: The median age was 72 years, age range between 16 and 96 years. Chronic AF was observed in 69.1% pts. There were 48.1% of males. Hypertensive heart disease (HHD) was the most common underlying heart disease (39.5%) followed by dilated cardiomyopathy (DCM), 25.1%, coronary artery disease (CAD), 13.9% and valvular heart disease (VHD), 11.3%. Lone AF was observed in 29.5% of pts, mostly in younger males (median age 48 years, range 29-60, men 71%). Hypertension and diabetes (DM) were found in 72.5% and 39.5% respectively, mostly in females. Thyroid gland disease (TH) was found in 6.3% of which 50% was hyperthyroidism.

Conclusion: Hypertension was by far the most prevalent associated medical condition in pts with AF. AF without underlying heart disease was present in only 1%, mostly in younger pts with transitory AF. Chronic AF was predominant in groups with advanced cardiac remodeling such as DCM and VHD, mostly in elderly pa-

Stepwise screening for atrial fibrillation in a 75-year old population and implications for stroke prevention

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Purpose: Atrial fibrillation (AF) is a frequent source of cardiac emboli in patients with ischemic stroke. AF may be asymptomatic and therefore undiagnosed. As oral anticoagulation (OAC) treatment is highly effective for stroke prevention, screening for silent AF seems suitable in risk populations. Little is known about the yield and cost-effectiveness of such screening. The aim of this study was to explore by extended screening the prevalence of asymptomatic AF in a population aged 75-76 years.

Methods: All inhabitants in the municipality of Halmstad, Sweden aged 75-76 years were invited to a stepwise screening program for AF. As a first step, participants recorded a 12-lead ECG and reported their relevant medical history. Those with sinus rhythm on 12-lead ECG, no history of AF and at least 2 risk factors according to CHADS2 were invited to a 2 week recording period using a hand-held ECG asked to record 20 or 30 seconds twice daily and if palpitations occurred. Results: 1368 inhabitants were invited of whom 847 (64%) participated. Previously undiagnosed silent AF was found in 10 (1%) among 847 who recorded 12-lead ECG. Among 79 persons with previously known AF, 32 (41%) were not on OAC treatment. Among 386 persons with at least 2 risk factors, 110 (28%) patients who completed the hand-held ECG event recording, 30 (7.8%, 95% CI 5.1-10.4) were diagnosed with paroxysmal AF. Thus 72/847 (8.5%, 95% CI 6.6-10.0) of the screened population were candidates for new OAC treatment and 56/72 actually commenced OAC treatment.

Conclusion: Stepwise risk factor-stratified AF screening in a 75-year old population yields a large share of candidates for OAC treatment for stroke prevention.

Effect on plasma d-dimer levels of angiotensin receptor blockade and maintained sinus rhythm after electrical cardioversion for persistent atrial fibrillation

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Purpose: Stroke risk in atrial fibrillation (AF) is related to plasma D-dimer levels. The present results might suggest an association between increased vagal activity as reflected by a low resting HR and a limited chronotropic response to exercise in fit men, and an increased risk of future AF.

Methods: In a double blind, placebo-controlled study (Candesartan in the Prevention of Relapsing Atrial Fibrillation, CAPRAF), 171 patients with persistent AF were randomized to receive candesartan 8 mg once daily or placebo for 3–6 months after electrical cardioversion (ECV) for persistent AF and the effect of the angiotensin receptor blocker candesartan on D-dimer levels.

Results: Despite all patients being on warfarin at baseline, D-dimer levels were still correlated with age (Spearman’s rho; r = 0.421; p < 0.001) and CHA2 DS2-VASc score (rs=0.258; P = 0.001). Baseline D-dimer levels were predicted by AF recurrence after ECV, and did not change during the course of the study in patients with a recurrence of AF. In 26 patients still in sinus rhythm 6 months after ECV and still on warfarin treatment, there was no change in D-dimer levels from baseline to end of study. However, in 13 patients still in sinus rhythm 6 months after ECV who had discontinued warfarin after ECV, D-dimer levels increased significantly from baseline (median 304 ng/mL, 25th, 75th quarti-

Conclusion: Hypertension is by far the most prevalent associated medical condition in pts with AF. AF without underlying heart disease was present in only 1%, mostly in younger pts with transitory AF. Chronic AF was predominant in groups with advanced cardiac remodeling such as DCM and VHD, mostly in elderly pa-

The impact of clinical types of AF on mortality after ischemic stroke in the Lund stroke register during 10-year follow-up

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Purpose: Atrial fibrillation (AF) is associated with poor prognosis after ischemic stroke (IS). However, whether AF clinical types impact on long-term prog-

Figure 1. Risk of chronic atrial fibrillation

Heart rate 100W (bpm) Unadjusted Multivariate adjusted Baseline BP

<table>
<thead>
<tr>
<th>Heart rate 100W (bpm)</th>
<th>Unadjusted</th>
<th>Multivariate adjusted</th>
<th>Baseline BP</th>
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<tbody>
<tr>
<td>≥ 100 (n=257)</td>
<td>1.40 (1.00-1.92)</td>
<td>1.52 (1.05-2.16)</td>
<td>2.06 (1.18-3.44)</td>
</tr>
<tr>
<td>&lt; 100 (n=1740 unif.)</td>
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Thus, inability to increase HR above 100 bpm after 6 minutes exercise on 100W is an independent long-term predictor of incident AF in initially healthy middle-aged men. The present results might suggest an association between increased vagal activity as reflected by a low resting HR and a limited chronotropic response to exercise in fit men, and an increased risk of future AF.

Table 1. Relative risk of AF in hazard ratios according to HR at 100W exercise
after IS has not been fully clarified. The aim of our study was to assess the impact of AF and its clinical type on the long-term prognosis after first-ever IS.

**Methods:** Patients with first-ever IS (n=336, age 74±1.2 years, 200 men) were enrolled in Lund Stroke Register from Mar 2001 to Feb 2002. AF history by admission (n=98), its clinical type and oral anticoagulation (OAC) at discharge (n=53) were assessed using medical records. AF was verified by ECG review using hospital catchment area ECG database. All-cause mortality during 10-years follow-up period was studied by record linkage with the Swedish Cause of Death Register.

**Results:** During follow-up, 200 patients died (59%). Total mortality was associated with age, heart failure and AF history at baseline, but only age >75 years (HR=2.7, 95%CI 2.1-3.5, p<0.001) and AF (HR=2.0, 95%CI 1.1-3.7, p<0.029) remained independent predictors in a multivariable model. The highest impact on mortality was observed for permanent AF (HR=10.7, 95% CI 2.4-47.6, p=0.002).

Separation between the survival curves for recurrent and permanent AF was observed after the 3rd year of follow-up (Figure). The lack of OAC at discharge predicted mortality in patients with AF discharged alive (n=89, HR=6.3, 95% CI 2.2-18.2, p<0.001).

Conclusions: Apart from age, AF history was the only independent predictor of long-term mortality after admission with first-ever IS. Permanent AF is associated with worse prognosis compared to recurrent AF. In AF patients, OAC after IS predicted favorable long-term prognosis, however, half of AF patients were not treated with OAC, likely due to underdiagnosis at the time of stroke.

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**P2351**

**Prognostic value of electrocardiographic left ventricular hypertrophy in patients with atrial fibrillation**

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The prognostic significance of left ventricular hypertrophy (LVH) diagnosed by electrocardiography (ECG) in atrial fibrillation (AF) has never been tested. We studied 13047 patients with AF at baseline enrolled in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Study. A single expert reader, who was unaware of treatment and clinical features of patients, examined all ECG tracings. We excluded patients with complete bundle block, pacemaker-induced rhythm, suboptimal quality tracings or sinus rhythm. Thus, we analyzed 10372 patients for ECG LVH. We defined ECG LVH by using the Perugia score, which is positive in the presence of a typical strain pattern or a Cornell voltage (sum of the height of the R wave in aVL plus the depth of the S wave in V3) >2.0 mV in women or >2.4 mV in men. LVH was found in 2353 patients (22.7%). During a median follow-up period of 2.9 years, 778 patients died (6.7%) and 303 patients developed stroke, 140 myocardial infarction (MI) and 3904 patients required hospitalization. In a Cox model, after adjustment for age, sex, diabetes, smoking, systolic blood pressure, prior stroke, prior MI and prior heart failure, LVH was associated with a significantly increased risk of all-cause death (RR 1.70; 95% CI 1.46-1.97), cardiovascular death (RR 2.07; 95% CI 1.72-2.48), MI (RR 1.67; 95% CI 1.17-2.39), stroke (RR 1.31; 95% CI 1.02-1.69) and hospitalization (RR 1.25; 95% CI 1.16-1.34).

These data show for the first time that LVH diagnosed in patients with AF portends an excess risk of mortality, MI, stroke and hospitalization. Such effect is independent of major risk factors and associated clinical conditions.

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**P2352**

**Determinants of platelet response to nitric oxide in association with atrial fibrillation: evidence for an acute suppression of response**

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**Purpose:** Resistance to nitric oxide (NO) signalling in cardiovascular disease is characterized by decreased inhibition of platelet aggregation in response to NO. Platelet hyporesponsiveness to NO represents an independent risk factor for atherothrombotic events, but has not been previously evaluated in the context of atrial fibrillation (AF). We examined the determinants of platelet NO response in a cohort of older patients admitted to hospital with AF of variable duration.

**Methods:** Platelet response to NO was determined using inhibition of adenosine diphosphate (ADP) – induced aggregation in whole blood with the NO donor glyceryl trinitrate (GTN). NO response was determined using the ADP- induced inhibition of RTA 306, a stable adrenergic antagonist. The NO response of platelets was determined using the ADP- induced inhibition of RTA 306. On multivariate analysis, only platelet response to NO was found to be associated with AF duration, OR 0.98 (95% CI 0.97-0.99, p=0.03). On multivariate analysis, platelet response to NO was found to be associated with AF duration, OR 0.98 (95% CI 0.97-0.99, p=0.03).

**Conclusion:** A proportion of patients with unexplained syncope are known to have concurrent AF, which was confirmed by ILR data. More importantly, continuous monitoring using an ILR with dedicated diagnostic algorithms for AF can reveal previously undiagnosed or new onset AF in patients without a prior history of AF. The clinical implications for managing the treatment of this patient cohort need to be further assessed in relation to the stroke risk.
hyperaggregability (β = 4.8, p < 0.001) and newly diagnosed AF (β = 2.5, p = 0.014) were significant correlates of impaired NO response.

**Conclusions:** 1) In the presence of AF, platelet hyperaggregability frequently impairs platelet NO responsiveness via physiological antagonism. 2) New onset AF is associated with impairment of NO responsiveness. The relationship between this phenomenon and thromboembolic risk is yet to be determined.

### P2353

**A global perspective of complications following discharge among patients presenting with atrial fibrillation in the acute care setting: the RHYTHM-AF study**

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**Purpose:** Atrial Fibrillation (AF) affects about 4.5 million in the EU. Complications following discharge among patients with AF in the acute care setting have not been well described.

**Methods:** RHYTHM-AF was fielded in 10 countries. Consecutive patients were enrolled from acute care centers from May 2010 to June 2011 in all (Australia, Brazil, France, Germany, Italy, the NL, Poland, Spain, Sweden, UK), and cumulative follow-up were collected at day 60 (~10) in all but Spain. Overall complication was defined as complications, major adverse events, death or AF recurrence; analyses exclude Spain.

**Results:** 86% (n=2965) of patients had complete follow-up. 26% (n=774) experienced 867 complications. AF recurrence (n=773), and rehospitalizations (n=479) were common. 57% of those with any complication, and 15% of all (n=440) had >1 rehospitalization (479 total). Only 12% occurred by day 5, 25% by day 10, and 60% by day 30. Patients age 75, having PVC on antithrombotic therapy (ATT) at discharge, and with first detected AF had 1.5, 2.0, 0.5, and 0.7 times (p<0.01) the adjusted odds of any complication. Those with history of stroke/TIA/thromboembolism, paroxysmal AF, ATT at discharge, and having PCV had 2.1, 1.5, 0.4, and 0.7 times (p<0.05) the odds of rehospitalization.

**Conclusions:** Age and history of TIA/stroke were independently associated with complications and rehospitalizations, respectively; mode of cardioversion, ATT and type of AF were associated with both.

### P2354

**ECG phenotypes and genetic risk variants in atrial fibrillation**

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**Purpose:** Inherited arrhythmia syndromes, electrophysiological (ECG) phenotypes point to underlying genotypes. Early repolarization pattern (ERP) and incomplete right bundle branch block (IRBBB) on the ECG have been linked with atrial fibrillation (AF) but their association with underlying genotypes is unknown. Here we tested the hypothesis that ERP and IRBBB are associated with common genetic variants on chromosomes 4q25, 1q21 and 16q22 known to confer AF risk.

**Methods and Results:** Among 589 consecutive patients with AF enrolled in the Leipzig AF Registry in 2004 to 2005, 131 patients with atrial fibrillation (61±10 years). 155 (31%) patients had IRBBB presence. Similar among all different ECG phenotypes (ER presence, location and type, IRBBB presence).

**Conclusions:** Early repolarization patterns and incomplete right bundle branch are frequently found in patients with AF with only 31% exhibiting neither ECG pattern. However, those ECG phenotypes do not associate with known common genetic AF risk variants.

### P2355

**Trends in atrial fibrillation hospitalisation in Scotland—an increasing cost burden**

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**Background:** Prevalence of atrial fibrillation (AF) is increasing in the aging population. The objective was to evaluate trends and costs of AF on secondary care in Scotland over 14 years.

**Methods:** Patient hospitalisation data collected by the Information and Statistics Division (Scottish National Health Service) from 2004 to 2008 were analysed.

**Results:** Over the 5-year period, AF related hospital discharges increased by 33% compared to 20% for all cardiovascular (CV) discharges (29 to 37 per 1000 population). There were increases of; 21% in number of hospitals treated (15 to 18 per 1000 population); 27% in AF related hospitalisations (20 to 24 per 1000 population); and 15% in duration of hospitalisation (241 to 264 days per 1000 population). Despite decreasing trends, duration of hospitalisation remained higher than for total CV conditions (10.9 vs 8.7 days), as was in-patient cost per patient (£6009 vs £5586). Overall, the burden of AF was higher among women and increased progressively with age: 18% patients per 1000 population ~59y to 26% in ~85y. Total hospital costs attributable to AF increased from £138.9 million in 2004 to £152.5 million in 2008, accounting for 24% of all CV hospital costs.

**Conclusion:** AF presents a significant and increasing burden on hospital care. As a proportion of total CV burden, AF costs account for nearly a quarter and is increasing at relatively faster.

### P2356

**Prevalence of atrial fibrillation in Spain. Preliminary results of the OFRECE study**

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**Purpose:** Atrial fibrillation is associated with substantial morbidity and mortality and both its incidence and prevalence are high. Nevertheless, comprehensive data on this condition in Spain are lacking. The aim of this study was to estimate the prevalence of atrial fibrillation in Spain.

**Methods:** We present provisional results from a cross sectional study done in the general Spanish population older than 40 years of age. Two-stage random sampling was used, where first stage units where primary care physicians randomly selected at every Spanish province and second stage units were 20 randomly selected persons drawn from every participating physician’s assigned population.

In the definite analysis, every participant will be weighted by the inverse of his probability of being selected, but not in this analysis. Reported prevalence were standardized for the age and gender distribution of the Spanish population. There was centralized reading of the ECG recordings.

**Results:** Overall, 6566 individuals recruited by physicians were evaluated. Mean age was 60±13 years (range, 40-110 years), 45.8% male. Prevalence estimates raised with increasing age, Table 1

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Prevalence (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>0.2</td>
<td>0.0-0.3</td>
</tr>
<tr>
<td>50-59</td>
<td>0.8</td>
<td>0.4-1.3</td>
</tr>
<tr>
<td>60-69</td>
<td>3.8</td>
<td>2.8-4.8</td>
</tr>
<tr>
<td>70-79</td>
<td>8.2</td>
<td>6.7-9.7</td>
</tr>
<tr>
<td>≥80</td>
<td>15.7</td>
<td>12.9-18.5</td>
</tr>
</tbody>
</table>

**Age adjusted prevalence was higher in men (4.2%, [3.6%-5.0%]) than in women (3.4%, [2.9%-4.0%]). Overall age-adjusted prevalence of atrial fibrillation was 3.8% (95% CI 3.4%-4.3%).**

**Conclusions:** Prevalence of atrial fibrillation in Spain is high, at 3.8%. The prevalence is higher in men than in women and rises steeply above 60 years of age.
Unrecognised atrial fibrillation and stroke risk in an otherwise healthy population over 65: a significant target for stroke prevention

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Purpose: About 22% of Atrial Fibrillation (AF)-related ischemic stroke occurs in incidentally documented AF. This prompted us to determine the proportion of the general population that may have unrecognized AF and may therefore be at risk of stroke. We hypothesized that a significant proportion of patients with incidentally found AF would have no symptoms and a CHA2DS2 score high enough to put them at risk of stroke.

Methods: We reviewed surgical pre-admissions ECGs, routinely performed in all patients over 40 years of age and examined medical records of those in AF. We then analysed the data for those patients >65 years, as this age group would be most likely to benefit from stroke prevention therapy.

Results: Of the 1459 ECGs in patients >65 years, 98 (6.7%) showed AF, and in 10 of these (0.7%) AF was an incidental finding. The mean age of patients with incidental AF was 74±6 years which was similar to those with known AF (78±7). Mean CHA2DS2 score of those with incidental AF was 2.2±1.5, with 7/10 having CHA2DS2 ≥ 2. Mean CHA2DS2VASc score was 3.8±2.0 in those with incidental AF compared to 4.5±1.7 in those with previously known AF. Only 65% of those with previously diagnosed AF and CHADS2 score ≥2 were prescribed anti-coagulation consistent with the known evidence-practice gap. Mean resting heart rate in incidental AF was low (78±14bpm), similar to that seen in known AF (77±16bpm). Additionally, only 20% with incidental AF reported palpitations.

Conclusion: AF is prevalent, and is unrecognized in about 1/140 of a relatively healthy population over 65. Unrecognized AF is generally not associated with symptoms as resting heart rate is not elevated. Those with unrecognized AF usually have CHA2DS2 or CHA2DS2VASc scores high enough to warrant anticoagulation. The presence of carotid plaque in incidental AF may be a factor for predicting stroke in those patients with atrial fibrillation.

Carotid plaque as a risk factor of stroke in atrial fibrillation

S.H. John, J.P. Park, S.E. Lee, J.H. Lim, J.Y. Rhee. Presbyterian Medical Center, Jeju, Republic of Korea

Purpose: Atrial fibrillation poses a significant burden of morbidity and mortality from stroke. The risk of systemic embolism can be assessed using the CHA2DS2-VASc score. Carotid plaque is also a powerful predictor of stroke. We examined whether carotid plaque could be a factor for predicting stroke in patients with atrial fibrillation.

Methods: From 425 patients (252 males, mean 71.1±10.0 years old) who received carotid ultrasound among patients with atrial fibrillation under our institution, patients with carotid plaque was assessed. The prevalent carotid ultrasound among patients with atrial fibrillation under our institution.

Results: Among 425 patients with atrial fibrillation, 229 patients (53.9%) had carotid ultrasound. Patients with carotid plaque and 17 patients without carotid plaque developed stroke. Significant difference was shown between the two groups (17.0% vs 8.7%, P=0.011). When comparing stroke incidence according to CHA2DS2-VASc score, patients with carotid plaque showed significantly higher incidence in case that CHA2DS2-VASc score is 2 (17.8% vs 3.4%, P=0.015). The comparison of stroke incidence according to the presence or absence of carotid plaque is showed in Table 1. The presence of carotid plaque may be useful in stratifying the risk of stroke.

Table 1. The comparison of stroke incidence according to the presence or absence of carotid plaque

<table>
<thead>
<tr>
<th>CHA2DS2-VASc score</th>
<th>Carotid plaque (+) n (%)</th>
<th>Carotid plaque (-) n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (n=425)</td>
<td>39/229 (17.0%)</td>
<td>17/196 (8.7%)</td>
<td>0.011</td>
</tr>
<tr>
<td>0 &amp; 1 (n=123)</td>
<td>5/31 (16.1%)</td>
<td>4/42 (9.5%)</td>
<td>0.396</td>
</tr>
<tr>
<td>2 (n=120)</td>
<td>8/45 (17.8%)</td>
<td>5/26 (3.4%)</td>
<td>0.016</td>
</tr>
<tr>
<td>3 (n=121)</td>
<td>11/74 (14.9%)</td>
<td>4/47 (8.5%)</td>
<td>0.301</td>
</tr>
<tr>
<td>4 (n=91)</td>
<td>10/50 (16.7%)</td>
<td>4/31 (12.9%)</td>
<td>0.637</td>
</tr>
<tr>
<td>5 &amp; 6 (n=27)</td>
<td>4/15 (26.7%)</td>
<td>3/12 (25.0%)</td>
<td>0.922</td>
</tr>
<tr>
<td>6-8 (n=10)</td>
<td>1/4 (25.0%)</td>
<td>0/6 (0.0%)</td>
<td>0.400</td>
</tr>
</tbody>
</table>

Conclusions: In patients with atrial fibrillation, the presence of carotid plaque is associated with the increased risk of stroke. When comparing patients of same CHA2DS2-VASc scores, we could confirm the presence of plaque made incidence rate of stroke comparatively high, although it is not statistically significant. Assessing carotid plaque may be useful in stratifying the risk of stroke.
Mortality post-discharge among patients presenting with atrial fibrillation in the acute care setting: a global perspective from the RHYTHM-AF study

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Atrial Fibrillation (AF) affects about 4.5 million in the European Union. Mortality following discharge among patients presenting with AF in the acute care setting has not been well described.

RHYTHM-AF is a prospective observational study fielded in 10 countries (Australia, Brazil, France, Germany, Italy, the Netherlands, Poland, Spain, Sweden, UK). Consecutive patients considered for cardioversion were enrolled from acute care centers between May 2010 and June 2011 at time of AF. Data were collected at AF presentation and cumulative followup data were collected at day 60 (±10) in all but Spain (where only baseline was collected). Analyses are based only on those with followup data.

Of 3465 patients enrolled, 86% (n=2965) had complete followup. Death occurred in 0.84% (n=25). Mortality was highest in France (1.97% of patients, n=11) and lowest (0%) in Sweden, UK and Brazil. Most (52%) deaths occurred ≥30 days after discharge. Risk by day 30 was 12% occurring by day 5, 16% by day 10, and 44% by day 30. This trend was fairly consistent whether or not patients were cardioverted.

Patients undergoing electrical cardioversion (ECV, with 5 of 7 deaths occurring after 30 days, compared to pharmacologic (PCV, 2 of 7 deaths after day 30), died later. Women and those on antithrombotic therapy (ATT) at discharge were independently associated with greater odds, and those >65, lesser odds of mortality with diabetes (HbA1c >9%) (HR 4.6 (1.3-16.4), 11.2 (3.6-34.8) and 0.21 (0.016-0.74), respectively, compared to men, those not on ATT, and those with followup data.

Increased risk of mortality was associated with increased age, female gender, and presence of ATT at discharge after adjustment for each other, as well as history of diabetes mellitus. The multivariable associations between risk factors and AF subtypes were: 52.2%, and with prolonged PQ, QRS and QT intervals (p < 0.05 for all comparisons). Overt atrio-ventricular block was present in 24.8%, and bundle branch block was evident in 28% of cardiac AL patients. None of the AL patients without cardiac involvement showed AF. Despite higher left atrial diameters and volumes, AF was present in only 14 patients with cardiac AL amyloidosis. The observed prevalence (8.7%) was much lower than expected when compared with the available literature data on patients with diastolic heart failure (ranging from 13 to 19%). According to Kaplan-Meier survival analysis, mortality was higher in the AF group when compared with the sinus rhythm group, both in the whole AL cohort (p=0.0001), and in patients with cardiac involvement (p=0.006). The presence of AF in cardiac AL patients was significantly associated with left atrial diameter, area and volume, as well as with NTproBNP levels (p<0.05 for all comparisons).

Conclusion: Our results confirm that the hospital burden of AF is considerable and caused by both cardiovascular and non-cardiovascular admissions. This stresses the importance for Western Health care systems in reducing the hospital burden of AF by clinical and pharmacological means.

P2363 Prevalence of atrial fibrillation in patients with AL amyloidosis: relationship with cardiac structure, cardiac biomarkers and prognosis

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Since cardiac amyloidosis is characterized by severe left ventricular diastolic dysfunction, an impact on atrial structure and function is expected, with possible atrial dilatation and dysfunction, as well as supraventricular arrhythmias and atrial fibrillation (AF), with all the well-known sequelae on cardiac pump function and on the risk of thromboembolism. Aim of the present study was to analyze the prevalence and the prognostic role of AF in 295 consecutive never-treated subjects, in whom a first diagnosis of primary AL amyloidosis was concluded between 2008 and 2009, according to the International Society of Amyloidosis criteria. Cardiac involvement was present in 193 out of 295 AL patients. Standard 12-leads electrocardiogram and echo-color-Doppler data were collected at diagnosis, and prognosis was evaluated after a median follow-up of 477 days. When compared with patients without cardiac involvement, cardiac AL amyloidosis was associated with a different electrocardiographic pattern (low voltages: 63.9%; pseudonormal-stasis: 52.2%), and with prolonged PQ, QRS and QT intervals (p<0.05 for all comparisons). Overt atrio-ventricular block was present in 24.8%, and bundle branch block was evident in 28% of cardiac AL patients. None of the AL patients without cardiac involvement showed AF. Despite higher left atrial diameters and volumes, AF was present in only 14 patients with cardiac AL amyloidosis. The observed prevalence (8.7%) was much lower than expected when compared with the available literature data on patients with diastolic heart failure (ranging from 13 to 19%). According to Kaplan-Meier survival analysis, mortality was higher in the AF group when compared with the sinus rhythm group, both in the whole AL cohort (p=0.0001), and in patients with cardiac involvement (p=0.006). The presence of AF in cardiac AL patients was significantly associated with left atrial diameter, area and volume, as well as with NTproBNP levels (p<0.05 for all comparisons).

No association was found between the presence of AF and the presence of peripheral low voltages, pseudonormality, left ventricular mass and wall thickness, or echo-derived indices of diastolic dysfunction.

Conclusion: In cardiac amyloidosis, AF prevalence is lower than expected when considering both the extent of diastolic dysfunction and other patients with diastolic heart failure. However, the presence of AF at diagnosis is associated with a much worse prognosis, indicating a more extensive cardiac damage despite the lack of association with the extent of amyloid deposition, as indicated by the left ventricular mass and wall thickness.

P2364 Impact of blood pressure and obesity on the risk of incident atrial fibrillation in the Suita Study: an urban cohort study

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Background: Atrial fibrillation (AF) is the most common chronic arrhythmia and is associated with an increased risk of mortality and stroke. However, no prospective study has examined the combined effect of blood pressure (BP) and body mass index (BMI) on the incidence of AF in the general population. We assessed the impact of the interaction between BP and BMI on the risk of incident AF in a 12.3-year prospective study of an urban general population.

Methods: A total of 6,570 participants (30-79 years old) in the Suita Study were...
initially free of AF and prospectively followed up for incident AF. Participants were diagnosed with AF if AF or atrial flutter was present on electrocardiogram from the routine Suita health check-up examination (every 2 years) or if AF was indicated as a present illness by questionnaires or by registration of cardiovascular disease events during follow-up. Categories of body mass index (BMI), calculated as weight (kg) divided by height (m) squared, were defined as follows: underweight, <18.5 kg/m²; normal weight, 18.5 to <25 kg/m²; overweight, ≥25 kg/m². Categories of systolic BPs taken as the average of the second and third measurements were defined as follows: optimal BP, <120 mmHg; prehypertension, 120-139 mmHg; and hypertension, ≥140 mmHg. Cox proportional hazards ratios (HRs) and 95% confidence intervals (CIs) were analyzed after adjusting for age, sex, diabetes, hyperlipidemia, smoking, and drinking at baseline.

Results: During 12.3 years of follow-up, 207 incident AF events occurred (3.73 and 1.60 per 1,000 person-years for men and women, respectively). Compared with the optimal BP, the adjusted HR (95% CI) of incident AF for hypertension was 1.42 (1.04 to 1.95). Compared with normal weight, the adjusted HR (95% CI) of incident AF for overweight was 1.95 (1.32 to 2.86). Compared with the combination of optimal BP and normal weight, the adjusted HRs (95% CI) of incident AF for prehypertension with overweight and hypertension with normal weight and overweight were 1.78 (1.02 to 3.11), 1.69 (1.06 to 2.68), and 2.65 (1.60 to 4.41), respectively (P for interaction between SBP and BMI=0.02). The risks of AF according to BP category when antihypertensive users were classified into one of the four BP levels were similar but slightly lower than those when such subjects were classified as hypertensive.

Conclusion: Systolic hypertension and overweight are important risk factors for incident AF. The combination of optimal systolic hypertension and AF. Appropriate BP and weight control are important for preventing AF in the general population.

ATRIAL FIBRILLATION: TREATMENT

P2365

Electrical cardioversion at first episode of Atrial Fibrillation in patients with heart failure

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Background: Aldosterone antagonist (AA) therapy is reported to significantly suppress development of new atrial fibrillation (AF) or atrial flutter (AFL) in many patients with mild systolic heart failure (HF) and to reduce cardiovascular death and hospitalization for heart failure.

We conducted this study to determine the efficacy of AA therapy to reduce the proportion of patients with HF that progresses to permanent atrial fibrillation after a rhythm control approach with Electrical Cardioversion (EC) for a first documented AF/AFL.

Methods: This study included 90 patients (pts), hospitalized for HF with systolic ventricular dysfunction and a first documented AF or AFL episode. Mean (±SD) age was 66.5±12.0 years, 64% were women. Patients were allocated to two groups: the first group was treated with Aldosterone Antagonist (AA), while the second group was treated with placebo. The primary endpoint was defined as new AF or AFL development at 1 year, with the following additional end-point definitions: cardiovascular death, all-cause death, hospitalization for HF and stroke.

Results: At 1 year of follow-up, 15 (16.7%) patients in the AA group and 14 (15.6%) patients in the placebo group developed AF or AFL. Differences in the incidence of AF or AFL did not reach statistical significance. The Kaplan–Meier survival curve analysis demonstrated that the proportion of patients with AF or AFL at 1 year was 24.4% in the AA group vs 25.6% in the placebo group. Differences in the occurrence of AF or AFL in the two treatment groups did not reach statistical significance.

Conclusion: This study did not find a significant difference in the incidence of AF or AFL at 1 year between patients treated with AA and those treated with placebo. However, further studies are needed to confirm these results and to evaluate the long-term efficacy and safety of AA therapy in patients with HF and AF or AFL.
Heart rhythm treatment of atrial fibrillation in an unselected population of patients managed by in-hospital cardiologists and internists: the ATA-AF survey

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Purpose: Guidelines for atrial fibrillation (AF) treatment have been widely disseminated. Unfortunately, observational studies show a gap between their recommendations and clinical practice. A possible explanation might be the different attitude of the attending physicians to treat AF. Aim of the study was to highlight differences in AF heart rhythm (HR) treatment between cardiologists and internists.

Method: ATA-AF is an observational, multicentre prospective study on the management of AF patients (pts) in Italy. From May to July 2010, 164 Cardiology (C) and 196 Internal Medicine Centres (IM) enrolled 6910 either hospitalized or ambulatory pts with a diagnosis of AF.

Results: Mean age was 75±11 yrs, 40% were admitted for AF (54% C vs 24% IM, p<0.0001); 25% had paroxysmal, 24% persistent and 51% permanent AF. Rate control (RcC) strategy was pursued in 51% (44% C vs 61% IM, p<0.001), rhythm control (RcR) in 28% (40% C vs 13% IM, p<0.001) and “strategy non defined” in 21% (7% C vs 26% IM, p<0.001). Multivariable analysis showed that AF type, setting of management, site (in/out-patient) of discharge, previous cardiovascular (CV) age, and left atrial diameters were in rank order the strongest variables independently related to the HR treatment choice. In the RHC subgroup: 50% under-achieve (RcR) (CV 43% C vs 74% IM, p<0.001), 37% achieve (CV 41% C vs 20% IM, p<0.001) and 6% (8% C vs 2% IM, p=0.001). PVC was performed with amiodarone in 62% (62% C vs 61% IM, p=0.75), propafenone in 26% (25% C vs 28% IM, p=0.44), flecainide in 10% (12% C vs 9% IM, p=0.001) and other drugs in 8% (6% C vs 12% IM, p=0.005). Medical treatment at discharge is shown in the Table.

<table>
<thead>
<tr>
<th>RHC</th>
<th>RcR</th>
<th>IM</th>
<th>p</th>
<th>RcC</th>
<th>IM</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone, %</td>
<td>34</td>
<td>30</td>
<td>0.20</td>
<td>12</td>
<td>9</td>
<td>0.004</td>
</tr>
<tr>
<td>Propafenone, %</td>
<td>8</td>
<td>10</td>
<td>0.16</td>
<td>0.6</td>
<td>0.9</td>
<td>0.91</td>
</tr>
<tr>
<td>Flecainide, %</td>
<td>13</td>
<td>5</td>
<td>&lt;0.001</td>
<td>1.2</td>
<td>0.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Betablockers, %</td>
<td>40</td>
<td>34</td>
<td>0.03</td>
<td>62</td>
<td>51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Digitals, %</td>
<td>6</td>
<td>7</td>
<td>0.41</td>
<td>38</td>
<td>41</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Conclusion: Our results show that in Italy: 1) pts admitted for AF are mainly managed in C, 2) the choice of HR treatment strategy is influenced by the attending physician characteristics and the site of pt discharge, 3) AF treatment differs between C and IM.

The surgical Cox Maze III procedure for the treatment of atrial fibrillation: Results from continuously monitored patients


Introduction: The Cox-Maze procedure has been shown to restore sinus rhythm in a significant proportion of these patients. However, most studies have employed intermittent follow up which has been shown to under-diagnose AF recurrence and overestimate procedural success. Aim of the present study is to investigate and at follow up rates of AF recurrence were the main outcome, investigated also with multivariate adjustment. Stroke and transient ischemic attack (TIA) represented the secondary end points.

Results: Consecutive patients underwent left atrial ablation procedure. 815 patients without thyroid disease, 78 with hyper and 72 with hypothyroidism were enrolled. AF recurrences. (Table 3.) multivariate analysis demonstrated that left anterior-posterior atrium diameter (OR: 1.3, 1.2-3.45 CI 95%; p=0.03) rhythm in a significant proportion of these patients. However, most studies have stroke and transient ischemic attack (TIA) represented the secondary end points.

Methods: Between 2007 and 2011, the Cox-Maze III procedure has been performed in 45 patients (32 long lasting persistent, 11 persistent, 2 paroxysmal). All patients were implanted with a leadless continuous heart rhythm monitoring device (Reveal XT, Medtronic, USA) and underwent regular follow up for a duration of 15.9 months.

Results: No complication related to the ablation procedure was observed. In 2 patients atrial fibrillation persisted in the early postoperative period and throughout the follow-up period. Early postoperative conversion to stable sinus rhythm was observed in 43, which remained till discharge. All patient received amiodarone during the early postoperative period. Throughout the observation period, the atrial fibrillation burden of the 43 patient was 1.3±±0.2%. The longitudinal development of AF burden in this population is displayed in Figure 1.

Conclusions: The Cox-Maze III procedure represents a gold standard for the treatment of patients with atrial fibrillation, continuous monitoring of patient after surgical ablation shows that complete absence of AF recurrence may be difficult to obtain. However even with in patients with long history of AF preoperatatively a significant reduction in AF burden can be obtained. Larger studies are needed to identify the clinical benefit of burden reduction in patients after ablation procedures.

Figure 1

Conclusions: Although the Cox-Maze III procedure represents a gold standard for the treatment of patients with atrial fibrillation, continuous monitoring of patient after surgical ablation shows that complete absence of AF recurrence may be difficult to obtain. However even with in patients with long history of AF preoperatively a significant reduction in AF burden can be obtained. Larger studies are needed to identify the clinical benefit of burden reduction in patients after ablation procedures.
**P2372** Should we change the definition of acutecardioversion of atrial fibrillation

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**Purpose:** It has been a common practice to cardiovert atrial fibrillation of short (<48 h) duration without precordial thromboembolic anticoagulation, but this practice has been recently called into question. We assessed whether a short duration of symptoms is related to lower incidence of thromboembolic complications after successful cardioversion acute atrial fibrillation in patients without periprocedural anticoagulation.

**Subjects and methods:** A total of 5652 cardioversions were performed in 2569 consecutive patients with atrial fibrillation lasting < 48 hours in 3 hospitals. Embolic complications were evaluated during the 30 days after 5325 successful cardioversions. In this analysis, only 3822 cardioversions with no periprocedural anticoagulation were included and divided into 2 groups according to the duration of preceding symptoms: < 12 hours or 12-48 hours.

**Results:** Thirty-five thromboembolic events (in 35 patients) occurred within 30 days after cardioversions and 27 (77.1%) were strokes. Thromboembolic events were significantly more common in the patients with longer duration of symptoms (1.3% vs 0.5%, p = 0.026). In multivariate analysis, long duration of symptoms (p>0.03, OR 2.3, 95%CI 1.1-5.0), female sex (p= 0.02, OR 2.5, 95%CI 1.2-5.4) and age (p<0.001, OR of 1 year 1.06, 95%CI 1.02-1.09) were the only independent predictors of embolic events.

**Table 1. Characteristics of patients with atrial fibrillation by the duration of symptoms**

<table>
<thead>
<tr>
<th></th>
<th>&lt;12 h (n=1936)</th>
<th>12–48 h (n=1986)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic events</td>
<td>0.5%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.3±10.3</td>
<td>60.8±12.4</td>
</tr>
<tr>
<td>Sex (males)</td>
<td>34.1%</td>
<td>29.5%</td>
</tr>
<tr>
<td>CHA2DS2-VASc = 2</td>
<td>50.7%</td>
<td>52.8%</td>
</tr>
</tbody>
</table>

**Conclusions:** The current time limit of “acute” AFib may be too long. Incidence of postcardioversion thromboembolic complications starts to rise within the first day when no periprocedural anticoagulation is used.

**P2373** Renal denervation and pulmonary vein isolation in patients with drug resistant hypertension and symptomatic atrial fibrillation

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**Introduction:** Hypertension is a risk factor for developing and maintaining atrial fibrillation (AF). Treating hypertension with renal denervation in drug-resistant patients might not only contribute to a decrease in blood pressure, but also to a decrease in AF recurrences in patients with paroxysmal (P) AF or persistent (Pers) AF. The aim of this prospective, single-center, randomized pilot study was the assessment of the impact of renal denervation and pulmonary vein isolation (PVI) in patients with history of AF and drug-resistant hypertension.

**Methods:** Patients with history of symptomatic PAF and/or PersAF and drug-resistant hypertension were enrolled in this study. Patients were randomized to pulmonary vein isolation (PVI) only or PVI + Renal Denervation. All patients were followed for 1 year to assess maintenance of sinus rhythm and to monitor changes in blood pressure.

**Results:** We enrolled 27 patients with symptomatic AF and drug-resistant hypertension: 14 randomized to PVI only and 13 to PVI + renal denervation. At 12 months FU the reductions in systolic and diastolic blood pressure were successfully and significantly maintained (p<0.001) in patients treated with PVI + renal denervation. On the contrary, no significant change in blood pressure was observed in the PVI only group. Nine (69%) of the 13 patients treated with PVI + renal denervation were AF-free at the 12-month post-ablation FU, versus 4 (29%) of the 14 patients in the PVI only group (Log-Rank test, p=0.033).

**Conclusions:** Renal ablation is effective in reducing systolic and diastolic blood pressure in patients with drug-resistant hypertension and history of atrial fibrillation. The benefit is maintained at 1 year after the procedure and it has an independent and positive impact on atrial fibrillation recurrences.

**P2374** Landiolol, an ultrashort-acting beta-blocker, for prevention of atrial fibrillation after catheter ablation

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**Introduction:** Immediate recurrence of atrial fibrillation (AF) after catheter ablation (CA) interferes with postoperative management. We investigated whether intravenous infusion of landiolol, an ultrashort-acting beta-blocker, could reduce immediate AF recurrence after CA in a randomized controlled trial.

**Method:** Patients with drug-resistant AF underwent CA were assigned to receive either landiolol or placebo after the procedure. In the landiolol group, small amount of landiolol (1 μg/kg/min) was continued for 3 days after the CA. The primary endpoint was occurrence/non-occurrence of AF, defined as supraventricular arrhythmia more than 5 min, up to 3 days after CA. Logistic regression analysis was performed to investigate risk factor.

**Result:** 34 and 15 patients were assigned to landiolol group and placebo group, respectively. There were no significant difference between both groups in changes from pre-CA to post-CA of systolic blood pressure (0.8±9.3 mmHg in landiolol group versus -1.2±5.5 mmHg in placebo group) and diastolic blood pressure (-0.7±8.9 mmHg in landiolol group versus -1.9±9.9 mmHg in placebo group). AF recurrence occurred in 7 patients (21%) in landiolol group versus 9 patients (60%) in the placebo group (P<0.008, Figure). Multivariable analysis revealed that landiolol infusion significantly reduced the risk of transient AF recurrence after procedure (Hazard ratio: 0.05, 95% confidence interval of hazard ratio: 0.004-0.65, P=0.02).

**Conclusions:** Short-term landiolol infusion successively decreased immediate AF recurrence after CA without lowering blood pressure. Administration of landiolol may become a new strategy to facilitate periprocedural management.

**P2375** The effect of strict rate control on BNP values and echocardiographic parameters in chronic AF

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**Introduction:** There are conflicting results about the role of strict rate control on cardiovascular outcomes in patients with chronic atrial fibrillation (AF). This study aimed to investigate the role of strict rate control on BNP values, and echocardiographic parameters in chronic AF patients.

**Methods:** Thirty-eight patients with chronic AF whom strict rate control were planned were enrolled to the study. Patients’ echocardiographic parameters, BNP values and 24 hour holter ECG findings were studied at baseline and monthly after till the end of the 3rd month. At the end of the 3rd month 25 patients achieved the target heart rate (group1 resting heart rate <80/min) while the remaining 13 were still rapidly responding (group 2). Laboratory and echocardiographic parameters at baseline and at the end of the study were assessed.

**Table 1**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
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<tbody>
<tr>
<td>Average heart rate (beats/min)</td>
<td>77±5</td>
</tr>
<tr>
<td>BNP (pg/dl)</td>
<td>29±20</td>
</tr>
<tr>
<td>LV end-diastolic volume (ml)</td>
<td>107±59</td>
</tr>
<tr>
<td>LV end-systolic volume (ml)</td>
<td>59±29</td>
</tr>
<tr>
<td>Left atrial area (cm²)</td>
<td>30±7.4</td>
</tr>
<tr>
<td>Right atrial area (cm²)</td>
<td>29±7.3</td>
</tr>
<tr>
<td>Septal e’</td>
<td>23±5.6</td>
</tr>
<tr>
<td>Mitral e’</td>
<td>11±6.2</td>
</tr>
<tr>
<td>Mitral e’/a</td>
<td>2.9±0.5</td>
</tr>
</tbody>
</table>

*p<0.05 between baseline and 3rd month, paired sample t test.

**Results:** In group 1 there were significant decrease in BNP, left ventricular systolic and diastolic volumes, left atrial and right atrial areas at the end of study. In group 2, BNP values were significantly higher at the end of the study despite of similar ventricular and atrial dimensions according to the baseline. Conclusions: Strict rate control in chronic AF patients yielded lowering of BNP values as well as reduction in cardiac chamber volumes.
Rate control efficacy in permanent atrial fibrillation: lenient versus strict versus inadequate rate control.

Data from the RACE II study

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Purpose: The RACE II showed no difference in outcome between lenient and strict rate control. However failure of achieving strict rate control may have influenced outcome. We aimed to investigate differences in outcome between patients with permanent AF treated with lenient, strict or inadequate strict rate control.

Methods: Of the 614 included patients, 311 were randomized to lenient rate control (resting heart rate <110 bpm). During the first two months follow-up visits occurred every two weeks until the heart rate target was achieved. Of the 303 patients randomized to strict rate control (resting heart rate <80 bpm and during moderate exercise <110 bpm), 203 achieved the rate control target, and 100 did not. The primary outcome was a composite of cardiovascular mortality, hospitalization for heart failure, stroke, systemic embolism, bleeding, and life-threatening arrhythmic events. Median follow-up was 2.9 (IQR range 2.4-3.0) years.

Results: There was a significant difference in heart rate after dose adjustment phase between lenient (93±9), strict (72±7) and inadequate strict (87±14) rate control (p<0.001). The primary outcome was reached in 38 (12.9%) patients in the lenient vs 27 (14.0%) patients in the strict group vs 16 (16.8%) in the inadequate strict group (p>0.05). The frequency of the components of the primary outcome was similar in the three groups. A landmark analysis (figure) performed at 2 months after the dose adjustment phase confirmed there was no difference in outcome between the groups.

Figure 1. Kaplan-Meier est. of landmark analysis

Conclusion: There is no significant difference in outcome between patients treated according to a lenient or strict rate control strategy, independent whether rate control is achieved.

Rhythm and heart rate control in an unsel ected population with atrial fibrillation: the AT-AF survey

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Background: Clinical trials did not demonstrate a superiority of rhythm control (RCh) vs rate control (RaC) strategy in atrial fibrillation (AF). Furthermore a strict RaC was not demonstrated to be superior to more lenient RaC over 2 to 3 years of follow-up in RACE II study. However, a controlled heart rate is desirable to minimize arrhythmia related symptoms and cardiomyopathy. Limited data are available regarding the RaC in patients (pts) with AF in clinical practice.

Aims: To describe the rate of pts with AF discharged in sinus rhythm or with controlled or not controlled HR in AF at discharge according to the selected antiarrhythmic strategy.

Methods: From May to July 2010, 360 centers (164 C and 196 IM), participating into the AT-AF survey, enrolled 7148 consecutive pts with current or previous (within 12 months) AF. Our analysis is carried out on 6910 pts with defined type of AF (permanent, paroxysmal, persistent).

Results: Out of 6910 pts, 54% were managed in C and 46% in IM units. Permanent AF was diagnosed in 50.8% of the pts, persistent in 24.4% and paroxysmal in 24.8%. RhyCh strategy was pursued in 27.5% of the pts, RaC was the preferred choice in 51.4% pts, while in 1465 pts (21.1%) an anti-arrhythmic strategy was not indicated. At discharge 33.8% of the pts were in sinus rhythm. Of the 4575 pts who at discharge were still in AF, 40.7% had a heart rate <80 bpm. The figure shows the rate of pts in sinus rhythm or with controlled or not controlled HR in AF at discharge according to the selected antiarrhythmic strategy.

Conclusions: RaC is the most selected strategy and more pts in RhyCh group are discharged in sinus rhythm.

Ranolazine added to amiodarone vs. amiodarone alone for the conversion of recent-onset atrial fibrillation

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Background: The efficacy of currently available drugs for cardioversion of atrial fibrillation (AF) is suboptimal. Amiodarone is one of the most widely used agents, yet it is limited by its delayed action that may prolong hospitalization. Ranolazine - an antianginal agent with increasingly appreciated antiarrhythmic properties – reduces AF occurrence in patients with acute coronary syndromes, and synergistically augments amiodarone’s AF-suppressing effect in animal models. However, the effect of ranolazine added to amiodarone for AF conversion in man is unknown.

Purpose: This randomized pilot study compared the safety and efficacy of ranolazine added to amiodarone vs. amiodarone alone for the conversion of recent-onset AF.

Methods: Consecutive patients with recent-onset (≤48h duration) AF eligible for pharmacologic cardioversion were enrolled. Patients with cardiogenic shock, recent acute coronary syndrome, QTc >440ms, hepatic, renal, or thyroid disorders, or those taking strong CYP3A inhibitors were excluded. Patients were randomized 1:1 to either ir amiodarone (loading dose of 5mg/kg followed by 50mg/h for 24h or until cardioversion if sooner than 24h) (A group), or to amiodarone at the same dosage plus oral ranolazine 1500mg at the time of randomization (A&R group). Patients remained on continuous ECG monitoring in the CCU. Successful treatment was pre-defined as conversion achieved within 24h.

Results: We enrolled 51 patients (33 male, age 63±8 years): 26 in the A group and 25 in the A&R group. The two groups were well balanced with similar clinical characteristics, and with no difference in left atrium diameter (4.3±0.5 vs. 4.5±0.4 cm in groups A vs. A&R, respectively; p=0.58). One patient in the A group had an allergic reaction leading to immediate amiodarone discontinuation. Conversion within 24h (primary endpoint) was achieved in 39 patients: 22 (86%) in the A&R group vs. 17 (68%) in the A group (p=0.06). Among successfully converted patients, time to conversion was shorter in the A&R group vs. the A group (9.8±4.1 vs.14.6±5.3 h; p=0.002). There were no cases of ventricular tachycardia, torsades de pointes, or ventricular fibrillation.

Conclusions: This proof-of-concept study provides first-in-man evidence of a synergistic effect of ranolazine and amiodarone for the conversion of recent-onset AF. Compared to amiodarone alone, the combination of amiodarone plus ranolazine is equally safe, it is associated with a trend for higher conversion rate and with faster conversion. Larger studies are warranted to affirm these preliminary results.
NEW PERCUTANEOUS CORONARY INTERVENTION TECHNIQUES

P2379
Long-term comparison of everolimus-eluting stents with sirolimus-eluting stents for saphenous vein graft intervention
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1Bern University Hospital, Department of Cardiology, Bern, Switzerland; 2Institute of Social & Preventive Medicine & Clinical Trial Unit, University of Bern, Bern, Switzerland; 3Erasmus Medical Center, Thoraxcenter, Rotterdam, Netherlands

Purpose: Newer generation everolimus-eluting stents (EES) have been associated with improved safety and efficacy as compared to sirolimus-eluting stents (SES) – the previous gold standard of early generation drug-eluting stents – in a large scale study during long-term follow-up to 4 years. It remains unclear whether this benefit is observed also among subjects with complex coronary artery disease, such as patients with saphenous vein aorto-coronary bypass grafts (SVG) lesions. The purpose of this analysis was to evaluate long-term efficacy and safety of newer generation EES as compared to the early generation SES in patients under 75 years of age with SVG lesions. Comparing more likely percutaneous revascularization of SVG lesions.

Methods: Long-term clinical outcomes were compared between patients treated with EES and SES in SVG lesions in the context of a large scale registry. Pre-specified subgroups were divided into two groups according to presence of cardiac death, myocardial infarction (MI), and target vessel revascularization (TVR).

Results: Out of 8,031 consecutive patients treated with EES or SES, 230 patients (2.9%) underwent percutaneous coronary revascularization of at least one SVG lesion – 127 patients received EES and 103 patients received SES. At 4 years, the risk of the composite primary outcome was similar for patients treated with EES and SES before (HR 0.87, 95% CI 0.56-1.34) and after adjustment for baseline differences (HR 1.06, 95% CI 0.62-1.80). No significant difference was observed between EES and SES treated patients for the single components of the primary outcome: cardiac death (crude HR 1.32, 95% CI 0.60-2.68, adjusted HR 1.18, 95% CI 0.49-2.84), MI (crude HR 1.02, 95% CI 0.38-2.73, adjusted HR 0.84, 95% CI 0.25-2.63), and TVR (crude HR 0.79, 95% CI 0.48-1.32, adjusted HR 0.92, 95% CI 0.49-1.75). Similarly, the risk of different MI (HR 1.28, 95% CI 0.29-5.74) and definite or probable stent thrombosis (HR 1.03, 95% CI 0.39-2.31) showed no difference between EES and SES treated patients. Conclusions: In this large-scale registry of consecutive patients undergoing percutaneous coronary intervention with drug-eluting stents, the use of newer generation EES among patients with SVG lesions showed similar safety and efficacy as compared to the use of early-generation SES during long-term follow-up to 4 years.

P2380
Age is not a bar to Percutaneous Coronary Intervention (PCI): insights from the longterm outcomes from off-site PCI in a real world setting
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Aims: Octo and nonagenarians are grossly under-represented in randomised studies with limited data on long-term outcomes following PCI. We aim to compare PCI outcomes of very elderly patients (>80yrs) to a cohort traditionally reported in the literature (75-80). Methods: All consecutive patients >80yrs were selected from the institutional database and outcomes compared to a cohort from our centre traditionally reported in the literature (75-80yrs). Primary end-point was MACCE, defined as a composite of cardiac death, MI, stroke, target vessel (TVR) and target lesion revascularisation (TLR). Secondary end points were target lesion failure (TLF) and stent thrombosis (ST).

Results: 624 lesions from 595 patients were identified with 99% clinical follow-up (31±4 months). Baseline characteristics were the same between the groups: 36% females, 17% diabetics and 9% smokers. The very elderly cohort were more likely to present acutely (49% vs. 58%, p<0.05, 16% PCI). In hospital peri-procedural mortality was 1.8% (75-80 vs. 4.2% (>80s), p<0.05, with 59% of the deaths occurring on PCI. At extended follow-up long-term mortality, TLF and MACCE tended to be non-significantly higher in the more elderly cohort (Figure). Definite and probable ST was 1.8% vs 45% of patients on dual antiplatelet therapy at 12 months and 6.4% TIMI major bleed. Despite majority bare metal stent use the restenosis rates were only 5% and TLF was 9.7% (75-80 vs 11.7% (>80s), p=0.42.

Conclusion: This study demonstrates an acceptable occurrence of MI, death, repeat intervention and ST in a high risk group with de novo lesions. Early revascularisation in stable patients appears to be more beneficial than intervention at the time of unstable symptoms. Age alone should not prohibit a patient from access to PCI.

P2381
Evaluation of antithrombotic pretreatment cooling-off strategy in patients with acute ST-elevation myocardial infarction having TIMI grade 3 flow on initial coronary angiography
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Purpose: We sought to evaluate antithrombotic pretreatment “cooling-off strategy” compared to emergent primary percutaneous coronary intervention (p-PCI) in patients with acute ST-elevation myocardial infarction (STEMI) having baseline TIMI grade 3 flow on initial coronary angiography.

Methods: We retrospectively enrolled 1792 patients with STEMI transferred immediately to catheterization laboratory within 12 h of chest pain. The patients were divided into two groups: emergent (n=158) and cooling-off strategy (n=102). In the cooling-off strategy PCI was performed 24-72 h after initial coronary angiography.

Results: In patients with baseline TIMI grade 3 flow, the frequency of postprocedural TIMI grade 3 flow (97.7% vs 67%, p<0.001) and left ventricular ejection fraction (LVEF) were higher; in-hospital (0.4% vs 4.5%, p<0.001) and 30-days (1.2% vs 5.8%, p<0.002) mortality rates were higher, compared to patients with baseline TIMI grade 3 flow. Among patients with initial TIMI grade 3 flow, there was no significant difference between the treatment subgroups (emergent [p-PCI vs cooling-off strategy] with respect to postprocedural TIMI grade 3 flow (97.5% vs 98%, p=0.7), LVEF (52±6.4 vs 51±6.5%, p=0.5), in-hospital (0.0% vs 1%, p=0.38) and 30-days (0.6% vs 2%, p=0.56) mortality rates. Further, there was no difference between the groups with respect to the incidences of reinfarction and target vessel revascularization.

Conclusions: The presence of baseline TIMI grade 3 flow is associated with better clinical and angiographic results in patients with STEMI. In patients with baseline TIMI grade 3 flow on initial coronary angiography, there is no difference between immediate p-PCI and cooling-off strategy with respect to clinical and angiographic outcomes.

P2382
Culprit only versus complete coronary revascularization during primary PCI
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Background: Current guidelines for management of patients with ST elevation myocardial infarction (STEMI) recommend treating only the culprit vessel in multivessel disease and that other vessels be addressed at a later procedure. Acute multivessel PCI (MVPCI) is recommended during the index procedure only for patients with hemodynamic compromise. Objectives: The purpose of this study was to examine differences in in-hospital clinical outcomes as well as short term and 1 year mortality for STEMI patients with multivessel disease as a function of whether they underwent culprit vessel or MVPCI. Methods: STEMI patients with multivessel disease undergoing primary PCIs between January 2001, and September 2010, were divided into those who underwent culprit vessel PCI (CVPIC) alone and those who underwent MVPCI during the index procedure. In-hospital adverse outcomes and mortality rates were compared.

Results: A total of 453 patients had multivessel disease. In 318 (70.2%) of them MVPCI was performed during the index procedure, in 135 (29.8%) patients CVPIC only was done. The rest of the revascularization was completed in the same hospitalization in 29 patients, and 1 to 3 months after in 106 patients. MVPCI during the index procedure was associated with a shorter hospitalization (4.4±1.27 vs 7.6±2.3 days, P=0.01), reduced incidence of in-hospital major adverse cardiac events (recurrent ischemia, reinfarction, acute heart failure and mortality (16.1% vs 35.5%, P=0.01). There was a significantly lower rate of recurrent ischemic episodes (7.2% vs 25.9%, P=0.02), myocardial reinfarction (3.9% vs 9.6%, P=0.01), and reintervention (9.4% vs 29.9%, P=0.001). Transient renal dysfunction was more common in MVPCI (8.4% vs 4%, P=0.01). In-hospital and one year mortality rates (4.1% vs 4.4% vs 9.6% vs 7.4%, p=0.32) were similar in both groups.

Conclusion: MVPCI in STEMI is feasible, safe and can result in improved clinical outcomes in select cases.
Impact of operator learning curve on success of percutaneous coronary intervention for chronic total occlusions

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Purpose: To evaluate the impact of operator learning curve on the technical success rate of PCI for chronic total occlusions (CTO) performed in a single center.

Methods: We included 1,108 consecutive patients who underwent PCI for CTO between January 2007 and December 2012. Patients were stratified into 6 categories of case volume experience (CVA) to assess the impact of case volume on PCI failure after adjustment for patient and lesion characteristics. All 6 categories of CVA were chosen for the analysis on the basis of minimum case volume for optimum clinical benefit, CTO-PCI cases were chronologically ranked and stratified into 6 case volume groups, as 1 to 50 (beginner operators), 51 to 100, 101 to 150, 151 to 200, 201 to 250, > 250, for several operators. A multivariable mixed effect logistic regression for clustered data was used to assess the impact of case volume on PCI failure after adjustment for patient and lesion characteristics, lesion difficulty graded by angiographic score, vessel size, procedural techniques.

Results: A total of 1,261 patients, median age 63 yrs-old (25th-75th percentile, 55-72yo), undergoing PCI for 1418 CTO were included. PCI success occurred in 1,008 (71%) lesions. Crude success rate was 69.6%, 62.2%, 69.6%, 76.1%, 70.2%, 77.8% across the 6 ordered case volume groups, respectively, p<0.04. At multivariable logistic regression, increasing case volume across the six categories was significantly associated with successful PCI (odds ratio (OR) 1.22, 95% confidence interval (CI) 1.13–1.32, p<0.001). The OR of success increased substantially and significantly with a case volume of at least 150 to 200, as compared to 1 to 50 case volume (2.09, 95% CI 1.18-3.70, p=0.012), reaching the highest value in case volume > 250 (OR 2.85, 95% CI 1.87-4.34, p<0.001), while the increase in odds ratio for case volumes > 150, as compared to 1 to 50 case volume, did not reach the statistical significance.

Conclusions: Operator experience in PCI for CTO is an independent predictor of success. A minimum case volume > 150 is required to increase significantly the chance of success compared to beginner operators.

Impact of the severity of unprotected left main stem (LM) stenosis on 12-month mortality after PCI of LM as a culprit lesion in patients with NSTE-ACS - an analysis from the PL-ACS Registry

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The left main stem (LM) stenosis as a culprit lesion is a serious cause of non-ST-segment elevation acute coronary syndrome (NSTE-ACS) leading to a high mortality. The aim was to analyze the impact of the severity of LM stenosis on 12-month mortality in patients with NSTE-ACS caused by the LM stenosis treated by PCI of the LM.

Methods: All patients with NSTE-ACS caused by LM stenosis and treated by PCI of the LM between 07/2007 and 11/2009 were included. Follow-up mortality was obtained from the government database.

Results: In PL-ACS Registry, from 16934 patients with NSTE-ACS, LM was chosen as a culprit lesion in 426 (2.5%) of cases. Most of them (225-53%) had bypass surgery done or planned after discharge. Non-invasive treatment was chosen in 40 (9%) of them. Immediate PCI was performed in 161 (38%). As was the severity of LM stenosis increased, the rates of hemodynamics disturbances as well as percentage of NSTEMI raised. Successful reperfusion (TIMI 3) was achieved less frequently as the severity of stenosis raised. 12-month mortality was significantly higher in patients with more severe stenosed LM.

Conclusions: The severity of left main stem stenosis in patients with NSTE-ACS treated by PCI is significantly associated with the 12-month mortality.
Radial versus femoral access for percutaneous coronary interventions in patients with chronic total occlusion

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Purpose: Femoral access (FEM) is usually employed in percutaneous coronary intervention (PCI) for chronic total occlusions (CTO) because this is considered to provide better catheter support, and allows the use of larger diameter guiding catheters. The aim of this study was to assess whether the use of radial access (RAD), which is typically 6-Fr catheter compatible, is comparable to FEM with respect to procedural success for CTO.

Methods: The study included all consecutive patients undergoing PCI for CTO at 3 tertiary PCI centres between January 2004 and December 2011. CTO lesions were graded as easy (score of 0), intermediate (1), difficult (2), and “very difficult” (≥3), according to the angiographic J-CTO score. A mixed variable effect logistic regression for clustered data was used to assess the impact of RAD on PCI success after adjustment for patient characteristics, lesion difficulty graded by angiographic score, vessel site, procedural techniques.

Results: A total of 1249 patients, median age 63 yrs-old (55.72, 25th-75th percentiles) undergoing PCI for 1402 CTO were included. RAD was used in 848 (60.5%) lesions. The use of 7-Fr (8% vs. 6.7%, p=0.01) or 8-Fr (0% vs 4.1%, p<0.01) guiding catheters was significantly lower in the RAD group than in the FEM group. The prevalence of difficult lesions (J-CTO score ≥ 2) was lower in the RAD group than in the FEM group (39.4% vs 48.4%, p<0.01). The use of 7-Fr or 8-Fr guiding catheters was significantly lower in lesions with J-CTO score ≥ 2 than in those with J-CTO score (61% vs 21%, p<0.001). PCI success rate was slightly higher in the RAD group than in the FEM group (72.6% vs 68.4%), although this difference did not achieve the statistical significance (p=0.09). At multivariable logistic regression the use of RAD, as compared to FEM, was not associated with procedural success (odds ratio 1.14, 95% confidence interval (CI) 0.88–1.48, p=0.33).

Conclusions: The use of RAD for PCI of CTO is feasible in the vast majority of lesions and is associated with a comparable success rate to that achieved using FEM.

Coronary Interventions in infants with congenital heart diseases

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Purpose: During the last decade the surgical and interventional techniques for the treatment of congenital heart diseases were constantly refined. Todays children, whom were considered to be inoperable some years ago undergo surgical or combined surgical-interventional treatment on a regular basis. This study focuses on coronary interventional procedures in children with CHD.

Population: During the last years we performed 16 coronary interventions in 14 patients. The age ranged from 9 days to 26 years, mean 6 years, the bodyweight from 1.7 kg to 65 kg, mean 18 kg.

Results: During 10/16 procedures closure of coronary fistulas was attempted and successful performed with a variety of implantable devices (coils, plugs). Coronary to right ventricular fistula in pulmonary atresia/intact ventricular septum were occluded in 3/14 patients. In 3/14 patients acute obstructed coronary artery were successfully treated in 2/3 cases with balloon dilation and by stent implantation (1.3). All procedures were successfully performed without any major complications. One patient with a bodyweight of 1.7 kg and balloon dilation of the left main coronary artery died 2 weeks after the intervention because of haemostatic complications. Conclusion: Balloon dilation or stent implantation is a realistic option in postoperative coronary stenoses. It helps to improve myocardial perfusion and function without reoperation in severely depressed patients. Closure of coronary arterial fistulas with some of the newer low profile devices is possible even in newborns. Fistulae with a short channel to the right ventricular caviurn remain critical for interventional closure if distal coronary perfusion has to be maintained.

12-month mortality of NSTEMI patients treated by PCI with multivessel disease and chronic total occlusions - analysis from the PL-ACS Registry

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The aim of this study was to assess the impact of chronic total occlusion during PCI for NSTEMI in patients with 3-vessel disease on 12-month mortality. Methods: All patients with NSTEMI treated by primary PCI, with 3-vessels diseases, registered in the PL-ACS from 7/2007 to 11/2009, were included. Patients with prior CABG as well as those with significant stenosis of left main were excluded. 12-month mortality was obtained from the coronary database.

Results: From 925 patients fulfilling inclusion and exclusion criteria, one or more CTO of main coronary arteries, different than artery related to NSTEMI, were found in 438 (47.4%). Successful reperfusion of infarct related artery by PCI (TIMI 3) was lower in patients with CTO (table). In-hospital as well as 12-months mortality was significantly higher in patients with CTO. After multivariable adjustment, presence of CTO remained significantly associated with higher 12-months mortality (relative risk = 1.42, 95%CI = 1.01-2.00, p=0.047).

Table 1

<table>
<thead>
<tr>
<th>Chronic total occlusion</th>
<th>No chronic total occlusion</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, %</td>
<td>438 (47.4%)</td>
<td>487 (52.6%)</td>
</tr>
<tr>
<td>Age, years ± SD</td>
<td>69.8±10.1</td>
<td>68.4±10.7</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>35.9</td>
<td>35.7</td>
</tr>
<tr>
<td>Prior myocardial infarction, %</td>
<td>37.9</td>
<td>20.1</td>
</tr>
<tr>
<td>Final TIMI flow grade 3 after PCI of NSTEMI related artery, %</td>
<td>91.6</td>
<td>95.0</td>
</tr>
<tr>
<td>PCI of 1 additional artery, %</td>
<td>20.3</td>
<td>24.0</td>
</tr>
<tr>
<td>Total revascularization by PCI (3 arteries), %</td>
<td>5.9</td>
<td>5.3</td>
</tr>
<tr>
<td>Bypass surgery (CABG) during hospitalization, %</td>
<td>1.9</td>
<td>0.8</td>
</tr>
<tr>
<td>CABG arranged after discharge, %</td>
<td>13.7</td>
<td>14.2</td>
</tr>
<tr>
<td>Mean left ventricular ejection fraction, % (SD)</td>
<td>42.5±10.7</td>
<td>47.8±16.6</td>
</tr>
<tr>
<td>In-hospital major bleeding, %</td>
<td>3.7</td>
<td>3.9</td>
</tr>
<tr>
<td>In-hospital stroke, %</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>In-hospital re-infarction, %</td>
<td>1.1</td>
<td>0.0</td>
</tr>
<tr>
<td>In-hospital death, %</td>
<td>5.3</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Conclusion: Chronic total occlusion(s) found in patients with 3-vessel disease and NSTEMI treated by primary PCI are associated with worse 12-months mortality.

Benefit in quality of life after percutaneous coronary intervention for chronic total occlusion

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Purpose: It is not clearly established whether percutaneous coronary intervention (PCI) provides similar incremental benefit in terms of health related quality of life (HRQoL) for chronic total occlusion (CTO) and non-CTO coronary lesions.

Methods: Consecutive patients undergoing PCI at our institution from September 2009 to October 2010 were evaluated. Clinical outcome was measured by the occurrence of clinically TVR. EQ-SD was used to measure quality-of-life at baseline and 12-months after PCI. Change in QALY at 1 year was considered between patients who underwent successful single-vessel CTO and non-CTO lesions PCI.

Results: Of 513 patients who underwent single-vessel PCI, 12.5% (n=4) were CTO and 87.5% (n=449) were non-CTO lesions. CTO PCI was successful in 84.4% (n=54) cases and failed in 15.6% (n=10) of cases. One year TVR rates were Higher in CTO (12.5%) than in non-CTO group (2.4%, p<0.01). Utility scores at baseline (0.53±0.40 vs. 0.43±0.42) and 12-month follow-up (0.79±0.22 vs. 0.80±0.21, p<0.02) were similar between patients undergoing CTO and non-CTO PCI. There was no significant difference in mean QALY gained between successful CTO (0.39) and non-CTO PCI (0.45). However, mean QALY gained after failed CTO intervention was significantly lower (0.14, p<0.01).

Conclusion: Successful CTO recanalization is associated with significant improvement in health-status comparable to non-CTO intervention despite higher rates of target vessel revascularization.

Second-generation DES vs first-generation DES in diabetic patients with coronary artery disease

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Background: Diabetes mellitus is a significant predictor of unfavourable outcomes after percutaneous coronary intervention (PCI). While drug-eluting stents (DES) have improved safety and efficacy outcomes compared to bare metal stents (BMS) in diabetic patients the optimal DES strategy still remains unclear. Therefore we compared effectiveness of everolimus-eluting stents (Xience) and sirolimus-eluting stents (Cypher) in patients with diabetes mellitus.

Methods: ISAR TEST-4 is a randomized trial of 2603 Patients with de novo native-vessel coronary lesions. This analysis is focused on a cohort of 377 Patients with diabetes mellitus randomly assigned to receive Xience (n=184) or Cypher (n=193).

The primary endpoint was the composite of cardiac death, myocardial infarction related to the target vessel, or target lesion revascularization (TLR) at three year follow-up. Secondary endpoints were binary restenosis; in-stent late lumen loss; all cause mortality; and incidence of definite/probable stent thrombosis (ST).
Results: Xience was comparable to Cypher concerning the incidence of the primary endpoint (21% vs. 24%, relative risk =0.87, 95% CI, 0.57-1.34; p=0.53), all-cause death (10% vs. 16%, relative risk =0.66, 95% CI, 0.37-1.18; p=0.16), TLR (14.7% vs. 16.6%, p=0.55) and ST (1.1% vs. 3.1%, p=0.19) at three-year follow-up. There was a significant difference in late lumen loss (0.22±0.46 vs. 0.44±0.60mm,p=0.01) and the incidence of angiographic restenosis (8.4% vs. 17%, p=0.02) at 6-8 months angiogram.

Conclusion: This analysis shows no significant difference between second and first generation DES regardless of clinical outcomes at 3 years, although angiographic restenosis measurements are in favor of second generation DES.

P2392 Primary PCI in patients with impaired renal function

Aim: To compare one-year outcomes after primary percutaneous coronary intervention (pPCI) in patients with vs. without impaired renal function (IRF)

Methods: Consecutive patients treated by PCI with at least one stent were included within 36 months and divided in 4 groups according to renal function (IRF/no-IRF) and the kind of PCI (pPCI/no-pPCI). IRF was defined by a CrCl < 60 ml/min and pPCI was used in case of acute myocardial infarction (AMI) and the kind of PCI (pPCI/no-pPCI). IRF/no-pPCI, 474 (17.1%) no-IRF/pPCI, 589 (21.3%) IRF/no-pPCI and154 (5.6%) IRF patients treated by PCI for other purpose than AMI have com-

Results: Among 2768 consecutive patients, 629 (23%) had pPCI and 749 (27%) had IRF. Patients were classified in 4 groups: 1551 patients (56.0%) with no

P2393 Mid-term outcomes following unprotected left main stenting with first- vs. new-generation drug-eluting stents: the fine registry
G.L. Buchanan, C. Bernelli, A. Chiechio, A. Ielasi, M. Montorsuo, A. Labb, F. Figini, C. Godino, M. Carlini, A. Colombo. San Raffaele Hospital (IRCCS), Interventional Cardiology Unit, Milan, Italy

Purpose: To assess clinical outcomes following first- vs. new-generation DES implantation in patients undergoing unprotected left main (ULMCA) percutaneous coronary intervention.

Methods: All eligible patients from our two-center prospective registry treated for ULMCA with DES implantation from October 2006 to November 2010 were ana-

Results: A total of 186 patients were included: 93 had first- (50%) vs. 93 (50%) with new-generation DES. No differences in baseline clinical and lesion character-

P2394 Impact of lesion length on chronic total occlusion intervention outcomes
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Background: Chronic total occlusion (CTO) intervention is still challenging be-

Results: Baseline clinical characteristics & procedure details were similar be-

Conclusions: IRF patients treated by PCI for other purpose than AMI have com-

Conclusions: IRF and AMI are independent predictors of MACCE.

Conclusions: Diffuse long CTO lesions needed more complex procedure tech-

Conclusions: In our study, new-generation DES have improved results with re-

Conclusions: This analysis shows no significant difference between second and first generation DES regardless of clinical outcomes at 3 years, although angiographic restenosis measurements are in favor of second generation DES.
Impact of chronic right coronary artery occlusion on outcomes of patients with acute myocardial infarction caused by left main stem stenosis - analysis from the PL-ACS Registry

M. Tajstra 1, M. Gerlotka 2, M. Gasior 3, M. Hawranek 4, K. Wilczyk 5, J. Wasilewski 6, M. Janion 7, L. Polonski 1 on behalf of PL-ACS Investigators. 1Medical University of Silesia, Silesian Center for Heart Diseases (SLCHD), Zabrze, Poland; 2University of Humanities and Science in Kielce, Cardiology Center, Kielce, Poland

The left main stem (LM) stenosis as a culprit lesion is a serious cause of NSTEMI as well as STEMI leading to a high mortality. The aim was to analyze the impact of chronic occlusion (CTO) of the right coronary artery (RCA) on outcomes of patients with NSTEMI and STEMI caused by the LM stenosis.

Methods: All patients with NSTEMI (N=192) and STEMI (N=105) caused by LM stenosis registered in PL-ACS between 7.2007 and 11.2009 were included. Follow-up mortality was obtained from the government database.

Results (table): In 297 patients with acute myocardial infarction with LM as a culprit lesion in 60 (20%) cases we found a CTO of RCA. These patients were older, had more frequently NSTEMI than STEMI, diabetes mellitus, peripheral artery disease, and a history of prior myocardial infarction. There was no difference in the rate of percutaneous or surgical revascularization procedures between the analyzed groups. Early as well as 12-month mortality was not significantly different in patients with and without CTO of RCA.

Table 1

<table>
<thead>
<tr>
<th>Number of patients, %</th>
<th>No CTO of RCA</th>
<th>CTO of RCA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSTEMI, %</td>
<td>76%</td>
<td>24%</td>
<td>0.012</td>
</tr>
<tr>
<td>STEMI, %</td>
<td>88%</td>
<td>12%</td>
<td>0.013</td>
</tr>
<tr>
<td>Age, years ± SD</td>
<td>67±12</td>
<td>68±10</td>
<td>0.0028</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>20%</td>
<td>35%</td>
<td>0.012</td>
</tr>
<tr>
<td>History of congestive heart failure, %</td>
<td>6%</td>
<td>13%</td>
<td>0.092</td>
</tr>
<tr>
<td>Prior myocardial infarction, %</td>
<td>16%</td>
<td>40%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cardiogenic shock on admission, %</td>
<td>16%</td>
<td>12%</td>
<td>0.44</td>
</tr>
<tr>
<td>Primary angioplasty (PCI), %</td>
<td>64%</td>
<td>60%</td>
<td>0.55</td>
</tr>
<tr>
<td>In-hospital bypass surgery, %</td>
<td>22%</td>
<td>28%</td>
<td>0.26</td>
</tr>
<tr>
<td>Left ventricle ejection fraction, % ± SD</td>
<td>43±13</td>
<td>37±14</td>
<td>0.0028</td>
</tr>
<tr>
<td>Major bleeding, %</td>
<td>10%</td>
<td>3%</td>
<td>0.11</td>
</tr>
<tr>
<td>In-hospital mortality, %</td>
<td>16%</td>
<td>12%</td>
<td>0.40</td>
</tr>
<tr>
<td>12-month mortality, %</td>
<td>33%</td>
<td>40%</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Conclusion: The presence of chronic total occlusion of the right coronary artery has no impact on outcomes in patients with acute myocardial infarction caused by the left main stem lesion who had coronary angiography performed.

Impact of the female gender in the outcomes of contemporary percutaneous coronary intervention


Purpose: Prior studies have shown there are differences in the clinical outcomes of percutaneous coronary intervention (PCI) between men and women. We tried to assess gender differences in clinical and angiographic presentation as well as in the in-hospital outcomes of patients undergoing contemporary PCI.

Methods: From 2002 to 2009, 6,067 consecutive patients were submitted to PCI, of these, 2,207 (33.3%) were women. The interventional strategy, including the type of stent implanted, was conducted at the operators discretion.

Results: The female gender was older and had a greater incidence of risk factors for atherosclerosis, except for smoking. Acute coronary syndrome without ST segment elevation was the most prevalent presentation in women. Women had a higher number of single vessel lesions and a lower prevalence of B2/C lesions, thromb lysis, and severe ventricular dysfunction. Patients were predominately treated with bare metal stents and no differences were observed for the diameter and length of the stents. No differences were observed for the inhospital incidence of major adverse cardiac and cerebrovascular events (1.5% vs. 1.4%; P = 0.76), death (0.9% vs. 0.6%; P = 0.15), stroke (0.05% vs. 0.005%; P = 0.005) and emergency myocardial revascularization surgery (0.1% vs. 0; P = 0.62). Diabetes, multivessel coronary artery disease, B2/C type lesions and total occlusions were the variables that best explained the occurrence of inhospital events.

Conclusions: Women correspond to one third of the patients undergoing PCI at our service and have a more severe clinical profile, but lower anatomic complexity than men. In our study, the female gender was not a predictor of inhospital adverse clinical events.

Clinical results of myocardial revascularization guided by functional assessment using invasive pressure wire: a single-center experience

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Purpose: The benefit of percutaneous revascularization in reducing cardiovascular events may depend on the extent of the territory at risk and the functional significance of coronary lesions. We sought to evaluate the clinical impact of revascularization guided by evaluation of Fractional Flow Reserve (FFR), in an unselected population.

Methods: From Jan 2007 until Oct 2010, we used PressureWire® for FFR determination with adenosine infusion >140 μg/kg/min in 183 cases (70%M, 65±9y): 75% were elective catheterizations, 16% had EF <50%, 43% had prior revascularization (88% PCI), 37% were asymptomatic or had atypical symptoms and 53% had done a prior functional test. We determined the rate of events during the first year (death, stroke, MI or any revascularization (MACCE)) related to deferred coronary lesions and compared to the expected rate, based on a validated score method.

Results: From a total of 527 lesions, 244 were evaluated by FFR (1.4pts, mean 0.82±0.09). 110 pts had 199 deferred lesions; 69 pts (37.7%) underwent PCI (1.26 stents/pts; 80% with >1 DES); and 4 pts (2.2%) were submitted to CABG. Mean FFR in the 45 treated lesions was 0.73±0.09 vs 0.84±0.07 in deferred lesions (p<0.0001). The MACCE incidence at 1 year was 17.4% (9 deaths, 6 MI, 22 CABG). Excluding programmed revascularization (4 CABG), the rate of MACCE was significantly lower than expected from the risk score: 11% vs 19.9% (OR 0.44 [0.2 to 0.98], p = 0.05). In 172 pts with follow-up-a 1 year (median 585 days [IQR 470, 572]), the rate of non-scheduled TLR in deferred coronary lesions was 1.2%.

Long-term clinical outcomes of coronary bifurcation stenting with sirolimus-eluting versus everolimus-eluting stent


Background: There is a paucity of data regarding comparison of sirolimus-eluting stent (SES) and everolimus-eluting stent (EES) for the treatment of coronary bifurcation lesion. We sought to compare long-term efficacy and safety of SES versus EES in patients undergoing coronary bifurcation stenting.

Methods and Results: We evaluated 486 patients who underwent percutaneous coronary intervention (PCI) with SES and EES for coronary bifurcation lesions.
New percutaneous coronary intervention techniques / Complex lesions, complex patients for PCI

P2399
Angiographic correlates of late and very late drug-eluting stent thrombosis: findings from the international multicenter Drug Eluting Stent Event Registry of Thrombosis (DESERT)

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Methods: In our registry data, coronary bifurcation stenting with DES showed better intermediate-term angiographic results. However, both group showed excellent and similar long-term clinical outcomes. These findings should be confirmed by propensity score matched analysis or large randomized controlled study.

COMPLEX LESIONS, COMPLEX PATIENTS FOR PERCUTANEOUS CORONARY INTERVENTION

P2400
Safety and efficacy of intense antithrombotic treatment and PCI deferral in patients with large intracoronary thrombus. A comparison with an ad hoc interventional treatment

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Background: Percutaneous coronary intervention (PCI) in patients with acute coronary syndromes (ACS) and large intracoronary thrombus (LIT) carry a high risk of complications. The optimal treatment of LIT is currently unclear, especially in stable ACS patients. We investigated in patients with these characteristics whether deferring PCI (d-PCI) allowing a period of intensive antithrombotic and antplatelet therapy (ATT) results in better in-hospital outcome than ad hoc, immediate PCI (i-PCI)

Methods: This is a prospective historical cohort–matched study of 133 patients admitted with ACS, with controlled symptoms at the time of angiography and presenting LIT. Primary PCI and ongoing angina were exclusion criteria. 89 patients underwent d-PCI (after ATT with Gp IIb/IIIa inhibitors, enoxaparin, aspirin and clopidogrel). The observed angiographic and in-hospital outcomes were compared with a 44 patient control group matched for TIMI flow and TIMI thrombus grade treated ad hoc with i-PCI. To assess the impact of ATT on thrombus burden, absolute thrombus volume was measured with dual QCA (volumetry) and edge detection) before and after ATT in cases suitable for this analysis (TIMI flow 1).

Results: All d-PCI patients remained asymptomatic during the ATT deferral period (60.0±30.8 hours) without need of urgent revascularisation. A significant reduction in TIMI flow (0.1±0.8 vs. 3.2±1.3; p<0.001) and stenosis grade (73.8% vs. 60.3±32.5%; p<0.001), as well as an increase in TIMI flow (1.7±1.3 vs. 2.2±1.2; p<0.001) were noted after ATT. In non-occluded vessels, dual QCA revealed a 37% thrombus volume reduction (70.9±56.0 vs. 44.6±38.0 mm³; p<0.001). PCI was performed more frequently in i-PCI group (100% vs. 76.4% in d-PCI; p<0.001). Despite that thrombus aspiration was performed in all (100%) i-PCI and only in 19 (21%) d-PCI procedures (p<0.001), distal embolization and/or no-reflow (31.6% vs. 7.9% in d-PCI; p<0.001) happened more frequently during i-PCI. Delayed PCI was therefore protective against these complications [OR 0.18 (95%CI 0.06-0.49); p<0.001], while major haemorrhagic complications did not differ between the 2 groups (9.7% in i-PCI vs. 8.0% in d-PCI; p=0.76).

Conclusions: In patients with ACS with LIT and controlled symptoms, and compared to i-PCI, deferral of PCI and concomitant ATT 1) is safe, 2) leads to an ob- jective reduction in thrombotic burden, 3) decreases the number of angiographic complications, and 4) reduces the need of revascularisation. These benefits are obtained without an increase in associated haemorrhagic complications.

P2401
Evolution of Percutaneous Coronary Intervention (PCI) in elderly patients over the last five years: results from the Belgian national data base on PCI

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Coronary interventions are performed increasingly in elderly and data on clinical outcomes and evolution over time are scarce. The present report focus on clinical data, management and outcomes of elderly patients undergoing PCI from 2006 to 2010.

Methods: Data of all PCI performed in Belgium in 2006-2010 were analysed. Data from each calendar year were assessed by quintiles and compared.

Results: Number of PCI decreased gradually from 25640 interventions in 2006 to 24230 in 2010. Mean age in the oldest quintile increased from 80.9 to 82.5 yrs. During this period, demographic data as well as indications for PCI remained similar. However, PCI performed via a radial approach and use of closure devices increased respectively from 7.0 to 22.7% and from 7.9 to 32.7%. Conversely, SVG PCI decreased from 6.2 to 4.7%. Serious vascular complications decreased from 1.9 to 1.3%. Acute stent thrombosis rates, Q wave MI post PCI and need for dialysis following PCI also decreased gradually. In hospital death rates and need for emergency CABG didn’t change over this period.

As compared to other population quintiles, the oldest group had more female (43.9%), a higher prevalence of previous CABG, history of stroke, peripheral vascular disease, heart and renal failure. There were fewer smokers but more hypertensive patients in the elderly. Fewer Primary PCI were performed in the oldest quintile (13.8 vs 27.6) in the former group (1.30 vs 0.68%), major bleeding (0.66 vs 0.31%), stroke (0.27 vs 0.08%), dialysis (0.56 vs 0.14%), stent thrombosis (0.35 vs 0.27%) and CABG (0.35 vs 0.27%). In hospital mortality from the first to the last quintile was respectively of 0.80, 0.68, 1.20, 2.06 and 3.74%.
Conclusions: These data confirm that the population undergoing PCI is getting gradually older. Improvement in vascular management has led to a significant decrease in serious vascular complications but, overall, no significant changes were observed for the other clinical outcomes. Mortality and morbidity still remain significantly higher among the elderly and is mostly related to more co-morbidities, more complex anatomy and poorer left ventricular function. Primary PCI for acute MI is the lowest among the oldest patients.

**P2402**

Drug eluting stents appear superior to bare metal stents in vein graft PCI in a propensity matched cohort

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**Purpose:** Trials have shown improved short-term outcome with drug-eluting stents (DES) vs bare metal stents (BMS) in Saphenous vein graft (SVG) PCI, primarily by reducing target vessel revascularisation (TVR). We assessed the outcomes in patients undergoing SVG stent implantation comparing DES vs BMS using a propensity matched analysis.

**Methods:** Clinical information was analysed from a prospective database on 512 patients who underwent SVG PCI between 2003-2010. 263 patients underwent PCI with BMS and 219 with DES Propensity scores representing the estimated probabilities of patients receiving either DES or BMS were developed based on 18 observed baseline covariates in a logistic regression model with stent type as the dependent variable. The nearest-neighbour-matching algorithm with Greedy 5-1 Digit Matching was used to produce two patient cohorts of 219 patients each balanced for baseline factors. We assessed major adverse cardiac events (MACE), defined as death, myocardial infarction (MI), stroke, and TVR out to a median of 3.3 years (IQR: 2.1-4.1).

**Results:** There was a significant difference in MACE between the two groups in favour of DES (17.9% DES vs 31.2% BMS group P=0.04) over the 5 year follow-up. MACE was driven by in-stent restenosis in both groups and the difference between groups was due to increased TVR in the BMS group (Figure 1). There was no difference in death, MI or stroke between the stent types. Propensity matched Cox analysis confirmed a decreased risk of MACE for DES compared with BMS (0.75 (95% confidence intervals 0.52-0.94) with no difference in the hazard of mortality (HR: 1.08 95% CI: 0.77-1.68).

**Conclusions:** In a selected CTO cohort with retrograde PCI technique CTOs late after CABG have higher lesion complexity compared to CTOs in patients without previous surgical revascularisation and procedural success rates are lower. However, even in these technically demanding lesions revascularisation success is encouraging with contemporary recanalisation techniques.

**P2404**

The effect of drug-eluting stents on clinical and angiographic outcomes in diabetic patients; 3 years result: multicenter registry in Asia

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**Background:** Chronic total occlusion (CTO) after coronary artery bypass grafting in a cohort with retrograde recanalisation technique

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**Background:** Chronic total coronary occlusions (CTO) after coronary artery bypass grafting (CABG), typically following late vein graft failure, represent a major challenge for percutaneous coronary intervention (PCI). We investigated characteristics of CTO lesions late after CABG compared to CTO lesions without previous surgical revascularisation and recanalisation success in a cohort with complex CTOs.

**Methods:** Consecutive patients with PCI of complex CTO lesions and retrograde recanalisation attempts (17% of all CTO interventions) were included. CTO was defined as TIMI 0 flow occlusion of >3 months duration. Procedural success was defined as <30% diameter stenosis of the CTO lesion after stent implantation.

**Results:** N=241 patients met the entry criteria. Mean age was 61±10 years. 12% were female, 30% diabetics, 44% had a prior myocardial infarction and 53% previous failed recanalisation attempts. Of the 241 patients 60 patients (25%) had prior CABG (Group A) and 181 patients (75%) no previous surgical revascularisation (Group B). Patients in Group A compared with Group B had more coronary 3 vessel disease (95% vs 48%; p=0.001) and CTO vessel distribution was different (left anterior descending, left circumflex, right coronary artery in 5%, 37%, 57% vs. 29%, 9%, 71%, respectively; p=0.001). CTO lesions in Group A had longer occlusion duration (144±72 vs 67±63 months; p=0.001), greater occlusion length (54±33mm vs 45±22mm; p=0.004), smaller reference vessel diameter (2.79±0.32mm vs. 2.96±0.32mm; p=0.005) and more moderate to severe calcification (63% vs. 39%; p=0.004). Conduits for retrograde guidewire passage were different in Group A and Group B (septal collaterals, epicardial collaterals, occluded vein grafts in 48%, 45%, 7% vs. 79%, 21%, 0%, respectively; p=0.001) and success rate for retrograde passage was similar (77% vs 81%; p=0.505). Total length of drug eluting stents implanted (91±30mmms. 86±22mm; p=0.304, fluoroscopic time (79±34min vs. 72±40min; p=0.195) and contrast volume (370±175 to 385±168mL; p=0.560) was comparable between groups. Procedural success was lower in Group A compared to Group B (72% vs 86%; p=0.015).

**Conclusions:** In a selected CTO cohort with retrograde PCI technique CTOs late after CABG have higher lesion complexity compared to CTOs in patients without previous surgical revascularisation and procedural success rates are lower. However, even in these technically demanding lesions revascularisation success is encouraging with contemporary recanalisation techniques.

**P2405**

Drug-eluting stents versus bare metal stents in patients with chronic kidney disease: a systematic review and meta-analysis

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**Objectives:** We conducted a systematic review and meta-analysis to compare clinical outcomes after drug-eluting stent (DES) and bare metal stent (BMS) use in patients with chronic kidney disease (CKD).

**Background:** CKD is a strong predictor of mortality and subsequent cardiac events after percutaneous coronary intervention. The safety and efficacy of DES in this population have not been adequately evaluated.

**Methods:** A search was conducted for published reports in MEDLINE, OVID, EMBASE and the Cochrane library databases from 2002 to 2011. Abstracts/presentations from this period at major cardiology conferences were also identified. Data were abstracted from studies comparing DES with BMS in CKD patients. Summary odds ratios (OR) for the mortality, repeat revascularisation, myocardial infarction (MI), major adverse cardiovascular events (MACE) and stent thrombosis were calculated.

**Results:** See table for clinical results.

**Conclusions:** The use of drug-eluting stents in patient with DM was safe with low acute complication. Patients treated with BES and EES showed lesser rate of restenosis compared with ECS.
Results: Data from 65088 patients in 2 past-hoc analyses from randomized controlled trials and 18 observational studies were included. Compared with BMS, DES were associated with significant reductions in mortality (OR, 0.86; 95% CI, 0.82 to 0.91; p < 0.0001), repeat revascularization (OR, 0.58; 95% CI, 0.46 to 0.73; p < 0.0001), MI (OR, 0.85; 95% CI, 0.79 to 0.92; p < 0.0001), and MACE (OR, 0.61; 95% CI, 0.49 to 0.76; p < 0.0001). Subgroup analysis showed that the benefit of DES versus BMS was restricted to unadjusted, retrospective observational studies, and studies with short-term follow-up period (<2 year). No difference in the likelihood of stent thrombosis between the two groups was observed (9.0% for DES, 0.48 to 1.71; p = 0.76).

Conclusions: Use of DES in CKD patients is associated with reduced rates of repeat revascularization, MI and MACE without increased risk of mortality or stent thrombosis. The true effect of DES versus BMS on mortality needs to be confirmed by further investigations.

P2406

Long-term efficacy and safety of triple versus double anti-platelet therapy after coronary intervention in the drug-eluting stent era


Background: There is a paucity of data regarding the impact of adding cilostazol to dual anti-platelet therapy on the clinical outcomes after coronary intervention. We sought to compare long-term efficacy and safety of triple anti-platelet therapy (TAPT) versus double anti-platelet therapy (DAPT) in patients undergoing DES implantation for coronary bifurcation lesions.

Methods and Results: We evaluated 800 patients who underwent percutaneous coronary intervention (PCI) with DES for coronary bifurcation lesions with side branch diameter ≥ 2.3mm from General Institute PCI database registry between April 2003 and December 2010. TAPT was defined as the addition of cilostazol for at least 3 months to conventional DAPT after PCI. Patients who had been taken cilostazol for at least 3 months 1 year after PCI (n= 68), and had other anti-platelet agents or warfarin (n= 17) were excluded. The primary endpoint was major adverse cardiovascular events (MACE), defined as the composite outcomes of cardiac death, myocardial infarction and target lesion revascularization (TLR). The secondary endpoint was definite or probable stent thrombosis (ST). The safety endpoints were Thrombolysis In Myocardial Infarction (TIMI) major and minor bleeding.

Results: Compared to DAPT, TAPT was not associated with a higher incidence of CIN and the secondary end point was the peak increase of serum creatinine (SCr). The mean peak increase of SCr was 0.5 mg/dL for ALA and placebo group (p=0.1). The mean peak increase of SCr was not different in ALA and placebo group (-0.01±0.02mg/dL vs. -0.05±0.02mg/mL, respectively (p=0.355). The SCr did not change from baseline of 1.25±mg/dL to 1.24±mg/dL (P=0.902) within 2 days in the ALA group and in the simple saline hydration group (from 1.21mg/dL to 1.16mg/dL, P=0.825).

Conclusion: We found for the first time that alpha lipoic acid as a well known antioxidant may not be beneficial in CIN prevention. This study may imply that not all antioxidants are preventive for CIN in patients undergoing coronary angiography.

P2407

Alpha-Lipoic acid for the prevention of contrast-induced nephropathy in patients undergoing coronary angiography: ALIVE study- a prospective randomized trial

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Background: N-acetylcysteine and ascorbic acid have been reported to be effective in preventing contrast induced nephropathy (CIN) after coronary angiography. However, there is a paucity of data regarding the impact of adding antioxidant- alpha lipoic acid (ALA) for prevention of CIN.

Methods: We conducted a prospective randomized controlled trial to evaluate the efficacy of ALA in CIN prevention. One hundred and sixty seven patients with renal basal insufficiency (creatinine clearance [CrCl] < 60mL/min) were randomized to have ALA for 2 days (650mg orally three times a day before and after coronary catheterizations totaling 1 day and n=80) or control (n=86). All the patients received hydration with iso-tonic saline at a rate of 1mL/kg/hour at least for 12hours before and after administration of contrast agent. Only iso- or low-osmolar contrast media were used in the procedure. The primary point was the incidence of CIN and the secondary end point was the peak increase of serum creatinine (SCr) within 2 days. CIN was defined as an increase in SCr of either ≥ 0.5 mg/dL or ≥ 25%.

Results: There were no differences in age, sex, prevalence of diabetes, prevalence of hypertension, baseline SCr, baseline left ventricular systolic function, and contrast media dose. The incidence of CIN was similar in both groups, 3.7% vs. 5.8% for ALA and placebo group (p=0.1). The mean peak increase of SCr was not different in ALA and placebo group (-0.01±0.02mg/dL vs. -0.05±0.02mg/mL, respectively (p=0.355). The SCr did not change from baseline of 1.25±mg/dL to 1.24±mg/dL (P=0.902) within 2 days in the ALA group and in the simple saline hydration group (from 1.21mg/dL to 1.16mg/dL, P=0.825).

Conclusion: We found for the first time that alpha lipoic acid as a well known antioxidant may not be beneficial in CIN prevention. This study may imply that not all antioxidants are preventive for CIN in patients undergoing coronary angiography.

P2409

Percutaneous coronary interventions (PCI) of the left main stem in clinical practice 2010: Results from the German ALKK PCI registry

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Background: Percutaneous coronary interventions (PCI) of the left main stem (LMS) is considered to be a co-primary indication for PCI for long term patients. Current evidence on clinical practice data led to paradigm change. However, there are few data on current use, patient characteristics and clinical outcome of LMS-PCI.

Methods: We analyzed data of the prospective ALKK PCI registry.

Results: In 2010 29045 PCIs in 27637 patients were included in the ALKK PCI registry from 47 hospitals. 900 (3.1%) of the PCIs were done for LMS disease: 688 (76.4%) of all unprotected LMS-PCI and 233 (6.6%) for protected LMS-PCI. The proportion of LMS-PCI per participating hospital was 2.8±1.7% of all PCIs (range: 0 – 6.9%). Patient and interventional characteristics as well as clinical results are given in detail in the table.

Conclusions: In current clinical practice of PCI in Germany 2010 3% of all PCIs were done for LMS: out of them 76% were done for unprotected and 24% for protected LMS. The proportion of LMS-PCI at the participating hospitals ranged from 0 – 6.9%. PCIs for unprotected LMS were more frequently performed in
patients with an ACS, especially during STEMI, which may be responsible for the higher mortality in these patients.

**P2410** Impact of insulin treatment on peri-procedural myocardial injury in patients undergoing elective coronary intervention

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**Background:** Insulin-treated diabetic patients were associated with worse clinical outcome after percutaneous coronary intervention (PCI) as compared to patient treated with diet or oral-hypoglycemic drugs. However association between insulin treatment and post-procedural myocardial injury (PMI) after PCI is unclear.

**Methods:** We evaluated 1111 consecutive patients who underwent elective coronary intervention (PCI) without troponin-T (TnT) elevation before procedure. Post-procedural myocardial injury (PMI) was evaluated by analysis of TnT 18 hours after PCI. PMI was defined as post-procedural TnT level of $>0.1ng/ml$ on the bases of manufacture’s statement.

**Results:** In study population, 160 (14.4%) patients were treated with insulin at the time of PCI. 509 (45.8%) diabetic patients were treated without insulin. Post-procedural TnT of patients treated with insulin was significantly higher than those of diabetic patients without insulin treatment or non-diabetic patients (0.224±0.193, 0.110±0.065 and 0.132±0.095, p<0.01 ANOVA, Figure). PMI was observed in 323 (29.1%) patients. Multiple logistic regression analysis showed that insulin treatment was independently associated with PMI after adjustment for age, gender, risk factor, chronic kidney disease, statin administration, maximum ballooning pressure, direct stenting and number of stents (OR:1.72, p=0.018).

**Conclusion:** Post-procedural TnT was significantly higher in the insulin treated diabetic patients, showing an association between insulin treatment and post-procedural myocardial injury.

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**P2412** Which drug-eluting stent is useful in Percutaneous Coronary Intervention for patients with Chronic Kidney Disease?

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**Background:** In percutaneous coronary intervention (PCI), patients with end stage renal dysfunction has had high rate of cardiovascular events. Our aim was to compare the clinical outcomes of chronic kidney disease (CKD) patients every type of drug-eluting stents (DES) after PCI.

**Methods:** 1168 consecutive patients (1582 lesions) on CKD (eGFR <60 [ml/min 1.73m²]) calculated by the simplified Modification of Diet in Renal Disease equation were treated with sirolimus-eluting stent (S group: 763 lesions), paclitaxel-eluting stent (P group: 467 lesions), zotarolimus-eluting stent (Z group: 143 lesions) or everolimus-eluting stent (E group: 209 lesions) implantation between April 2007 and December 2010, and were follow up to 8 months. The primary endpoints were angiographic outcomes and MACE (death, AMI, CABG, target lesion revascularization: TLR). For statistical analysis, chi-square test and ANOVA were used. No significant difference was detected in the baseline demographic, angiographic and lesion characteristics. In 8 months follow up, the mean values of late loss were significantly lower in the E group (0.1±0.6mm) than other group (S group: 0.3±0.6mm, P group: 0.4±0.7mm, Z group: 0.6±0.7mm, P=0.001). TLR was significantly lower in the E group (S group: 4.1%, P group: 7.1%, Z group: 6.3%, E group: 1.9%; p=0.02). However no significant difference was detected in MACE (S group: 5.5%, P group: 7.7%, Z group: 7.7%, E group: 2.9%).

**Conclusion:** EES implantation improved the TLR with influence of CKD, however clinical outcomes of CKD patients were similar in every type of DES implantation.
Effects of oral contraceptive usage on angiographic outcomes and in-hospital mortality in patients undergoing primary percutaneous coronary intervention (p-PCI)

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Purpose: Although the association between oral contraceptives (OC) and the risk of ST-segment elevation myocardial infarction (STEMI) has been intensively studied in literature, and conclusions are controversial; there is no data about clinical prognosis of STEMI occurred during OC usage.

Methods: 1637 patients in 30 months period admitted to our hospital emergency service within first 12 hours of chest pain and undergone primary percutaneous coronary intervention (p-PCI) were our study population. Patients were divided in two groups according to OC usage, OC user (n=12), OC non-user (n=1528).

Results: Inflammatory markers were higher in OC-user group: CRP (13.7±13 vs. 25.9±20.3, p<0.001), BNP (121±145.4 vs 229.1±235.3, p<0.003). In OC-user group angiographic outcomes were worse; high grade thrombus burden ratio [67% (41.8% vs 9 (7.5%)] (p<0.001), no-reflow ratio [192 (11.8%) vs 4 (33.3%), Left ventricular ejection fraction was lower in OC-user group (47±8 vs 40±9, p<0.011). In-hospital mortality and congestive heart failure were higher in OC-user group (0.097 vs 0.031, respectively, P<0.001).

Conclusion: The severity of renal dysfunction impacted on neointimal proliferation after SES implantation, but not after EES implantation. Further study should be warranted to evaluate the angiographic effect of EES in patients with renal dysfunction.

Reduction in mortality from thrombin inhibition in CHF patients: results from the premier hospital database

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Background: Patients with congestive heart failure (CHF) in the ACS setting may be particularly susceptible to the pro-apoptotic effect of thrombin. Thrombin inhibition has been shown to reduce infarct size and improve myocardial contractile function in animal models of ischemic injury. We therefore hypothesized that thrombin inhibition would be associated with improved outcomes among ACS patients with CHF who underwent PCI.

Methods: Within the PREMIER Hospital Database (PHD), between 2004-2010, there were 489,919 ACS adult patients (pts) who underwent PCI and received either bivalirudin alone or heparin with GP2b/3a inhibition during index PCI; only pts with an ICD-9 code for CHF (428.XX) were included in the analysis (n=69,421). Chi-square tests were used to compare in-hospital clinical outcomes in observed and propensity-score matched samples.

Results: Among PCI patients with CHF, those who received bivalirudin vs. heparin + GP2b/3a were older and less likely to be male or present with STEMI. The unadjusted rate of all-cause in-hospital death was 2.2% in the bivalirudin alone group vs. 6.1% in the heparin + GP2b/3a group (OR 3.6, p<0.001). After propensity score matching, administration of bivalirudin was associated with a 37% RRR in mortality (2.7% vs 4.3%, p<0.001). Patients in the bivalirudin group had a significantly lower rate of clinically apparent bleeding (8.4% vs. 14.6%, p<0.001) and were less likely to require a transfusion (7.5% vs. 13.8%, p<0.001).

Conclusion: Among patients with CHF in the PREMIER hospital database, direct thrombin inhibition with bivalirudin during PCI was associated with significantly lower mortality and bleeding compared to heparin + GP2b/3a treatment. Further studies are needed to confirm the benefits of thrombin inhibition, which may minimize reperfusion injury and apoptosis, among patients with CHF.
quires endless patience from the cardiologist. There is no need to abuse the resources of the cath lab if we follow the protocol of TO BELIEVERs. Excellent results can be obtained if CTO intervention done by using these basic equipments.

**P2418**
The effect of drug-eluting stents on clinical and angiographic outcomes in renal failure patients with dialysis: multicenter registry in Asia

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**Background:** Patients treated with renal failure have been reported having high incidence of mortality and other complications rate after PCI. Optimal treatment of PCI for renal failure patients with dialysis is still unknown. Aim: The aim of this study is to compare the safety and efficacy of Sirolimus (SES), Paclitaxel (PES), EPC capture (ECS), Zotarolimus (ZES-R/Endeavor Resolute), BiolimusA9 (BES) and Everolimus-eluting stent (EES) on the outcome of percutaneous coronary intervention in renal failure patients with dialysis (CRF-HD).

**Methods:** A prospective analysis of 1013 patients with CRF-HD (258 SES, 244 PES, 77 EPC, 118 ZES-R, 128 BES, 188 EES) in six high volume Asian centers after successful stenting was performed. The study endpoints were 30 days major adverse cardiac events (MACE) and 12, 24 and 36 months target lesion revascularization (TLR) and MACE.

**Results:** The baseline clinical characteristics between 5 groups were similar. See table for clinical results.

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<tr>
<th></th>
<th>SES</th>
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</table>

*p<0.05 vs. SES, ECS, ZES-R and BES.

**Conclusion:** The use of drug-eluting stents in patient with CRF-HD was safe with low acute complication. Patients treated with PES and EES showed lesser incidence of restenosis rate and TLR compared with other drug-eluting stents.

**P2419**
The impact of bifurcation stenting strategy on health related functional status - a quality of life analysis from the BBC ONE trial

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**Purpose:** Several studies have compared simple versus complex bifurcation stent techniques, with regard to MACCE outcomes and angiographic follow-up. However another key goal of stenting is symptom control and improvement in functional status. There is a lack of published data comparing results from different bifurcation techniques in this respect. Here, we report the findings of the prospectively collected quality of life data from the BBC ONE trial.

**Methods:** The BBC ONE trial randomized 500 patients with bifurcation lesions to simple (provisional T) versus complex (crush or culotte) treatments. Study subjects completed a 19-item Seattle Angina Questionnaire (SAQ) at baseline, 6-month and 12-month follow-up. Data was analyzed using Mann-Whitney testing to compare scores between groups at each time point. Chi-Square testing was used to compare the groups in terms of proportions of patients changing scores over the follow-up period.

**Results:** There was no significant difference between the overall Simple and Complex stent strategy groups with regard to baseline scores on any of the 5 scales of the SAQ.

At follow-up, there was no significant difference in the overall scores on any of the scales between the simple and complex groups.

**Conclusion:** Elderly patients who underwent PCI experienced similar improvement in quality of life comparable to younger patients. Our findings suggest that age per se should not deter against revascularization because of potential benefits in quality of life.
Does murray's law apply to all types of bifurcation lesions treated with provisional side-branch stenting?

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Purpose: In relation to bifurcation lesions, the Finet-Murray's law postulates that proximal segment = 0.678 (distal segment + side branch). According to this law, proximal stent non apposition would occur in all patients in whom stent size is selected according to bifurcation distal reference diameter. This hypothesis however, has not been tested in "in vivo". The aim of this study was to analyse the practical implication of this law and to determine the need for systematic proximal main vessel stent post-dilation.

Methods: We analysed 132 patients (61±11 year old) with all types of Medina bifurcation lesions treated by provisional stenting in whom an intravascular ultrasound study (IVUS) was available after main vessel stent implantation. The stent diameter was selected according to the distal reference segment. In all patients, an IVUS pull back was performed at the main vessel stent from distal to proximal arterial reference segment. Measurements were obtained at the distal edge, immediately under the side branch origin and at the proximal segment. Proximal stent non apposition was defined as the lack of contact at any site between stent struts and the arterial wall.

Results: Proximal stent non apposition was observed in 54 patients (41%), requiring an additional proximal post-dilation. Parasidically, full apposition was found in the remaining 78 patients (59%). Non apposition was more frequent in large vessels as determined by IVUS (proximal reference lumen area 10.75±3.75 vs 8.24±2.47 mm², p<0.01; distal reference lumen area 6.71±2.74 vs 5.51±1.82 mm², p<0.01). These findings were confirmed by angiography (mean distal reference diameter 3.34±0.58 mm vs 3.03±0.41 mm, p<0.05; side branch diameter 2.51±0.33 mm vs 2.35±0.28, p<0.05). Left main bifurcation lesions showed a higher rate of non apposition than other bifurcations (65% vs 37%, p<0.05). Patients were followed up during a mean of 14 months. The incidence of major cardiac events was similar among patients with initial full stent apposition (no proximal post-dilation) and those who required additional balloon post-dilation (5% vs 6%, p=ns).

Conclusions: Finet-Murray's law has a low clinical impact on some patients with bifurcations lesions treated by provisional side branch stenting. This fact is more evident in bifurcation lesions located in smaller vessels. Proximal vessel post-dilation was not necessary to obtain good stent apposition in more than 50% of the studied patients.

In the absence of recommendations: angioplasty of the culprit lesion or multivessel angioplasty in acute myocardial infarction with ST segment elevation?

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The approach of multivessel (MV) coronary artery disease (CAD) in the primary angioplasty (PCI) in patients (pt) with acute myocardial infarction (AMI) with ST elevation (STEMI) remains unclear on the international recommendations.

Purpose: To evaluate the impact of primary PCI of the culprit lesion or MV angioplasty on in-hospital morbidity and mortality of pt with STEMI.

Methods: Between October 1, 2010, and October 1, 2011, 1336 pt with STEMI were included in a national multicenter registry;we studied 399 pt undergoing coronary intervention (PCI) in patients with STEMI may be undersized, and associated with stent malaposition and a stent thrombosis. The aim of the study was to evaluate the changes of reference vessel diameter (RVD) of the infarct-related artery (IRA) before (Pre-PCI), immediate after (post-PCI), and at follow-up by Quantitative Coronary Analysis (QCA).

Methods: We studied 307 STEMI patients (231 men, 64±13 years) who had a complete QCA data in pre-PCI and immediate post-PCI, and 163 patients who underwent PCI of the IRA before PCI (Pre-PCI, post-PCI, and 1 year follow-up).

Results: The RVD increased from pre-PCI to post-PCI (5.16±0.44 mm; p<0.0001) and maintained from post-PCI to follow-up (3.17±0.42 mm; p<0.05). The RVD at before PCI was smaller than the RVD at follow-up in significance (p<0.0001). These findings showed similar tendency with the result of each coronary arteries (Figure 1).

Conclusion: RVD changed significantly from pre-PCI to immediate post-PCI and follow-up in patients with STEMI. Especially, RVD of IRA in pre-PCI was smaller than that in post-PCI and follow-up. Therefore, when operators choose a stent or balloon catheter, they should consider that actual RVD may become enlarged as time goes on.
A novel non-polymeric ciglitazone-eluting stent inhibits neointimal proliferation stronger than the Xience V stent: an experimental study using optical coherence tomography in rabbit iliac arteries

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Background: The benefit of drug-eluting stents (DES) to cut restenosis is partially offset by delayed endothelial healing, due in part to polymer resorption. Nonpolymeric local drug delivery might improve safety and efficacy of newer DES. Optical coherence tomography (OCT) is a high-resolution intravascular imaging technique that accurately distinguishes structures of the arterial wall and stent struts, allowing to precisely quantify neointimal proliferation. We investigated ciglitazone, a peroxisome proliferator-activated receptor-gamma agonist as a novel stent coating.

Methods: Non-polymeric ciglitazone-eluting stents (CDES) were produced by coating bare metal stent (2.5x12 mm micro porous Yukon Choice, Translumina) with ciglitazone at a drug load of 39 mcg/mm stent length. As a comparator we used commercially available everolimus-eluting stents (EES): 2.5x12 mm Xience V, Abbott Vascular. Thirteen NZW rabbits, fed with high cholesterol diet, underwent DES implantation in both common iliac arteries (left: CES, right: EES). The stents were imaged in vivo using OCT and postmortem by Elastica-van-Gieson staining. At 5 days, the study stent showed partial EC with a mean strut coverage of 46.3±1% which was lower than the historic control at 85.5±5% (p=0.02). The endothelium overlying the struts showed extensive leukocyte adhesion, while the struts not covered by endothelium often showed vasa vasorum giant cells. At 28 days, a time point associated with 100% endothelialization in historic controls, the study stent struts were still incompletely covered and showed approximately 90% endothelial coverage with small areas devoid of endothelium as well as areas with poor cell-cell contact and leukocytes adhesion. At 90 days the struts were completely covered by an endothelium with distinct cell-cell borders and only scarce impaired cell-cell contact, although we did observe continuous inflammatory response at either time point. Morphometry at 28 days shows a similar IH between the study stent and the historic controls (219±37 μm vs. 210±17 μm, p=0.6). At 90 days IH remained stable in the study stent with 238±47 μm. However, the historic control showed regression of IH to 185±31 μm (p=0.04). When using regression analysis for IH (using acute gain, B/A ratio, stent, injury score and follow-up time as workload parameters) there was no statistical significance between stent types.

Conclusion: Delayed EC, an indicator of delayed healing, does not negatively affect maximal intimal thickening in a porcine coronary model. This data questions the hypothesis that improved EC reduces restenosis.

Neither presence nor absence of post PCI endothelium affects intimal thickness, a surrogate for restenosis

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Delayed endothelialization (EC) in bare metal stents (BMS) is associated with increased intimal hyperplasia (IH). Hence, accelerating EC by, for example, promoting the survival of some residual or newly generated positive cells (GENOUS), was thought to decrease IH and thus restenosis. This approach however, was found to be unsuccessful. We aimed to assess whether delayed EC as seen in a BMS (suboptimal surface, not via denudation) would increase IH at 28 days, traditionally seen as the time point of maximal thickness in preclinical models (in BMS), and at 90 days (possible IH regression).

Methods & Results: Experiments were performed in Yorkshire swine according to standard clinical protocol. All stents were placed with a balloon-artery ratio of 1.1. At 5 days (early endothelialization; n=8), 28 days (maximal IH; n=14) and 90 days follow-up (n=6; completed healing, IH stabilization), arteries were harvested and prepared for scanning electron microscopy (SEM) followed by histology and morphometry. Data were compared to clinical grade historic BMS controls also at 5 (n=5), 28 (n=5) and 90 days (n=6). Six weeks after DES implantation, the d/m-ratio in the proximal, stented, and distal part were resp.: 1.722±0.119 (p proximal vs. distal and stented part are resp. 0.030 and 0.029). The endothelium overlying the struts showed extensive leukocyte adhesion, while the struts not covered by endothelium often showed vasa vasorum giant cells. At 28 days, a time point associated with 100% endothelialization in historic controls, the study stent struts were still incompletely covered and showed approximately 90% endothelial coverage with small areas devoid of endothelium as well as areas with poor cell-cell contact and leukocytes adhesion. At 90 days the struts were completely covered by an endothelium with distinct cell-cell borders and only scarce impaired cell-cell contact, although we did observe continuous inflammatory response at either time point. Morphometry at 28 days shows a similar IH between the study stent and the historic controls (219±37 μm vs. 210±17 μm, p=0.6). At 90 days IH remained stable in the study stent with 238±47 μm. However, the historic control showed regression of IH to 185±31 μm (p=0.04). When using regression analysis for IH (using acute gain, B/A ratio, stent, injury score and follow-up time as workload parameters) there was no statistical significance between stent types.

Conclusion: Delayed EC, an indicator of delayed healing, does not negatively affect maximal intimal thickening in a porcine coronary model. This data questions the hypothesis that improved EC reduces restenosis.

Purpose: Drug eluting stents (DES), especially first-generation DES, have been associated with abnormal coronary vasomotor function as compared with bare metal stents (BMS), being the suggested cause the reduced expression of endothelial nitric oxide synthase (eNOS) observed in immature endothelium. The objective of this study is to analyse the relationship between the morphological and functional characteristics of the endothelium after BMS and DES implantation and the vasomotor response to endothelium-dependent drugs.

Methods: In 18 domestic juvenile swine (25±3 kg), one stent per coronary artery was implanted with an intended stent-to-artery ratio of 1.1 to 1.2. We used 18 stainless-steel BMS, 18 paclitaxel eluting stents (PES), 9 siamstatin+ paclitaxel eluting stents (SpES) and 9 balloon eluting stents (BES). Quantitative coronary angiography was performed after 28 days to assess the vasomotor response measuring the vessel diameter distal to the stent after intraocular infusion of Acetylcholine 10-6M as compared with basal status. Morphometric analyses of the neointimal hyperplasia (hyperplasia in-artery wall: circumferential extent of luminal surface coverage with flattened, confluent endothelial cells) and eNOS expression (percentage of endothelial cells positively immuno-stained) were calculated at 90° from each stent sample. The neointimal hyperplasia index measures the proportion of the whole luminal surface covered by eNOS+ endothelial cells.

Results: The vasomotor responses were significantly different among stents: change in diameter, BMS +3% (SD 9), PES +2% (SD 12), BES +6% (SD 10), (p=0.04). The eNOS+ endothelialisation indexes were also significantly different among groups: BMS 88% (SD 8), PES 78% (SD 11), SpES 76% (SD 7), BES 94% (SD 3), (p=0.0001).

Conclusions: The paclitaxel eluting stents used in this normal coronary arteries swine model showed impaired 28 days after the implantation. This fact can be revealed either as an abnormal coronary vasomotor function as well as loss of functional endothelialisation. Nonetheless, the association between histological and vasomotor findings is very weak, raising the chance of different causal mechanisms other than eNOS reduced activity.

Effect of paclitaxel-eluting balloon on physiologic vasodilatory capacity of porcine peripheral arteries, combined with safety and efficacy preclinical studies M. Gyongyosi1, I. Sabbyushaev1, V. Lamin1, N. Pavo1,2, E. Szentirmai2, O. Petnehazy2, Z. Petrasz2, C. Plas1, G. Maurer1,2

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Purpose: Drug eluting balloon (DEB) prevents neointimal hyperplasia in coronary arteries. In contrast to the muscular type coronary vessels, the peripheral (iliac and iliac) arteries are large elastic arteries, differing from coronary arteries in size, relative composition of elastic and muscle tissue and by physiologic functional properties. The present study was conducted to prove the safety and efficacy of the paclitaxel (PTX)-coated peripheral periphereal percutaneously balloon expandable FREENWAY (Euroco, Germany) in prevention of neointimal hyperplasia and to investigate the vasomotor response of the peripheral arteries to DEB in comparison with plain balloon use.

Methods: Twenty-six domestic pigs underwent percutaneous FREENWAY overstretch balloon dilation (1.31 balloon/artery ratio) for 1 min of both iliac (balloon 6-7 mm of size, 40 mm of length) and femoral (balloon 5-6 mm of size, 40 mm of length) arteries using carotid access. Measurements of tissue PTX concentration (preclinical safety study) were performed by harvesting of the dilated arteries at 15 min, 1h, 3 and 9 days follow-up (FUP). The development of neointimal hyperplasia in peripheral arteries was assessed in a randomized pre-clinical efficacy study. The vasomotor response of the iliac and femoral arteries was determined after 5h, 1, 3 and 7 days. During the FUP, the animals were treated with propofol and aspirin.

Results: The achieved tissue PTX concentration showed a significant correlation with the applied balloon inflation pressure 1h post delivery in femoral arteries (r=0.597, p=0.05). The tissue PTX concentration was 433±122, 185±20, 4±0.1 and 1.4±0.5 µg/ig in iliac, and 131±260, 54±8, 30±6 and 5.2±1.7 µg/ig in femoral arteries at 15min, 1h, 3 days and 9 days post-dilation, respectively. The injury score was similar in all arteries. The degree of neointima was small in peripheral arteries after overstretch injury, but the difference in neointimal area was significant: 2.4±0.03 vs 1.51±0.48 mm² in femoral arteries and 0.62±0.24 vs 1.21±0.04 mm² in iliac arteries treated with FREENWAY or plain balloon, respectively. In contrast to coronary arteries, use of DEB did not lead to addition to vasconstriction of the vessels, and no difference between the FREENWAY and plain balloon was observed regarding the impaired endothelium-dependent vasodilation capacity post-intervention.

Conclusions: FREENWAY DEB reduces effectively the neointimal hyperplasia in peripheral (iliac and femoral) arteries, and does not lead to worse vasodilatory capacity as compared to plain balloon.


Purpose: The ISAR-REACT-4 clinical trial patients undergoing PCI for non-ST-segment myocardial infarction demonstrated that antiaggregation with abciximab plus unfractionated heparin did not confer any advantage in comparison to bivalirudin but was associated with an increased overall risk of bleeding. The interaction of anti-thrombotic therapy with patient age was not fully scrutinised and it remains unclear if any age group is subject to an increased risk.

Methods: The cohort of patients from the ISAR-REACT-4 - a clinical trial comparing anti-thrombotic therapy with abciximab plus unfractionated heparin with bivalirudin - were divided into quartile groups according to age (Q1 n=426; Q2 n=431; Q3 n=427; Q4 n=437) and outcomes compared. The primary end-point was the composite of death, large recurrent MI, urgent target vessel revascularization (TVR) or major bleeding within 30 days. The secondary endpoints comprised cardiovascular death, any recurrent ischemic events or TVR (efficacy endpoint) and major bleeding (safety endpoint) within 30 days.

Results: 1721 patients were analysed. The primary clinical endpoint occurred in 11.8% vs 11.2% in Q1 and Q3, 12.3% vs 12.3% in Q2 and 11.0% vs 12.4% in Q4 in patients treated with abciximab and heparin or bivalirudin respectively. There was no overall interaction between age and occurrence of the primary endpoint (P=0.4) for either therapy. There was an interaction between age and clinical outcome for the secondary efficacy endpoint (P=0.84) or for the primary safety endpoint (P=0.59) (Figure 1).

The GPVI-Fc fusion protein reveapct improves atherosclerosis and reduces thrombus formation in vivo M. Ungerer1, Z.M. Li1, C. Baumgartner1, S. Wagner1, H.P. Holhoff1, M. Gawaz2, G. Muech1, C. Zimmerm GmbH, Martinsried, Germany; 2Medical Clinic III, University of Tuebingen, Tuebingen, Germany

Background: GPVI is a key platelet receptor mediating plaque-induced platelet activation, and consecutive atherothrombosis, but GPVI is also involved in platelet-mediated atheroprogession. Various options to interfere with GPVI mediated platelet activation can be conceived. An ideal imagined anti-thrombotic agent would combine optimal potency, specificity and safety especially regarding bleeding complications. Methods and Results: We investigated the effects of the soluble GPVI receptor, Reveapct, an antagonist of collagen-mediated platelet activation, in a relevant animal model of atherosclerosis: Revasive (8 mg/kg) was given twice weekly for 4 weeks and compared to a Fc only control group in twenty week old rabbits fed a cholesterol-rich diet for 8 weeks. Pharmacokinetics indicated a slight accumu-

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Impaired production of anti-atherosclerotic interleukin-10 by coronary intraplaque hemorrhage in patients with acute coronary syndrome and early diabetes

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Background: In 50 ACS patients, atherothrombotic debris was retrieved during primary PCI with filter-based distal protection device (Filter). The debris was stained with antibodies to CD163, CD14 (a proinflammatory macrophage marker), CD20 (a B cell marker), and IL-10. Based on the level of glycated Hb (HbA1c(NGSP) -6.5%) and insulin resistance (HOMA-IR -2.5), Pts were divided into 18 diabetes (DM), 13 non-diabetes with insulin resistance (IR) and 19 normals (NR).

Results: Compared to NR (8.7±8.3%), GSP staining were increased significantly in DM (21.0±15.2%, p<0.05), but not significantly in IR (14.7±10.6%). Compared to NR (10.7±7.9%), CD14 macrophages were increased in DM (38.9±21.6, p<0.05) and in IR (18.4±7.3, p<0.05), and all three groups contained similar amount of IL-10 staining (DM: 45.4±24.0%, IR: 52.0±25.4%, NR: 43.5±32.7%). IL-10/CD163 ratio were significantly decreased in DM (15.1±1.0, p<0.05) and IR (15.6±1.0, p<0.05), compared to NR (11.8±1.3, p<0.01).

Conclusions: Coronary IPH was frequent in ACS with DM. Proinflammatory macrophage accumulation were exaggerated in patients with DM and even with IR, but IL-10/scavenging macrophage accumulation were not different among the three groups. Anti-atherosclerotic IL-10 production by Hb scavenging macrophages were impaired in patients with DM and even in those with IR. These findings may explain underlying mechanism of coronary plaque progression in early diabetic patients.

Serum and carotid plaque lesion are major determinants of a stable plaque phenotype, insights from the OPAL study

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Purpose: The links between human and atherosclerotic carotid plaque phenotype and related symptomatology remain unclear. In the present study, we examined this relationship in patients with carotid atherosclerosis.

Methods: One hundred and forty six consecutive patients scheduled for carotid endarterectomy were included in the OPAL study and underwent blood and plaque sampling. Plaque-related symptoms (recent history of stroke or transient ischemic attack) were recorded for each patient. 75 were classified as symptomatic and 30 asymptomatic.

Results: Plaque and blood biomarkers (basal, 6 months) were measured at the beginning of the study. The patients were divided into two groups according to the presence or absence of symptoms (symptomatic (n=75) vs asymptomatic (n=30)). VSMC content, VSMC proliferation rates, and ERK1/2 activation were assessed using paraffin-embedded plaques and peripheral blood mononuclear cell cultures.

Conclusions: Increased plaque vascularity and inflammation contribute to plaque instability and vulnerability.

Coronary intraplaque hemorrhage (IPH) accelerates atherosclerosis by both US (GSM) and HR-MRI allows a better “in vivo” and non-invasive insight into the evolution of the atherosclerotic plaque burden and its vulnerability.

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Background: It has been previously demonstrated that patients with increasing carotid echolucency quantified by decreasing gray-scale median (GSM) lesion and negative plaque remodeling as assessed by high-resolution plaque magnetic resonance imaging (HR-MRI) are at high risk for midterm major adverse cardiovascular events. The relation between “in vivo” non-invasive quantitative assessment of plaque instability with GSM analysis and plaque/vessel geometry evaluation as assessed by HR-MRI has not been investigated so far.

Objective: To evaluate plaque stability by GSM values variations of carotid plaques, at repeated carotid ultrasound (US) examinations, in relation to quantitative variations in carotid arterial geometry assessed by high spatial resolution magnetic resonance imaging (HR-MRI).

Methods: We performed an echographic evaluation with GSM analysis and a HR-MRI at the level of carotid arteries at baseline and at 1 and 2 year follow-up in a cohort of 30 patients (mean age 68.5±8.8 females) with mild-to-moderate carotid atherosclerosis and with high Framingham general cardiovascular disease 10-year risk score, on standard medical therapy. The changes on GSM levels were evaluated as the difference between the 2 years values and the baseline ones. HR-MRI studies were evaluated in consensus reading by two experienced readers for lumen area (LA), total vessel area (TVa) and vessel wall area (VWA= TVa - LA).

Results: Increasing echolucency plaques in the lower tertile of GSM values distribution (quantified by GSM decrease) and activation of ERK signaling pathway mediating GSM proliferation (pERK/total ERK ratio).

Conclusions: The tissue characteristics of coronary plaque with microchannel structure in patients with Coronary Artery Disease assessed by OCT and IB-IVUS

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Background: Assessment of the coronary plaque composition has recently become possible using high-resolution imaging modalities. Integrated backscatter intravascular ultrasound (IB-US) provides histological informations, and optical coherence tomography (OCT) does detailed microstructural informations such as microchannels. However, relation of microchannels to tissue characteristics of coronary plaque is not known.

Methods: A total of 29 consecutive patients with coronary artery disease were studied. Diagnostic OCT images of coronary plaques were obtained 2 times in each patient. Histological images were obtained during IB-US imaging and OCT. The presence and characteristics of microchannels were assessed.

Results: Lipid volume was significantly larger in the microchannel group than in the no-microchannel group on IB image analyses (57.5±8.3 vs 35.3±6.8%, p<0.05). Fibrous tissue was significantly smaller in the microchannel group than in the no-microchannel group (38.7±6.8 vs 68.2±5.8%, p<0.005). In the microchannel group, both lipid volume and fibrous tissue were significantly lower than in the no-microchannel group.

Conclusions: These results demonstrate, for the first time, that serum and carotid plaque levels of leptin are significantly associated with more stable plaque characteristics and less related symptoms. Moreover, serum and plaque leptin are related to plaque VSMC proliferation, providing a mechanism for the observed association with a more stable plaque phenotype.
Mechanism of no-reflow phenomenon induced by stent deployment in thin cap fibroatheroma area in acute coronary syndrome: histological evaluation


Purpose: It has been reported that post-stenting no-reflow is associated with thin cap fibroatheroma defined by virtual histology-intravascular ultrasound (VH-IVUS) in patients with acute coronary syndrome (ACS), however it is unclear why stent deployment of VH-TCFA can induce no-reflow phenomenon. To clarify the above-mentioned mechanism, we examined the correlation between stenting in VH-TCFA area and histology of retrieved material using filter and thrombectomy in ACS.

Methods: Seventy-three consecutive ACS patients who received VH-IVUS-guided coronary intervention with distal protection filter device and thrombectomy were enrolled. We divided our patients into VH-TCFA group in which VH-TCFA was found before stent deployment and non VH-TCFA group in which VH-TCFA was not found. We compared the incidence of filter no-reflow (FNR), histology of retrieved material between the two groups.

Results: The incidence of FNR and atheromatous substances in the retrieved material was significantly higher in VH-TCFA group than non VH-TCFA group (45% vs 0%, p=0.01). The incidence of FNR was to induce FNR more frequently than only fibrinous clot or thrombus. After removing the filter, no patients show slow or no-reflow phenomenon.

Conclusions: VH-TCFA area is associated with the presence of atheromatous substances which can induce no-reflow phenomenon. The filter protection device should be used if VH-TCFA is found before stenting.

Insulin resistance is associated with coronary plaque vulnerability: an Optical Coherence Tomography study

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Purpose: Recent studies have reported that hyperinsulinemia have an important role in progression of atherosclerosis. There are no reports about relationship between insulin resistance (IR) and coronary plaque instability. The aim of this study was to evaluate the association between IR and coronary plaque characteristics identified by optical coherence tomography (OCT).

Methods: This study included 30 patients undergoing percutaneous coronary intervention. OCT was performed in the most diseased 20-mm segment around the culprit lesions. We assessed lipid-rich plaque (>2 quadrants), calcification, minimum fibrous cap thickness, frequency of thin-cap fibroatheroma (TCFA) and ruptured plaque identified by OCT. IR was defined as the homeostasis model assessment of insulin resistance (HOMA-IR). We compared plaque characteristics according to clinical variables including IR, HbA1c and other coronary risk factors.

Results: There were no significant differences in the presence of lipid-rich plaque and calcified plaque between IR group (HOMA-IR ≥2.5, n=17) and normal group (HOMA-IR <2.5, n=13). IR group showed thinner minimum fibrous cap thickness (86.1±41.8 μm vs 106.5±34.2 μm, p=0.029) and higher frequency of TCFA (21.6% vs 58.8%, p=0.007). Regarding other clinical variables including HbA1c, there were no significant differences in these plaque characteristics.

Conclusions: This study suggests that IR may be a contributing factor for plaque vulnerability compared with diabetes severity.

Clinical and angiographic predictors of neointimal rupture as a culprit for very late stent thrombosis. Insights from optical coherence tomography


Purpose: Recent investigations have suggested neointimal rupture as a mecha-

rism for very late stent thrombosis (VLST). However, the incidence and predictors of this entity have not been described in detail. We investigated by frequency do-
minal optical coherence tomography (OCT) the incidence and predictors of neo-
timal rupture as a culprit for thrombosis in patients with VLST.

Methods: We included 29 patients undergoing cardiac catheterization from 1/1/2009 to 31/1/2012 with VLST, in whom OCT was performed in the culprit stented segment following thrombus aspiration. Demographic and clinical data were collected retrospectively. Neointimal rupture was identified as a fibrinous cap disruption with cavity formation inside the stent and adjacent thrombus.

Results: Median interval from initial implantation was 5.5 years (range 2-16). There were 14 culprit stents in the LAD, 1 in the LCx and 14 in the RCA. Analysis of OCT images revealed 14 cases with VLST due to neointimal rupture. There were also 2 cases with atheromatous plaque rupture at the stent edge. Factors significantly associated with neointimal rupture as a cause for VLST were interval from initial implantation (OR 1.41; p<0.05) and family history of coronary disease (OR 0.19; p<0.05) (Table).

Conclusions: Neointimal rupture is a frequent cause of VLST and is more common in long intervals since implantation and in patients without family history of coronary disease.

Comparison of no-reflow incidence with angiographic and cardiovascular magnetic resonance criteria

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Introduction: No reflow (NR) is the inability of a previously ischemic region to be reperfused despite patency of the culprit coronary artery. It is more frequently observed after ST-segment elevation myocardial infarction (STEMI) with an inci-
dence ranging between 10 and 50% depending on how it is assessed. Here we report the preliminary data of an ongoing prospective study to ascertain the incidence of NR in STEMI based on angiographic and cardiovascular magnetic resonance (CMR) criteria.

Methods: We enrolled 125 consecutive STEMI patients within 12 hours of symp-
toms onset who underwent primary percutaneous coronary intervention (PCI). Angiographic criteria of NR were TIMI flow grade <3 and/or blush grade <2. The CMR (Philips Medical Systems 1.5 T) criterion of NR was the presence of microvascular obstruction (MVO). The myocardial salvage index (MSI) was calculated as area at risk (AAR) - late gadolinium enhancement (LGE) area/AAR.

Results: For patients (Group B) had NR based on angiographic criteria (TIMI flow grade <3 and two myocardial blush grade <2 - in two). The AAR was comparable (34.7±% vs 29.4±% of LV mass) between Group B patients and those without angiographic NR (Group A). All Group B patients had evidence of early or late MVO whilst the latter was evident in 8/25 (32.5%) of Group A patients. The ratio of MVO area/AAR was significantly higher in Group B (17.4±% vs. 7.1±% for Group A). The MSI was lower in Group B (43 ±14.0% vs 25 ±18.1%, p=0.05) and was always concurrent with MVO. The LGE area was similar in patients of Group B and A (26.3±3 mm² vs. 25.0±10 mm²). LGE was transmural in 3/4 (75%) patients in Group B and 5/8 (62.5%) patients in Group A. In Group A there was a greater MSI compared to group B (43±14.0% vs. 25±18.1%, p=0.05). Only one patient with evidence of MVO had an MSI >50% whereas all patients without MVO had MSI >50%. Early and late MVO were inversely related to left ventricular ejection fraction at CMR (r = -0.629, p = 0.029 and r = -0.838, p = 0.001, respectively). Post-PCI final TIMI flow grade was inversely related to the area of early MVO (r = -0.899, p < 0.0001) and to the MVO/AAR ratio (r = 0.785, p = 0.002).

Conclusion: These preliminary data seem to indicate that the CMR changes ob-
served in STEMI patients meeting the angiographic criteria of NR occur also in some of the patients who do not meet the angiographic criteria of NR. Future follow up data will indicate whether these CMR signs have an independent prog-
nostic value.
Percutaneous coronary intervention mobilizes vascular resident CD34+CD45- cells directly through mechanical vascular injury

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Background: The pathophysiological significance of circulating CD34+CD45- cells is unknown, however they are increased in association with coronary atheroma burden. We assessed the behaviour of CD34+CD45- cells in response to discrete vascular injury during percutaneous coronary intervention (PCI).

Methods and results: Using flow cytometry we quantified circulating CD34+CD45- cells, in addition to traditional CD34+VEGFR-2+ EPCs, angiogenic monocytes (CD14+VEGFR-2+Tie-2+) and intercellular adhesion molecule expression, before and during the first week following diagnostic angiography (n=13) or PCI (n=23). Vascular endothelial growth factor A (VEGF-A) and C-reactive protein (CRP) were quantified by enzyme-linked immunosorbant assays. Percutaneous coronary intervention, but not angioplasty alone, caused a neutrophilia and an increase in CRP, peaking at 24 and 48 hours respectively (P<0.002 for both). Serum VEGF-A concentration was unaffected by either procedure (P=0.2 for both), but were transiently increased six hours following PCI [median (IQR): 0.93 (0.43-1.49) versus 1.15 (0.96-2.15) x106 cells/L; P<0.01], returning to normal by 24 hours. The concentrations of traditional EPCs, CD34+ adhesion molecule expression, and angiogenic monocytes were unaffected by either procedure (P>0.1 for all).

Conclusions: PCI causes a transient release of CD34+CD45- cells into the peripheral circulation, without an increase in CD34+ adhesion molecule expression or VEGF-A production, suggesting that CD34+CD45- cells are released directly from the vessel wall following mechanical injury. Traditional putative EPCs and angiogenic monocytes are unaffected by PCI, and are unlikely to be important in the acute response to vascular injury.

P2441 High-sensitivity troponin T for earlier diagnosis of acute coronary syndrome with initially negative rapid Troponin T test - sub-analysis of HS-TnT-NET study focused on coronary angiographic findings

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Background: High-sensitivity Troponin T assay (hs-TnT) has attracted much attention in diagnosis of acute coronary syndrome (ACS). We conducted an additional analysis to predict presence of significant stenosis for percutaneous coronary intervention (PCI) in ACS.

Method: In a multi-center prospective hs-TnT-NET study, the patients with chest pain and suspected ACS were enrolled at 5 sites from Dec 2009 to Jan 2011 in Japan. The first sample was drawn at a time of enrollment (T0) at presentation. In case of which rapid TnT test at T0 was negative, second and third samples were drawn at 3 and 6 hours later enrollment. Other cardiac biomarkers (cTnT, conventional troponin I, CKMB, and H-FABP: heart-type fatty acid-binding protein) were simultaneously measured. In this subanalysis, we reviewed raw data of EKG and coronary angiogram of all patients at the core lab. ACS lesion was described as described in our study, fQRS was significantly related to infarction and myocardial infarction (STEMI) who underwent PCI. Presence or absence of IQRs on pre and post-PCI ECGs and its change by PCI were investigated. In addition, independent predictors of IQRs were also investigated. Patients with significant organic valve disease and patients having any MRI scans with MRI du- ration >120 ms as well as patients with permanent pacemakers were excluded from the study.

Results: Patients with IQRs on admission ECGs had higher leukocyte counts (p<0.001), lower CK-MB (p=0.005), increased time to balloon time (p=0.004), higher Killip score (p=0.001), prolonged QRS time (p=0.001), higher Gensini score (p=0.001) and more frequent Q waves on ECG (p=0.001) in comparison to patients who did not fragmented QRS. In addition, these patients usually had an infarction of anterior territory related to a lesion in proximal LAD and wider jeopardized myocardium (p=0.001). The number of IQRs were negatively related with percentage of total ST resolution and myocardial reperfusion score while QRS duration and the extent of coronary involvement were positively related. Both before and after PCI, patients without IQRs achieved decreased ST resolution, higher reduction in QRS duration and better myocardial reperfusion in comparison to patients with IQRs on any ECG. In multivariate analyses, presence of IQRs before and after PCI was related to wider jeopardized myocardium and infarction, but presence of IQR after PCI was not directly related to myocardial reperfusion.

Conclusion: In our study, IQRs was significantly related to infarction and myocardial reperfusion parameters before and after PCI. In the setting of STEMI, absence of IQRs on admission ECG predicted increased ST resolution, higher reduction in QRS duration and better myocardial reperfusion. IQRs may be useful in identifying patients at higher cardiac risk with larger areas of ischemic jeopardized or necrotic myocardium.

AORTIC VALVE DISEASE

P2443 Incidence, characteristics and diagnosis of prosthetic valve endocarditis after transcatheter aortic valve implantation

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Purpose: Transcatheter aortic valve implantation (TAVI) has recently developed into an accepted alternative to conventional surgery in high-risk patients with symptomatic aortic stenosis. According to only few current data, post-TAVI endocarditis seems to occur very rarely. In the present study, we will however report five cases and discuss special characteristics of prosthetic valve endocarditis (PVE) in the context of TAVI.

Methods: To assess safety and efficacy of TAVI, the first 180 consecutive patients undergoing this intervention at our institution between August 2008 and December 2010 were followed by telephone contact in 2011. During follow-up (median, 319 days), the diagnosis of suspected PVE was made more frequently than expected. We therefore verified this diagnosis by applying modified Duke criteria.

Results: TAVI-patients were characterized by a mean age of 82±5 years and long-expected. We therefore verified this diagnosis by applying modified Duke criteria. The diagnosis of suspected PVE was made more frequently than expected. Two of three deaths of post-TAVI endocarditis during follow-up. After Kaplan-Meier-analysis, this represents an estimated PVE-incidence of 3.4%.
Aortic regurgitation after TAVI can be predicted on the basis of intraprocedural hemodynamics

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Aortic regurgitation after TAVI can be predicted on the basis of intraprocedural hemodynamics

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Introduction: The importance of TAVI (transcatheter aortic valve implantation) in the management of severe aortic valve stenosis is increasing, especially in multi-morbid patients with high surgical risk (Euroscore > 20%). One of the most common shortcomings of this treatment option is post-interventional paraprosthetic regurgitation. This is currently assessed primarily by aortography after implantation of the prosthesis. This approach is limited in patients with reduced renal function.

Our hypothesis was, that the pressure difference between diastolic aortic pressure and LVEDP could equally detect aortic regurgitation and might be used to reduce nephrotoxic contrast exposure.

Methods: A total of 200 patients (age: 81.66±5.66 years, f/m:108/92) with severe aortic valve stenosis were treated by using TAVI using standard procedures in a transfemoral approach (n = 168 CoreValve, n = 32 EdwardsSAPIEN). All patients underwent an aortography, a measurement of LV pressures to determine the difference between diastolic aortic pressure and LVEDP before and after any post-dilatation of the valve. In 56 patients (n = 56) a post-dilatation of the prosthetic valve was performed because of significant paravalvular regurgitation. The pressure conditions before and after dilatation were documented and compared to the remaining aortic regurgitation as determined by aortography.

Results: By using prosthetic valve post-dilatation a significant reduction in aortic regurgitation as determined by aortography could be demonstrated, without showing any periprocedural adverse effects. Among the patients in whom the prosthetic valve was post-dilated, the mean difference between diastolic aortic pressure and LVEDP increased from 13.89±10.73 mmHg to 36.23±10.73 mmHg, p < 0.001. After post-dilatation the pressure difference between diastolic aortic pressure and LVEDP is comparable to the patients who after TAVI did not show a relevant aortic regurgitation in the aortography (mean difference 37.88±10.77 mmHg).

Summary: Post-dilatation is an effective and safe method for the reduction of aortic regurgitation after TAVI. Potentially the assessment of the pressure difference between diastolic aortic pressure and LVEDP could be sufficient to determine the severity of aortic regurgitation after TAVI.

The evaluation of aortic regurgitation by using hemodynamic data has the potential to reduce the amount of contrast agent used.

30-day mortality in patients after transfemoral Transcatheter Aortic Valve Implantation (TAVI): predictive value of EuroSCORE II as compared to EuroSCORE

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The logistic EuroSCORE is commonly used to identify high-risk or “inoperable” patients undergoing aortic valve implantation (TAVI). However, the predictive value and accuracy of the EuroSCORE is currently intensely discussed in view of TAVI and there is recent evidence for over-prediction of procedural risk in those patients. Therefore, a new model (EuroSCORE II) has been prepared to overcome these limitations. The purpose of our study is to examine the performance characteristics of EuroSCORE and EuroSCORE II with respect to predictive accuracy in high-risk patients with severe aortic valve stenosis who underwent transfemoral TAVI.

Between September 2007 and September 2011, 100 consecutive patients (female/male 68/32; mean age 82 years) in whom either a CoreValve (n=79) or an Edwards Sapien bioprosthesis (n=21) was implanted were included for analysis. Logistic EuroSCORE II and EuroSCORE II were calculated on a prospective and retrospective basis, respectively. Observed 30-day mortality of the entire cohort was 10.0%. The predicted 30-day mortality was 22.4±15.9% and 9.9±8.9% based on logistic EuroSCORE and EuroSCORE II, respectively. In patients who died within 30 days after TAVI EuroSCORE was significantly higher compared to those patients who were alive (31.9±17.1% vs. 21.3±13.5%; p = 0.02). In contrast, no significant difference was observed for EuroSCORE II between non-survivors and survivors (12.8±13.3% vs. 9.5±8.3%). Pearson coefficient revealed no correlation between both scoring systems (r = - 0.17).

In patients undergoing transfemoral TAVI, 30-day mortality is more accurately reflected by EuroSCORE II than by EuroScore. However, EuroSCORE may still play its role in identifying patients who are at the highest risk for transfemoral TAVI.

3 Predictors of prolonged hospital stay after TAVI

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Background: Transcatheter aortic valve implantation (TAVI) has become a valuable alternative to aortic valve replacement (AVR) for surgical high-risk patients with severe aortic stenosis. Due to technical improvements and increased operator experience the valve implantation success has become very high. Nevertheless, the post procedural recovery in these elderly patients is often prolonged. We aimed to evaluate clinical and demographic predictors of a prolonged hospital stay in patients undergoing TAVI.

Methods: We included 187 consecutive patients with severe aortic stenosis who underwent TAVI. The valve was implanted by transfemoral technique in 160 (86.3%), transapical in 2 (1.1%) and via the subclavian artery in 5 (2.7%) patients. We implanted 160 (85.6%) CoreValve and 27 (14.4%) Edwards Sapien prostheses.

Logistic regression was used to determine the factors affecting length of stay longer than median.

Results: Median of length of stay was 7 days. Pulmonary hypertension above 60mmHg, prior ischemic stroke, EuroSCORE II above median (5.3%) and previous cardiac surgery did not have a significant influence on the length of hospital stay (LOS). The following parameters could be identified as predictors of a hospital stay > 7 days (Table 1):

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>State of chronic renal failure ≥ 3</td>
<td>1.9</td>
<td>1.1-3.5</td>
<td>0.002</td>
</tr>
<tr>
<td>STS-Score &gt; median (5.6%)</td>
<td>2.5</td>
<td>1.4-4.5</td>
<td>0.003</td>
</tr>
<tr>
<td>EuroSCORE Log. &gt; median (14.7%)</td>
<td>1.9</td>
<td>1.1-3.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Age &gt; 85</td>
<td>2.6</td>
<td>1.3-5.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Female Gender</td>
<td>2.0</td>
<td>1.1-3.9</td>
<td>0.03</td>
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Conclusions: Age above 85, STS-Score above median (5.6%), female gender, state of chronic renal failure ≥ 3, logistic EuroSCORE above median (14.7%) but not EuroSCORE II above median (5.3%), previous cardiac surgery, pulmonary hypertension above 60mmHg and prior ischemic stroke are associated with an increased risk of prolonged hospital stay after TAVI.

Influence of concomitant coronary artery disease on clinical outcomes of patients with severe aortic stenosis undergoing transcatheter aortic valve implantation


Objectives: Coronary artery disease (CAD) is a known risk factor in patients undergoing surgical aortic valve replacement and concomitant coronary revascularization is usually performed at the time of valve surgery. Whether outcomes after transcatheter aortic valve implantation (TAVI) are also negatively impacted by the presence of CAD is unclear at present.

Methods: We retrospectively analyzed our prospective database of 281 patients undergoing TAVI using the Edwards SapienTM device via a transapical (TA, n=177), or transfemoral (TF, n=104) approach from March 2008 through September 2011. Relevant CAD was considered present if patients had undergone previous coronary artery bypass grafting or percutaneous coronary intervention or if PCI was performed in a single-stage operation immediately prior to TAVI.

Results: Relevant CAD was present in 45.6% (n=128) of the overall TAVI population and it was significantly more frequent in the TA group compared to the TF group (53.1% vs. 32.7%, p = 0.001). Overall 30-day mortality in 281 patients undergoing TA- or TF-AVI was 0.4%. Patients with CAD had a higher median logistic EuroSCORE (26.4±14.8% vs. 19.9±11.9%, p = 0.003) and a lower mean left ventricular ejection fraction (0.50±0.11 vs. 0.56±0.09, p = 0.01) compared to patients without CAD. However, 30-day mortality was not significantly different between
TAVI vs. surgery vs. medical treatment in an all-comer population: Residual platelet aggregation is associated with a high risk for conventional aortic valve replacement: effect on NYHA classification at 2 years

**Background:** With regard to mid-term survival of elderly patients with symptomatic degenerative aortic valve stenosis (AS), Transcatheter aortic valve implantation (TAVI) has been proven to be superior to optimal medical therapy in patients deemed at too high risk for conventional aortic valve replacement (AVR) and to be competitive to surgery in high-risk populations. In the very elderly, not only data on survival, but also on the impact on quality of life is important with regard to optimal assignment of patients to these different treatment modalities.

**Methods:** We report mid- (1 year) and longer term (2 and 3 years) follow-up of assessment of NYHA classification in 166 patients (median age 83y (IQR 80–87y)) with symptomatic AS at high risk for conventional AVR. Patients were extensively screened and, based on score systems and clinical judgment, proposed to undergo TAVI, AVR, or medical treatment (± percutaneous transluminal aortic valvuloplasty (PTAV)).

**Results:** NYHA classifications at baseline and after 1, 2, and 3 years are presented in Figure 1.

In a highly symptomatic patient population (84% in NYHA class III and IV at baseline), 88% and 79% of patients treated with TAVI were scored in NYHA class 1 or 2 at one and respectively 2 years after treatment. These results aortic valve implantation (TAVI) has been shown to be superior to optimal medical therapy in patients deemed at too high risk for conventional aortic valve replacement (AVR) and to be competitive to surgery in high-risk populations. In the very elderly, not only data on survival, but also on the impact on quality of life is important with regard to optimal assignment of patients to these different treatment modalities.

**Conclusion:** Our results show that TAVI has a profound and durable impact on the two groups (CAD 7.0%, no CAD 13.0%, p=0.117). Timing of concomitant coronary revascularization by means of PCI (staged vs. single-stage procedures) did not influence postprocedural outcomes.

**Conclusions:** CAD is a frequent finding in patients undergoing TAVI. Even though patients with concomitant CAD had a higher predicted procedural risk and worse ventricular function compared to patients without CAD, this was not associated with an increased 30-day mortality rate in our experience. Whenever needed, concomitant coronary revascularization can be safely performed in a staged or single-stage fashion.

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**P2445**  
**Aortic stenosis and acquired type 2A von Willebrand syndrome: correlation between severity of aortic stenosis and activity of ADAMTS-13**

**Background:** Aortic stenosis (AS) complicated with Wilhelmsen type 2A von Willebrand syndrome (VWS-2A). However, the prevalence and the cause of hemostatic abnormality in AS are not widely recognized.

**Methods:** We investigated 37 patients who were diagnosed moderate to severe AS by echocardiography. We analyzed echocardiographic data and other clinical or biochemical parameters. To assess the significance of WVS-2A in AS patients, association between severity of AS and serum levels of 3 subtypes von Willebrand factor were analyzed. And we also investigated the correlation between severity of AS and activity of ADAMTS-13.

**Results:** The median age was 79 years. The median left ventricular-aortic pressure gradient (LV-Ao PG) was 82.0 ± 31.1 mmHg. Fifteen patients received aortic valve repair. Twenty-three patients (62%) were diagnosed moderate AS by echocardiography. We analyzed echocardiographic data and other clinical or biochemical parameters. To assess the severity of WVS-2A in AS patients, association between severity of AS and serum levels of 3 subtypes von Willebrand factor were analyzed. And we also investigated the correlation between severity of AS and activity of ADAMTS-13.

**Conclusions:** Acquired type 2A von Willebrand syndrome complicated with AS (Heyde’s syndrome) may be related to the increasing activity of ADAMTS-13 caused by high LV-Ao PG (shear stress). Deficiency of high-molecular-weight multimers of von Willebrand factor may be associated with impaired ClpR.

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**P2449**  
**Residual platelet aggregation is associated with a significant platelet decrease after transfemoral aortic valve implantation (TAVI) which predicts poor outcome**

**Background:** After CoreValve implantation patients (pts) are treated usually with dual antiplatelet therapy consisting of aspirin (ASA) and clopidogrel (Clp) for 6 months to prevent procedural-related thrombocytopenia.

**Aim of the study:** The aim of this study was to investigate the effect of residual platelet aggregation (RPA) on platelet decrease after CoreValve implantation and its relation to outcome.

**Methods:** Platelet function was assessed in pts who underwent TAVI at our hospital. All pts were loaded with 600 mg Clp and 500 mg ASA the day before intervention. Platelet aggregation (Plag) was evaluated by the Multiplate system (Dynabyte, Munich, Germany) before (T0) and directly after intervention (T1) and on day 1, 2, 3, and 4. Preoperative RPA was defined with a maximal ADP (5mM)-induced Plag > 50 AUC. Platelet activation (PA) was simultaneously assessed with the use of immunologic markers of platelet activation (SD1F and PAC-1) by flow cytometry.

**Results:** We consecutively analyzed 132 pts (age 80.4±0.6 years) with severe aortic stenosis (mean pressure gradient 45±1.2 mmHg, aortic valve area 0.7±0.01 cm², mean ejection fraction 51±1.0) and high surgical risk (log Euroscore 24.7±1.1) who underwent successfully TAVI using the CoreValve Relining device.

In our study group 26 (19.6%) pts with enhanced RPA (median AUC T (25th-75th percentile) = 60 (54-81)) were classified as Clp low responder. Enhanced RPA was associated with a significant decrease in platelet count (93±8.3 versus 67.4±1.0; p=0.006) before T0 (directly before intervention) and day 3 (T4) compared to pts with decreased RPA and classified as Clp Responder (ClpR). ClpLR showed an enhanced expression of SDF1 and PAC-1 (median immunofluorescence (25th-75th percentile): SDF1= 37 (33-55) versus 34 (26-39); p= 0.02 and PAC-1 = 5.3 (4.6-6.4) versus 4.5 (4.1-5.1); p= 0.016. Endstage renal disease seemed to be associated with RPA, because seven of ten patients with dialysis were ClpR.

**Conclusions:** Our study shows that RPA is associated with a significant platelet drop in pts after TAVI. Since platelet decrease represents besides dialysis an independent predictor for poor outcome it is tempting to speculate that an alternative platelet therapy in patients with enhanced RPA might be beneficial.

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**P2452**  
**Cysts predict the hypertrophic response in hypertrophic cardiomyopathy mutation carriers**

**Purpose:** Hypertrophic cardiomyopathy (HCM) is a heterogeneous disease in which overt disease manifestation is accompanied by adverse clinical outcome. Current genetic testing identifies an increasing number of phenotype negative HCM mutation carriers with subtle signs of diastolic dysfunction. Data on de-
development of hypertrophy and left atrial (LA) remodeling in these patients are scarce. Therefore, we used serial cardiovascular magnetic resonance imaging (CMRI) to monitor LV mass and LA volumes. Also, we aimed to identify predictors for changes of these parameters, including the presence of intramyocardial crypts.

Methods: A total of 27 HCM mutation carriers (11 male, age 40±13 years of MIVS≥15mm) and TPM1 (n=5) gene mutation carriers were subjected to serial CMRI acquisitions. Mean follow-up duration was 4.8±0.9 years. A tailored CMRI protocol was performed including long- and short-axis cine (SSFPI) images with additional modifications to two chamber cines. Images were analyzed with dedicated software (Mass, Medis, Leiden) and volumes were indexed for body surface area (BSA). Comparisons were made with a paired Student’s t-test or non-parametric test when necessary. Logistic regression analysis was used to identify potential predictors for changes in LV mass or LA volumes. P-values <0.05 were considered statistically significant.

Results: During follow-up, LV mass increased from 45±9 g m⁻² to 48±8 g m⁻², p=0.001. Also, maximal and minimal LA dimensions showed increments over time (54±11 mm L⁻² vs 58±10 mm L⁻², p<0.01 and 24±6 mm L⁻² vs 29±7 mm L⁻², p<0.001, respectively). Regression analysis revealed that mycardial crypts were an independent predictor for the increase in LV mass. Thus, crypts may be used to identify patients at risk for developing HCM phenotype. In addition, left atrial dimensions increased, reflecting the deterioration of diastolic function over time.

Conclusions: This CMRI study with 5 year follow-up of pre-hypertrophic HCM mutation carriers revealed that the presence of myocardial crypts was an independent predictor for the increase in LV mass. The results of this study support the hypothesis, that crypts may play a role in the development of hypertrophy and diastolic heart failure.

P2454
Non-invasive assessment of the haemodynamic range -2-240, r= 0.637, p= 0.001. We performed ROC curves in patients for TWEAK levels, attending at impaired left ventricular ejection fraction (≤50%). The c statistic in the ROC curve for TWEAK was 0.81 (95%CI 0.67-0.96; p=0.042), the optimal cut-off point was 61.5 pg/mL. The AUC for NT-proBNP attending at a low effort capacity (maximal oxygen consumption values under 25 percentile in our patients’ population) The c statistic in the ROC curve for NT-proBNP was 0.72, (95%CI 0.52-0.92; p=0.03), the optimal cut-off point was 704.2 pg/mL, which had a sensitivity 75% and specificity 59%. We found significant correlation between effort capacity (as assessed as maximal oxygen consumption values) and TWEAK serum levels (r= 0.37, p=0.017). Effort capacity negatively correlated with NT-proBNP and age (r=-0.50, p<0.001; and r=-0.37 p=0.006, respectively). We found significant association between maximal oxygen consumption and sex (p=0.01) and atrial fibrillation (p=0.023). In the multivariate analysis, TWEAK and NT-proBNP levels, as well as sex, remained independently associated to the effort capacity (p=0.016, p=0.010 and p=0.002, respectively) with a r2 value: 0.58 and p<0.001 of the model.

Conclusions: TWEAK and NT-proBNP levels are biomarkers of disease severity independently associated with the effort capacity in HCM patients.

P2455
A portuguese multicenter screening of fabry disease in patients with hypertrophic cardiomyopathy

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Background: The prevalence of Fabry disease (FD) in patients with an echocardiographic pattern of hypertrophic cardiomyopathy (HCM) is not clear. Nakao et al. reported a FD prevalence of 3% in male patients presenting left ventricular hypertrophy (LVH) with a thickness of >30 mm. Sachtel et al. reported a prevalence of 6.3% in male patients with late-onset HCM (IVS thickness ≤13 mm). However, the recent ACES study reported a much lower prevalence of 0.5% in patients with HCM (IVS thickness ≤15 mm).

Aim: To determine the prevalence of FD in patients with HCM.

Methods: We performed a multicenter screening study of FD in patients with HCM. We included 129 patients from 4 Portuguese hospital centers. All patients presented an echocardiographic pattern of HCM: (1) LVH with maximum thickness of the IVS ≥15 mm, that was unexplained by hypertension, valve disease or other condition; or (2) Apical form of HCM. FD screening was performed using a dry blood spot test to quantify the enzymatic activity of α-galactosidase A. FD was excluded in male patients with normal enzymatic activity. Molecular analysis was performed in all female patients, regardless of the enzymatic activity, in order to exclude FD.

Results: Patients with HCM were 59±15 years and 59.7% were males. The pattern of LVH was asymmetric (61.2%), symmetric (29.5%) or apical (11.6%). Mean VS1 thickness was 18±5.6 mm. Obstructive HCM was found in 31.8% of the patients. FD was identified in 8 of the 129 patients with HCM (6.2%). Fabry patients were 55±14 years and 3 of them were males (37.5%). The majority of Fabry patients presented asymmetric LVH (75%), but also symmetric LVH (25%), or apical (12.5%) patterns of LVH were also found. Mean VS1 thickness was 18.6±6.3 mm. One Fabry patient was already on a dilated stage of HCM. None had obstructive HCM. Four probands harbored the most common Fabry gene. These patients were from the same geographic region, but no family connection was identified. A genetic study is ongoing to search for a possible founder effect in this geographic region.

Conclusions: In this study, the prevalence of FD in patients with HCM was 6.2%. A founder effect may explain the high prevalence of FD in one of the geographic regions included in the study. Nevertheless, this study supports the hypothesis, suggested by previous studies, that the prevalence of FD in patients with HCM is probably around 3-4% and not as low as 0.5% as reported in the recent ACES study.

ADVANCES IN ECHO CONTRAST

P2456
Nanobody-coupled microbubbles as novel molecular probe

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Purpose: Cameld-derived single-domain antibody-fragments (~150kDa), called nanobodies, are a new class of molecular tracers that are routinely identified with
nanomolar affinity for their target and that are easily tailored for molecular imaging and drug delivery applications. We hypothesized that they are well-suited for the design of targeted micro bubbles (μBs) and aimed to develop and characterize eGFp- and VCAM-1-targeted μBs.

Methods and results: Anti-eGFp (cAbGFp4) and anti-VCAM-1 (cAbVCAM1-5) nanobodies were site-specifically biotinylated in bacteria. This metabolic biotinylation method yielded functional nanobodies with one biotin located at a distant site of the antigen-binding region of the molecule. The biotinylated nanobodies were coupled to biotinylated lipid μBs via streptavidin-biotin bridging. The ability of μB-cAbGFp4 to recognize eGFp was tested as proof-of-principle by fluorescent microscopy and confirmed the specific binding of eGFp to μB-cAbGFp4. Dynamic flow chamber studies demonstrated the ability of μB-cAbVCAM1-5 to bind VCAM-1 in fast flow (up to 5 dynes/cm²). In vivo targeting studies were performed in MC38 tumor-bearing mice (n=4) (Figure 1), μB-cAbVCAM1-5 or control μB-cAbGFp4 were injected intravenously and imaged using a contrast-specific ultrasound imaging mode. The echo intensity in the tumor was measured 10 minutes post-injection. μB-cAbVCAM1-5 showed an enhanced signal compared to control μBs (p<0.05).

Conclusions: Using metabolic and site-specific biotinylation of nanobodies, a method to develop nanobody-coupled μBs was described. The application of VCAM-1-targeted μBs as novel molecular ultrasound contrast agent was demonstrated both in vitro and in vivo.

P2457 An experimental and clinical comparison of new and conventional integrated backscatter intravascular ultrasound (IB-IVUS) systems

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Background: While the utilization of integrated backscatter intravascular ultrasound (IB-IVUS) for the quantitative in vivo assessment of coronary plaque continues to grow, the validity of IB-IVUS images obtained from newly developed and conventional systems remains uncertain.

Methods and Results: To assess the accuracy and reliability of a newly developed IB-IVUS system (VISIWAY) as compared to the conventional system (Clearview), we compared quantitative IB-IVUS plaque characteristics in two systems using 125 post-mortem specimens from 26 coronary arteries in 11 cadavers, as well as using 200 clinical plaques in 32 patients undergoing coronary intervention. The overall agreement between the histological and IB-IVUS diagnoses using VISIWAY (Cohen’s κ = 0.82, 95% CI: 0.73-0.90) was similar to that using Clearview (Cohen’s κ = 0.80, 95% CI: 0.71-0.89). The two systems also demonstrated comparably high sensitivity and specificity. In the direct comparison, the overall agreement between IB-IVUS diagnoses using VISIWAY and Clearview was also excellent (Cohen’s κ = 0.87, 95% CI: 0.76-0.95). In the clinical comparison, measured plaque dimensions were similar (VISIWAY: 8.27±3.46mm² vs. Clearview: 8.31±3.46mm², p=0.44) and there was strong concordance between both grayscale and IB-IVUS parameters.

Conclusions: There was close agreement of analyzed results in both systems when as compared with the gold standard of histology. Both systems are able to reliably and accurately characterise coronary plaque and thereby make a valuable contribution to our understanding of atherosclerosis.

P2458 Association of ultrasound characteristics, angiogenesis and thermal heterogeneity in mild atherosclerotic carotid artery disease


Purpose: Both plaque angiogenesis and inflammation contribute to the development and progression of atherosclerosis. Contrast-enhanced ultrasound (CEUS) provides direct visualization of the adventitial vasa vasorum and intraplaque neovascularization. Microwave radiometry (MR), a new non-invasive method, allows in vivo measuring of internal temperature of tissues, reflecting inflammatory activation. We investigated in vivo in human carotid arteries whether plaque neovascularization and plaque temperature 1) are associated with standard ultrasound findings 1) have a positive correlation.

Methods: Consecutive patients with significant coronary atherosclerosis and carotid atherosclerosis (intima-media thickness ≥1mm in one or both carotid arteries) underwent carotid artery examination by basic ultrasound imaging, CEUS and MR). During ultrasound study the segment with the highest IMT value was designated as the “segment under investigation”. During CEUS analysis of the “segment under investigation” the contrast enhancement (CE) was defined as the percentage of signal intensity difference, prior and post contrast infusion. Thermal heterogeneity (ΔT) by MR was assigned as the temperature of the “segment under investigation” minus the minimum temperature along the carotid artery. Association of the findings between matching cross sections of standard ultrasound, contrast enhancement and MR was performed.

Results: Eighty-eight patients (86 carotid arteries) met the inclusion criteria and were included in the analysis. Fatty plaques had higher CE% compared to mixed and calcified plaques (21.4±2.70 vs 17.1±5.23 vs 8.55±2.42%, p<0.01). Heterogeneous plaques had higher CE% compared to homogeneous (21.44±2.70 vs 14.66±6.02%, p<0.01). Plaques with irregular surface had higher CE% compared to plaques with regular (18.29±5.09 vs 13.64±6.06%, p<0.01). Fatty plaques had higher ΔT compared to mixed and calcified plaque (1.13±0.27 vs 0.83±0.37°C, p<0.01). There was a positive correlation between mean ΔT and CE (R=0.60, p<0.001).

Conclusions: Carotid plaque thermal heterogeneity by MR was associated with pronounced neovascularization on CEUS examination. In vivo non-invasive assessment of the functional characteristics of carotid artery atherosclerotic plaques may serve as an additional screening tool to identify “high risk” patients for future cerebrovascular events.

P2459 Operator-independent soft computing-based assessment of extravascular lung water by ultrasound

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Purpose: B-lines obtained with lung ultrasound (LUS) evaluation have been recently proposed for the assessment of extravascular lung water (EVLW). However, LUS suffers from operator-dependence and lack of precise quantification. Our aim was to combine state-of-the-art technologies and innovative solutions to develop a soft computing-based B-lines analysis for an objective, automated and quantitative classification of the severity of EVLW.

Methods: One hundred and forty-five subjects with EVLW, independently assessed by gold-standard radiological techniques (CT and/or chest X-ray), and 62 control subjects underwent LUS examination by an experienced gold-standard radiologist. A soft computing-based modelling approach was applied in order to develop a model predictive of severity of EVLW. The soft computing method was based on artificial neural network.

Results: The model was able to discriminate 4 levels of severity of EVLW (normal, mild, moderate and severe). The model correctly identified 100% of patients with severe and 100% of patients without EVLW. It also identified 92.3±7.7% of patients with a mild degree, misclassifying 7.7% of "high risk" patients for future cerebrovascular events.
Neuronal network-based texture analysis allows Carotid plaque vasa vasorum by contrast enhanced imaging. These results were obtained for a red component of CPS color scale and contrast-enhanced myocardial texture studied 7 days after reperfused ST-elevation MI without need for stress testing. Myocardial contrast enhancement allowed a diagnostic analysis of echocardiogram may provide useful data on myocardial viability early after reinfarction.

Aim: Defining early post-infarction (MI) viability is significant early after myocardial infarction. Current methods are either related to isotopic stimulation (dobutamine) or not ready for bedside use (CMR). We hypothesized that native or contrast-enhanced myocardial texture studied 7 days after reperfused ST-elevation MI contains prognostic information regarding the transmurality of necrosis.

Methods: In this pilot study we used 226 heart echo images (native or contrast - obtained in myocardial perfusion echocardiography by iv Sorovue injection and Contrast. The aim of this study was to detect in-stent neointima the apical camera window from 26 patients for texture analysis with custom software (MaZDa 4.20). 299 image features were calculated for defined regions of interest in each image (including 9 features for intensity from gradient matrix, 20 from run length matrix, 220 from co-occurrence matrix, and 44 from wavelet transform). 8 most reproducible parameters were selected based on lowest intra class variance and error minimization approach. Each patient underwent a CMR study with gadolinium late enhancement imaging to define the % transmurality of necrosis. Linear and non-linear(neuronal network) discriminative analysis was performed to identify the optimal analytic method correlating with CMR information regarding the necrosis extent.

Results: Neuronal network approach allowed correct classification regarding the absence of necrosis in 79% of segments and in 84% of images representing different levels of transmurality (~50% or ~50%), based on resting contrast imaging. These results were obtained for a red component of CPS color scale as mean values of 5-fold network cross-validation. A similar feature selection and classification procedure applied for native grayscale images yielded worse results (68% and 79% correct classification). Among athletes RA volume index showed a significant correlation with RASa (r=-0.49, p=0.02), RASRa (r=-0.43, p=0.03) and right A wave VTi (r – 0.5, p < 0.01). Athletes with LA volume > 40 mL/m² (~7) showed reduced LAsA, LASRa and left A wave VTi compared to athletes with LA volume < 40 mL/m² (~1.0±0.1 vs. 1.9±0.2; p=0.02, 1.0±0.09 and 1.66±0.15 ± 1 s, p=0.03 and 3.7±0.2 vs. 4.9±0.2 cms, p=0.01 respectively).

Conclusions: A proportion of athletes showed reduced deformation and stroke volumes together with an enlarged LA and RA, suggesting adverse remodelling. This may act as a substrate for further atrial arrhythmia development.
Moreover, semi-automated image analysis had very good to excellent reproducibility (intraclass correlation coefficient: 0.90).

Conclusions: CAP images obtained by CEUS may have a different pattern for stable and unstable plaques, while plaque brightness enhancement may not always represent a denser microvessel network. This should be taken into account if CEUS is used for the identification of VV and microvessels within carotid atherosclerotic plaques as a screening test for plaque vulnerability.

**P2465**

The impacts of conventional echocardiographic parameters for the prediction of the recurrence of chronic atrial fibrillation after pulmonary vein isolation

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**Background:** Although, recent technological advances have improved the outcome of the pulmonary vein isolation (PVI), PVI is considered insufficient to cure chronic atrial fibrillation (CAF) and little is known whether several conventional factors also predict recurrence after PVI.

**Method:** To evaluate predictors of CAF-recurrence, in 109 patients (90 men, mean age 59.5±8.7 years) with CAF underwent PVI, AF duration, LVEF, left atrial volume index, appendage (LAA) flow, PV flow, LAA tissue doppler imaging (TDI) were measured before PVI. All patients underwent 4 PVI and additional ablation of non-PV foci if present.

**Results:** Only 33 patients (30.2%) kept sinus rhythm after 1st PVI procedure. TDI was the only one factor that made significant difference between patients with and without AF recurrence. The case with TDI of <20cm/s, the success rate went up to 78%. On the other hand, 67 patients (61.4%) had remained AF-free after three times of PVI. Compared to the patients who underwent PVI once, the success rate increased dramatically (from 30.2% to 61.4%). However, the case with TDI of <10cm/s, the success rate was only 21%.

**Conclusion:** LA TDI could be useful to identify CAF patients at high risk of AF recurrence after PVI. In addition, the case with low TDI(<10cm/s), it could be difficult to maintain sinus rhythm regardless the number of PVI.

**P2466**

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


**Background:** Recent studies showed improvement of left atrial (LA) geometry following cardiac resynchronization therapy (CRT), but little is known about the impact in LA function.

**Purpose:** To assess LA function response to CRT.

**Methods:** Prospective, longitudinal study of 62 consecutive patients undergoing CRT between October 2009 and March 2010 in a single centre. Fourteen patients were excluded due to atrial fibrillation and 11 due to low quality pictures: Standard echocardiographic evaluation and LA deformation analysis by two-dimensional speckle-tracking echocardiography (2DSE) was performed prior to and up to 12 months after implantation. Left atrial longitudinal late peak diastolic strain (LPDS) was used as a surrogate of LA function. Response to CRT was defined as >15% reduction in left ventricular end-systolic volume.

**Results:** Mean age was 65.5 years, with a male predominance (64.9%). Regarding etiology, 73% were idiopathic and 27% were ischemic. The majority of the population was in NYHA class III, the mean basal QRS duration was 140.9±22.1 ms and the mean left ventricular ejection fraction (LVEF) 23.9±7.1%. Pre-CRT, LPDS was -0.21±0.64% and improved with the device (-0.93±1.21, p<0.001).

There was no correlation between LA volume, LVEF and LPDS. LPDS was a predictor of CRT response (AUC=0.70, p<0.03). A -0.24% LPDS cut-off value had a 74% specificity and 60% sensitivity to predict a CRT echocardiographic response.

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

**P2467**

Noninvasive mapping of cardiac electrophysiology in patients with ventricular arrhythmias

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**Aim of the study:** The aim of this study was to test the accuracy of the noninvasively obtained ventricular activation as compared with that of standard invasive mapping in patients with premature ventricular contraction (PVC) and ventricular tachycardia (VT).

**Patient population:** 47 patients (21 male and 26 female; mean age 42.6 years) with ventricular arrhythmias were examined. All patients underwent noninvasive electrophysiologic examination, which was performed with Amycard 01C System and subsequent intracardiac mapping and radiofrequency cather ablation of the arrhythmogenic focus.

**Results:** 13 patients had an arrhythmogenic focus in the left ventricle (LV), according to the invasive electrophysiological examination and successful RF ablation procedure: 2 – in anterior position of the left ventricular outflow tract (LVOT); 3 – in posterior position of LVOT; 1 – in the projection of left coronary artery ostium; 3 – in the posterior-septal projection of the LV middle parts; 1 – in the anterior wall of the LV basal parts; 2 – in the lateral wall of the LV basal parts and 1 – in the posterior wall of the LV basal parts. 28 patients had an arrhythmogenic substrate in the right ventricle (RV): 3 – in the anterior-lateral wall of the right ventricle outflow tract (RVOT); 5 – in the anterior wall of the RVOT; 12 – in the anterior-septal position of the RVOT; 6 – in the septal position of the RVOT; 1 – in the apex parts of the RV free wall; 1 – in the anterior-septal position of the RV middle parts. The same results we obtained during noninvasive imaging. In 6 patients we had discrepancy: 2 had the arrhythmogenic focus in the septal position of RVOT, according to the intracardiac electrophysiological examination and successful RF ablation procedure, but the noninvasive mapping showed the area of the noncoronary sinus of LVOT and the LV lateral wall correspondingly; 1 – in the anterior wall of RVOT, but the noninvasive examination again showed the area of the noncoronary sinus of LVOT and the LV lateral wall correspondingly; 1 – in the posterior-septal position of the LV basal parts, but the noninvasive mapping showed the lateral wall of the LV basal parts and 1 more patient had the arrhythmogenic substrate under the Tricuspid annulus, near His’ bundle, however, the noninvasive examination showed the area of the RV apex.

**Conclusions:** The individual cardiac anatomy model obtained for each patient enables accurate noninvasive electrocardiographic imaging of ventricular pre-excitation in patients with PVCs and VT (the accuracy is 87.2%).
Automatic detection and classification of heart sounds and systolic murmurs based on reassigned spectrogram

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Purpose: Successful discrimination of innocent from abnormal heart murmurs in childhood is a prerequisite for an effective heart disease screening based on cardiac auscultation. We aimed to develop and validate the clinical efficacy of an automatic detection and classification system of pediatric heart sounds based on reassigned spectrogram

Methods: 40 randomly selected digital phonocardiograms from pediatric cardiology outpatients (corresponding to 20 innocent and 20 abnormal systolic murmurs), consisted the training data base for our system, while 10 further cases (5 innocent, 5 abnormal murmurs) were used for the final system testing. Diagnosis was based on a detailed echocardiographic study. Heart sounds were recorded from three standard auscultation sites using a sensor based electronic stethoscope with incorporated 3-lead ECG and transferred to a laptop PC for offline analysis. R-waves in the synchronous ECG signal were used as reference for the detection of the first heart sound and a fixed segment of 400 ms was selected in the beginning of every heart cycle, as systolic interval, for subsequent analysis. Sound signal analysis was carried out using reassigned spectrogram. Using an information theoretic criterion based on the Mutual Information between systolic murmur classes (i.e., innocent/abnormal) and features, the relevance of certain frequencies at specific time instants in the heart cycle segment could be quantified. The initial time-frequency representation was transformed to a lower-dimensional domain using higher order singular value decomposition (HOSVD). The classification system was evaluated through cross-validation experiments on a further random database of recordings from functional and abnormal heart murmurs obtained as previously described.

Results: Using support vector machines (SVM) for classification, the suggested approach achieved an Equal Error Rate (EER) of 7.07±3.65% and an Area Under the Curve (AUC) score of 0.973±0.0213. The sensitivity of 95% and specificity of 72% was achieved at a probability cut-off point of 0.45. This performance is comparable to the reported accuracy achieved by pediatric cardiologists while significantly better than that of pediatricians.

Conclusions: An automated murmur classification method could serve as a first line tool for clinical screening of cardiac disease in children, and probably as a useful aid in practice of pediatric cardiac auscultation for non-cardiologists.

Solitary hypertrophic papillary muscle: the difference from hypertrophic cardiomyopathy


Background: Solitary Hypertrophied papillary muscle (HPM) can show electrocardiographic abnormalities suggestive of hypertrophic cardiomyopathy (HCM). The aim of this study is to elucidate the clinical difference between HPM and HCM patients with 2-dimensional transthoracic echocardiography (2DE).

Methods: HPM was defined papillary muscle diameter in short axis view was 11mm or larger as previously reported. All our solitary HPM patients have revealed a normal ventricular hypertrophy with 2DE. HCM patients represented an asymmetrical septal hypertrophy or apical hypertrophy or both of them with 2DE. 50 patients with HPM (Group A), 50 patients with HCM (Group B) and 20 age-matched control patients (Group C) were examined with 2DE. Tissue Doppler imaging was also obtained in addition to the conventional 2DE.

Results: All study patients had sinus rhythm and normal left ventricular ejec- tion fraction. Left atrial diameter of Group A (40±6.7cm) was larger than Group C (35±5.4cm: p<0.01) and smaller than Group B (49±5.6cm: p<0.01). Tissue Doppler septal e′ of Group A (5.7±1.6cm/s: p<0.05) was lower than Group C (6.7±1.9cm/s: p<0.05) and higher than Group B (4.2±1.2cm/s: p<0.05). 4 cases of cardiac events (2 cases of percutaneous septal ablation, 1 case of ICD implantation, and 1 case of ablation for paroximal atrial fibrillation) were reported in Group B, but no event was reported in Group A.

Conclusion: HPM patients had better prognosis than HCM patients. HPM patients showed decreased diastolic function than control patients but better than HCM patients. Tissue Doppler septal e′ could be used to distinguish HPM patients from HCM patients.

Left atrial deformation parameters predict left atrial appendage function and thrombus in patients in sinus rhythm with suspected cardioembolic stroke

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Purpose: Cardioembolism is an important cause of ischemic stroke. One of important origins of embolism is left atrial appendage thrombus. A number of non-invasive parameters that predict LAA thrombi have been studied but none has been done to evaluate the association with left atrial appendage parameters.

Methods: 107 ischemic stroke patients (66 males, 41 females) in sinus rhythm who were suspected of having cardioembolism were included in the study. Clinical and demographic characteristics and laboratory parameters of all patients were recorded. The patients underwent conventional 2D echocardiogram and 3D speckle tracking echocardiogram of the left atrium. Left atrial peak strain, left atrial reservoir value (LA-4C-RES) and left atrial pre-contraction strain (LA-4C-PUMP) were measured. Patients were divided into two groups according to the presence of thrombus in the LAA in tranesophageal echocardiography (TEE). The non-invasive predictors of LAA thrombus were investigated.

Results: Decreased LA deformation parameters were found to be associated with impaired LAA functions and LAA thrombus. Both LA-4C-RES and LA-4C- PUMP values were found to be significantly lower in patients with LAA thrombus (P<0.05 vs. controls). A good inverse correlation was present between LA-4C-RES values and LAA morphologic parameters (with LAA area: r = -0.77, p < 0.001, with LAA length: r = -0.69, p < 0.001), and a good positive correlation was present with LAA emptying velocity with pulse Doppler (r = 0.78, p < 0.001). The area under the receiver-operating characteristic curve of the LA-4C-RES was 0.91 (0.86-0.97, p < 0.001), for the LA-4C-PUMP, the area was 0.88 (0.82-0.95, p < 0.001) to predict LAA thrombus. LA-4C-RES and high-sensitivity C-reactive protein were found to be independent predictors of LAA thrombus in multivariate analysis (Odds Ratio (OR): 0.34, 95% confidence interval (CI): 0.13 – 0.91, p = 0.031 and OR: 1.76, 95% CI: 1.01 – 3.04, p = 0.043, respectively).

Conclusion: Left atrial deformation parameters measured by 2D speckle tracking method was found to predict impaired LAA functions and the presence of LAA thrombus in cardioembolic stroke patients with suspected cardioembolism but who are in sinus rhythm.

In vivo fluorescence-mediated tomography demonstrates atorvastatin promoted reduction of macrophages in atherosclerotic lesions of apoE−/− mice

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Purpose: Brief statin treatment prevents peri-procedural myocardial infarctions. (1) Underlying mechanisms are unknown. Atherosclerotic lesion progress- tion, destabilization and rupture are driven by macrophages (MØ). We used non-invasive fluorescence-mediated tomography (FMT) to image MØ homing to vulnerable atherosclerotic plaques. MØ recruit into aortic and brachiocephalic artery plaques. After 4 days, 20MØ were injected IV 2 days prior to treatment. FMT-scans were performed on d0, d1, and d4. Atorvastatin was administered at 40mg/kg BW atorvastatin or vehicle twice daily for 4 days. Peritoneal MØ from eGFP/labeled mice were used to assess overall MØ content. Plasma was collected on d4 for lipoprotein analysis. Data were evaluated for significant differences (p<0.05) by Students t-test. Results are mean or mean ±% of baseline ±SEM.

Results: After IRB approval and in accordance with the principles of labora- tory animal care (NIH Publication no. 85-23) 14 ApoE−/− mice were fed a high- cholesterol diet to establish complex plaques. After 16 wks on diet mice received 40mg/kg BW atorvastatin or vehicle twice daily for 4 days. Peritoneal MØ from eGFP/labeled mice were injected IV with near-infrared fluorescent dye DIR. 10E7 eGFP/DIR-MØ were injected IV 2 days prior to treatment. FMT-scans were performed on d0, d1, and d4. We labeled MØ infiltration into aortic and brachiocephalic artery plaques. eGFP/DIR-MØ that infiltrated plaques were counted on fixed-sections of athero- sclerotic arteries by fluorescence microscopy. Lesion size was measured on H&E stainings. Immunohistochemistry (CD68) was utilized to assess overall MØ content. Plasma was collected on d4 for lipoprotein analysis. Data were evaluated for significant differences (p<0.05) by Students t-test. Results are mean or mean ±% of baseline ±SEM.

Results: Longitudinal FMT scans detected an increase of DIR-signal derived from indicator MØ recruited into aortic and brachiocephalic artery plaques. After 4 days of high-dose statin the signal was lower than in controls (75±5 vs. 175±35, p<0.05). Reduction of recruited eGFP/DIR-MØ to atherosclerotic plaques was confirmed by fluorescence microscopy (50±13 vs. 125±23, eGFP/DIR pos. cells/lesion, p<0.02). Plaque size was not affected (p>0.67). Statin treat- ment reduced the plaque area that stained pos. for CD68 by 35% (p<0.05). Total cholesterol was reduced in statin animals (351±21 vs. 504±58, mg/dl, p<0.01). Triglycerides, phospholipids, HDL, LDL and VLDL did not differ (p>ns).

Conclusions: In vivo FMT optical imaging proved its high potential for clinical applicability to track infiltration of DIR-labeled MØ into vulnerable atherosclerotic plaques. FMT-based quantification of MØ recruitment demonstrated a stabiliza- tion of atherosclerotic lesions in ApoE−/− mice by 4-day atorvastatin treatment. This rapid and likely lipoprotein-independent effect could explain the reduction in cardio-vascular events after brief statin therapy. (1) Circulation. 2011;123:1622.
Gender disparities in the association of epicardial adipose tissue volume and coronary atherosclerosis: a 256-slice multidetector computed tomography study


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Purpose: Epicardial adipose tissue (EAT) may play a role in the development of coronary artery disease (CAD). Although it is well known that abdominal fat distribution is dissimilar between men and women, gender difference in EAT distribution has never been studied. We explored gender disparities in EAT volume and its impact on coronary atherosclerosis.

Methods: The study consisted of 90 consecutive patients (age 63±12 years: 47 men, 43 women) who underwent 256-slice multi-detector computed tomography (MDCT) coronary angiography. EAT volume was measured as the sum of cross-sectional epicardial fat area on CT images (0.675-mm thickness, range 300 to 320 slices per heart) from the lower surface of the left pulmonary artery origin to the apex. Patients were divided into CAD group (≥50% coronary lumen narrowing) or non-CAD group.

Results: In men, EAT/body surface area (BSA) was significantly larger in CAD group than those in non-CAD group in ≤65 years (61±16 vs 34±10 cm²/m², p<0.0001) and in >65 years (62±11 vs 28±12 cm²/m², p<0.0001). In women, EAT/BSA was not different between CAD and non-CAD groups. Multivariate logistic analysis showed that EAT/BSA was the single predictor for ≥50% coronary lumen narrowing only in men (p<0.0001). Age, body mass index, hypertension, diabetes mellitus, and hyperlipidemia were excluded from predictors.

Conclusions: Increased EAT volume is strongly associated with coronary atherosclerosis only in men. EAT volume is a men-specific determinant for coronary atherosclerosis.

A new method of manufacturing flexible heart replicas of congenital heart disease for simulation surgery in combination of stereolithography and vacuum casting method


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Stereolithography is a rapid prototype technique whereby an ultraviolet laser beam selectively solidifies photosensitive liquid plastic. By using this technique, 3D volumetric data of MSCT can be converted into plastic models that enhance our spatial perception of real-life anatomy. However, the solid materials of the original stereolithography are not satisfactory for idealistic simulation surgery. Recently, a vacuum casting method has been developed, where more detailed prototypes with flexible materials can be manufactured.

Methods: Six biomodels of various congenital heart diseases were manufactured in this study. The patients include SRV (4m), DORV (1y), ccTGA (3y), VSD (3y), ASD (9y), and TOF (6y). Three-dimensional volumetric datasets of MSCT angiography were converted into STL files to guide the laser beam. Plastic replicas representing the both outer and inner surface of the heart tissues were initially made with stereolithography. Then, urethane materials with stiffness of the real heart tissue were used to assess the best ACS cut-off points for RA requirement. After solidification of the urethane materials, the casts were carefully removed and the final products were obtained.

Results: The vacuum casting in association with stereolithography enabled us to manufacture precise replicas with similar texture of the real individual heart in all the 6 cases. This technique also allowed the surgeon to cut and suture, facilitating the simulation of the surgical operation.

Conclusions: The vacuum casting method in association with stereolithography is a promising technique for medical education, preoperative rehearsal, simulation of individual surgery, and planning of novel and innovative surgical procedures of congenital heart disease.

Coronary calcification versus plaque formation in symptomatic South Asians and Caucasians: a computed tomography coronary angiography (CTCA) study

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Background: Differences in the prevalence and severity of coronary artery disease (CAD) between ethnic groups are well documented and attributed to cardiovascular (CV) risk factors variation. This study investigates the differences in coronary artery calcification (CAC) and stenosis between two groups of patients with symptomatic angina, one of South Asian (SA) and another of Caucasian origin matched for age, gender and CV risk factors.

Methods: Retrospective study; 101 symptomatic angina patients of SA origin who underwent computed tomography coronary angiography (CTCA) and CAC scoring (CACs) were compared with 101 age, gender and risk factors matched Caucasian patients.

Results: SA had a greater mean number of affected coronary segments, with both obstructive and non-obstructive plaques, than Caucasians. Presence of CAC was reported in 54.5% of South Asians vs. 43.5% of Caucasians. Furthermore, SA had a higher mean CACs (p<0.0001). In the CACs categories >100 (101-400, 401-1000 & >1000) there were more SAs than Caucasians, although the difference was not statistically significant in the latter. SAs had a higher number of arterial segments with calcified and non-calcified plaques. These results were more marked in patients aged >50; in those ≤50, the mean CACs was not significantly different between the two ethnic groups (p=0.28). In regards to plaque morphology; SAs were affected more than Caucasians, although the difference did not reach statistical significance. Moreover, CAD prevalence and severity in this age group was not significantly different between SAs and Caucasians.

Conclusion: Despite similar CV risk factors for CAD, symptomatic SAs seem to have more diffused arterial calcification compared to Caucasians. These differences are more profound over the age of 50, suggesting potential genetic or other risk factors yet to be determined.

Usefulness of agatston calcium score by multidetector computerized tomography to recommend rotational atherectomy in patients with calcified coronary lesions


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Purpose: Many calcified coronary lesions (CL) that are not crossable or are inadequately distensible with conventional coronary intervention (PCI); are finally referred for rotational atherectomy (RA). There is no diagnostic method to predict which patients will require RA. Our objective was to assess if Agatston calcium score (ACS) is able to predict those CCL untreatable by conventional PCI.

Methods: We studied 19 patients (mean age 72) with clinical PCI indication and at least one CCL with >70% stenosis in a main coronary vessel. Severe calcification was assessed by fluoroscopy by two independent interventional cardiologists. They underwent ACS quantification (global, coronary and segmentary) by multi-detector computerized tomography (MCT), and subsequent PCI. Semi-compliant balloons (sized 0.8 to 1.0 to the reference vessel diameter) were used in an initial cross and dilation attempt. If the CCL was dilated, conventional PCI was performed (PCI group); if the operator was unable to cross or dilate the CCL, RA was performed (RA group). A receiver-operator characteristic (ROC) curve was used to assess the best ACS cut-off for RA requirement with calcium volume, global ACS and vessel ACS were 0.58, 0.53 and 0.74 respectively. The best AUC was obtained for segmentary ACS (0.808). Using the ROC curve of the segmentary ACS, we selected a cut-off point of 383 units, above which failure of conventional PCI and requirement of RA could be predicted (100% of sensitivity and 64% specificity for RA requirement).

Conclusions: Stenotic severely calcified lesions untreatable with conventional PCI that will require rotational atherectomy may be predicted with a pre-procedure MCT using the segmentary calcium score analysis.
Adrenomedullin as marker of coronary atherosclerosis detected by computed tomography in non-diabetic renal patients

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Background: High levels of the plasma peptide mid-regional pro-adrenomedullin (MR-proADM) is elevated in various pathological states including cardiovascular and inflammatory diseases in the general population. Data in patients with chronic kidney disease are very limited. We therefore investigated the association of MR-proADM levels with calcium in plaques of coronary arteries in non-diabetic chronic kidney disease. The present study investigated whether an increased MR-proADM level is a marker of coronary atherosclerosis detected by coronary CT angiography in asymptomatic subjects with early chronic kidney disease.

Methods: We determined plasma MR-proADM levels in 62 patients, aged 40-86 years (56.5% male), studied without documented coronary events in stage 2 and 3 chronic kidney disease. Coronary artery calcification (CAC) and noninvasive coronary angiograms were performed by 64-multi-detector computed tomography (Siemens, Germany). Coronary artery stenosis of at least 50% was considered significant. Laboratory data MR-proADM were collected and analysed to CT findings.

Results: The median and mean MR-proADM plasma levels were 0.80 nmol/l and 0.81±0.3 nmol/l, respectively. Adrenomedullin correlated with coronary artery calcification (r=0.34; p=0.02), glomerular filtration rate (r=-0.55; p=0.02) and age (r=0.27; p=0.05). Patients with CAC score 0 to 400 had lower MR-proADM (0.71 nmol/l±0.18) than patients with CAC >400 (MR-proADM 1.05 nmol/l±0.37) (p=0.001). In the high CAC group, however, there was no significant difference in the adrenomedullin between patients with or without coronary stenosis (1.0 vs. 1.1 nmol/l, p=0.65). A receiver operating characteristic (ROC) curve analysis predicted significant coronary stenosis revealed that the area under the curve (AUC) of the low CAC group was significantly larger than that of the high CAC group (0.672 vs. 0.417, p<0.05). When compared to patients without coronary stenosis, patients with one or more vessel stenosis had a no significant difference in MR-proADM levels (0.73 vs. 0.91 and 0.84 nmol/l, p=0.313).

Conclusions: Our findings suggest the possibility that plasma MR-proADM is a sensitive marker for the presence of atherosclerotic lesions in patients with chronic kidney disease and the power of adrenomedullin to predict significant coronary stenosis was stronger in patients with CAC <400.

Prognostic value of dual-source multidetector computed tomography coronary angiography in patients with stent implantation

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Aim: To evaluate the prognostic value of dual-source 64-slice multidetector computed tomography (MDCT) in patients with coronary stents.

Methods and Results: The study included 173 patients (mean age 59.9 years) with previous stent implantation who underwent dual-source MDCT for evaluation of CAD and stent patency between 2006 and 2009. Stented vessel segment was evaluated as patent without neointimal hyperplasia (NIH), nonobstructive NIH (<50% luminal narrowing), or obstructive NIH (>50% luminal narrowing). Patients were evaluated for major cardiovascular events (MACES) to demonstrate association between stent patency and clinical outcome.

Results: Our results indicated that patients who had a patent stent without any NIH on MDCT had a good prognosis, whereas an increased event rate was observed in patients with nonobstructive or obstructive NIH on MDT.

Computed tomography 409

The correlation between CT coronary angiography and low to moderate pre-test probability for coronary artery disease in patients with acute chest pain. A retrospective comparative analysis

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Purpose: CT coronary angiography (CTCA) is now a recognised diagnostic tool for patients admitted with chest pain who have low to intermediate probability of having coronary artery disease (CAD) as per recent guidelines by the European Society of Cardiology (ESC) on acute coronary syndromes. The National Institute for Clinical Excellence (NICE) advocates using CADScore for risk stratification.

The aim of this study is to assess the correlation between the pre-test probability (as determined by TIMI and CADScore).

Methods: Patients presenting with acute chest pain were included in the study if they had a low to moderate likelihood of having CAD with a TIMI score ≤2 or when troponin and ECG were inconclusive. Their CADScore was calculated retrospectively and patients were risk stratified into low-10% and high-61-90% risk groups. Sensitivity and NPV for exclusion of disease on CTCA were calculated for patients in low CADScore, low-moderate CADScore and low TIMI score.

Results: 63 patients with TIMI score ≤4 underwent CTCA. The mean patient age was 59.9 years (range 40-86 years), 41 (65.1%) patients were male. 48 (76%) patients had normal or mild coronary artery disease and 13 (21%) patients had significant stenosis (stenosis diameter reduction ≥50%). 2 patients had an inconclusive study. 56 (89%) patients had a low TIMI score (≤2) and 7 (11%) patients had intermediate TIMI score (3-4). Using the retrospectively calculated CADScore, 12 (19%) were classified to have a low and 18 (29%) were classified to have a moderate, and 33 (52%) were classified to have a high pre-test likelihood. The mean radiation dose for the cohort was 310±90 mSv per patient. CADScore had a higher NPV than TIMI as a predictor for a negative CTCA (100% vs. 79.6%). CADScore also had a higher sensitivity (100% vs. 54.5%) although the sensitivity for TIMI was very low, possibly due to the insufficient number of patients in the intermediate TIMI group. The combined low and moderate CADScore groups as a predictor for negative CTCA yielded a NPV of 86.2% and a sensitivity of 69.2%.

Conclusions: CTCA results correlate well with pre-test likelihood for CAD. CADScore demonstrated better performance in risk stratification, particularly in the low to moderate risk groups. Given its excellent NPV, CTCA is a highly effective and inexpensive tool in the exclusion of CAD in patients admitted to hospital with chest pain leading to efficient, safe and early discharge of patients.
Follow-up at 3 months revealed four late revascularizations (no deaths or myocardial infarctions), all of whom had obstructive CAD with calcium on CT at presentation.

Conclusions: Coronary CTA outperforms calcium imaging in the triage of patients suspected of developing ACS. Absence of plaque on coronary CTA allows safe discharge. Coronary CTA has incremental value to clinical risk scores and has the potential to reduce unnecessary hospital admissions.

P2482 Atherosclerotic plaque burden on coronary CT angiography in cocaine abusers presenting with acute chest pain at the emergency department

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Purpose: Cocaine-associated chest pain accounts for a substantial proportion of emergency department (ED) visits in the United States. Such patients are known to be at an increased risk of acute coronary syndrome and advanced atherosclerosis. We used coronary CT-angiography (cCTA) to evaluate the prevalence, extent, and composition of coronary atherosclerotic lesions in patients with history of cocaine abuse and acute chest pain in whom the presence of ACS had been excluded.

Materials and Methods: Retrospectively, we studied 78 patients (52 men, mean age 44 ± 17 years, 56% with a history of cocaine abuse and 40 with acute chest pain and underwent dual-source cCTA. Patients with ACS did not undergo CT and were not included in this study. Each coronary artery segment was evaluated for presence of atherosclerotic plaque, plaque composition (calcified, non-calcified, or mixed), and the presence and degree of stenosis. Findings were compared with a matched control cohort of 78 patients (52 men, mean age 45 ± 6 years).

Results: The presence of significant stenosis was not significantly different between patients with and without cocaine use (12.8% vs. 5.1% of patients, p > 0.05). Cocaine use was not associated with a higher prevalence of overall plaque (48.7% vs. 35.9%, p = 0.05), calcified plaque (30.8% vs. 21.8%, p = 0.05), or non-calcified plaque (16.7% vs. 7.7%, p = 0.05). In contrast, patients with a history of cocaine abuse had a higher prevalence of mixed plaque (34.6% vs. 15.4%, p < 0.05) and mixed plaque volume (59.7 ± 33.3 mm³ vs. 25.6 ± 12.6 mm³, p = 0.05).

Conclusion: In patients undergoing cCTA for acute chest pain in the ED, those with cocaine abuse have a higher prevalence and volume of mixed coronary plaque than those without cocaine abuse. Although larger studies are needed, our results suggest that coronary plaque composition may play a role in the development of ACS in this patient population.

P2483 Integration of CT calcium scoring and CT coronary angiography in a rapid access chest pain clinic: A tertiary hospital experience

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Purpose: UK guidelines were published in 2010 for assessment of patients with chest pain of recent onset based on their pre-test likelihood (PL) for coronary artery disease (CAD). A novel aspect was the use of a computed tomography (CT) calcium score (CaS) and CT coronary angiography (CTCA) to exclude CAD in low risk patients. Here we report our experience of integrating this approach to our Rapid Access Chest Pain Clinic (RACPC) over a 17 month period.

Methods: Data was retrospectively analysed from consecutive patients attending RACPC, referred for CT. Both CaS and CTCA were performed by default by our radiology department, regardless of CaS, using older 64-multislice and newer generation 128-multislice CT scanners (the latter capable of flash acquisition and prospective gating). The radiation dose (RD) in milli-Sieverts (mSv) received by each patient was calculated from the dose-length product. Patients with significant CAD on CTCA (at least 1 > 50% lesion) were referred for invasive angiography (XA).

Results: Sixty-seven patients were included (52.2% male; median age 51 [23- 68]). The median RD received was 10.74 mSv (8.78-20.56); patients scanned in the newer generation CT scanner (n=24) received significantly less RD than those in the older scanner (median 2.24 [1.23-8.16] vs 11.64 [8.40-25.6] mSv respectively; p < 0.001) provided they were in sinus rhythm with a well-controlled heart rate. Thirty-nine patients had a CaS of 0 (35.9% male; median age 50 [23-68]). Of these, 6 (15.4%) were found to have CTA pathology. Three of these had significant CA confirmed CAD, 2 of which were aged 33 and 40 years respectively.

Conclusions: A CaS of 0 in symptomatic patients does not rule out significant and probable CAD, particularly in younger patients. Prospective gating with 128-slice multiset CT scanners in patients with optimum heart rate and rhythm significantly reduces the RD. In light of this and given that almost 50% of our patients referred by new guidelines for XA had no significant disease on CTCA, it is reasonable to consider CaS & CTCA as a 1st line investigation in selected high risk patients. Our findings in the highest risk patients (PL CAD >90%) suggest that this group may benefit from investigation, with XA being the most appropriate choice.

P2484 Accuracy of prospectively ECG-triggered very-low-dose coronary DSCT angiography using iterative reconstruction for the evaluation of coronary artery stents: comparison with invasive catheterization

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Introduction: Raw-data based iterative reconstruction (IR) allows substantial reduction of image noise and hence the use of very low dose data acquisition protocols in coronary CT angiography. However, despite first reports about the accuracy of IR in evaluation of native coronary arteries, its value in assessing coronary artery stents has not yet been investigated.

Methods: 40 symptomatic patients (age: 64 ± 9 years, BMI: 28 ± 3 kg/m², heart rate: 59 ± 6 bpm after beta blocking) with 72 coronary stents (31 BMS, 41 DES, mean diameter 3.0 ± 0.5 mm) underwent coronary Dual-Source CT (DSCT) angiography prospectively ECG-triggered at 70% of RR interval, 80kV, 165 mAs, 2/128×0.6mm collimation, 60ml contrast at 6mL/sec prior to invasive catheterization. DSCT images were reconstructed both using standard filtered back projection (FBP) and using an IR algorithm. Subsequently, the accuracy to detect significantstenoses (>50%) in native coronary arteries as well as in coronary stents was assessed for FBP and IR by two independent observers blinded to the results of invasive catheterization. Additionally, differences in subjective image quality (4-point scale), image noise, signal-to-noise-ratios (SNR), contrast-to-noise-ratios (CNR) were determined between FBP and IR. Mean effective radiation dose was calculated based on the dose-length product.

Results: Mean DLP and patients radiation dose of prospectively ECG-triggered coronary DSCT angiography was 47.3 ± 3 mGy/cm and 0.65 ± 0.05 mSv. IR led to significantly improved image quality in comparison to standard FBP (image quality score: 1.8 ± 0.6 vs. 1.5 ± 0.5 points, p = 0.05; image noise: 70 ± 14 vs. 93 ± 20 HU, p = 0.001; SNR: 10 ± 3 vs. 8 ± 3, p = 0.001; CNR: 12 ± 3 vs. 8 ± 3, p = 0.001).

In standard FBP reconstructions, sensitivity, specificity, PPV and NPV of DSCT angiography to detect a significant coronary stenosis were 95% (25/26), 57% (8/14), 81% (25/31), 89% (8/9) on a per-patient, 98% (34/35), 81% (99/122), 60% (34/57), 96% (99/103) on a per-vessel and 78% (7/9), 78% (46/53) (7/21), 96% (49/51) on a per-stent based analysis, respectively. After IR, values improved to 100% (26/26), 71% (10/14), 87% (26/30), 100% (10/10) per patient, 100% (40/40), 87% (104/120), 71% (40/56), 100% (104/104) per vessel and 100% (9/9), 78% (49/63), 39% (9/23), 100% (49/49) per stent.

Conclusions: Raw-data based iterative reconstruction along with prospective ECG-triggering improves diagnostic accuracy for evaluation of patients with coronary artery stents when compared to standard filtered back projection and allows substantial reduction of radiation exposure in coronary DSCT angiography.

P2485 Prognostic value of MSCT for coronary artery disease in low-intermediate risk Mediterranean population

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Introduction and Objectives: Although multislice computed tomography (MSCT) detects obstructive coronary artery disease (CAD) with high diagnostic accuracy, there are not much data about MSCT long-term prognostic value. Our aim is to assess the prognostic utility of MSCT coronary angiography in patients with suspected CAD followed for a period of 2 years.

Methods: All consecutive patients with suspected CAD and a MSCT performed in our hospital between October 2007 and July 2011 were screened. Those with previous documented CAD were excluded. Framingham score and its adaptation to Mediterranean population (Regicor score) were used to assess cardiac risk. Non-invasive coronary angiography was performed with a 64-slice MSCT scanner. Patients with a heart rate over 65 bpm received propranolol (1mg/ml) intravenously, in order to reduce heart rate. A bolus dose of 80 ml of contrast (iodixanol, 320 mg of iodine per ml. Visipaque, GE Healthcare UK) was infused at 5 mls and saline solution was infused immediately after iodine contrast to reduce hyperattenuation in the right heart (20ml at 5ml/s). Patients were categorized as follows: No CAD, mild CAD (+50% lesion) and severe CAD (at least +50% lesion). Patients and their follow-up was performed by telephone interview and review of electronic clinical data, registering death, acute myocardial infarction and coronary artery revascularization.

Results: 617 patients and 205 met criteria and were included. The
average age was 59.1±12.5 years. Male. Most of them had low risk of present-
ing cardiovascular disease (Framingham score 10%, Regicor 4%). There were 46 patients (22%) with severe CAD, 67 patients (33%) with mild CAD and 81 (40%) without CAD. In 10 cases (5%) MSCT was inconclusive. The mean radi-ation dose was 14.1±3.8 mSv. Mean follow-up was 19.6±11.6 months. Three cardiac deaths, 2 non-cardiac deaths, 3 myocardial infarctions and 10 cases of percutaneous coronary revascularization were detected. In 148 patients with mild or no CAD, event free-survival was 97%, while in 46 patients with severe CAD by MSCT, event free survival was 82% (Log-rank statistic p value =0.01).

Conclusions: In low-intermediate risk patients, MSCT adds useful information over those obtained from risk scores. Patients without severe CAD in MSCT present an excellent long term prognosis.

### Results:

**Diagnostic accuracy of dual-source coronary computed tomography angiography in patients after bypass grafting: comparison with invasive coronary angiography**


**Purpose:** Previous studies with multidetector coronary computed tomography angiography (CCTA) demonstrated satisfactory accuracy for detection of significant graft disease and limited usefulness in the assessment of native coronary circulation in patients after coronary artery bypass grafting (CABG). We aimed to investigate the diagnostic accuracy of dual-source CCTA with improved temporal resolution in the comprehensive assessment of symptomatic post-CABG patients.

**Methods:** Dual-source CCTA was performed in 80 (74 men, mean age 67 ± 9.6 years) symptomatic patients from the prospective ANNI Computed Tomography Angiography Registry, 9±6.5 years after CABG. A total of 202 grafts (67 arterial grafts, 135 venous grafts) and 1105 native coronary segments with a diameter of ≥1.5 mm were evaluated for the presence of significant stenosis (≥50% diameter reduction). Results were compared with invasive coronary angiography (ICA) as the standard of reference.

**Results:** Sensitivity, specificity, and positive and negative predictive values of dual-source CCTA for the detection of significant lesions in bypass grafts were 99%, 96%, 94%, and 99%, respectively. Segment-by-segment analysis of native coronary arteries for the detection of obstructive disease yielded sensitivity of 91% with specificity of 92%. If analysis was restricted to nongrafted and distal runoff segments, sensitivity was 88% with specificity of 96%. The diagnostic accuracy was significantly lower for the evaluation of severely calcified native coronary segments compared to moderately and noncalcified coronary segments (85% vs. 93%, p<0.001).

**Diagnostic accuracy of dual-source CCTA**

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<th>All Grafts (n=202)</th>
<th>Arterial Grafts (n=67)</th>
<th>Venous Grafts (n=135)</th>
<th>Nongrafted and runoffs segments (n=781)</th>
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<tr>
<td>Sensitivity [%]</td>
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**Conclusions:** Dual-source CCTA allows successful evaluation of suspected graft disease in symptomatic post-CABG patients, whereas ICA is still required for the assessment of significant disease in distal runoffs and native coronary arteries.

### Results:

**Reasons for inaccurate diagnoses in coronary computed tomography angiography:**


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**Introduction:** Coronary CT angiography has demonstrated high diagnostic accuracy for non-invasive detection of coronary artery stenoses. However, false positive diagnoses occur and the underlying reasons for misclassification have not yet been systematically evaluated.

**Methods:** We retrospectively analyzed, data sets of 400 consecutive symptomatic patients (289 male, 111 female) with an intermediate likelihood for coronary artery disease who showed at least one significant stenosis (>50% lumen reduction) in coronary CT angiography (dual source CT, 24128x0.6 mm collimation, 60 mL contrast agent at 6 mL/s), and who were referred for invasive catheterization over a time period of 3 years. The number of false-positive diagnoses in CT angiography compared to invasive angiography as well as the respective coronary artery (LM, LAD, LCX, RCA) were assessed. Subsequently, the underlying reasons for inaccurate interpretation were evaluated using 4 classifications: calcification, motion artefact, image noise and small vessel diameter. Data sets with correct and incorrect interpretation were compared with respect to differences in mean heart rate, BMI, Agatston score, image noise and effective radiation dose.

**Results:** Of 400 data sets, 33 (8.3%) patients (23 male, 11 female) and 46 (2.9%) coronary arteries (LM: n=9, LAD: n=16, LCX: n=13, RCA: n=17) showed at least one false positive diagnosis in coronary CT angiography. False-positive findings were caused by calcium in 16 cases, motion artefact in 11 cases, image noise in 5 cases and were attributable to a small vessel diameter in 1 case. Mean heart rate, BMI, Agatston score, image noise and effective radiation dose for data sets with accurate interpretation and for data sets with inaccurate interpretation were 61±10 and 61±12 bpm (n.s.), 27.4±4.1 and 28.8±5.4 kg/m² (n.s.), 556±799 and 557±495 (n.s.), 26.8±30.9 HU (p=0.02), 10.2±4.7 and 11.7±7.0 mSv (n.s.), respectively.

**Conclusions:** Despite the reported high accuracy of coronary CT angiography, false-positive diagnoses occur in daily routine practice and are most frequently caused by regional vessel calcification and motion artefacts. The significantly higher image noise in misclassified DSCT data sets emphasizes the important role of image quality for a correct identification of significant stenoses in CT angiography.

### Results:

**Computed tomographic pulmonary angiography and prognostic significance in patients with Acute Pulmonary Embolism**

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**Purpose:** Patient with acute pulmonary embolism (APE) present with a broad spectrum of symptoms. Computed tomographic pulmonary angiography (CTPA) has been established as a first line test in the APE diagnostic algorithm, but estimation of short term prognosis by this method remains to be explored.

**Methods:** In 62 consecutive patients with APE were divided into three groups according to their clinical presentation: dyspnea (n=49), impending circulatory fal-
Coronary artery angiography by catheter.

**Results:** During 3 month follow-up, 17 patients died (25%). The mortality rate was 14.2%, 26%, and 0% in the three groups, respectively. Neither systolic aortic blood pressure nor the pulmonary arterial pressure could predict the patient outcome. In contrast, a significant correlation with mortality was found using the systolic blood pressure (p < 0.001) and heart rate (p < 0.001), as well as from imaging parameters including pulmonary obstruction index (p < 0.0001) and right ventricular dysfunction (p < 0.001).

**Conclusion:** CTCP quantification of RVD and pulmonary vascular obstruction index are accurate predictors of mortality in patients with APE.

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**P2490**

**The clinical value of coronary artery angiography by dual-source computed tomography in children with Kawasaki disease**

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**Objective:** To evaluate the feasibility, safety and advantage of coronary angiography by dual-source computed tomography (DSCT) in diagnosing coronary artery lesions due to Kawasaki disease in children.

**Methods:** We included 200 children with Kawasaki disease admitted to the department of Pediatric cardiology during August in 2007 and July in 2010 were complicated with coronary lesions screened by transthoracic echocardiography and completed coronary angiography by DSCT. Four cases with giant aneurysm had coronary angiography by catheter.

**Results:** 1. All children underwent coronary angiography by DSCT uneventfully and acquired good image within five to six minutes. The smallest child was two month old, 24 cases were found to have coronary artery lesions after DSCT examination. There were 144 coronary artery lesions including 73 light coronary lesion, 45 coronary aneurysm and 26 giant aneurysms. The maximum diameter of aneurysm was 1.48cm (mean 0.63±0.33cm). 84 lesions were located in left coronary artery, of which 37 were in left main trunk, 36 in left anterior descending branch (LAD), and 11 in left circumflex branch. 60 aneurysms were located in right coronary artery, 60 lesions were located in right coronary artery, including 29 in proximal segment, 18 in medium segment and 8 in distal segment. In addition, Seven thrombus were found in six children by DSCT and meanwhile four of them detected by transthoracic echocardiography. All of the thrombus developed in giant aneurysm which located in left main trunk, proximal segment of LAD, proximal and medium segment of right coronary artery, respectively. 3. The results of coronary artery angiography by DSCT in four children consistent with that done by catheter completely.

**Conclusion:** Coronary Angiography by DSCT is an efficiency, safe, and reliable method in diagnosing coronary artery lesion due to Kawasaki disease in children.

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**P2492**

**Risk stratification of non-high-risk pulmonary embolism by the use of a novel rapid immunoturbidimetric H-FABP assay**

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**Background:** Heart-type fatty acid-binding protein (H-FABP) is a promising biomarker for risk stratification of non-high-risk pulmonary embolism (PE). However, currently available quantitative H-FABP assays are not suitable for clinical routine. Therefore, we tested a novel CE-approved clinical chemistry H-FABP assay for its usefulness for risk stratification of non-high-risk PE.

**Methods:** We prospectively examined 271 normotensive patients (120 men (44.3%); median age, 70 years) with acute PE. Baseline H-FABP levels were measured by a novel fully automated clinical chemistry immunoturbidimetric assay (Randox®, Crumlin, United Kingdom) and by ELISA (HyCult®, Uden, The Netherlands).

**Results:** H-FABP levels measured by the immunoturbidimetric assay were higher compared to ELISA (5.2 ± 2.9 [1.1-5.4] ng/ml, p < 0.001). Thus, more patients were diagnosed with elevated (>6 ng/ml) H-FABP levels by the immunoturbidimetric assay (45.4 vs. 25.8%; p < 0.001).

During the first 30 days after diagnosis, 16 patients (5.9%) had an adverse outcome, defined as all-cause death, cardiorespiratory resuscitation, intubation, or catecholamine administration. As expected, these patients had higher H-FABP concentrations with both assays (p < 0.001 each).

ROC analysis yielded an AUC of 0.78 (95% CI, 0.66-0.90) for H-FABP determined by ELISA and of 0.81 (0.71-0.91) by the novel assay. The predefined cut-off value of 6 ng/ml was associated with a higher sensitivity and specificity compared with the immunoturbidimetric assay when compared to the ELISA (94 and 68 vs. 63 and 82%). Only one patient (0.7%) with H-FABP < 6 ng/ml measured with the immunoturbidimetric assay had an adverse outcome (compared to 12.2% with H-FABP ≥ 6 mg/ml; p < 0.001) while H-FABP > 6 ng/ml determined by ELISA had an unfavourable clinical course (compared to 17.9% with H-FABP ≥ 6 mg/ml; p < 0.001).

**Conclusion:** Our findings indicate that the novel immunoturbidimetric H-FABP assay appears suitable for risk stratification of non-high-risk PE. However, H-FABP alone does not appear sufficient to identify candidates for outpatient treatment.

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**P2493**

**Validation of NT-proBNP cut-off values for risk stratification of acute non-high-risk pulmonary embolism**

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**Background/Aims:** N-terminal pro-brain natriuretic peptide (NT-proBNP) is a repeatedly studied biomarker for risk stratification of non-high-risk pulmonary embolism (PE). However, optimal cut-off values remain controversial. In this study, we validated and compared different proposed cut-off values for NT-proBNP regarding their prognostic value in a large European multicenter cohort.

**Methods:** We prospectively examined 688 consecutive normotensive patients (326 men (47.4%); median age, 70 years) with acute PE. NT-proBNP levels were measured on admission using a routine assay (Elecsys 1010/2010 Roche Diagnostics, Mannheim, Germany) and yielded a median value of 683 pg/ml (25th-75th percentile, 160-2591 pg/ml).

**Results:** During the first 30 days after diagnosis, 39 patients (5.7%) reached the primary end-point (all-cause death, cardiopulmonary resuscitation, intubation, or catecholamine administration); secondary end-points were met by 29 patients (all-cause death: 4.2% and 18 patients (PE-related death: 2.6%). As expected, patients who reached the endpoints had significantly higher levels of NT-proBNP (p < 0.001, and p = 0.01), respectively.

ROC analysis yielded an AUC of 0.71 (95% CI, 0.62-0.79) for NT-proBNP (primary endpoint). A cut-off value of 600 pg/ml was associated with the best prognostic sensitivity and specificity (96% and 50%) compared to the cut-off values of 1,000 or 500 pg/ml. Using logistic regression analysis, this cut-off value was associated with the highest Odds Ratio (5.7; 95% CI, 2.3-13.7; p = 0.001) for predicting an adverse 30-day outcome, which remained significant after correction for sex, age, renal insufficiency, and congestive heart failure. Similar results were obtained with regard to secondary endpoints.

**Conclusion:** Among 1924 patients under surveillance from August 2005 to April 2011, we assessed safety profiles in 1890 patients treated with monteplase and
analyzed clinical background, efficacy and 30-day prognosis for 1242 patients in whom acute PE was confirmed from diagnostic imaging and categorized as massive or submassive.

**Results:** Among 1242 patients (median age, 66 years; 25% of patients ≥75 years; 59% females), monteplase was administered to 491 patients (40%) with massive PE and 751 patients (60%) with submassive PE. Massive PE patients underwent combined therapy requiring non-surgical or medical procedures, including catheter interventions (15.3% vs. 7.7%, p < 0.001), surgical embolec-tomy (1.8% vs. 0.4%, p = 0.02) and percutaneous cardiology pulmonary support device (15.1% vs. 0.7%, p < 0.001). The response rate of PE to monteplase was 94% in pulmonary circulation evaluation judged from imaging results and 93% in clinical efficacy assessment. No significant differences in efficacy analysis were seen according to dose of monteplase and age, but massive PE patients showed significantly lower clinical efficacy than submassive PE patients (90.9% vs. 94.3%, p = 0.03) and patients with collapsed circulation showed much lower clinical efficacy than those without (74.3% vs. 95.9%, p < 0.001). The 30-day survival rate assessed using the Kaplan-Meier method was 89.2%. Survival rate was significantly lower with massive PE than with submassive PE (77.9% vs. 96.6%, p < 0.001) and in patients with collapsed circulation than in those without (41.1% vs. 95.3%, p < 0.0001). Among the 1890 patients in the safety analysis set, 34 (1.8%) developed intracranial hemorrhage (ICH). No significant differences in occurrence of ICH were seen according to dose or age, but ICH occurred more frequently in females than in males (2.3% vs. 1%, p = 0.03), in massive PE patients than in submassive PE patients (2.7% vs. 1%, p = 0.03) and in patients with history of cerebrovascular disorder than in those without (9.4% vs. 1.3%, p < 0.001).

**Conclusions:** The present study shows outcomes of thrombolytic therapy with monteplase for acute PE in daily clinical practice in Japan.

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**P2494**

**Time since symptom onset influences interpretation of troponin elevation in intermediate risk pulmonary embolism**

N. Meneveau, D. Dos Santos, S. Janin, R. Chopard, M.F. Seronde, Y. Bernard. *University Hospital of Besancon - Hospital Jean Minjoz, Besancon, France*

**Background:** Troponin dosage plays an increasingly important role in risk stratification of pulmonary embolism (PE), especially in patients (pts) without hemodynamic compromise. Troponin elevation in the setting of acute PE is of small magnitude and short duration and can go unnoticed in pts referred late after symptom onset.

**Methods:** Prospective, single-center registry of pts with confirmed intermediate-risk PE, defined as at least 1 echocardiographic finding of right ventricular (RV) dysfunction (RV/left ventricular end-diastolic diameter ratio ≥ 1 in the 4-chamber view, paradoxical septal systolic motion or pulmonary hypertension defined as RV/trialtrel gradient > 30mmHg), or positive troponin test. Combined in-hospital endpoint was defined as death, non-fatal recurrent PE, or residual pulmonary vascular obstruction (RPVO) > 35% as measured by V/Q scan before discharge.

**Results:** 282 pts were included, average age 66 ± 14 years, 59% women, 174 (62%) referred ≥ 5 days after symptom onset, 108 (38%) after < 5 days. Troponin elevation was observed in 126 (72%) treated within ≤ 5 days, and in 60 pts (56%) treated after > 5 days (p = 0.004). Prognostic value is shown in table. Positive troponin was an independent predictor of adverse outcome (OR=1.43 [1.08-5.56]). ROC curves show that prognostic value of positive troponin test was lower in pts referred ≥ 5 days after symptom onset (p < 0.01).

**Conclusions:** There is a significant difference between troponin elevation and symptom onset in patients with intermediate-risk PE. Time since symptom onset does not give a significant increase in interpretation when interpreting troponin elevation in this population. Negative predictive value of troponin elevation is adequate in pts treated early (< 5 days) but is suboptimal in pts treated > 5 days after symptom onset.

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**P2495**

**Can the “Bleeding Academic Research Consortium” (BARC) classification be applied to pulmonary embolism?**

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**Background:** Bleeding complications are associated with increased risk of subse-quent adverse outcomes in pulmonary embolism (PE). The “Bleeding Academic Research Consortium” (BARC) developed a classification of bleeding events combining laboratory and clinical parameters. However, this classification was mainly based on acute coronary syndrome patients. We investigated whether this classification is applicable in the context of PE, where no standard bleeding definition exists.

**Methods:** Prospective, single-center registry of patients with confirmed PE. We excluded bleeding events classified as BARC types 1 or 4, considered not to be applicable in acute PE. BARC type 2 bleeds were defined as any overt bleeding requiring therapy more frequent care, or leading to hospitalisation. Type 3 bleeds were defined as drop of > 3g/dl in haemoglobin, any transfusion, tamponade, intracranial hemorrhage, or bleeding requiring surgical intervention. Type 5 bleeds were defined as any fatal bleed.

**Results:** Between 2007 and 2011, 666 patients with confirmed PE were included in the registry; average age 66 ± 18 years; 52% women; 25% low-risk, 61% intermediate-risk and 14% high-risk PE. Treatment was: unfractionated heparin in 93 (14%), enoxaparin in 200 (30%), fondaparinux in 375 (56%). Thrombolysis was given in 167 (25%). Sixty patients (9%) experienced bleeding (n=13, 43 and 4 for BARC types 2, 3 and 5 respectively). Main in-hospital events are shown in the table. By multivariate analysis, independent predictors of in-hospital death were: cardiological shock (OR 12.6 [4.8-20.8]); chronic obstructive pulmonary disease (OR 5.27 [2.5-8.43]); acute right ventricular dysfunction (OR 2.98 [1.25-6.96]) and any bleeding (BARC 2.35 [OR 5.15 [1.34-7.37]).

**Conclusions:** Our data suggest that the BARC classification can be applied to patients with acute PE, and that in this population, bleeding events are associated with unfavourable in-hospital outcome. We suggest that the BARC definitions could be used as the standard classification of bleeding events in PE, particularly in clinical trials.

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**P2496**

**Accuracy of multi-organ ultrasound (venous, cardiac and thoracic) for the diagnosis of pulmonary embolism: Suspected Pulmonary Embolism Sonographic assessment (SPES) multicenter prospective study**

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**Purpose:** Multi-detector Computed Tomography Pulmonary Angiography (MCTPA) is the standard of care for the detection of Pulmonary Embolism (PE); unfortunately it involves radiation exposure, is not feasible in unstable patients, is not always available and has contraindications. Ultrasound (US) is an inexpensive, safe, bedside diagnostic tool, however the accuracy of a multi-organ US approach for the diagnosis of PE is unknown. We investigated the accuracy of multi-organ US (venous, cardiac and thoracic) scan for the diagnosis of acute PE.

**Methods:** Consecutive patients presenting to four emergency departments with clinical suspicion of PE and with a simplified Wells score of 4 (PE likely) or with a pretest probability of PE ≥ 50% (or both) were enrolled. MCTPA was considered the gold standard for PE diagnosis. Multi-organ US was performed before MCTPA. PE was considered echocardiographically present if venous US was positive for limb deep vein thrombosis or cardiac US was positive for right ventricular dysfunction or at least one pulmonary subpleural infarct was detected with thoracic US. The accuracy of the single organ US were calculated. Multi-organ US accuracy was calculated in patients with a complete US (compression US of bilateral femoral and popliteal veins, good acoustic window for cardiac US and both anterior and posterior thoracic US).

**Results:** Among 123 patients MCTPA was positive for acute PE in 46 (37%). A complete multi-organ US was obtained in 114 (93%) patients. Table 1 shows the diagnostic performance of single and multi-organ US.

**Table 1. Accuracy of single and multi-organ ultrasound in patients with suspected acute pulmonary embolism**

<table>
<thead>
<tr>
<th>Ultrasound</th>
<th>Sens % (95%CI)</th>
<th>Spec % (95%CI)</th>
<th>PPV % (95%CI)</th>
<th>NPV % (95%CI)</th>
<th>LR +</th>
<th>LR -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous</td>
<td>67 (53.79)</td>
<td>95 (87.98)</td>
<td>89 (79.94)</td>
<td>73 (64.79)</td>
<td>13.0 (4.944)</td>
<td>0.3 (0.3-0.5)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>24 (13.39)</td>
<td>89 (79.94)</td>
<td>55 (43.75)</td>
<td>67 (57.76)</td>
<td>2.2 (0.97-5)</td>
<td>0.8 (0.7-0.9)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>65 (49.78)</td>
<td>90 (84.95)</td>
<td>78 (61.89)</td>
<td>83 (73.90)</td>
<td>6.8 (3.12-4.2)</td>
<td>0.4 (0.2-0.6)</td>
</tr>
<tr>
<td>Multi-Sens</td>
<td>93 (80.98)</td>
<td>72 (60.82)</td>
<td>62 (52.78)</td>
<td>94 (84.99)</td>
<td>3.3 (2.3-4.9)</td>
<td>0.1 (0.1-0.3)</td>
</tr>
<tr>
<td>Sens + Spec</td>
<td>Sensitivity, Specificity, PPV+ + Negative Predictive Value, NPV- + Positive Likelihood Ratio, -LR+ - Negative Likelihood Ratio</td>
<td>95% CI</td>
<td>95% CI</td>
<td></td>
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</tr>
</tbody>
</table>

**Conclusions:** A complete multi-organ US scan is possible in more than 90% of patients with suspected PE and his sensitivity is superior to all single organ US. Multi-organ US has a high negative predictive value and could be a good tool to rule-out PE.
P2497
Low Risk Pulmonary Embolism Decision Rule - A new and improved decision score for low risk pulmonary embolism
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Purpose: Non-massive Pulmonary embolism (PE) has low intrahospital and post-discharge mortality rates when an accurate diagnosis is made. However, some patients initially considered to be low risk show progressive deterioration. This research aims at developing a new and improved score that allows detection of low risk patients who are eligible for outpatient treatment.
Methods: Retrospective cohort study involving 142 asymptomatic or mildly symptomatic and hemodynamically stable patients with PE and no clinical or echocardiographic signs of right ventricular dysfunction. Collected data: risk factors, analytical and gasometric parameters, admission echocardiogram, thoracic CT angiography. Patients followed for 6 months. Primary endpoint: 1-month all-cause mortality. Secondary endpoints: Intrahospital and 6-month all-cause mortality. A new score allowing detection of patients eligible for early discharge and outpatient treatment was developed and its prognostic accuracy compared to that of the Geneva and simplified PESI scores through area under the curve (AUC) on ROC curve analysis and the net reclassification improvement index.
Results: A score for predicting 1-month all-cause mortality (Low Risk Pulmonary Embolism Decision [LR-PED] rule) was obtained using Binary Logistic Regression and included: age, atrial fibrillation at admission, previous heart failure, admission heart rate, creatinine, troponin I and C-reactive protein at admission. ROC curve analysis assessed its overall accuracy for predicting 1-month, intrahospital and 6-month mortality (AUC=0.776, 0.763 and 0.854, respectively, when compared to Geneva and simplified PESI). The LR-PED rule showed higher sensitivity and negative predictive value for the detection of the lowest risk patients, with a rate of false negative of zero per cent in our cohort. Although the ROC areas under the curve of the three models were not significantly different (the Geneva rule: 0.80, simplified PESI: 0.76), the net reclassification improvement index revealed very significant upward risk reclassification by the LR-PED model of patients who reached primary or secondary outcomes.
Conclusions: LR-PED rule further stratifies low risk patients, allowing identification of those at very low risk and who could benefit from outpatient treatment. Prospective validation of this score in larger cohorts is important before its potential implementation as a decision aid for outpatient treatment and the safety of early low-risk patient discharge further evaluated.

P2498
Prognostic value of plasma lactate levels among patients with acute Pulmonary Embolism: the thrombo-embolism lactate outcome study (TELOS)
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Objective: To investigate the prognostic value of plasma lactate in patients with acute pulmonary embolism (PE).
Methods: Consecutive adult patients with symptomatic, objectively confirmed acute PE were prospectively included. Plasma lactate and troponin I levels were tested within six hours from presentation. Based on a previous retrospective analysis, plasma lactate values ≥ 2 mmol/L and troponin I values > 0.10 ng/ml were considered abnormal. Right ventricular dysfunction (RVD) was prospectively assessed by echocardiography. Primary endpoints were all-cause death and the composite of all-cause death and clinical deterioration (defined as progression to shock, rescue thrombolysis, mechanical ventilation or cardiopulmonary resuscitation) at 30 day follow-up.
Results: From January 2007 to April 2010, 270 patients were included, 151 were females (55.9%), with a mean age of 73 ± 12.7 years. Twelve patients (4.4%) showed shock/hypotension (shock or arterial pressure < 90 mmHg) at presentation, 109 (40.4%) had RVD. 93 (34.4%) and troponin I > 0.10 ng/ml (0.10 mg/dl) were considered abnormal. Right ventricular dysfunction (RVD) was prospectively assessed by echocardiography. Primary endpoints were all-cause death and the composite of all-cause death and clinical deterioration (defined as progression to shock, rescue thrombolysis, mechanical ventilation or cardiopulmonary resuscitation) at 30 day follow-up. Patients died (63.3%) and 37 (13.7%) reached the composite endpoint. At multivariable Cox proportional hazard regression analysis, plasma lactate was associated with all-cause death (HR 9.03; 95%CI: 2.94–27.70) and with the composite endpoint (HR 5.46; 95%CI: 2.68–11.14) independent of shock/hypotension, RVD or elevation of troponin I.
Conclusions: Patients with PE and elevated plasma lactate are at increased risk of death and adverse outcome, independent of overt hemodynamic impairment or of markers of right ventricular injury/dysfunction.

P2499
Pulmonary anatomopathologic analysis and clinical manifestations related to different diseases in patients with pulmonary thromboembolism. An autopsy study
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Purpose: Patients who died due to pulmonary thromboembolism (PTE), may present different clinical manifestations and symptoms depending on their underlying diseases. The anatomopathological findings are still unknown in literature. The objective of this study was describing demographic and etiologic data, anatomopathological findings and in-vivo manifestations (Acute Respiratory Failure [ARF], Hemodynamic Instability [HI] or Sudden Death) associated to the variety of diagnosis extracted from autopsy reports of PTE patients.
Methods: From 2.000 to 2.008, were reviewed 291 autopsies of patients whose cause of death was PTE. The following data were obtained: age, sex, clinical in-vivo manifestations, post-mortem pathologic patterns and main associated underlying diseases. The pulmonary histopathological changes were categorized in: diffuse alveolar damage (DAD), pulmonary edema (PE), alveolar hemorrhage (AH) and lympho/plasmacytic interstitial pneumonia (LPIP). Odds ratios of certain associated diseases developing a specific clinical manifestation and/or a specific anatomopathologic finding were calculated. Moreover, the relation between certain clinical manifestation and a specific anatom pathologic pattern was analysed too. Odds ratio was considered significant when p < 0.05.
Results: A total of 127 (43.6%) men were studied. The median age was 64 years. Neoplasias were present in 49.1% of cases and 31.2% of patients developed PTE in a postpartum period, mainly from cervix and sim abdominal and neurosurgery. The most common clinical manifestation was ARF (28.9%), followed by CPR (27.5%) and HI (26.8%). The most prevalent pulmonary finding was PE (26.8%). Chronic Obstructive Pulmonary Disease was positively correlated to LPIP (p = 0.04), Linking in-vivo manifestations to pulmonary changes were found significant relations between: ARF and PE (OR, 2.99; 95% IC, 1.25 – 7.21; p = 0.014); ARF and AH (OR, 2.70; 95% IC, 1.02 – 7.23; p = 0.03); ARF and DAD (OR, 8.79; 95% IC, 1.11 – 69.42; p < 0.009); HI and HA (OR, 3.39; 95% IC, 1.27 – 9.99; p = 0.015) and HI and DAD (OR, 11.43; 95% IC, 1.46 – 89.46; p = 0.02). The multivariate analysis didn’t exhibited significant association between different clinical manifestations and specific diseases.
Conclusions: In autopsies of patients with PTE, the most prevalent disease was neoplasia. The most associated histological finding was PE. The most frequent clinical manifestation was ARF. We noticed important relation between COPD and LPIP. ARF was positively related to PE, AH and DAD; as well HI to AH and DAD.

P2500
Prognostic value of coronary sinus diameter measured by CT pulmonary angiography in acute pulmonary embolism
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Background: Several parameters measured by computed tomographic pulmonary angiography (CTPA) have been advocated in prognostication of patients with acute pulmonary embolism. We hypothesized that the prognostic value of the diameter of coronary sinus measured by multi-slice CTPA.
Methods: Consecutive adult patients with symptomatic acute PE diagnosed by multi-slice CTPA were included. The angiographic diameter of right coronary artery was defined as the one of the following: catecholamine infusion for sustained hypotension, shock, endotracheal intubation, rescue thrombolysis, cardio pulmonary resuscitation or recurrent PE. Coronary sinus diameter together with the Ganadi score, RV/LV ratio and planar diameters of main pulmonary artery, inferior vena cava, superior vena cava and axzogos veins were measured by two independent readers blinded to all other clinical data. After dichotomization of CTPA parameters based on ROC curve analysis, logistic regression analysis was used to assess the association of CTPA parameters with the composite endpoint and with right ventricular dysfunction (RVD) as assessed by echocardiography.
Results: Overall 99 patients were included. The angiographic diameter of coronary sinus was not correlated to the composite endpoint at 30 days. Coronary sinus diameter measurements were highly reproducible (k=0.94). The inter-observer variability was too high for inferior and superior vena cava measurements and they were excluded from subsequent analysis. At logistic regression analysis the coronary sinus diameter ≥ 10 mm (OR 8, CI 95% 2.7-24.9) together with the Ganadi score > 11 (OR 10, CI 95% 1.3-78.9) and RV/LV ratio > 1 (OR 4, CI 95% 1.3-17.0) but not the axzogos vein and pulmonary artery diameters were significantly associated with the composite endpoint. A significant association was found also between coronary sinus diameter ≥ 10 mm (OR 3.7, CI 95% 1.5-9.1) and the presence of RVD as assessed by echocardiography.
Conclusions: In patients with acute PE, coronary sinus diameter was a highly reproducible parameter, associated with increased risk of short-term adverse outcome and with echocardiographic evidence of RVD.
Right ventricle stroke work index predicts mortality in inoperable patients with chronic thromboembolic pulmonary hypertension

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Purpose: Right ventricle (RV) failure due to an increased afterload is the main cause of mortality in pulmonary hypertension (PH). Complex physiology and geometry of RV suggests the need for new parameters to assess its function. The stroke work index (RVSWI) may be the best surrogate for isolated function of RV, if measures the work performed in each contraction corrected by heart rate and pressure (normal: 8-12 g.m/m²). RVSWI has been applied in other scenarios as mean pulmonary arterial pressure (normal: 8-12 g.m/m²). RVSWI has been applied in other scenarios as

Methods: We studied the prognostic value of RVSWI in p affected by chronic thromboembolic pulmonary hypertension. Between July 2003 and December 2011, 104 patients (mean age 71.2±4.6 years) studied the site of the obstruction. Patients were treated with PDE5-I, 12 with ERA and 3 with combination therapy. Mean hemodynamic parameters at baseline and after treatment are shown in the table.

Results: 50 patients were treated with phosphodiesterase type-5 inhibitors (PDE5-I), 33 with endothelin receptor antagonists (ERA), 5 with prostanoids and 16 with combination therapy; 20 patients were treated with PDE5-I, 12 with ERA and 3 with combination therapy. Mean hemodynamic parameters at baseline and after treatment are shown in the table:

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Medical Therapy</th>
<th>PEA-Treated Patients</th>
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<tbody>
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Conclusions: PAH-approved drugs improve exercise capacity and hemodynamics in operable and inoperable CTEPH. The improvement of hemodynamics before PEA may favourably influence the surgical results in operable subjects.

Effects of medical treatment for operable and inoperable chronic thromboembolic pulmonary hypertension

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Background: The elective therapy for chronic thromboembolic pulmonary hypertension (CTEPH) is pulmonary endarterectomy (PEA) but around 40% of patients are deemed inoperable for several reasons. Specific PAH drug therapy may play a role in improving hemodynamics in operable and inoperable patients.

Methods: Between July 2003 and December 2011, 104 patients (mean age 67±6.1 years) with operable CTEPH and 44 patients (mean age 61±1.8 years) with operable CTEPH received PAH-approved drugs. Six-minute walk distance (6MWD) and right-heart catheterization data were collected at baseline and after 3-4 months of treatment in the inoperable patients; at baseline, immediately before PEA and 6 months after PEA for surgically treated patients.

Results: 1) Inoperable patients: 50 patients were treated with phosphodiesterase type-5 inhibitors (PDE5-I), 33 with endothelin receptor antagonists (ERA), 5 with prostanoids and 16 with combination therapy; 2) Operable patients: 28 patients were treated with PDE5-I, 12 with ERA and 3 with combination therapy. Mean hemodynamic parameters at baseline and after treatment are shown in the table.

Conclusions: PAH-approved drugs improve exercise capacity and hemodynamics in operable and inoperable CTEPH. The improvement of hemodynamics before PEA may favourably influence the surgical results in operable subjects.
Right ventricular stroke work index predicts mortality after surgery in patients with chronic thromboembolic pulmonary hypertension suitable for pulmonary thromboendarterectomy

A. Jurado Román1, M.J. Ruiz-Cano2, E. Zatarain Nicolás3, M.T. Velázquez Martín4, E. Barrios García-Lestache2, E. Pérez De La Sota2, J. Cortina5, P. Escobar Subias6,1, University Hospital 12 de Octubre, Department of Cardiology, Madrid, Spain; 2University Hospital 12 de Octubre, Department of Heart Transplant and Pulmonary Hypertension, Madrid, Spain; 3Institute of Heart Sciences, ICICOR, University Clinic Hospital, Valladolid, Spain; 4University Hospital 12 de Octubre, Department of Hematopathy, Madrid, Spain; 5University Hospital 12 de Octubre, Department of Cardiac Surgery, Madrid, Spain

Purpose: Pulmonary thromboendarterectomy (PTE) is the therapy of choice in suitable patients (p) with chronic thromboembolic pulmonary hypertension (CTPH). Right ventricle (RV) function is one of the main risk factors for survival after surgery. The complex geometry of the RV suggests the need for new parameters to assess RV function. The RV stroke work index (RVSWI) may be the best surrogate for isolated function of the RV, because it measures the work performed by the RV with each contraction, corrected for heart rate and pressure. RVSWI is an important parameter to assess the risk of RV failure in patients that require assessment for heart transplantation but it has been never tested in the vascular field.

Objective: To study the ability of RVSWI to predict in-hospital mortality (<30 days) after pulmonary thromboendarterectomy (PEA) in patients with CTPH.

Methods: 102 consecutive CTPH patients were studied at a national reference institution for PH between 2001 and 2011. Retrospective hemodynamic data during right-side catheterization were obtained in 55 suitable for PEA (56.6% male, 53.2±14.7 years, body surface area 1.8±0.10 m²) at the time of diagnosis. RVSWI was calculated by the formula: systolic volume index (m³/m²) (mean pulmonary artery pressure – central venous pressure) (mmHg)/0.0136 (g/ml).

Results: 69.8% were in NYHA functional class III-IV at the time of diagnosis.

Hemodynamic mean values were: right atrium (RA) 8.3±0.07 mmHg, mean pulmonary artery pressure (PAPm) 46.9±1.6 mmHg, pulmonary wedge pressure (PWP) 8.9±3.3 mmHg, pulmonary vascular resistance (PVR) 9.8±1.5 WU and cardiac index (CI) 3.3±0.5 l/min/m². Mean RVSWI was 15.3±4.5 mm²/g. In hospital mortality after PEA was 7.5% (4p), all of them due to right heart failure. RVSWI was lower in non-survivors (15.95±8.45 mm²/g; p=0.005). According to ROC analysis, a cut-off value of RVSWI ≤10.4 mm²/g predicts in-hospital mortality with sensitivity of 80% and specificity of 89%. (Area under the curve=0.87±0.07; p=0.006).

Conclusion: RVSWI is a hemodynamic parameter to assess RV function. We describe for the first time its ability to predict short-term mortality in patients with CTEPH that undergo PTE.

Exercise training improved exercise capacity and quality of life in patients with inoperable or residual chronic thromboembolic pulmonary hypertension (CTEPH)

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Background: Aim of this prospective study was to evaluate the effects of exercise training (ET) in patients with inoperable or residual chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: Thirty-five consecutive patients with invasively confirmed inoperable or residual CTEPH (16 women;19 men; mean age 61±15 years, mean pulmonary artery pressure, 63±20 mmHg; primary inoperable n=33, persisting pulmonary hypertension after pulmonary endarterectomy n=2) on stable disease-targeted medication received ET in-hospital for 3 weeks and continued training at home for 15 weeks. Medication remained unchanged during the study period.

Efficacy parameters have been evaluated at baseline and after 15 weeks by blinded-observers. Survival rate has been evaluated in a follow-up period of 36±15 months.

Results: All patients tolerated ET without severe adverse events. In week 15, 6-minute walking distance was significantly improved compared to baseline (by 71±70 m; p<0.001), as well as scores of quality-of-life questionnaire SF36, peak oxygen consumption (from 933±335 to 1111±304 ml/min; p<0.014) and maximal workload (from 64±28 to 90±22 watt; p<0.01). The 1- and 2-year survival rate was 100%, the 3-year survival rate 91%.

Conclusion: ET as add-on to medical therapy may be effective in patients with CTEPH to improve work capacity, quality of life and further prognostic relevant parameters and possibly improves survival. Further multicentric randomized controlled trials are needed to confirm these results.

PULMONARY ARTERIAL HYPERTENSION: DIAGNOSIS AND TREATMENT

Serum soluble ST2 levels in patients with pulmonary arterial hypertension and their relationship with right ventricular structure and function

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Purpose: Prognostic stratification in pulmonary arterial hypertension (PAH) currently relies on clinical assessment and invasive hemodynamics, even though right ventricular (RV) dilatation and function assessed by cardiac magnetic resonance (CMR) have been demonstrated to independently predict survival. Soluble ST2 (sST2), a marker of cardiomyocyte stress, is increased in left-sided heart failure, especially when right-sided decompensation coexists. Aim of this study was to explore sST2 levels in PAH, and their correlation with cardiac remodeling as assessed by CMR.

Methods: 25 patients with PAH underwent contrast-enhanced CMR and measurement of serum sST2 levels by means of an ELISA assay. We excluded patients with congenital heart disease, 10 age-matched healthy individuals served as controls.

Results: PAH patients showed increased sST2 levels compared with healthy controls (28.9±19.9 vs. 14.8±19.0 ng/ml; p<0.001). According to ROC analysis, the cut-off value of sST2 >54.6 ng/ml predicts high RV pressure >35 mmHg with sensitivity of 89% and specificity of 77%.

P2507 Oral therapy in patients with porto-pulmonary hypertension

E. Concifieni, M. Palazzini, F. Dardi, A. D’Adamo, F. Terzi, A. Rinaldi, C. Bachetti, A. Manes, A. Branzi, N. Galie1, Institute of Cardiology, University of Bologna, Bologna, Italy

Rationale: Phosphodiesterase type-5 inhibitors (PDE-5) and endothelin receptor antagonists (ERA) are oral drugs effective in patients with idiopathic pulmonary arterial hypertension (PAH) and PAH associated with connective tissue diseases. We assessed the effects of these drugs in patients with PAH associated with portal hypertension (PoPAH).

Methods: Between February 2001 and December 2011, 39 patients with PoPAH received PDE-5 i-monotherapy and 10 patients received ERA monotherapy. At baseline and after a mean treatment period of 4.6±2.6 months patients underwent clinical evaluation, 6-minute walk distance (6MDW) assessment and right-heart catheterization.

Results: Mean age was 53±11 years. Etiology of portal hypertension was hepatitis C virus [14], alcohol abuse [13], hepatitis virus + alcohol abuse [12], cryptogenic [4], primary biliary cirrhosis [1] and autoimmune hepatitis [1]. Mean trans-hpatic pressure gradient at baseline was 12.6±9 mmHg. Two Patients died during follow-up above and below the median differed significantly in terms of WHO class, walking distance, RV volumes, and RV ejection fraction (table). Fibrosis at the RV insertion points was also more common in patients with high sST2 levels. Analysis of CMR data showed significant correlation between sST2 levels, RV end-systolic volume, and RV ejection fraction (p<0.001 for all).

Conclusions: Serum sST2 levels are elevated in patients with PAH, and they are strictly correlated with the severity of right heart remodeling and RV dysfunction. Soluble ST2 appears as a promising novel biomarker in the field of pulmonary vascular disease, and a potentially useful tool for the non-invasive assessment of RV dysfunction in this high-risk population.

P2505 Oral therapy in patients with porto-pulmonary hypertension

E. Concifieni, M. Palazzini, F. Dardi, A. D’Adamo, F. Terzi, A. Rinaldi, C. Bachetti, A. Manes, A. Branzi, N. Galie1, Institute of Cardiology, University of Bologna, Bologna, Italy

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Conclusions: Serum sST2 levels are elevated in patients with PAH, and they are strictly correlated with the severity of right heart remodeling and RV dysfunction. Soluble ST2 appears as a promising novel biomarker in the field of pulmonary vascular disease, and a potentially useful tool for the non-invasive assessment of RV dysfunction in this high-risk population.
Conclusions: PDE-5 I and ERA monotherapy is associated with improvements in functional class, exercise capacity and hemodynamic parameters in patients with Po-PAH. The effects of these drugs in patients with Po-PAH are similar to those observed in patients with other forms of PAH.

**P2508**

Comparison of clinical, functional and haemodynamic characteristics of patients with pulmonary arterial hypertension associated with portal hypertension (HIV-PAH) with HIV infection (HIV-HIPAH) and with Po-PAH.

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**Background:** Pulmonary arterial hypertension (PAH) is a rare complication of HIV infection and portal hypertension (Po-PAH). These two clinical conditions have different pathophysiological background but may concur in the same patient mainly due to similar risk factors for transmission of viral infections (HIV) and hepato-cirrhosis.

**Purpose:** To compare clinical, functional and haemodynamic characteristics of patients with PAH associated with portal hypertension (Po-PAH), HIV infection (HIV-Po-PAH) and both (HIV-Po-PAH).

**Methods:** From March 1993 to December 2011 we assessed baseline characteristics of patients with Po-PAH, HIV-Po-PAH and HIV-PAH. All patients underwent right heart catheterization, including mean trans hepatic pressure gradient (mTHG), and all underwent echocardiographic examination.

**Results:** We analysed 145 patients with Po-PAH, HIV-Po-PAH and HIV-PAH. Pathology and mTHG were: 1) Po-PAH: pre-hepatitis [8]; cirrhosis (virus [25], alcohol [17], alcohol-virus [19], cryptogenic [6], autoimmune hepatitis [1], primary biliary cirrhosis [1], hemocromatosis [1], Budd-Chiari [1]; mTHG = 12.5 ± 5 mmHg; 2) HIV-Po-PAH: cirrhosis (virus [22], alcohol-virus [4], Budd-Chiari [1]; mTHG = 10.5 ± 5 mmHg. Characteristics of each group are shown in the table.

**Conclusions:** Patients with HIV-PAH are younger but with a worse haemodynamic profile as compared with Po-PAH. Patients with HIV-Po-PAH have intermediate characteristics as compared with the two groups: in fact they are young, with an high cardiac output and as a consequence they have the better exercise capacity.

**P2509**

Utility of a diagnosis algorithm for detection of pulmonary hypertension in patients with lupus

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**Introduction:** The prevalence of pulmonary hypertension (PH) in patients with systemic lupus erythematosus (SLE) has been reported between 0.5 and 14%, but some studies have suggested that a mild degree of PH may be more common. Only a few studies have been carried out in caucasians using an algorithm for systematic evaluation with confirmation by right heart catherization (RHC). Objective: To assess the utility of a clinical algorithm for evaluation of PH in patients with SLE.

**Methods:** Prospective cross-sectional study of 158 patients with SLE. The study included clinical evaluation of the dyspnea (Borg scale), Doppler echocardiography (Doppler), using capacity for CO (DLC0), and NT-proBNP in all patients, with confirmation by RHC in cases of PAPs (DIEcho=) 45 mmHg or exercise D echo positive (pAPs>=) 20 mmHg), except for those with PH related to known left heart disease.

**Results:** Mean age: 45 (± 12.9) years, 94.3% women. Years of evolution of SLE: 14 (± 8.0). Dyspnea at the time of evaluation 21 patients (13.4%). 11 (6.9%) had some degree of PH. Three patients with structural heart disease had PH which was diagnosed by DEcho, three had postcapillary PH after exercise and one at baseline, with a total of 7 patients in group 2 (Dana Point 2008). One patient had thromboembolic disease (group 4). Only 3 out of 158 patients (2.5%) had precapillary PH directly attributable to SLE (group 1), in two cases the diagnosis was made before the study. The 11 patients (100%) with PH had dyspnea (Borg >= 2) versus 10 (6.8%) of 146 without PH (p = 0.001) (Fishier I). Patients with PH had lower DLC0: 59% (± 14) vs. 88% (± 15) (p = 0.048). 54% of patients (6 of 11) with PH had a NT-proBNP > 395 pg/mL, compared with 41% of controls, with significant differences in medium NT-proBNP (685±663 vs 191±578), p = 0.000 (U Mann-Whitney). Cardiovascular involvement was more frequent in patients with PH: 27.3 (11/1) vs. 6.8% (15/146) (p = 0.05). Considering only the 7 patients with PH at baseline (excluding stress), it remains significantly associated with dyspnea (p = 0.000), cardiac involvement (p = 0.014), number of patients with NT-proBNP > 395 pg/mL (p = 0.000). There were no difference in SLE clinical characteristics between SLE patients with vs. without PH.

**Conclusions:** There is low prevalence of precapillary PH in patients with SLE. The cardiac etiology predominates, and are mostly detected by stress test. A unselected screening program of PH based on echocardiography, NT-proBNP and pulmonary function testing is not cost-effective and should be restricted to SLE patients with unexplained dyspnea.

**P2510**

Right ventricular parameters predict survival in patients qualified for liver transplantation

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**Background:** Liver transplantation (LT) is an established treatment for end-stage liver disease (ESLD). The aim of this study was to identify the prognostic value of echocardiographic parameters in patients evaluated for LT due to liver failure.

**Methods:** We followed 131 patients (44 women, age 25 to 65 years, mean age 57.6 ± 14.5) referred for liver transplantation (LT) in 2007-2009. 80 underwent LT during the duration of the study. In addition to the complete transthoracic echocardiographic study, pulmonary vascular resistance (PVR), S’ tricuspid annular plane systolic excursion (TAPSE), aortic valve LVOT, left atrial volume (LAV) were assessed. All Doppler echocardiographic measurements were performed according to ESC standards. Pulmonary vascular resistance was estimated by echocardiography using the Abbas equation: PVR=TRV*VTI x 10. Total mortality, cardiovascular mortality and serious complications (heart attack, stroke), non-fatal hospitalization for cardiovascular reasons was analyzed over 6-months follow-up.

**Results:** In the whole group of liver transplantation candidates a higher risk of all-causes death was associated with increased tricuspid regurgitant velocity (TRV) (p=0.039), enlarged dimension of the right ventricle (p=0.030), and elevated right ventricular systolic pressure (p=0.036). The only independent echocardiographic risk factor for total mortality was a higher value right ventricular outflow tract RVOT VTI (p=0.05, OR 1.15, 95% CI 1:02-1:31) - beside male gender and inability to perform LT. Other echocardiographic parameters were not statistically significant predictors of death or other endpoints. In the group of patients who did not undergo LT we observed a statistically significant relationship between death and the parameters of the morphology and function of the right ventricle. Risk factors of mortality in this group were: the dimension of the right ventricle above 26 mm (p=0.028, OR 12.3), the tricuspid velocity regurgitant above 2.9 m/s (p=0.012, OR 7.4) and right ventricular systolic pressure above 37 mm Hg (p=0.041, OR 3.83). In patients undergoing liver transplantation lower value of PVR (p=0.021, OR 0.04), TRV (p=0.017, OR 0.06) and RVSP (p=0.015, OR 0.06) were correlated with reduced risk of total mortality. No independent risk factors were identified in this group.

**Conclusions:** Parameters reflecting right ventricular overload and increased pulmonary flow but not left ventricular dysfunction were prognostic for short-term clinical course in this relatively young group of patients qualified for orthotopic liver transplant.

**P2511**

Survival and hemodynamic response to first-line single or combination therapy in idiopathic, familial and systemic sclerosis-associated pulmonary arterial hypertension

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**Purpose:** Idiopathic (IPAH), familial (FPAH) and systemic sclerosis-associated (SSc-PAH) pulmonary arterial hypertension are severe diseases with poor prognosis. This retrospective registry study compared survival and hemodynamic response to first-line single or combination therapy in patients with IPAH/FPAH or SSc-PAH.

**Methods:** IPAH/FPAH (n=40) or SSc-PAH (n=32) patients >18 years registered in the Lund cohort of the Swedish PAH Registry from 2000-01 to 2010-12 were included if devoid of multiple pulmonary hypertension diagnoses. Hemodynamic effects were investigated in patients where right heart catheterization data was available at baseline and first follow-up. Patients receiving first-line single or combination therapy at registry baseline were analyzed separately. Patients were treatment naive at baseline except for a few SSc-PAH patients who for different reasons had received PAH drugs before registry inclusion. 3-year survival was estimated by Kaplan-Meier curves for the entire population. Patients were censored at transplantation and 2011-12 ±3 years since diagnosis. Values were mean±SEM. P<0.05 was considered significant.

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Results: In IPAH/FPAH patients, at follow-up after 5.5±0.5 months, first-line single therapy (n=23) had not consistently altered (p=ns) mean pulmonary artery pressure (mPAP), mean right atrial pressure (MRAP), pulmonary capillary wedge pressure (PCWP), cardiac output (CO) or pulmonary vascular resistance (PVR). At follow-up after 6.5±0.5 months, first-line combination therapy (n=8) had decreased (p<0.05) mPAP by 6.5±2.2 mmHg and PVR by 3.8±1.1 WU, and increased (p<0.05) CO by 6.8±0.4 min⁻¹, while MRAP and PCWP were unaltered (p=ns). In patients with SSc-PAH, at follow-up after 7.2±1.5 months, first-line single therapy (n=18) had decreased (p<0.05) mPAP by 4.6±1.4 mmHg and PVR by 1.0±0.4 WU, whereas MRAP, PCWP and CO were unaltered (p=ns). At follow-up after 11.8±6.5 months, first-line combination therapy (n=6) had not consistently altered (p=ns) mPAP, MRAP, PCWP, CO or PVR, 1-2- and 3-year survival were 90, 81 and 70% for IPAH/FPAH, and 84, 56 and 38% for SSc-PAH. Median survival-time was 907 days for SS-PAH, but better (p<0.05) for IPAH/FPAH.

Conclusions: Survival has improved for IPAH/FPAH and SSc-PAH since introduction of PAH-specific treatments and is better for IPAH/FPAH than SSc-PAH. The different hemodynamic effects to first-line single or combination therapy indicate individual variation in severity of disease and responsiveness to different treatments, emphasizing the need for new biomarkers to identify responders to specific PAH treatments.

P2514 Pulmonary arterial compliance is severely altered in severe primary pulmonary hypertension

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Purpose: There has been suggestion that pulmonary vascular reserve, measured by echocardiography by reduced pulmonary vascular resistance (PVR) and increased transit time of agitated contrast, might be associated with increased exercise capacity. This could be even more relevant at altitude, where PVR is increased because of hypoxic vasodilation. Furthermore, a larger pulmonary vascular reserve could be associated with higher lung diffusing capacity. We investigated whether larger pulmonary vascular reserve at sea level and high altitude predicts an improved exercise and lung diffusing capacity.

Methods: We reviewed echocardiographic estimates of PVR and measurements of the lung diffusing capacity for nitric oxide (DLNO) and for carbon monoxide (DLCO) at rest and incremental cardiopulmonary exercise tests in 64 healthy subjects at sea level and during 4 different medical expeditions at altitudes around 5000m.

Results: Altitude exposure was associated with a decrease in maximum oxygen uptake (VO2max), from 42±10 to 32±8.8 ml/min/kg and increases in PVR, ventilatory equivalents for CO2 (VE/VCO2), DLNO and DLCO. At univariate analysis VO2max was predicted at sea level and at altitude by VE/VCO2 (p<0.001), mean pulmonary arterial pressure (Ppa, p<0.05), stroke volume index (SVI, p<0.05), DLNO (p<0.02) and DLCO (p<0.05). At multivariate analysis, VO2max at sea level and at altitude was predicted by VE/VCO2, Ppa, SVI, and DLNO. The multivariate analysis also showed that the altitude-related decrease in VO2max was predicted by increased PVR and VE/VCO2.
The epidemiology of pulmonary arterial hypertension in HINPULSAR Registry showed areas for improvement in Argentina: promote early identification, improve the diagnostic strategy and treatment

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The epidemiology and management of pulmonary arterial hypertension (HAP) in Argentina is poorly known. We sought to characterize the clinical profile, diagnosis, evaluation and treatment strategies for this condition.

Method: Between Jan-10-Dec-11, 422 patients with diagnosis of PH were prospectively included in 31 centers from 13 provinces. The inclusion criteria were clinical diagnosis of PH and one of the following: systemic pulmonary arterial pressure (SPAP) ≥ 40 mmHg or mean pulmonary arterial pressure (MPAP) obtained by right heart catheterization (RHC) ≥ 20 mmHg. In total, 124 (29.4%) with diagnosis of HAP were included in the present analysis.

Results: Mean age was 45 ± 17 years and 78% were women. 53% were referred from other centers, 26% were incident cases and 27% did not have social insurance. According with Dana Point classification, the distribution was idiopathic 51.6%, inherited 1.6%, drugs 2.4%, connective tissue disease 15.3%, portal hypertension 1.6% and congenital heart disease 27.4%. Diagnosis was made by SPAP ≥ 40 mmHg in 95% (mean 81 ± 26 mmHg). The most frequent symptoms were dyspnea 92% (62% in functional class III-IV at the diagnosis), fatigue 49%, syncope 10%, chest pain 15%, palpitations 18% and heart failure 41%. Right heart catheterization was performed in 80 (65%) with SPAP ≥ 40 mmHg and MPAP 55 ± 20 mmHg, vasoactivity test in 48, which was positive in 21. Distribution according with functional class (FC) at diagnosis was: I: 9%; II: 26.7%; III: 17.7%; IV: 15.6%, and with previous history of heart failure (HF) in 41%. The treatment was different in patients in FC I to IV with diuretics (27, 57, 79 and 95%, p ≤ 0.001) and spironolactone (36, 49, 70 and 90%, p ≤ 0.004). Calcium antagonist were prescribed in FC I to IV in 9, 26, 16 and 26%, 17 and 28% vasoreactive and non vasoreactive subjects, both p = NS. Specific drugs were prescribed in FC I to IV in 9, 26, 16 and 26%, 17 and 28% vasoreactive and non vasoreactive subjects, both p = NS. Specific drugs were prescribed in FC I to IV in 9, 26, 16 and 26%, 17 and 28% vasoreactive and non vasoreactive subjects, both p = NS. Specific drugs were prescribed in FC I to IV in 9, 26, 16 and 26%, 17 and 28% vasoreactive and non vasoreactive subjects, both p = NS. Specific drugs were prescribed in FC I to IV in 9, 26, 16 and 26%, 17 and 28% vasoreactive and non vasoreactive subjects, both p = NS. Specific drugs were prescribed in FC I to IV in 9, 26, 16 and 26%, 17 and 28% vasoreactive and non vasoreactive subjects, both p = NS. Specific drugs were prescribed in FC I to IV in 9, 26, 16 and 26%, 17 and 28% vasoreactive and non vasoreactive subjects, both p = NS.

Conclusion: First line treatment with sildenafil or bosentan appears to have similar effects on hemodynamics and RV function capacity after 4.0 ± 0.9 months of treatment. Long term evaluation is ongoing.
function was identified in all patients with PH and in 36/72 (50%) patients with no PH. RV MPI, r = 0.5 (p < 0.01), RV IVA, r = 0.5 (p < 0.01), and sYs, r = 0.5 (p < 0.01) correlated with mPAP.

Conclusion: The present study has demonstrated impaired subclinical RV global and systolic function even in GOLD II in this cohort of COPD patients compared to controls. RVMPI seems to be the best echo index to identify reduced RV function in these patients.

### Table 1

<table>
<thead>
<tr>
<th>Variables (unit)</th>
<th>Controls (n=34)</th>
<th>COPD (n=58)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV MPI (mV/m)</td>
<td>0.30±0.04</td>
<td>0.45±0.10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>RV basal strain (%)</td>
<td>31±4.1</td>
<td>22±1.4</td>
<td>-0.01</td>
</tr>
<tr>
<td>RV IVA (m/s²)</td>
<td>3.1±0.7</td>
<td>2.0±0.4</td>
<td>0.01</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>NA</td>
<td>18±3</td>
<td>29±4</td>
</tr>
<tr>
<td>CI (m/min/m²)</td>
<td>NA</td>
<td>2.9±0.4</td>
<td>3.2±0.6</td>
</tr>
<tr>
<td>RV IVA (cm²)</td>
<td>NA</td>
<td>7.4</td>
<td>11±4</td>
</tr>
</tbody>
</table>

Values are mean ± SD. *Significantly different (p < 0.01) from controls. **Significantly different (p < 0.01) from no PH. NA Not available by invasive measurement.

### P2519

Immediate impact of successful percutaneous mitral valve commissurotomy on echocardiographic measures of right ventricular contractility

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**Purpose:** Functional analysis of the right ventricle (RV) cannot reliably evaluate cavitally oriented echocardiography techniques owing to complex geometry and load dependence of ejection phase indices. Dp/dt, the Tei-index, and myocardial acceleration during isovolumic contraction (IVA) are parameters of RV contractility unaffected by RV geometry. However, the effect of loading conditions on these parameters is controversial. The aim of this study was to examine the effect of PTCM before and after on RV dp/dt and IVA indexes.

**Methods and results:** Fifty eight patients (mean age 30.0±8.3 years old, 58males and 52 females) with isolated rheumatic MS, eight of whom had atrial fibrillation, were studied before and 24–48 hr after PTCM. Immediately following PTCM, RV dp/dt and IVA indexes were measured by echocardiography machine.

There was a significant decrease in systolic pulmonary artery pressure from 42.1±4.9 to 39.6±4.2 mmHg (p<0.001), RV IVA and systolic velocity (SV) at the lateral tricuspid annulus assessed by tissue Doppler imaging did not change. There was weak positive correlation among Tei index, dp/dt and SPAP before PTCM (respectively, r=0.3, p=0.06, and r=0.05, p=0.05) but not after (respectively, r=0.17, p=0.02, and r=0.02, p=0.9).

**Conclusion:** This study suggests that RV dp/dt and Tei indexes are weakly load dependent whereas IVA is unaffected by acute change in RV afterload.

### P2521

Role of tissue doppler echocardiography in detecting preclinical cardiac involvement in systemic sclerosis patients

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**Purpose:** Primary myocardial involvement is common in systemic sclerosis (SSc), but often underestimated. Clinically apparent myocardial involvement has significant therapeutic implications and is an important prognostic factor. Cardiac involvement may occur years before clinical manifestation. Limited data are available on preclinical cardiac involvement assessment. In this study, we investigated whether preclinical cardiac dysfunction could be detected by echocardiographic Tissue Doppler Imaging (TDI) in SSc patients.

**Methods:** We prospectively studied 33 consecutive female patients (mean age = 52.3±12.3 years old) with SSc without cutaneous hypertension, arterial hypertension or renal failure, and in NYHA class. Results were compared with 16 age and sex-matched healthy controls (mean age = 48.8±5.6 years; p=0.93). Patients underwent standard echocardiography, along with measurements of longitudinal velocities by TDI to assess right ventricular (RV) function.

**Results:** Systolic right ventricular function, as assessed by peak systolic tricuspid annular velocity, was lower in patients than in controls (mean ± SD 8.0±2.4 vs 10.6±1.1; p=0.0005).

**Conclusion:** Evaluation of ventricular function by TDI is an effective tool to detect preclinical systolic and diastolic cardiac involvement in SSc patients, when therapeutic options are supposed to be more effective.

### P2522

Clinical characteristics of pulmonary arterial hypertension (PAH) associated with congenital heart disease: baseline results from the THALES (Turkish Congenital Heart Disease-associated PAH) Registry

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**Purpose:** THALES is the first national multicenter prospective observational registry, providing demographic and clinical characteristics, laboratory data, prognostic and treatment patterns in pulmonary arterial hypertension (PAH) associated with congenital heart disease (APAH-CHD) in Turkey.

**Methods:** Patients (>3 months of age) with APAH-CHD (mean pulmonary arterial pressure [mPAP] >25 mmHg, pulmonary capillary wedge pressure (PCWP) ≤15 mmHg, and pulmonary vascular resistance index [PVRI] <3 Wood units/m²), were enrolled at 61 centers in Turkey. First results of baseline characteristics of patients enrolled to date are presented.

**Results:** Between May 2009 and October 2011, 1034 patients (male:female=1:1.38) aged 3 months–79 years (mean 16.9±17.9 years) were enrolled. 249 patients (24.1%) were <2 years, 349 (33.8%) were 2–15 years, and 436 (42.1%) were >15 years of age. Mean mPAP was 54.6±22.15 mmHg, PVRI 10.23±10.84 WU/m², 55.4% and 34.5% of patients had Eisenmenger’s syndrome (Group A) or PAH associated with systemic-to-pulmonary shunts (Group B), respectively. Both groups had similar pulmonary artery hypertension with significant residual defects. 1.2% had PAH with small defects (Group C), 7.3% had PAH after repair of CHD in the absence of significant residual defects (Group D), and 1.6% had PAH associated with unrepaired or partially repaired complex cyanotic CHD and increased pulmonary blood flow (Group E). Dyspnea was the most frequent symptom (69.8%), followed by chest pain (10.4%), and hemoptysis (6.9%). Syncope/pre-syncope was reported in 5.9%, the highest percentage recorded in group D (16.2%). Functional class was predominantly III in Group A (48.2%), and II in groups B-E (75.8%, 83.3%, 57.5%, 66.7%, respectively), 415 (40.1%) patients received targeted PAH therapies (monotherapy in 80.7%, combination in 19.3%). Bosentan was the most frequently prescribed agent; 80% of patients. Bosentan/Procrit and Bosentan/Sildenafil were the most common drug combinations (54% and 32%, respectively). Overall treatment rate for FC III-IV patients was significantly higher than FC II (74% vs 36%, p<0.001). Patients on inhaled Procrit had significantly lower baseline 6-minute walking distance than those receiving oral agents.

**Conclusion:** This is the first study characterizing APAH-CHD patients in Turkey. Overall treatment rates for FC II patients are lower compared to FC III-IV suggesting under-utilization of therapies in patients with milder disease. Further analysis regarding disease course, prognosis, the impact of surgical/interventional procedures and long term efficacy of targeted therapies is planned.

### P2523

Prevalence of pulmonary hypertension among asymptomatic school children in India

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**Purpose:** The prevalence of pulmonary artery hypertension (PAH) among asymptomatic school children in India is not known. Conventionally, auscultation has been used for screening for heart disease, but echocardiography with Doppler may be more sensitive and specific. Hence, in the RHEUMATIC study designed to identify echocardiographic prevalence of rheumatic heart disease, we estimated the prevalence of PAH.

**Methods:** We carried out a cross sectional survey to diagnose heart defects in asymptomatic school children aged 5-15 years, living in rural areas, using portable echocardiography. The data was collected in 8 centers. After history and physical examination, echo-Doppler was performed, using a bedside portable echocardiography machine.

**Results:** A total of 11,177 asymptomatic children (mean age 10.7±2.7 years) were screened and 50.9% were boys. Echo-Doppler diagnosed pulmonary hypertension in 4 cases, giving a prevalence of 0.3/1000 school children (95% CI 0.1 – 0.9/1000 children). The cardiac lesions associated with PAH identified by echo-Doppler included: rheumatic heart disease (2 patients), Eisenmenger syn-
Impaired functional capacity in patients with systemic sclerosis is related to right ventricle dysfunction

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Systemic sclerosis (SSc) is characterised by cardiovascular abnormalities, which may affect patient’s clinical symptoms. Aim: was to assess whether the impaired exercise tolerance in patients with SSc without overt cardiopulmonary complications is related to left ventricle (LV) or right ventricle (RV) dysfunction and vascular remodeling.

Methods: Forty-seven patients (F/M:36/11, age57±9.9) with diagnosed SSc and clinical symptoms (NYHA III) were enrolled into the study. In all the patients, pulmonary arterial hypertension (PAH), pulmonary fibrosis, left ventricle (LV) systolic dysfunction and valvular heart diseases were excluded. The following tests were performed: echocardiography, ultrasound vascular indexes: flow mediated dilatation, nitroglycerin mediated dilatation and arterial tonometry parameters: pulse wave velocity, pulse pressure and augmentation index. The above indexes were related to the 6 minute walk test (6MWT) results.

Results: The 6MWT mean value was 440±72m. LV diastolic function parameters did not correlate with 6MWT. RV systolic dysfunction (fraction area change<−32%), decreased tricuspid annular plane systolic excursion (TAPSE <20mm) or low peak systolic velocity of lateral tricuspid anulus (TDI: RV S’<20cm/s) were found in 1 (2.1%), 5 (10.6%), 43 (91.5%) patients, respectively. The 6MWT values correlated with TAPSE (r=0.318, p=0.030, Fig 1) and TDI: RV S’ (r=−0.295, p=0.048). There were no significant correlations between ultrasound parameters and 6MWT values.

Conclusion: After exclusion of typical causes of low exercise capacity in SSc, the shortened 6MWT distance observed in this group seems to be related to the RV systolic impairment, which supports regular echocardiographic screening for early detection of cardiac complications in SSCs.

Echo in the cath-lab: reliability of non-invasive versus invasive evaluation in an heterogeneous pulmonary hypertension population

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Aim: Doppler echocardiography (DE) is recommended for screening of pulmonary hypertension (PH) but the ultimate diagnosis of PH is currently established by right-heart catheterization (RHC). Aim of this study was to evaluate the accuracy of DE in estimating the key measurements of RHC: mean pulmonary artery pressure (mPAP), cardiac index (CI), capillary wedge pressure (CWP) and pulmonary vascular resistances (PVR).

Methods: All consecutive patients referred to our PH tertiary center from January to December 2011 underwent standard DE within 1 hour of a clinically indicated RHC to compare non-invasive hemodynamic estimates with invasively measured values.

Results: One hundred thirty-five patients were evaluated. Twelve/135 (9%) did not have PH. Of 123 PH patients with PH, 54 (43%) had group 1, 39 (29%) group 2, 22 (16%) group 3, and 8 (6%) group 4 PH. DE showed a satisfactory correlation to invasive evaluation (Table). Nevertheless, it was inaccurate in defining the presence of pre-capillary (CWP ≤15 mmHg, groups 1, 3, and 4) versus post-capillary (CWP >15 mmHg, group 2) PH leading to a misclassification in 22/123 (18%) of analyzed patients. In particular, sensitivity of echo for pre-capillary PH was 82% and specificity 83%.

Conclusion: Doppler echocardiography is an essential tool for the screening of PH, but it only provides an initial approach to the patients with suspected PH.

Acute hemodynamic effects of levosimendan in right heart hypertrophy and failure

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Purpose: Levosimendan is an inotropic calcium sensitizer used in the treatment of severe left heart failure. We investigated the hemodynamic effects of levosimendan in two different in vivo animal models of right ventricular hypertrophy and failure.

Methods: Wistar rats were randomised to pulmonary trunk banding (PTB) producing isolated RV pressure overload with a fixed afterload (n=8), sham operation (n=8) or monocrotaline (MCT) (n=7) inducing pulmonary vascular remodelling.

Results: Our models of PTB and MCT caused hypertrophy, diastolic failure and RV failure. In all three groups levosimendan increased RV stroke volume (RVS) (sham: 21.7±3.3%, CI: 13.3±1.8%, MCT: 24.1±2.4%, PTB: 19.8±6.3%, p<0.05) compared to baseline. Levosimendan markedly increased RV stroke volume (RVS) measured by MRI in the MCT group (24.1±6.6%, p<0.05), did not change RV SV in the PTB group (1.3±2.9%, p=0.68) and decreased RV SV in the sham group (-12.5±4.5%, p<0.05). See Fig. 1. The reduction in RV SV in sham animals was due to preload reduction.

Role of ERK and Akt/eNOS signalling in chronic volume overload induced right ventricle remodelling

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Purpose: Chronic volume overload induces right ventricle (RV) failure and pulmonary hypertension. Molecular mechanisms for ventricular and vascular remodelling remain unclear. This study examined some of the signal pathways, which are known to regulate pro- or anti-apoptotic proteins and nitric oxide homeostasis.

Methods: Aceto-caval (AC) shunt was surgically created in 20 male Sprague-Dawley rats (350-450 g). Shunt operated rats (n=20) were considered as control. Animals were assessed for hemodynamic signs of RV dysfunction and pulmonary hypertension at 20 weeks after operation. RV and lungs were examined to determine: apoptosis-associated signal transduction mechanisms, endothelial nitric oxide synthase (eNOS) expression/activation, oxidative stress by reduced to oxidized glutathione (GSH/GSSG) ratio, high energy phosphates content, and apoptotic index.

Results: Hemodynamic data indicated the presence of severe RV dysfunction, pulmonary hypertension and impaired ventricular-vascular coupling in AC shunt rats. Western blot analysis revealed a significant increase in phosphory-
Impact of dopamine and dobutamine support at the initiation of epoprostenol as compared with 76.6% in DOA and/or DOB support: 66

Results: At the initiation of epoprostenol, 25 patients did not receive neither DOA nor DOB support. Eight patients received DOA support, 24 patients DOB support and 14 patients DOA and DOB support, respectively. No significant difference was found in mean pulmonary artery pressure between 4 groups (non-support: 65±16 mmHg, DOA support: 57±16 mmHg, DOB support: 65±16 mmHg, DOA and DOB support: 66±20 mmHg). Eight patients died and one patient received lung transplantation during hospitalization of epoprostenol initiation. The use of noradrenaline and mechanical supports (percutaneous cardiopulmonary support device and intubation) during hospitalization was associated with poor short-term outcome. Eighteen patients required mechanical support to the end of hospitalization.

Conclusion: DOA and DOB support by our strategy at the initiation of epoprostenol was not associated with short and long-term survival in patients with PAH.

Can the clinical classification of congenital heart disease associated pulmonary arterial hypertension be used in pediatrics? Analysis of the TOPP registry

Methods: The aim of our study was to evaluate the impact of dopamine and dobutamine support at the initiation of epoprostenol as compared with the group with neither DOA nor DOB support. The patients were stratified into 4 groups: (1) non-supported group, (2) DOA-supported group, (3) DOB-supported group, and (4) DOA and DOB-supported group. The primary endpoint was survival at 1 year post-repair.

Conclusion: If consensus was not obtained, the patient was considered “not categorized” (NC). Demographics and PVR are shown in the table. 27 patients diagnosed as idiopathic PAH had some type of CHD and were recategorized in (B) (3/27), (C) (10/27), and (D) (6/27). The largest est group was PAH after repair (48/142) but a significant number were NC (18/142). The current PAH-CHD classification into 4 groups seems feasible for pediatric patients in group A, B and D but was difficult to apply to group C with the diversity of absolute defect size. The largest PAH-CHD group in this pediatric PH Registry was D, characterized by high PVR (>1 year post-repair) raising concerns about the appropriateness of performing the prior surgical repair. A significant number of patients with complex CHD or PAH who never had shunts were difficult to categorize. A more tailored description appears necessary for PAH-CHD in children, in particular those with small defects (defining small being different among the spectrum of pediatric ages) or complex CHD.

Evaluation of response to oral therapy in portopulmonary hypertension

Methods: 83 patients (pts) with PoPH were prospectively included in this open-labelled uncontrolled study from 2004 to 2010. PoPH was defined by a mean pulmonary arterial pressure >25 mmHg, pulmonary capillary wedge pressure ≤15 mmHg and pulmonary vascular resistance ≥240 dynes.s.cm-5 on right heart catheterization. Eighteen patients received oral RHC with portal hypertension. RHC was repeated after initiation of oral treatment by endothelin receptor antagonist (ERA) or phosphodiesterase-5 (PDE) inhibitor.

Results: PoPH was mainly caused by alcoholic cirrhosis (n=63, 76%). At diagnosis, mean pulmonary arterial pressure was 49.3±1.4 mmHg, mean cardiac index 2.8±0.1 l/min/m² and mean 6-MW distance was 337±12 m. Of the 83 screened pts, 57 (69%) underwent a second evaluation. Twenty-three pts died before control, mainly from complications of cirrhosis. Twenty-five pts (44%) were started on ERA, 26 pts (46%) on PDE inhibitor and 4 pts (7%) on both in combination. On RHC, cardiac index significantly improved (p=0.0001), mean pulmonary arterial pressure and pulmonary vascular resistance significantly decreased (p<0.001 and p=0.0001, respectively). New York Heart Association (NYHA) score and 6-MV distance significantly improved (p<0.0001 and p<0.0003, respectively) and BNP decreased (p=0.01). No significant variation in transaminases or hemoglobin levels was noticed, especially in the subgroup receiving ERA.

Conclusion: In this study of 57 consecutive pts with PoPH, we have shown that oral treatment (ERA, PDE inhibitors), alone or in association, can significantly improve clinical parameters and hemodynamic responses without adverse effect on hepatic function.

Ventricular geometry and strain determinants of NT-proBNP in arterial hypertension

Methods: 30 patients (8 men), age 66±13.5 years, with PAH (thromboembolism 14, 11 systemic disease, 1 congenital, idiopathic 4) on specific therapy. Median NT-proBNP 724, TAPSE 20.0±6.0, right ventricle (RV) ejection fraction 37.4±18.4%, Left ventricle (LV) EF 61.0±16.0%, pulmonary artery systolic pressure (PASP) 88.6±15 mmHg. Complete echocardiography including 2D, Doppler, TDI mitral annulus septal (SmI, Emd, Amt) and tricuspid (Str Vti, Etr, Atr), T1 index, diastolic (IE-D) and systolic (IE-S) Eccentricity index; longitudinal myocar-

Objective: Determine in patients with pulmonary arterial hypertension (PAH) the relationship between NT-proBNP, ventricular geometry and ven-tricular contractility.

Results: (1) The NT-proBNP correlates with: (i) RV Function - STR Vti (r = -0.611 po.001), STR (r = -0.408 po.001), TAPSE (r = -0.367 po.051), T1 index Tr (r = 0.411 po.037), RS-GV (r = -0.506 po.005), RV-GSpra (r = -0.571 po.003), (ii) LV Function - SmI (r = -0.45 po.001), Amt (r = -0.421 po.001), LV-GSpra (r = -0.412 po.003) and LV-GSri (r = 0.45 po.028), (iii) Geometry: IE-D (r = -0.409 po.027), IE-S (r = -0.432 po.019). (iv) Independent predictors of the NT-proBNP (multiple regression): (i) RV Function: T1 index (r = 0.001), STR

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Impact of dopamine and dobutamine support at the initiation of epoprostenol on short and long-term survival in patients with pulmonary arterial hypertension

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Evaluation of response to oral therapy in portopulmonary hypertension

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Ventricular geometry and strain determinants of NT-proBNP in arterial hypertension
Effect of medical therapy in patients with out-of-proportion pulmonary hypertension due to parenchimal lung disease

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Background: Pulmonary hypertension (PH) is a complication of parenchimal lung disease and it is associated with poor survival. A small subgroup of these patients may present with out-of-proportion PH, defined by a mean pulmonary arterial pressure ≤ 40 mmHg. Currently, the safety to efficacy ratio of targeted therapies approved for pulmonary arterial hypertension (PAH) in cases with out-of-proportion PH due to lung disease is unknown.

Purpose: To evaluate the safety-to-efficacy ratio of specific PAH therapy in patients with lung disease and out-of-proportion PH.

Methods: Between November 2008 and January 2012, 33 patients (15 with interstitial lung disease, 12 with chronic obstructive pulmonary disease and 6 with a combination of both) were treated with endothelin receptor antagonists drugs (12, ERA) and phosphodiesterase type-5 inhibitors (21, PDE5-i). At baseline and after a mean treatment period of 4 to 6 months, patients underwent 6-minute walk test (6MWT) and right-heart catheterization.

Results: Mean age was 67±9 years. Three patients did not perform the exercise and haemodynamic assessment due to death (1) or clinical deterioration (2); 2 patients withdrew from the therapy due to side effects (both in the PDE5-Igroup). 3 patients have not been studied yet. To date, 25 patients have completed the study (mean period of treatment 4.3±1.0). Hemodynamics and 6MWT parameters are shown in the table.

Table: Hemodynamics and 6MWT Parameters

<table>
<thead>
<tr>
<th>Baseline</th>
<th>4 weeks</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAP (mmHg)</td>
<td>mRAP (mmHg)</td>
<td>mSAP (mmHg)</td>
<td>CI (%)</td>
</tr>
<tr>
<td>15.1±1.9</td>
<td>14.9±1.9</td>
<td>15.2±1.9</td>
<td>15.2±1.9</td>
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Conclusions: In patients with out-of-proportion PH due to parenchimal lung disease able to complete 4 to 6 months of therapy with PAH-approved drugs (76%), a moderate haemodynamic improvement was observed. However, no changes in exercise capacity and a trend towards the reduction of finger oxygen saturation at end-exercise were detected.

Pulmonary hemodynamic changes, functional capacity and clinical events in pulmonary arterial hypertension: A meta-analysis of 16 randomized trials


Purpose: In patients with pulmonary arterial hypertension (PAH) it is unknown whether changes in pulmonary hemodynamic parameters induced by therapy correlate with functional capacity and clinical events (CE).

Methods: MEDLINE, Cochrane, ISI Web of Science and SCOPUS database were searched for randomized trials investigating PAH therapy until November 2011. Measuring hemodynamic parameters by right heart catheterization at baseline and at end of follow-up and reporting CE (all-cause death, hospitalization for PAH and/or lung or heart-lung transplantation, initiation of PAH rescue therapy). Meta-analysis and meta-regression analysis were performed to assess the effects of treatments on outcomes and the relationship between hemodynamic parameters and CE. Spearman correlation was used to test the relationship between changes in hemodynamics and 6 minute walking distance (6MWD).

Results: 16 trials enrolling 2,353 patients were included in meta-analysis. Treatment significantly reduced composite outcome (all CE) (OR: 0.459; 95% CI: 0.346 to 0.624; p<0.01) as well as all-cause death (OR: 0.467; CI: 0.292 to 0.747; p<0.01), hospitalization for PAH and/or lung or heart-lung transplantation (OR: 0.384; CI: 0.218 to 0.674; p<0.01), initiation of PAH rescue therapy (OR: 0.341; CI: 0.200 to 0.582; p<0.01). No relationship was found between changes of hemodynamic parameters and CE, whereas changes of cardiac index and PVR significantly correlated to changes of 6MWD (r=0.638, p<0.035; r=0.547; p<0.043 respectively). No heterogeneity among trials included in meta-analysis, potential confounding variable or publication bias was detected.

Conclusions: In PAH patients, improvement of pulmonary hemodynamic parameters correlates with functional capacity changes but do not predict CE.

6-minute walk distance and clinical events in pulmonary arterial hypertension: a meta-analysis of 22 randomized studies

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Purpose: 6-minute walk distance (6MWD) has usually been employed as end-point (often primary) in clinical trials to assess the benefit of therapies in pulmonary arterial hypertension (PAH). The aim of the current study was to verify whether changes in 6MWD reflects clinical events in PAH patients.

Methods: MEDLINE, Cochrane, ISI Web of Science and SCOPUS databases were searched for articles about PAH treatment until August 2011. Study inclusion criteria were: report of 6MWD at baseline and at end of follow-up, and of clinical end-points (all-cause death, hospitalization for PAH and/or lung or heart-lung transplantation, initiation of PAH rescue therapy); randomized protocol design. Meta-analysis was performed to assess the influence of treatments on outcomes. Meta-regression analysis was performed to test the relationship between 6MWD changes and outcomes. The influence of potential effect modifiers and the presence of publication bias were also explored.

Results: 22 trials enrolling 3,112 participants were included. Active treatments led to significant reduction in the risk of all-cause death (OR: 0.459; CI: 0.346 to 0.624; p<0.01), hospitalization for PAH (OR: 0.384; CI: 0.218 to 0.674; p<0.01), hospitalization for PAH and/or lung or heart-lung transplantation (OR: 0.384; CI: 0.218 to 0.674; p<0.01), initiation of PAH rescue therapy (OR: 0.341; CI: 0.200 to 0.582; p<0.01), and composite outcome (OR: 0.459; CI: 0.313 to 0.630; p<0.01; h=0.345). In meta-regression analysis, no relationship between 6MWD changes from baseline to end of follow-up and outcomes was observed. No publication bias was detected.

Figure 1. Meta-regression between 6MWD and events

Conclusions: In patients with PAH, improvement in 6MWD, induced by pharmacological treatment, does not reflect reduction in clinical events.
The innate immune system, NLRP3 inflammasome, in epicardial adipose tissue intensifies human coronary atherosclerosis


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Background: The emergence of chronic inflammation could enhance obesity-induced insulin resistance and atherosclerosis, but the underlying mechanisms remain unclear. The Nod-like receptor (NLR) family of innate immune cell sensors, such as pyrin domain-containing-3 (NLRP3) inflammasome are implicated as one candidate to elicit nonmicrobial originated signals in atherosclerosis. Objectives: We determined association between the NLRP3 inflammasome signals in epicardial adipose tissue (EAT) and coronary atherosclerosis in human.

Methods: Pair samples were obtained from epicardial and subcutaneous adipose tissue during elective cardiac surgery for coronary (CAD, n=40) or non-coronary artery disease (non-CAD, n=40). Expression of NLRP3 in EAT was analyzed by immunohistochemical staining using antibodies against NLRP3, CD68 and IL18. Expression of pro- and anti-inflammatory adipocytokines in EAT was evaluated by quantitative real-time polymerase chain reaction (qPCR).

Results: By immunohistochemical staining, NLRP3 signals were well detected in EAT of the CAD group, but rarely in EAT of the non-CAD group. The signals were co-localized with macrophages in EAT determined by anti-CD68 or anti-F4/80 immunostaining. By qPCR, signals of NLRP3, TLR1, TLR2, TLR4, but not TLR3, TLR5 and TLR9, were increased in EAT of the CAD group as compared to that of the non-CAD group. Signals of MyD88, but not MD-2, were also enhanced in EAT of the CAD group. Signals of IL-18 and adiponectin were decreased in EAT of the CAD group.

Conclusions: We, for the first time, showed that NLRP3 inflammasome signals were enhanced, but signals of IL-18 and adiponectin were decreased, in EAT of the coronary atherosclerotic lesions. We conclude that atherogenesis in human coronary arteries may be caused in part by NLR signals in infiltrating macrophage of epicardial adipose tissue.

Adiponectin and its receptor 1 inhibit lipid accumulation, oxidative stress and autophagic damage in the hypertropic heart of diet-induced obese mice

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Background: Adiponectin and its receptors (AdipoR1 and 2) have been demonstrated to play important roles in regulating glucose and lipid metabolism in mice. Obesity, type 2 diabetes and cardiovascular disease are highly correlated with downregulated adiponectin signaling. The functions of AdipoR1 have not been demonstrated in vivo. In this study, we generated mice overexpressing AdipoR1 transgene to study its functions in against hypertrophic heart. Wild-type and AdipoR1- transgenic male mice were fed ad libitum with a standard chow diet or a high-fat/sucrose diet (HFDSD) for 24 wk, beginning at 6 to 7 wk of age.

Results: Upon challenged with HFDSD to induce obesity, AdipoR1-transgenic mice were found to be protected from developing obesity and heart hypertrophy. AdipoR1 transgene decreased the elevating cardiac troponin I expression caused by HFDSD, demonstrating an improvement of cardiac damage by AdipoR1. HFDSD induced mRNA expression of CD68 and CPT1, whereas adipoR1 reversed them, implying the potential role on decreasing lipid accumulation in the heart. Suppressing cardiac SOC mRNA expression by HFDSD was improved by AdipoR1 transgene. HFDSD caused a higher autophagic gene expression of Beclin 1 and Lamp 2A in the heart, whereas AdipoR1 transgene ameliorated them, implying a protection from HFDSD-induced autophagic death by AdipoR1.

Conclusion: AdipoR1 transgene resisted diet-induced obesity, decreased lipid accumulation, oxidative stress and autophagic damage, which might contribute to the improvement of heart functions of diet-induced obese mice.

Is cardiac frequency on admission, a prognostic factor for acute pericarditis?

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Purpose: Rest is usually recommended in acute pericarditis, as it could help to lower cardiac frequency, and contribute to limit "mechanical inflammation". Whether cardiac frequency on admission can predict clinical evolution of pericarditis is not known.

Methods: Between March 2007 and February 2010, a retrospective study was performed for all patients admitted in our center for acute pericarditis, diagnosed if 2 criteria among the 4 following: typical chest pain, friction rub, pericardial effusion on cardiac echography, or typical ECG findings. We evaluated hospital events (heart failure, acute pains, death) and biology during hospitalization (CRP on admission, on days 1, 2, 3, peak). At one month, clinical events were recorded through phone calls when not noticed in clinical settings.

Results: We included 73 patients. Mean age was 41.0 y (CI 95% 37.2-44.8) and mean hospitalization duration was 3.5 d (2.5-4.5). Among patients with pericardial effusion (27% of patients), we observed that CRP on admission and peak of CRP were significantly more elevated that in those without (59.4 mg/L (24.9-93.9) versus 18.9 (9.7-28.1); p< 0.04) Heart rate on admission was 86.0 bpm
Our data show that two populations of MSC of HF patients with recurrences, heart rate on admission and peak of CRP were significantly higher (96.6 (89.3-105.0) versus 80.0 (74.4-85.5), p < 0.002). CRF (61.0-124.5) versus 37.6 (21.7-53.4), p = 0.007). Fever was scarcely observed (21%), and was not correlated to heart rate nor CRP.

**Conclusion:** In acute pericarditis, cardiac frequency at admission is correlated with cardiac recurrence and with CRP levels, and could be a new prognostic marker.

### STEMC CELLS

**P2539**

*Altersations in cytokine gene expression and secretion in mesenchymal stem cells derived from bone marrow and adipose tissue of the patients suffering from chronic heart failure and co-morbidities*


The purpose of the present study was to elucidate the properties of mesenchymal stem cells (MSC) in patients with heart failure (HF) and co-morbidities (obesity and diabetes mellitus (DM)) in terms of their relationship to the clinical severity of the disease and cardiovascular function.

**Methods:** A group of 36 HF patients enrolled included 11 with isolated HF, 16 with comorbid obesity, and 11 with DM and obesity. Body composition analysis was performed using osteodensitometry. Exercise tolerance was assessed by cardiopulmonary testing (CPX). Blood samples were collected to perform blood chemistry tests. Bone marrow (BM) and subcutaneous adipose tissue (Ad) derived MSC cultures of patients with HF were evaluated at passage 3 for gene expression and secretion of a set of cytokines involved in modulation of cardiac remodeling, neovascularization, and inflammatory response (transforming growth factor β (TGFβ)), interleukin 6 (IL-6), and monocyte chemotactic protein 1 (MCP-1)).

**Results:** BM- and Ad-MSC of patients with HF having exercise intolerance profoundly demonstrated poor proliferative activity: mean population doubling time (PD) in “high tolerance” group was 3.60, vs 6.02 days in “low tolerance” group (p = 0.037) for BM-MSC, and 2.16 vs 3.30 days for Ad-MSC (p = 0.013). A correlation was observed in BM-MSC PD time and serum NT-proBNP (r = 0.35, p = 0.01) and blood glucose (r = 0.51, p = 0.001). TGFβ secretion correlated with body fat (r = 0.61, p = 0.020; r = 0.65, p = 0.015 for BM-MSC and Ad-MSC, respectively), body mass index (BMI) (r = 0.60, p = 0.029 for BM-MSC) and CPX peak oxygen consumption (r = 0.64, p = 0.019; r = 0.538, p = 0.039 for BM-MSC and Ad-MSC, respectively). IL-6 was up-regulated in BM-MSC at both protein and mRNA level in obese: secreted IL-6 level correlated with body fat (r = 0.54, p = 0.046) and BMI (r = 0.647, p = 0.017) and the level of IL-6 gene transcripts correlated with waist and hip circumference (r = 0.57, p = 0.004; r = 0.67, p = 0.004, respectively). There was a correlation in BM-MSC CCL2 gene expression and BMI (r = 0.55, p = 0.03). In contrast, no significant correlation with the above-mentioned clinical parameters was established for IL6 and CCL2 in Ad-MSC derived from the same patients.

**Conclusions:** Our data show that two populations of MSC of HF patients with recurrences, heart rate on admission and peak of CRP were significantly higher (96.6 (89.3-105.0) versus 80.0 (74.4-85.5), p < 0.002). CRF (61.0-124.5) versus 37.6 (21.7-53.4), p = 0.007). Fever was scarcely observed (21%), and was not correlated to heart rate nor CRP.

**P2541**

*In vivo non-invasive bioluminescence imaging monitoring of cTnl and CD31 gene expression in cardiac adipose tissue-derived progenitor cells (ATDPCs) implanted in a mouse model of myocardial infarction*


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**Purpose:** The population of progenitor cells isolated from human cardiac adipose tissue (cardiac ATDPCs) proved to be a valid cell source for cardiac regeneration in rodent models of myocardial infarction. These cells, however, do not express cardiac troponin I (cTnI) in basal conditions in culture, although de novo expression was achieved in co-culture with neonatal cardiomyocytes. Low levels of CD31 were found when cells were cultured in standard conditions. Whether cTnI and CD31 expression are upregulated in vivo after cell delivery in cardiac regeneration protocols is unclear. The purpose of this study was to monitor in vivo cTnI and CD31 gene expression of cardiac ATDPCs delivered through a fibrin patch in the murine model of myocardial infarction by means of non-invasive bioluminescence imaging (BLI).

**Methods:** ATDPCs of cardiac origin were transduced with two lentiviral vectors for bioluminescence and fluorescence monitoring: CMV-Rluc-RFP-tk (constitutive expression) and cTnI-Fluc-RFP-EGFP-human-specific cTnI and CD31 expression respectively). Next, cells were loaded in a 3-D fibrin patch and transplanted covering injured myocardium in a mouse model of myocardial infarction. Sham-operated animals (cells implantation and no infarction) were used as controls. Bioluminescence images were obtained and light was quantified at 0, 1, 2 and 3 weeks post-implantation. Mouse hearts were excised and processed for immunostaining.

**Results:** Bioluminescence images indicated that de novo expression of cTnI was already induced one week post-implantation in cardiac ATDPCs. BLI quantification results revealed a 30-fold increase of cTnI expression in cells transplanted into infarcted animals, while only 4-fold increase was found in sham group (p = 0.037). These results were confirmed by protein expression as analysed by immunofluorescence. CD31 expression also increased, getting to a maximum at 2 weeks post-implantation in both groups (132-fold increase). Additionally, vessel density was significantly higher in cardiac ATDPCs treated animals compared with controls (p < 0.01).

**Conclusions:** Our work indicates that de novo expression of cTnI in cardiac AT-DPC implanted into a mouse infarcted myocardium already occurred one week post-implantation. Comparative analyses between infarcted and sham groups showed that cardiac injury might enhance cardiac AT-DPCs differentiation into cardiomyogenic cells. On the other hand, cardiac environment importantly upregulates CD31 expression in transplanted cardiac ATDPCs. This was reflected as an increase in myocardial vessel density.
**P2542**

**Skp2 rescues endothelial progenitor cell senescence in vitro and in vivo**

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**Purpose:** Cell cycle retardation is a prominent feature of senescence in proliferating cells. p53 phase kinase-associated protein-2 (Skp2), an F-box subunit of SCF/Skp2 ubiquitin ligase responsible for proteasomal degradation of many cell cycle proteins, is a key regulator for G1-S transition. It remains poorly understood whether Skp2 plays a role in the regulation of endothelial progenitor cell (EPC) senescence.

**Methods:** Senescence of human EPC was induced in vitro by serial passages and confirmed by an arrest at 100% of cells doubling time. Skp2 overexpression and silencing were achieved by using adenoviral vector and siRNA, respectively. EPC function was tested in vitro by injection of EPC into ischecmic nude-mouse hindlimb which was induced by ligation and dissection of femoral artery.

**Results:** Compared with young EPC, Senescent EPC showed remarkably reduced cell proliferation due to G1 arrest, downregulated p21cip/waf1 (p21) expression, along with a typical increase of senescence-associated β-galactosidase (SA-βGal) activity. To further elucidate the pivotal role of Skp2 in the EPC senescence, Skp2 was silenced by siRNA in long-term EPC. We found that in a senescent-alone was sufficient to result in an increase of SA-βGal activity. Moreover, Adenovirus-mediated expression of Skp2 in senescent EPC was able to significantly reverse SA-βGal activity, cell proliferation, and PAI-1 expression. Compared with mononuclear cells isolated from bone marrows of young rats (3 months, n=5), those from old rats (24 months, n=4) had prominently reduced cell proliferation and increased SA-βGal activity, both of which were also significantly reversed by Skp2 overexpression. Finally, to test whether Skp2 expression would rejuvenate senescent EPC function in vivo, senescent EPC infected with adenoviral vectors expressing Skp2 or β-galactosidase were injected into ischemic hindlimbs of nude mice. Surprisingly, adenoviral expression of Skp2 was able to rejuvenate senescent EPC function to enhance limb salvage (88% vs. 71%, p<0.05) and laser Doppler detected recovery of limb perfusion (44% vs. 30% of non-ischemic limb, n=8, p<0.05) after induction of hindlimb ischemia.

**Conclusions:** This data suggests that Skp2 downregulation plays a crucial role in EPC senescence. Enhancement of Skp2 may provide a promising potential to rejuvenate senescent EPC and slow down aging-related atherosclerosis.

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**P2544**

**Safety and effect of adipose tissue derived stem cell implantation in patients with critical limb ischemia**


**Introduction:** We performed intramuscular multiple injection of ADSCs to patients with critical limb ischemia which was composed of DM foot, Buerger’s disease and ASO.

**Methods:** The study comprised 15 patients (15 men) who had critical limb ischemia, defined as ischemic rest pain in a limb with or without nonhealing ulcers, necrotic foot. The patients received intramuscular multiple injections of ADSCs into the gastrocnemius muscle, the intermetatarsal region, and the feet dorsum (n=15). Primary end points were avoiding major or minor amputation, from baseline to 6 months follow-up, and the safety and feasibility of the treatment. Secondary end points were changes in ankle-brachial pressure index, claudication, peak walking time, the angiographic evidence of collateral vessel formation or remodeling and color change on thermography. ADSCs were isolated from adipose tissue of patients and were cultured by standard methods. ADSCs were plated in a 10mm culture dish at a density of 60 cells/dish. The cell numbers in each colony were counted after 1 week. Adipogenic differentiation was shown by the use of Oil-Red O stain as an indicator of intracellular lipid sequestration (VALS-1). Osteogenic differentiation was evaluated by Alizarin red stain of matrix multiplication.

**Results:** Intramuscular multiple injection of ADSCs was not associated with any complications. The mean follow-up time was 6 months. 71%(11/15) of patients was improved clinically. Five patient required minor amputation during follow-up. All of amputation sites were healed clearly. There were no complications in the ankle-brachial pressure index during 6 months. At 6 months, patients demonstrated a significant improvement in pain scores, peak walking time, claudication walking time. Digital subtraction angiography studies and thermography before and after ADSCs implantation showed numerous vascular collateral networks had formed across the affected arteries. In a CFU assay, B-ADSCs displayed lower colony numbers and cell numbers per colony than ADSCs. Cell counting at the indicated days after plating of 5 x 103 cells/well showed that B-ADSCs had slower growth than control ADSCs. However, B-ADSCs showed normal proliferating ability compared to those of control ADSCs and there was no difference in adipogenic and osteogenic differentiation between B-ADSCs and control ADSCs.

**Conclusions:** Intramuscular multiple injection of ADSCs could be a safe alternative to achieve therapeutic angiogenesis in patients with critical limb ischemia.

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**P2543**

**Metabolic selection for pluripotent stem cell-derived cardiomyocytes**

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Heart-regenerative cell therapy using pluripotent stem cells (PSCs) including embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) is a promising divergent therapeutic strategy for patients with severe heart failure. Mass production of highly purified cardiomyocytes is a critical bottleneck in realizing heart regenerative therapy. Our recently established non-genetic purification method of cardiomyocytes using mitochondrial dye is efficient but not suitable to produce large scale cardiomyocytes due to the usage of FACs. This study was designed to establish a large-scale purification method for PSC-derived cardiomyocytes based on cell-specific differences in metabolism and nutrition source. We first approached this issue by focusing on the possible metabolic differences between cardiomyocytes and ESCs by transcriptome and metabolome analysis. Transcriptome analysis delineated marked differences in isozyme expression and mRNA levels between metabolic pathways including glycolysis and the TCA cycle. Fluxome analysis using [13C]-labeled glucose revealed that ESCs used glucose mainly for biomass synthesis, while cardiomyocytes used glucose primarily for ATP production via TCA cycle. Lactate was discarded by ESC, but it was incorporated into cardiomyocytes and converted to lactate by PSCs for ATP production. To purify the bulk of PSC-derived cardiomyocytes using original culture media. This culture media enabled us to obtain > 98.5% pure cardiomyocytes derived from human ESCs which did not form tumors when transplanted into the immune deficient mice. In this study, we report a novel method to purify a bulk of cardiomyocytes from PSC derivatives based on the findings from transcriptome and fluxome analyses. We believe that our novel and inexpensive method termed "Lactate Method" will resolve the bottleneck and directly facilitate human heart-regenerative therapy.

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**P2545**

**Highest VCM-1 expression three days after ischemia/reperfusion injury of the porcine heart: best time-window for cell therapy?**

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**Purpose:** Bone marrow-derived mononuclear cells (BM-MNCs) injected intracoronary into the site of acute myocardial infarction (AMI) in a porcine model of reperfused AMI leads to a reduction in infarct size. Cardiac function, however, was not improved. Mononuclear cells were unable to enter the infarcted area upon infarction. Therefore, expression of adhesion molecules was investigated. The second aim is to investigate which subset of injected BM-MNCs is retained in the infarcted area. For this purpose, qualified antibodies were validated. The third aim is to determine the peak of VCM-1 expression, an indicator of intracellular lipid sequestration (VALS-1). Osteogenic differentiation was evaluated by Alizarin red stain of matrix multiplication.

**Results:** VCM-1 expression appeared highest in the infarcted area at 3 days of reperfusion: 30.3±8.7 vs 3.3±0.7 (p<0.05) in the remote area at 3 days follow-up, and compared to 4.3±1.0, 9.5±2.3, 12.7±1.2 and 8.2±3.2 (mean±SEM) in the infarcted areas of the 1, 7, 14 and 35 days reperfused hearts, respectively. For the second aim, proper antibody staining was ascertained for the flow cytometric and immunofluorescent characterization of porcine mononuclear cells, leukocytes, T-cells, B-cells, monocytes and the α and j2-subunit of integrins.

**Conclusions:** The expression of VCM-1 differs most significantly between infarcted and remote myocardium after 3 days of reperfusion. Therefore, it is suggested that injection of BM-MNCs at 7 days is less effective and that retention may be increased when injected at 3 days of reperfusion. This will be investigated. The characterization of retained cells will provide us with suggestions to increase the adherence of injected cells to the endothelial cells even further and will assist in...
the selection of appropriate subsets. This will aid in cell therapy-based studies and subsequent improved cardiac function with better prognosis.

P2546

**Cell Tracking of CXCR4+ cells in the ischemic heart utilizing a novel CXCR4 (BAC)-EGFP transgenic murine model**


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**Objective:** Recently published data from our lab indicate that stabilization of the cardiac SDF-1/CXCR4 axis preserves myocardial function and attenuates ischemic cardiomyopathy. However, the basic mechanisms of SDF-1/CXCR4 mediated cellular repair are barely understood. Here, we aimed to track the fate of CXCR4+ cell populations in the bone marrow, peripheral blood and the heart under normoxaemic and ischemic conditions utilizing novel CXCR4(BAC)-EGFP reporter mice.

**Methods:** In order to track the fate of CXCR4+ cells, genetically tagged CXCR4-EGFP+(BAC) reporter mice were used. These mice carry an EGFP sequence downstream of the translational (ATG) start side of a corresponding ca. 150-200kb large bacterial artificial chromosome (BAC), including all regulatory sequences. FACs- and immunohistochemical analyses of CXCR4+EGFP+(BAC) bone marrow, peripheral blood (PB) and heart cells were performed under normoxaemic and ischemic conditions.

**Results:** Mice were able to generate two different CXCR4+ murine HSC lineages: CXCR4+CD31+CD45+lin− cells, as well as stem cell populations like CXCR4+CD11b+monocytes and CXCR4+Flik+ cells were upregulated. In the PB the most frequent populations were CXCR4+/CD31+ and CXCR4+/Sca-1+, which were upregulated after ischemia. In the heart CXCR4+ expressing CD11b+monocytes, angiogenic CD31+, CD34+, c-kit+, and Flk1+ cells, as well as stem cell populations like ACC133+ and Lin−/c-kit+/Sca-1+ cells were significantly upregulated after ischemia. Immuno-fluorescent staining revealed only few CXCR4-EGFP+(BAC) cells in non injured hearts, whereas tissue ischemia strongly increased the number of CXCR4-EGFP+(BAC) cells in capillaries after ischemia.

In conclusion, our data suggest that CXCR4 is highly expressed on angiogenic and on stem cell populations in the BM, PB and the myocardium. In the heart, CXCR4-EGFP+(BAC) cells are upregulated after ischemia and target to vascular structures.

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P2547

**Four-and-a-half LIM domain protein-2 inhibition enhances survival, migratory capacity and paracrine function of early outgrowth endothelial progenitor cells: implications for endothelial regeneration**

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**Inhibition of Four-and-a-half LIM domain protein-2 (FHL-2) attenuates atherosclerosis-like lesion formation and increases endothelial cell migration. Endothelial progenitor cells (EPCs) substantially contribute to endothelial repair. We investigated the role of FHL-2 in the regulation of early outgrowth EPC number and function in vitro and in vivo.**

**Human early outgrowth EPCs were cultured from peripheral blood. FHL-2 knockdown in EPCs by small interfering RNA (siRNA) resulted in a significant increase in EPC numbers. Cell proliferation was low in EPCs (<1% Ki67 positive cells). FHL-2 knockdown induced a significant reduction of apoptosis, as indicated by a decrease of cleaved caspase-3 and reduced Bax/Bcl-2 expression ratio. This was mediated through increased phosphorylation and membrane translocation of sphingosine kinase-1 (SK-1) and Akt phosphorylation. Furthermore, FHL-2 knockdown significantly enhanced SDF-1-induced EPC migration. This was associated with an upregulation of v-α/β3 and v-α/β5 integrins and increased cortactin expression. v-α/β3 and v-α/β5 blockage by antibodies and v-α/β5 blocking antibodies (PK2) knockdown-induced reduction of apoptosis, increase of EPC migration and cortactin expression were abolished by the specific SK-1 inhibitor CAY10621.**

**Within 54 days after MI the number of CMs in the infarct area increased 3 fold in wt + G-CSF + DiprotinA (70mg/kg/BID) or saline for 7 days. Echocardiography, morphometric and immunohistochemical analyses were performed. Proliferation index and total numbers of CMs in the infarct area were quantified.**

**Results:** Although infarct size was similar in mice with stem cell mobilization/homing and/or cell cycle induction, vessel density and infarct thickness were significantly increased in transgenic mice treated with G-CSF and DPP-IV inhibitor. The CM proliferation index was 3400 fold increased in G-CSF-treated mice. The number of CMs in the infarct area increased 3 fold in transgenic mice with G-CSF plus DPP-IV inhibitor treatment. Total numbers of CMs within the area of infarction were 9.3 fold increased in G-CSF + Dppa animals compared to wt + saline. CMs in the infarct area were connected through CX43 gap junctions. Functionally, G-CSF treatment and DPP-IV inhibition combined with cardiomocyte cell cycle activation additionally increased myocardial function.

**Conclusion:** In conclusion, our data suggest that stem cell mobilization and targeted homing combined with cell cycle activation in CMs increase myocardial regeneration.
Simultaneous overexpression of CXCR4 and prostaglandin receptor-2 increase myocardial function of hematopoietic progenitor cells in a murine model of autoimmune myocarditis


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Purpose: In this study homing of murine hematopoietic progenitor cells (HPC) to damaged myocardium should be improved by simultaneous overexpression of the chemokine receptor CXCR4 and the prostaglandin receptor PST2 (PG2). A potential transdifferentiation of HPC to cardiomyocytes should be investigated after overexpression of Mesp I, an early cardiac transcription factor.

Methods: Heart failure was induced in 24 animals with bone marrow of autologous mice triggered by subcutaneous injection of cardiac Tropinin I. Lin- and c-kit+ HPC were isolated from bone marrow of transgenic RFP (Red Fluorescent Protein) reporter mice. CXCR4 and PG2 were simultaneously overexpressed using nucleofection of 5ug of mRNA, respectively. In the recipient mice the aorta ascending was ligated and HPC were injected into the cavum of the left ventricle. One week later mice were sacrificed and the fate of HPC and RFP was investigated by tracking of RFP. Aortically hearts were examined histologically for CD3+ lymphocytes and CD68+ macrophages. Clinical effects were investigated by running wheel and echocardiography.

To investigate a potential transdifferentiation of administered HPC to cardiomyocytes HPC were isolated from Ncx/GFP transgenic mice. Here cardiogenesis is indicated by GFP expression. To enhance cardiac differentiation HPC were nucleofected with 5ug of mRNA for Mesp I. Hearts were histologically examined for GFP positive cells.

Results: While RFP+ cells were detectable in all hearts of mice that received CXCR4/PST2-overexpressing HPC only 53% of the control group was positive for RFP. (+p<0.05 vs. n=15) CD3 and CD68 were distributed equally in both groups. However, increased homing of HPC was not related with improved clinical parameters.

Successful overexpression of Mesp I was shown in vitro by PCR analysis. In contrast, no evidence for a transdifferentiation of HPC to cardiomyocytes was gained. In our groups we were not able to detect GFP positive cells definitely.

Conclusion: Simultaneous overexpression of CXCR4 and PG2 in HPC resulted in an increased myocardial homing. A clinical consequence was missing most likely because of the relatively short follow-up period and the still low number of HPC that was found within the heart. Furthermore, we could not gain evidence, that HPC transdifferentiate to cardiomyocytes after homing in the damaged myocardium. Nevertheless, this therapeutic approach represents a proof of principle for an in vivo application of genetically modified HPC. As the mRNA-nucleofection is GMP-adapted basically this protocol could be transferred into a clinical setting.

Cultured human MSCs secretome contains anti-inflammatory cytokines and reduces in vitro ischemia reperfusion lesions and T lymphocyte proliferation after allogeneic stimulation

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Mesenchymal stem cells (MSCs) may reduce ischemia reperfusion injury by paracrine activation of cardioprotective pathways. MSCs may also modulate allogeneic rejection by secretion of cytokines. We hypothesized that human MSCs secretome can contain an anti inflammatory cocktail of cytokines that could reduce both ischemia reperfusion injuries and allogeneic rejection at the time of organ transplantation.

Methods and results: Serum free conditioned media (secretome) was harvested after 24, 48, and 72 hours from cultured human MSCs. The best results were obtained with 72 hours conditioned media. We didn’t observe any differences of cytokine secretion obtained after conditioned media harvested after 24, 48, and 72 hours of culture. Addition of human MSCs secretome at the time of ischemia-reperfusion injury in in vitro model of ischemia reperfusion of neonatal rat’s cardiomyocytes significantly reduced (-15% to -16%) cell death assessed by MTT staining. Addition of human MSCs secretone on mixed lymphocytes reaction significantly reduced (-22% to 3%) T lymphocytes proliferator assessed by the amount of radioactivity measured in a scintillation counter after 3H thymidine incorporation. Multiplex analysis of human MSCs secretome (IL-1, IL-6, IL-10, IL-12, IL-17, TNF-a, VEGF) showed an anti inflammatory profile of cytokine concentration.

Conclusion: Our preliminary in vitro data suggest that human MSCs secretome features an anti inflammatory cytokines profile that may favor the reduction of ischemia reperfusion injuries and modulate allogeneic rejection.
entire intra-peritoneal cavity involving the liver and kidneys. Flow-Cytometry detected the cells primarily within the lymphatic-organ and only in low levels within the heart.

Conclusion: For the first time, we demonstrate the principal feasibility of intrauterine, direct intra-myocardial stem-cell transplantation in the immunotolerant fetal sheep after MI. Using combined cell-tracking protocols comprising advanced imaging technologies and in-vitro tracking logs, this novel in vivo model offers a unique possibility to assess human cell-fate after intra-myocardial transplantation without the necessity of immunosuppressive therapy.

P2554 Cardiac progenitor cells coexpressing the surface markers CD34 and Flk1 can be generated from germine-derived pluripotent stem (gPS) cells

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Purpose: The efficacy of current cell-based therapies of heart failure is low as these are mostly relying on functionally impaired autologous bone marrow-derived cells. Recently, we obtained germine-derived pluripotent stem (gPS) cells from adult mouse unipotent germline stem cells. Therefore, the purposes of the present project are to generate cardiovascular progenitor cells from gPS cells and to characterize them in vitro to eventually reveal their capability to promote cardiac repair in murine models of heart failure.

Methods: Standard protocols for embryonic stem (ES) cells were applied to cultivate and to differentiate gPS cells. Cxcr4/Flk-1 double-positive cells were isolated by flow cytometry based cell sorting. To characterize their differentiation potential they were cultivated either on OP9 stromal cells or under specific feeder-free conditions and the expression of markers indicative for cardiovascular differentiation (e.g. alpha cardiac actinin for cardiomyocytes) was analyzed by immunofluorescence detection and real time RT –PCR. In gPS cell-derived EBs Cxcr4/Flk1 double-positive cells appeared with a similar kinetics as compared to ES cell-derived Cxcr4/Flk1+ cells (peak values at days 3, 4 and 5). The proportions (peak values) of Cxcr4+/Flk1+ cells were 10% (gPS cell-derived) or 13% (ES cell-derived), respectively, of all cells constituting the EBs. gPS cell-derived Cxcr4+/Flk1+ cells analyzed immediately after FACS-based isolation expressed the cardiomyocyte progenitor cell markers Nkx2.5 and Mesp1. After cocultivation with OP9 stromal cells for 8 days or culti-vation under specific feeder-free, differentiation-promoting conditions for 10 days beating areas containing cells (co)-expressing the markers alpha smooth muscle actin (alpha-SMA) (marker of immature cardiomyocytes and vascular smooth muscle cells) and alpha cardiac actinin (marker of partially and fully differentiated cardiomyocytes) were detected in addition to cells expressing only one of these markers each. Extended coculture led to an increase of the proportion of cells expressing alpha cardiac actinin only while the numbers of cells expressing alpha-SMA alone or in combination with alpha cardiac actinin decreased. Cells expressing the endothelial markers CD31 or VEGF were not detected.

Conclusions: gPS cells were shown to constitute a source of Cxcr4/Flk1 coexpressing cardiac progenitor cells. Current experiments are clarifying whether they can act as an alternative cellular source to the ethically problematic ES cells in cardiac repair in murine models of heart failure.

STEM CELLS DELIVERY

P2555 Intravenous delivery of bone marrow monocytes is a robust method of stem cell delivery: stem cell enhancement external counterpulsation a preliminary report

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Bone marrow stem cell (BMSC) therapy for treatment of ischemic heart disease and dilated cardiomyopathy (DCMP) has been claimed to be effective only by intramyocardial or intracoronary delivery of BMSC (Streuer and Steinhoff). The purpose of the current report is to show that despite certain hypothetical calculations, to the contrary, BMSC could be delivered to the heart with remarkable success by intravenous (IV) route under EECP therapy. We report a pilot study of IV delivery route of BMSC in cardiac patients under EECP. The results of therapy of 28 patients (21 male, 7 female) are summarized below: All patients had end-stage ischemic cardiomyopathy, except two who had primary dilated cardiomyopathy. Age was 51.4±18.8 years. The results pre and post are summarized below: Ejection Fraction improved from 38.1±10.2% (P<0.0001) to 47.8±9.0% (P<0.0001). Diastolic BP (mmHg): 82.1±11.4 vs 69.1±8.6 (P<0.0001); LV diastolic dimension (cm): 6.2±0.8 vs 5.9±1.1 (P<0.0005), left atrial volume index (mL/m²): 50.8±25.6 vs 52.5±1.1 (P<0.0002). 6- walk (m/min) vs 34.2±16.1 vs 52.9±20.5 (P<0.0005). NYHA class decreased one or two grades in all patients. To this date, all patients are alive and well. We would like to stress that "homing in" and other hypothetical mechanisms for vasculogenesis are not the basic mechanism of the beneficial effects of BMSC therapy. We summarize expert remarks, about cardiac BMSC therapy: Almost every clinical and animal experiment has shown improved left ventricular (LV) function (ejection fraction, ventricular arrhythmia substrate) without the necessity of immunosuppressive therapy.

P2556 The intramyocardial injection of undifferentiated induced pluripotent stem cells could improve the ventricular arrhythmia substrate in a porcine acute myocardial infarction model

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Introduction: Intramyocardial delivery of the iPSCs cells represented a suitable autologous cell source for heart disease therapy. To indentify whether myocardial direct injection of iPSCs cells delivered to the damaged tissue via systemic circulation. The intravenous route for BMSC delivery recruits the humoral factors, is noninvasive, less hazardous, cost-effective and available for repeated BMSC delivery.

Methods: Standard protocols for embryonic stem (ES) cells were applied to cultivate and to differentiate gPS cells. Cxcr4/Flk-1 coexpressing cells were isolated by flow cytometry based cell sorting. To characterize their differentiation potential they were cultivated either on OP9 stromal cells or under specific feeder-free conditions and the expression of markers indicative for cardiovascular differentiation (e.g. alpha cardiac actinin for cardiomyocytes) was analyzed by immunofluorescence detection and real time RT –PCR. The results of therapy in 28 patients with STEMI and stable CAD is analyzed. MSC count was assessed by the presence of surface antigens CD34 and CD133 as

P2557 Influence of percutaneous coronary intervention on CD271+ mesenchymal stem cells of patients with STEMI and stable coronary artery disease

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Purpose: Stem cells are mobilized from bone marrow following myocardial infarction. Some studies indicate that stem cells may be recruited following vascular injury. Hypothetically stem cells recruitment in STEMI may partially be caused by percutaneous coronary intervention (PCI) related vascular injury. The aim of the study was to investigate this hypothesis.

Methods: Overall 43 patients were enrolled to the study. 23 patients were admitted due to STEMI and treated with primary PCI. 20 patients were admitted due to stable coronary artery disease (CAD) in order to perform PCI. All patients underwent successful PCI with stem cell implantation. First blood sample was obtained directly after PCI completion and second sample the next day. No periprocedural myocardial infarction was observed in stable CAD group (troponin I <0.05 ng/ml). Blood samples were harvested with heparin (100 IU/ml) and processed by density gradient centrifugation cell sorting (FACS) analysis. Both mesenchymal (MSC) and hematopoietic (HSC) stem cells following PCI in STEMI and stable CAD group was analyzed. MSC count was assessed by the presence of surface antigens CD34 and CD133 as
well as novel MSC marker CD271, while HSC count was assessed according to ISHAGE protocol. MSC and HSC count was assessed using beads for absolute cells counting.

Results: Mean age in STEMI and stable CAD group was similar (64.6±10 vs 60.1±11 years, ns). In both groups MSC and HSC count in blood samples taken directly after PCI was similar. Number of double CD133+/CD271+ cells was increased significantly one day after PCI in STEMI group (19.2±12.6 cells/μl vs 25.0±14.5 cells/μl, p<0.02) without significant change in separate CD133+ cells (13.5±9.0 cells/μl vs 14.8±8.1 cells/μl, ns) and CD271+ cells (22.1±12.3 cells/μl vs 12.5 cells/μl, ns). Number of CD271+ cells significantly increased one day after PCI in stable CAD group (17.2±8.5 cells/μl vs 24.9±14.9 cells/μl, p<0.05) without significant change in separate CD133+ cells (12.6±11.4 cells/μl vs 13.2±10.4 cells/μl, ns) and double CD133+/CD271+ cells (16.6±19.3 cells/μl vs 14.8±10.2, ns). Number of HSC (ISHAGE) didn’t differ significantly, between first and second blood sample, in both groups, STEMI and stable CAD (1.0±0.1 cells/μl vs 0.8±1.3 cells/μl, ns. 0.75±0.9 cells/μl vs 0.8±1.0 cells/μl, ns, respectively).

Conclusions: Acute myocardial infarction causes double CD133+/CD271+ cells mobilization. Vascular injury due to PCI in stable CAD is followed by CD271+ cells mobilization and thus may be in part responsible for CD271+ mesenchymal stem cells recruitment in STEMI patients treated with PCI.

P2559 Intramyocardial injections of bone marrow stem cells induced QT prolongation
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Aims: We aim to evaluate the effects of intramyocardial (i.m.) injections of Bone Marrow Stem Cells (BMSCs) on development of arrhythmias in an ischemia/reperfusion animal model.

Methods: In New Zealand rabbits an ischemia/reperfusion damage was induced by temporary ligation of anterior descending coronary artery. Homologous BMSCs were isolated, cultured and re-suspended for injection. We compared i.m. injections of BMSCs at the peri-infarcted area with intravenous (i.v.) administration of cells. A control group of animals was treated with i.m. injections of saline, to evaluate pro-arrhythmic effect of needle puncture. The hourly number of ventricular premature contractions (VPC), QT interval time and QTC time were recorded and calculated.

Results: After injections, temporary but frequent VPC were observed in the i.m. BMSCs group as compared with i.m. saline and i.v. injections of cells. QTc time interval was prolonged during ischemia and recovered in control and in the group treated with i.v. BMSCs whereas it remained longer in rabbits treated with i.m. (Table 1).

<table>
<thead>
<tr>
<th>Time</th>
<th>BMSC SAL</th>
<th>BMSC I.M.</th>
<th>BMSC I.V.</th>
</tr>
</thead>
<tbody>
<tr>
<td>QT baseline</td>
<td>425±16</td>
<td>419±20</td>
<td>420±20</td>
</tr>
<tr>
<td>QT during ischemia</td>
<td>432±21</td>
<td>427±23</td>
<td>434±29</td>
</tr>
<tr>
<td>QT post ischemia</td>
<td>429±19</td>
<td>421±19</td>
<td>426±29</td>
</tr>
<tr>
<td>QT 30 days</td>
<td>432±20</td>
<td>429±19</td>
<td>430±20</td>
</tr>
</tbody>
</table>

*p<0.05.

Conclusions: BMSCs injections were associated with changes in cardiac electrophysiological properties as shown by QTc prolongation. The combination of cell clustering as barriers to electrical impulse propagation and of cytokines released by cells would contribute to the development of arrhythmias. Data need to be confirmed by further studies, evaluating a longer follow-up, before translating information to clinical studies.

P2560 Co-transplantation of non-cardiomyocytes increases persistence of highly purified murine induced pluripotent stem cell derived cardiomyocytes after intramyocardial injection into syngeneic mouse hearts
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Purpose: Cardiac cell replacement therapy is a promising approach to improve cardiac function in heart failure. Embryonic or induced pluripotent stem cells can differentiate into functional cardiomyocytes (iPS-CM or ES-CM), which integrate into host myocardium after transplantation and thereby improve heart function. However, while highly purified cells are needed to avoid teratogenic risk, both iPS-CM and ES-CM have limited engraftment into cardiac tissue after intramyocardial injection which might be due to their purity. Thus, we tested the co-transplantation of non-cardiomyocytes to improve cell persistence.

Methods: iPS-CM (and ES-CM as control) were derived from transgenic murine stem cells and highly purified using an antibiotic resistance under a cardiac-specific promoter. 300,000 ES-CM or iPS-CM with or without addition of 300,000 syngeneic wild-type mouse embryonic fibroblasts (MEF) or 300,000 syngeneic wild-type mesenchymal bone-marrow cells (MSC) were intramyocardially injected into healthy hearts of syngeneic wild-type mice. Hearts were harvested immediately (0h) or after 6 or 24 h, DNA was isolated and the number of transplanted cardiomyocytes was determined by quantitative RT-PCR using specific primers. As control (=100%), one cell aliquot was mixed with an explanted heart ex vivo at each surgery day.

Results: Immediately after intramyocardial injection, we detected 28.4±4.0% of the transplanted iPS-CM and 16.9±6.1% of the transplanted ES-CM in the recipient heart. Values decreased over time in both groups to 2.6±0.9% of iPS-CM and 11.0±2.5% of ES-CM after 6 and down to 0.6±0.2% of iPS-CM and 0.9±0.3% of ES-CM after 24h, confirming our previous results for transplanted ES-CM. After co-transplantation with non-cardiomyocytes, the number of detectable iPS-CM after 24h was more than 2-fold and with ES-CM alone, respectively, corresponding to absolute numbers of approx. 4.200 or 4.600 iPS-CM as compared to approx. 1.800 iPS-CM without co-transplantation. Highly purified murine cardiomyocytes derived from both ES or iPS showed a massive cell loss already during or shortly after intramyocardial injection into syngeneic healthy recipient hearts and a poor persistence of less than 1% of the injected cells at 24h. Since this number was enhanced 2-fold by co-transplantation of non-cardiomyocytes (MEF or MSC), this strategy should be further investigated to optimize the effectiveness of cardiac cell replacement therapy and to facilitate the possible therapeutic benefit.

P2561 Repeated transendocardial bonemarrow cell injection in a porcine model of chronic ischemic heart disease improves diastolic function
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Purpose: Success of cell therapy is limited by low cell survival upon single cell injection, leading to a temporary improvement in ejection fraction(EF). This study was designed to assess the long-term effect of repeated transendocardial (TE)
bone marrow cell delivery in a porcine model of chronic myocardial infarction (MI).

Methods: Nineteen animals underwent repeated TE cell delivery using echocardiographic mapping guidance at 4 and 8 weeks after MI. Animals received 107 autologous stem cells and were allocated to 3 groups: (1) bone marrow-derived mononuclear cells (BMMNC) + mesenchymal stem cells (MSC), (2) MSC + placebo or (3) placebo-placebo delivery. Cardiac function was assessed by echocardiography, pressure-volume loops, intracoronary flow and ex vivo force indentation compliance tests. Explanted hearts were processed for collagen content and capillary density assessment.

Results: APE was significantly improved in cell treated groups compared to placebo treatment (Group 1 18±3%, Group 2 18±3%, vs. Group 3 9±3%; all P<0.01). However, no difference was observed between the single and repetitive cell injected groups in EF (P=0.67). Interestingly, the improvement in diastolic function was more pronounced after repeated cell injection assessed by a significant reduction in EDP and diastolic stiffness (Eed) (Fig. 1). Repeated cell injection was associated with a greater decrease in coronary microvascular resistance, increased angiogenesis, lower collagen density and improved myocardial compliance.

Conclusions: This study showed that cell injection improves systolic function in a chronic ischemic heart disease model, moreover, repeated rather than a single injection further improved diastolic function.

Figure 1. Diastolic parameters

Transplantation of highly purified murine embryonic stem cell derived cardiomyocytes in clusters together with adult mesenchymal bone-marrow cells yields enhanced engraftment but poor persistence

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Purpose: Transplanted embryonic stem cell derived cardiomyocytes (ES-CM) can integrate into host myocardium and improve cardiac function in heart failure. Since this therapy’s effectiveness is limited by low engraftment and persistence of transplanted ES-CM, we tested the intramyocardial injection of in-vitro grown clusters of ES-CM together with adult mesenchymal bone-marrow cells (MSC) as a novel approach to facilitate early cell retention.

Methods: Male murine ES-CM were generated and highly purified (~97%) using antibiotic resistance under cardiac specific promoter and MSC were isolated from syngeneic wild-type male mice. Both cell types were then grown in co-culture on special dishes enabling gentle detachment of the in-vitro grown mixed clusters which were then intramyocardially injected into healthy hearts of syngeneic wild-type female mice. Hearts were harvested immediately (0h) or after 48h or 48h post injection. While native explanted hearts with ex-vivo added cluster aliquots served as controls (ctrl=100%). In all samples, numbers of male and transgenic cells were determined using quantitative real-time PCR with specific primers for Y-chromosome and transgene.

Results: Immediately after intramyocardial injection of in-vitro grown mixed clusters of ES-CM and MSC, we detected 24±7.9% of transgenic cells (i.e. ES-CM+MSC) injected and numbers decreased over time down to 11.1±6.0% at 24h and 3.7±0.9% at 48h (p<0.06 for linear trend). With selective quantification of transplanted ES-CM alone, we detected 24.7±7.8% of transgenic cells (i.e. ES-CM) injected at 0h, 10.5±5.4% at 24h and 1.0±0.4% at 48h (p<0.001 vs 0h, P<0.01 for linear trend). Thus, the fraction of ES-CM within the detectable cells injected changed from ~50% (0h, 24h) to ~20% at 48h. Although similarly low at 48h, retention of injected ES-CM at 0h and 24h was remarkably higher than in previous studies with intramyocardial injection of similar ES-CM alone (0h: 13.3±2.8%, P<0.01 and 24h: 0.8±0.3%, p=0.05).

Conclusions: Highly purified murine embryonic stem cell derived cardiomyocytes show remarkably enhanced engraftment but poor persistence when intramyocardially injected in-vitro grown clusters together with adult mesenchymal bone-marrow cells. Nevertheless, transplantation of in-vitro grown clusters seems to delay or even prevent the massive early loss of transplanted single cells presumably by increasing volume, surface and adhesiveness of injected particles and by providing a beneficial milieu within the injected clusters and should therefore be further investigated.

Systemic administration of allogenic fetal membrane-derived mesenchymal stem cells suppressed Th1 and Th17 T-cell immunity in experimental autoimmune myocarditis

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We reported that intravenous injection of autologous bone marrow or allogenic fetal membrane (FM) derived mesenchymal stem cells (MSCs) similarly attenuated myocardial injury in rats with experimental autoimmune myocarditis (EAM). Because EAM is a T cell-mediated autoimmune disease, and recent evidence has indicated that both autologous and allogenic MSCs exert an immunosuppressive effect on T cell activity, we focused on T cell differentiation in allogenic FM-MSC administered EAM rats. EAM was induced in Lewis rats by injecting porcine cardiac myosin (day 0). Allogenic FM-MSCs, obtained from major histocompatibility complex mismatched ACI rats, were intravenously injected (5×106 cells/rat) on day 7, 10 or 14 (D7, D10 or D14 group). At day 21, severe deterioration of cardiac function and inflammation were observed in control EAM rats (MyoC group). We found that intravenous administration improved cardiac function and reduced inflammation, significantly in the D10 and D14 groups (ejection fraction: 74.4±1.3% in D10, 74.9±2.2% in D14, vs. 62.6±2.1% in MyoC, P<0.01; macrophage infiltration: 95.8±13.9 cells/mm2 in D10, vs. 146.6±9.9 cells/mm2 in MyoC, P<0.05). To evaluate T cell differentiation, we used intracutaneous cytokine flow cytometry to determine the percentage of interferon (IFN)-γ positive Th1 and interleukin (IL)-17 positive Th17 cells in peripheral CD4-positive lymphocytes. At day 16, the percentage of Th1 cells was significantly lower in the D10 (13.4±1% and 14.1 (1.5%) groups compared to the MyoC group (23.6± P<0.05), as was the percentage of Th17 cells in the D10 group (1.85%) compared to the MyoC group (22.1%, P<0.05). Immuno-histochemical staining of IL-17 in EAM hearts on day 21 demonstrated that FM-MSC administration significantly decreased the infiltration of IL-17 positive cells in the D10 group compared to the MyoC group (D10: 50.1±13.2 cells/mm2 vs. MyoC: 92.1±10.9 cells/mm2, P<0.05). Therefore, intravenous injection of allogenic FM-MSCs in EAM model attenuated myocardial dysfunction and inflammation, associated with systemic Th1 and Th17 suppression. In vitro, human CD4+ T cells co-cultured with human FM-MSCs exhibited reduced Th1 cell-differentiation and proliferation. These results suggested that intravenous administration of allogenic FM-MSCs ameliorates EAM via suppression of Th1 and Th17 immunity.

Stem cells delivery 431

Cell sheet transplantation in porcine ischemic cardiomyopathy model; comparison of skeletal myoblast and bone marrow-derived mesenchymal stem cell

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Introduction: The therapeutic effects of cell transplantation are determined by cell-source, cell-delivery mode, and target cardiac pathology. Cell sheet technique is one of the most promising cell delivery systems to maximize the therapeutic efficacy. We herein compare skeletal myoblast(SMB) and bone marrow-derived mesenchymal stem cell(MSC), both of which have proved to be feasible, safe and potentially effective in clinical studies, in treating ischemic cardiomyopathy(ICM) by cell-sheet technique.

Methods and Results: Primary SMBs and MSCs were isolated and expanded to create cell-sheet on the thermoresponsive dishes.Total cell number:SMB=3×108, MSC=1×108. Either SMB or MSC cell-sheets were successfully transplanted onto the ICM model of a porcine ICM model induced by placing ameroid constrictor on LAD. There were no procedure related complications(SMB group=5, MSC group=5, Sham group=5). Premature ventricular contractions(PVC) were rarely detected by Holter ECG in each group during 24 hours after the transplantation, but the number of PVC in the SMB group was significantly higher than that in the SMB group (26±15 vs 11±1.5, P<0.01). On echocardiography, cardiac performance of the S and M group were significantly better than that of C group at 8 weeks after the transplantation(EF: S; 50±0.3%, M; 51±0.5%, C; 35±0.5%, S vs C P<0.001, M vs C P<0.01, S vs M ns). On histological examination 8 weeks after the transplantation, size of cardiomyocytes or interstitial collagen in the S and M group was significantly attenuated compared with the C group(S vs M:cardiomyocyte size:12±2 μm vs 13±1 μm, P<0.001, S vs M, C vs M, P<0.001, S vs M ns, interstitial fibrosis:2.4±2.4 vs 2.2±0.3% P=0.04, S vs M, C vs M P<0.001, S vs M ns). In addition, vascular density in the border area from the infarction assessed by immunohistochemistry for vWF, was significant greater in the S and M group and the sham group(S vs M vs C: 869±86 units/mm2 vs 773±91 units/mm2 vs 157±80 units/mm2, S vs C P<0.0001, M vs
Transplantation of cardiac tissue sheets including human induced pluripotent stem cells (hiPSCs), efficient differentiation from hiPSCs to defined cardiac cell populations (cardiomyocytes [CMs]/endothelial cells [ECs]/vascular mural cells [MCs]), and transplantation technique for fair engraftment are required.

Methods: After 4 days of culture, we successfully collected self-transferred onto temperature-responsive culture dishes (UpCell dishes; CellSeed, Tokyo, Japan) and these cells differentiation day 15 (n=12). Then, these cells induced were harvested and analyzed for functional parameters.

Results: Coronary flow always remained within TIMI III definitions and no ventricular arrhythmias were found in the treated group. No MPC-related side effects occurred. Cell retention in the anterior wall was 47±2.6%, whereas no shedding was found to occur at remote myocardial segments.

Infarct size significantly decreased in MPC treated sheep. Global LVEF in controls deteriorated to 38±6.2%, whereas it was enhanced in treated sheep to 45±1.4% (P<0.001; n=12). Regional angiogenesis function increased by 25% (P=0.002/). Wall thickness in the antero-septal wall improved from 13.3±1.6% to 9.5±1.1% in controls to 39.1±1.8% in treated animals (P=0.001) and in the anterior wall from 13.8±3.6% to 34.7±1.9% (P<0.001). End-systolic elastance (P=0.002) and pre-load recruitable stroke work (P=0.007), all PV loop derived, load independent parameters of contractile function, were significantly enhanced in the MPC treated group as compared to the control group. LV remodeling was abrogated by MPC therapy, resulting in significant differences in end-systolic and end-diastolic volumes. Collagen content was reduced by more than 50% in both border and remote areas of MPC treated animals. Also, a 59% increase in capillary density in the infarct border zone, as well as a 122% increase in arterioles in the infarct area.

Conclusion: IC infusion of allgenic MPC is safe, feasible and highly efficient following AMI. MPC infusion preserved left ventricular systolic function, and reduced LV remodeling and fibrosis, evoked by myocardial salvage and increased angiogenesis.

Insufficient electrical integration and maturation of transplanted neonatal ventricular patches

Methods: Neonatal hearts expressing green fluorescent protein under control of the alpha-actin promoter were harvested at day 1 p.p. from transgenic C57BL/6 mice. The left ventricular wall was dissected into patches of approximately 2.5 mm diameter. In an open chest surgery, NVP were sutured to the left ventricular wall of adult wild-type C57BL/6 mice or 6 or 12 days after surgery; hearts were examined. Slices were cut and cultured in vitro for 6 days. Postnatal day 5 (P5), which decreases during native murine development, was regarded as best indicator of the grade of maturation. All data are presented as mean ± SEM.

Results: In 5 of 20 hearts we found an electrical integration of the transplanted NVP. Synchronous blocks occurred at a stimulation frequency of 4.9±0.17 Hz. APD50 of NVP at day 12 after transplantation (44.1±3.3 ms, n=16) was significantly decreased as compared to NVP at day 6 after transplantation (69.5±4.1 ms, n=34), but still much longer than in host cardiomyocytes (9.4±0.89 ms, n=7).
both, mRNA and protein level. Silencing of SPRED1 in EOCs from patients with CHF due to ICM significantly improved their pro-angiogenic capacity, whereas anti-hR-126 transfection of EOCs from H5 markedly impaired their capacity to stimulate tube formation. Conversely, miR-126-mimic transfection of EOCs from patients with CHF due to ICM enhanced the tube formation capacity. Moreover, in vivo cardiac repair capacity was improved in miR-126-mimic as compared to scrambled transfected EOCs from patients with CHF. Neither the injection of any of the tested biomaterials nor fibroblasts could prevent the massive early loss of cardiomyocytes derived from murine embryonic stem cells after intramyocardial injection. Therefore, other strategies to improve engraftment, persistence and survival of transplanted cells must be identified to optimize the effectiveness of cardiac cell replacement therapy and to facilitate the possible therapeutic benefit.

**P2570**

High mobility group box 1 released from dead donor cells plays a key role in bone marrow mononuclear cell transplantation for treating heart failure


**Purpose:** Transplantation of bone marrow mononuclear cells (BMMNCs) is a promising approach for treating heart failure, but the mechanism underlying the therapeutic effect remains unclear. Given that the majority of donor cells are dead after injection, we speculated that dead BMMNCs might also contribute to the effect. High mobility group box 1 (HMGB1) is a nuclear protein that stabilizes nucleoprotein complexes and also acts as a pro-inflammatory cytokine when released from damaged cells. We have previously reported that administration of HMGB1 improves the function of post-infarction failing hearts. Here we examined possible contribution of HMGB1 released from dead donor cells to the effect of BMMNC transplantation.

**Methods and Results:** One month after coronary artery ligation in rats, 1×10⁵ syngeneic BMMNCs or PBS only were intramyocardially injected (BM or CO group). In addition, BMMNC injection was performed with 50μg of anti-HMGB1 antibody or control IgG (AB or IG group; n=6 in each group). One hour after injection, HMGB1 level in peripheral blood was elevated in BM group compared to CO group (16.2±2.5 versus 6.3±1.9 ng/ml, p<0.01). Four weeks after treatment, echocardiography and catheterization showed enhanced cardiac function in BM group compared to CO group. This effect was abolished in AB group, but not in IG group. Reduced fibrosis, improved neovascular formation, and increased proliferative activity (Ki-67+ cell) were observed as underpinning factors for the function recovery in BM group, while all these were eliminated in AB group. Accumulation of CD45+ inflammatory cells was increased in AB group.

**Conclusion:** HMGB1 released from dead donor cells plays an important role in the therapeutic effects of BMMNC transplantation for treating heart failure.

**P2572**

Effects of bone marrow mesenchymal stromal cells implantation vs. intramyocardial plasmid pVEGF165 gene transfer on infarct size and left ventricular function in sheep with acute myocardial infarction

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**Purpose:** Implantation of bone marrow-derived mesenchymal stromal cells (MSCs) in the left ventricular (LV) myocardium has been shown to induce beneficial effects in animal models of acute myocardial infarction (AMI). On the other hand, we have shown that the intramyocardial injection of a plasmid encoding VEGF165 (pVEGF) in an ovine model of AMI limits infarct size and enhances LV function. We thus aimed to compare, in the same model, the efficacy of MSCs versus pVEGF in decreasing infarct size and improving LV function.

**Methods:** Adult sheep underwent surgical acute occlusion of 2nd and 3rd diagonal branches of the left anterior descending artery. One week later, sheep were randomized and randomized to receive 20 million MSCs (n=5), pVEGF165 (3.8 mg) or placebo (PBS, n=5) in ten 0.2 ml intramyocardial injections distributed along the infarct border. At 3 and 30 days post-treatment infarct size (as %LV mass) was measured by magnetic resonance imaging and LV function [end diastolic volume (EDV), end systolic volume (ESV), ejection fraction (%EF)] by echocardiography. Heart function data, baseline, pre-treatment LV function and LV function at 30 days post-treatment were also assessed.

**Results:** Infarct size showed a significant 27% decrease in the pVEGF group (from 17.6±3.4% to 12.7±2.7%, X±S.D, p<0.01, ANOVA-Bonferroni), a marginally significant 23% decrease (from 10.2±3.0% to 7.9±2.9%, p<0.07) in the MSCs group and no significant change in placebo. Between 3 and 30 days post-AMI, EDV increased significantly in the placebo group (from 64.4±13 to 64.3±15.4 ml, p<0.01) but not in the VEGF group (from 64.1±16 to 73±17.7 ml, p>NS) or MSCs (from 59.2±16 to 74±16.7 ml, p>NS) groups. While ESV did not change significantly in any groups, LV %EF showed marginally significant increases (from 38.6±12.1 to 52±12.2%) and MSCs (from 40.1±8.9 to 51.1±9.4%) but not in the other two groups. Further, %EF was marginally significant in the VEGF group (from 38.6±12.1 to 52±12.2%) and MSCs (from 40.1±8.9 to 51.1±9.4%) but not in the other two groups.

**Conclusion:** According to these preliminary results, we conclude that in sheep with AMI pVEGF gene therapy decreases infarct size more than MSCs implantation; however, as regards LV performance, the difference is not clinically relevant on account that both treatments tend to increase LV %EF to the same extent, suggesting that, in clinical terms, either treatment may prove similarly effective.

**STEM CELLS AND CARDIAC REGENERATION**

**P2573**

The potential role of a PARP-inhibitor in the myocardial stem cell regeneration

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**Introduction:** Ischemic myocardial damage leads to cell death, scar formation which determines the morbidity and mortality of postinfarction patients. It is known from literature that circulating stem cells deriving from bone marrow take a relevant part in myocardial regeneration. Previous examinations showed that thymosin beta-4 (TB4) occurs in embryonic heart, stimulates migration of cardiomyocytes, improves their survival and in adult heart it increases the mobilization of myocardial progenitor cells. It was also proved that TB4 exerts its favorable effect via the Akt-1 signal transduction pathway. The PARP-inhibitor L-2286 was examined in several models by our group also exerts its protective effect via Akt pathway. Based on these evidences we assumed that L-2286 could enhance the survival of certain stem cell mark for Y-chromosome.

**Methods:** CD1 type mice were divided into 5 groups. Controls received placebo, the others 80 mg/kg isoprotensol (ISO) on the first day. On the 2nd day 6 mice received ISO, 6 mice ISO and 5 mg/kg L-2286, other 6 ISO, L-2286 and 150 ug
thymosin, and the last group ISO and thymosin. 1 week later we examined the activation of different signal transduction pathways and the presence of stem cell markers CD117 and CD133 expression in hearts with confocal laser microscopy and immunoblot.

Results: Comparing control and ISO treated mice the number of CD117 positive cells increased significantly in the subepicardium and myocardium of the injured hearts. Activation of CD117 positive cells increased in ISO and thymosin treated mice but the highest elevation could be seen in ISO, thymosin and L-2286 treated animals. This difference was also significant (p < 0.05) using Western blot.

Conclusion: These results suggest that PARP inhibition via the activation of Akt-1 is able to affect stem cell renewal shortly after cardiac injury.

P2574 Force of contraction of human right atrial trabeculae after temporary hypoxia is increased after injection of neonatal rat cardiomyocytes

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Purpose: Cardiac cell replacement therapy is a promising therapeutic option to improve impaired cardiac function by replacing lost or injured myocardium with transplanted new contractile cells. However, integration of transplanted cells is crucial for successful therapy. Methods: Single trabeculae were prepared from temporarily hypoxic human right atrial auricles obtained from patients undergoing cardiac surgery with heart-lung machine. Trabeculae were continuously stimulated under optimized conditions without treatment (Ctrl, n=5), after central injection of 1μl alginate suspension alone (Alg, n=4) or with 300,000 freshly isolated neonatal rat cardiomyocytes (NCM, n=5), and force of contraction was recorded for at least 11 hours. Consecutively, the trabeculae were fixed and cut for histological and immunohistochemical analyses.

Results: There were no differences between groups in the time span until maximal force of contraction (ANOVA p=0.59), as well as in the total duration of constant contractions (ANOVA p=0.24). While the force of contraction at baseline was similar (ANOVA p=0.58), the maximal force of contraction was significantly different with 2.4±0.4mN in Ctrl, 2.1±0.2mN in Alg and 2.6±0.2mN in NCM (ANOVA p=0.03). AUC analysis revealed that force of contraction was significantly higher in NCM vs. Alg (p=0.01) and vs. Ctrl (p=0.05, ANOVA p=0.003). In immunohistochemistry, transplanted NCM were identified by alpha-smooth muscle-actinin stained positive for Connexin 43 in 25% of analyzed samples at baseline and in 75% of analyzed samples after constant contractions (Chi² p<0.05) suggesting viability and integration of transplanted cells.

Conclusion: Contracting human right atrial trabeculae are a valuable in-vitro model for cardiac cell therapy, facilitating the analysis of transplanted cells within viable human cardiac tissue and their interactions over time. For neonatal rat cardiomyocytes we demonstrated an increase in force of contraction of cell treated trabeculae and an enhanced expression of connexin 43 in transplanted cells over time.

P2575 Roles of aldehyde dehydrogenase (ALDH) isoforms and retinoic acids in the growth and differentiation potential of human adult cardiac progenitor cells


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Aim: We have studied human adult cardiac progenitor cells (CPCs) based on high aldehyde dehydrogenase activity (ALDH-hi), a property shared by many stem cells across tissues and organs. However, the role of ALDH in stem cell function is poorly known. In humans, there are 19 ALDH isoforms with different biological activities. The isoforms responsible for the ALDH-hi phenotype of stem cells are not well known but they may include ALDH1A1 and ALDH1A3, which function in all-trans retinoic acid (RA) signaling. ALDH activity has been shown to regulate hematopoietic stem cell function via RA. We aimed to analyze ALDH isoform expression and the role of RA in human CPC function.

Methods: Human adult CPCs were isolated from atrial appendage samples from patients who underwent heart surgery for coronary artery or valve disease. Atrial samples were cultured as primary explants or enzymatically digested and sorted for ALDH activity by FACS. ALDH isoforms were determined by qRT-PCR. Cells were cultured in the presence or absence of the specific ALDH inhibitor DEAB, with or without RA. Induction of cardiac-specific genes in cells cultured in different differentiation medium was measured by qRT-PCR.

Results: While ALDH-hi CPCs grew in culture and could be expanded, ALDH-low cells grew poorly. CPC isolated as primary explant outgrows expressed high levels of ALDH1A3 but not of other isoforms. CPC isolated from cardiopathies expressed relatively high levels of all the 11 isoforms tested. In contrast, expanded CPCs and cardiosphere-derived cells expressed low levels of all ALDH isoforms. DEAB inhibited CPC growth in a dose-dependent manner, whereas RA rescued CPC growth in the presence of DEAB. In differentiation medium, ALDH-hi CPCs expressed approximately 300-fold higher levels of cardiac troponin T compared with their ALDH-low counterparts.

Conclusions: High ALDH activity identifies human adult cardiac cells with high growth and cardiomyogenic potential. ALDH1A3 and, possibly, ALDH1A1 isoforms account for high ALDH activity and RA-mediated regulation of CPC growth.

P2576 Stimulation of circulating angiogenic cells by statins in chronic heart failure

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Chronic heart failure (CHF) management is a complex process that can involve a large number of pharmacological and non-pharmacological approaches. Patients with CHF show endothelial dysfunction. Endothelial progenitor cells (EPCs) play a crucial role in endothelial repair and statins have been shown to stimulate these progenitor cells in patients with coronary artery disease. However, there are few data regarding the effect of statins in patients with CHF. Observational studies suggest that adding statins to standard therapy may improve survival in patients with CHF. Nevertheless, there is still a lot of controversy about the possible benefit of statins in these patients.

Our work aimed to analyze the effect of statins on the pattern of mobilization of EPCs in advanced heart failure. EPCs were analyzed in the peripheral blood of 30 consecutive patients with CHF scheduled for cardiac resynchronization therapy (CRT). Inclusion criteria were: normal sinus rhythm, left ventricular ejection fraction (LVEF) >55% and New York Heart Association (NYHA) functional class II or IV. Patients with concomitant inflammatory disease, active infections, cardiogenic shock or taking regular nonsteroidal anti-inflammatory drugs or on anticoagulants were excluded. Circulating EPCs were quantified by flow cytometry using 5 directly conjugated antibodies against human FITC-conjugated CD34, PE-conjugated KDR, APC-conjugated CD133, APC-Cy7-conjugated CD45 and PE-Cy5-conjugated CXCR4. We determined the number of CD34+CD133+, CD34+KDR+ and CD133+KDR+ double positive EPCs.

Patients were divided in 2 groups: 1) previous treatment with statins for >3 months (16 patients) and 2) no previous treatment with statins (14 patients). There were no significant differences between groups regarding: age, gender, hypertension prevalence, LVEF or percentage of patients receiving the guideline-recommended drugs for CHF. However, patients previously treated with statins showed a significantly higher prevalence of diabetes and hyperlipidemia (44% vs. 0%, p<0.006 and 81% vs. 29%, p<0.009, respectively). Levels of CD34+CD133+ were significantly higher in the statin group (0.0042±0.0004% of total events, p=0.009), despite the significant percentage of diabetic and hyperlipidemic patients in this group. Regarding CD34+KDR+ and CD133+KDR+ levels there were no significant differences between groups. In conclusion, these results indicate that statins stimulate the mobilization of the CD34+CD133+ stem cells to the peripheral circulation suggesting that statins may be beneficial in advanced heart failure.

P2577 Multipotent human mesangioblast mobilization induced by heparin

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The identification of clinically applicable drugs, which mobilize endogenous mesen- chymal progenitor cells, is of major importance for treatment of cardiovascular dis- easedharacters. We recently identified multipotent mobilizing mesenchymal cells that co-express endothelial markers (so-called circulatingmesangioblasts, cDMABs) in patients undergoing heart surgery (HS). cDMABs differentiate into endothelial cells, smooth muscle cells and cardiomyocytes, and enhance functional recovery after ischemia. More recently, we showed that hepaticocyte growth factor (HGF) induces the mobilization of cDMABs. Since HGF only has a short half life, we investigated whether heparin might be useful to endogenously increase HGF levels, thereby, inducing the mobilization of cDMABs.

Heparin was infused in patients undergoing heart catheterization at a concentration of 100μg/kg (n=7), 200μg/kg (n=11) and 300 μg/kg (n=11) and serum HGF lev- els were determined by ELISA. Peripheral blood-derived mononuclear cells were isolated by Ficoll density gradient centrifugation and were plated on a fibronectin- coated dish.

Consistent with published studies, heparin dose-dependently increased HGF levels (28.1±3.0, 34.4±1.9, 42.8±0.9 ng/ml, respectively). Moreover, hepar- in dose-dependently increased the number of circulating mesenchymal cell
Progenitor cells expressing stage-specific embryonic antigen-1 (SSEA-1) can be isolated from human adult hearts and show mesenchymal progenitor cell characteristics

Background: Mesenchymal stem cells (MSC) are stromal cells with multilineage differentiation potential. They express CD73 and CD105 but not hematopoietic markers. Most of these features are shared with cardiac fibroblasts, however, and no single marker identifies MSC with highest potency. Stage-specific embryonic antigen-1 (SSEA-1/CD15) is expressed by embryonic cells and multipotent cardiac progenitor cells in nonhuman primates. We assessed whether this marker would also be expressed by human adult cardiac cells.

Methods: Atrial appendage samples were obtained from patients undergoing heart surgery for coronary artery or valve disease. They were enzymatically digested and cultured as tissue explants. Cell outgrowths were seeded on poly-D-lysine-coated dishes in cardiomyocytes (CS) medium. CS were plated on fibronectin-coated flasks and expanded as CS-derived cells (GCC). Surface markers were analyzed by flow cytometry and immunocytochemistry. SSEA-1+ cells were purified by magnetic immunosorting (MACS).

Results: Cell outgrowths from cardiac explants contained 17% SSEA-1+ cells (Figure; left panel) which were CD105+ but negative for other markers known to be expressed in CS (α-KS, CD309), and for CD14 and CD34 (3% CD45+ cells). SSEA-1+ cells were purified by MACS (right panel) and expanded as clones. SSEA-1 expression increased when SSEA-1+ cells were cultured as CS or CS+GCC, but decreased when cells were cultured in Mesenchynal medium.

Conclusions: The human adult heart contains SSEA-1+ cells that express MSC markers, form CS, and are clonogenic. Therefore, SSEA-1+ cells have many features of MSCs. Their differentiation potential is currently being analyzed. Recent data in nonhuman primates suggest that human SSEA-1+ cardiac progenitors may be an attractive source for cell therapy applications.

Methods and Results: We first examined cardiomyocytes of Fucci-expressing transgenic mice during development. Fucci probes indicated that the S/G2/M phase cardiomyocyte cycle population decrease during development (11.5; 19.0%; ± 5.3%; P1: 2.5%; vs HS: ± 1.0%). This consistent finding supported Fucci as a novel method to analyze cardiomyocyte cell cycle. Next, for establishing an ex vivo culture system, murine heart was sliced (200µm-300µm) horizontally, and 2h cycle transition was examined by 5-ethyl-2'- deoxyuridine (EdU) staining for 24 hours. The number of EdU positive cardiomyocytes showed that our method successfully replicated the in vivo cell cycle transition (ex vivo: 27.4%; ± 5.4%, in vivo: 29.1%; ± 8.9%). Finally, our ex vivo culture system visualized the cell cycle progression of Fucci-expressing cardiomyocytes and we assessed the length of S/G2/M phase. Interestingly, S/G2/M phase length in cardiomyocytes elongated during development (11.5±0.6 h, P1:15.2±0.1h).

Enhanced expression of myocardin A and telomerase by combined gene transfer improved survival in cyclinD2-overexpressing mice

Methods and Results: MSCs from the bone marrow of 24 months-old C57BL/6 male mice were efficiently transduced or co-transduced with 3rd generation lentiviral vectors (SFFV-LTR-WPRE) carrying the cDNAs coding for TERT yellow fluorescence protein (YFP) or McA-V5 epitope fusion proteins driven by a CMV promoter, at MOI 10-40. Evidence for interaction between TERT and McA was obtained by co-immunoprecipitation and bioluminescence resonance energy transfer assay. Transduction with TERT and to a less extent, McA, but not empty vectors (mock), elevated cell viability (assessed by flow cytometry), proliferation (by BrdU uptake), and self-renewal (by colony formation). MSCs with TERT and McA transduction showed decreased apoptotic responses to Fas induction, as they had lower levels of Annexin V and propidium iodide (PI) staining (Table). In-
creased expression of endogenous Mcα and smooth muscle α-actin occurred in MSCs with overexpressed TERT (n=3, P<0.05 by ANOVA vs mock- transduced). MSCs with co-expression of both TERT and Mcα showed enhanced expression of cardiac and smooth muscle α-actin, as well as the stem cell oncogene Oct-4 and promyogenic genes Nxk2-5, MLC2v, MLC2c and Mcα. The cells also showed increased activity of serum response factor.

Conclusions: Delivery of the TERT and Mcα genes may reseuscitate MSCs from aged mice by increasing cell ability of survival, proliferation and differentiation into cardiomyogenic cells. Thus, detrimental effects of aging on the heart may be reversed by transplantation of MSCs following their in vitro rejuvenation by TERT and Mcα gene transfer.

P2583
Alogeneic adipose tissue-derived stem cells in myocardial infarction: immune response and timing of administration
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Aims: To analyse the immune response and the histological and functional effects of allogeneic adipose tissue-derived stem cells (ADSCs) in a porcine model of reperfused myocardial infarction and determine the effect of administration timing. Methods and Results: Acute myocardial infarction (AMI) was induced in 24 pigs with coronary artery ligation. Viable myocardium was assessed by culture medium at 15 minutes after reperfusion (n=6); ADSCs 15 minutes after reperfusion (n=6); culture medium 7 days after AMI (n=6); or ADSCs 7 days after AMI (n=6). At three weeks follow- up, immunohistochemistry, alloantibodies and histological analysis were evaluated. The administration of ADSCs after reperfusion and 7 days after AMI resulted in similar rates of engrafted cells; some of those cells expressed endothelial cells, smooth muscle cells and cardiomycocytes markers. ADSCs administered after reperfusion compared to the ones administered at 7 days were more effective in increasing expression (2.92±0.4 vs 1.3±0.4, P<0.01). ADSCs therapy did not change ejection fraction but generated alloantibodies.

Conclusions: Allogeneic ADSCs elicited an immune response, when administered after reperfusion were more effective in increasing expression of vascular endothelial growth factor and neovascularisation.

P2584
Transient complete inhibition of TGF-beta/activin/nodal signaling enhances cardiogenesis induced by canonical Wnt signaling in ES cells
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Purpose: Cardiomyocytes derived from ES cells are promising cell source for cardiac repair. Previously we showed that Wnt-3a induced cardiac mesoderm cells resulted in remarkable enhancement of cardiogenesis and a specific inhibitor of Activin receptor-Ikeokinasine (ALK) 4/5/7 increased further. However, the mecha- nisms underlying the enhancement by the specific inhibitor are little understood. Therefore, we investigated the machinery of the cardiogenesis not only to understand stem cell biology but also to improve cardiogenesis in ES cells for clinical application.

Methods and Results: R1 mouse ES cells were differentiated in suspension for 7 days to form embryoid bodies (EBs) and grown under adherent conditions for another 7 days. EBs received 100 ng/ml of mouse recombinant Wnt-3a from day 2 to 6 to induce cardiac mesoderm cells. EBs were additionally stimulated with 10 μmol/l of SB431542 (SB), which is a specific inhibitor of ALK 4/5/7 and inhibits downstream of every TGF-beta/activin/nodal signaling, at various period (day 0-2, 2-6 or 6-9). The proportion of beating EBs (%) beating EBs was examined under microscope at day 9, 11 and 14. The alpha-myosin heavy chain (MHC) expres- sion normalized for GAPDH expression was examined by quantitative RT-PCR at day 14. Addition of SB from day 0 to 2 significantly enhanced % beating EBs (SB+ Wnt-3a: 70.2±5.1%, Wnt-3a only: 51.0±3.6%, p<0.01, n=3) and alpha and MHC mRNA expression (2.92±0.12-fold vs. Wnt-3a only, p<0.01, n=3) at day 14. Next, EBs were additionally stimulated with 30 μg/ml of neutralizing monoclonal anti-TGF-beta 1/2/3 antibody and/or 0.1-10μg/ml of neutralizing monoclonal anti-activin and/or anti-nodal antibody from day 0 to 2 instead of SB. However, only inhibition of TGF-beta and/or activin signaling did not significantly enhance % beating EBs at day 14 (TGF anti- body + Activin antibody + Wnt-3a: 56.0±10.9%, Wnt-3a only: 56.9±5.7%, n=3).

Conclusions: The transient complete inhibition in the downstream of TGF- beta/activin/nodal signaling in the beginning of cardiac differentiation enhances cardiogenesis induced by canonical Wnt signaling. Not only TGF-beta/activin sig- naling but also nodal signaling at the onset of cardiac differentiation plays a critical role in early cardiogenesis.

P2585
Characterization of Oct-4+SSEA-4+ very small embryonic-like stem cells in human myocardium
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Very small embryonic-like cells (VSELs) express pluripotent stem markers (Oct-4, Nanog, SSEA-4). Bone marrow (BM)-derived VSELs in adult mice may be ex- panded and differentiated into all three germ layers. VSELs were also identified in humans in umbilical cord blood and peripheral blood (PB).

Aim: Identification and characterization of VSELs in human myocardium and PB and comparison with cardiac stem cells.

Methods: 29 patients with CAD undergoing CABG were enrolled. Samples of right atrial appendage (RAA), left ventricle (LV) and BM were collected during the procedure. PB samples were drawn before surgery, after weaning from cardiopulmo- nary bypass, after 24 hrs and 5-7 days. Samples of RAA and LV were cut (0.5-1.0 cm3), incubated, digested in collagenase (2 mg/ml) for 30-45min in 37oC, passed through 70um cell strainer, cen- trifugated with 2%FBS, stained with antibodies CD34 FITC/CD133 APC/SSEA- 4PE/CD45 APC-Cy7 for 30min. Nuclei were stained in 10mM of Hoechst dye. VSELs did not express c-kit, express pluripotent markers (Oct-4, Nanog, SSEA-4), are markedly smaller (4.7±0.2μm vs. 7.7±0.4μm). Both populations are Isl-1 negative. My- ocardin contained also subpopulation of Oct-4+SSEA-4+ VSELs which express Isl-1 marker and are of intermediate size (5.7±0.7μm) and might form more ma- ture population of progenitors.

Conclusion: Human myocardium contains population of VSELs expressing early developmental markers (SSEA-4, Oct-4). VSELs have phenotype distinct from cardiac stem markers.

P2586
Mechanical stretch modulates calcium handling during direct cardiac reprogramming of resident progenitor cells in human heart
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Background: Although recent work suggests that defined transcription factors suffice to induce cardiac fibroblasts to undergo cardiocyte-like cells in mice, the possible effects of cardiac reprogramming in humans remain to be inves- tigated. Here, we propose that stretch activation might be essential to achieve effective contraction and differentiation during direct cardiac reprogramming.

Methods: Human cardiac progenitor cells (CPCs) were isolated and transduced with lentiviral vectors encoding human GATA4, Tbx5, and Mef2C. For cardiomycocytes identification, alpha-MHC promoter directing fluorescent proteins (eGFP) and mitochondoria labeling fluorescent dye, tetramethylrhodamine methyl ester perchlorate (TMRE), were used. Differenitiated cardiomycocytes were character- ized by immunofluorescent staining, calcium oscillation imaging, and FACS analy- sis with signal-regulatory protein alpha (SRIPA), a cell-surface marker specific to cardiomycocytes. Reprogrammed CPCs by defined factors were kept static or subjected to pulsatile stretch (110% elongation) to test cardiac differentiation.

Results: Factors-based reprogrammed-CPCs could give rise to a small popu- lation of alpha-MHC/eGFP positive cardiomycocytes in culture at 1 week. The differentiated cells typically contained mitochondrial membrane potential verified by TMRE uptake as ∼15%. Similarly, SRIPA expression was increased and alpha/beta-MHC, cardiac troponin T, MLC-2a, and Hand1 expressions were sig- nificantly upregulated at 2 weeks after reprogramming; however, these cells never showed spontaneous cardiac beating during the differentiation process. We tested the possible contribution of cardiac induction by cyclic mechanical stretch along with the factor-based reprogramming. We found that physiologic stretch for
3 days rapidly induced cellular elongation and orientation vertical to stretch di-
rection in culture. This triggers an increased frequency in calcium oscillation for
> 2.5-fold as well as enhanced cardiac structural gene expressions for ≈2-fold in
reprogrammed CPCs. However, cyclic stretch significantly suppressed the ex-
pression of yanoid receptor and sarcoplasmic reticulum calcium-ATPase, re-
sulting in reduced calcium transport and connexin43 expression in reprogrammed
CPCs.

Conclusions: Our results indicate that defined cardiac transcription factors are
indispensable but not sufficient to induce CPCs to functional human cardiomy-
ocyes. Mechanical stretch accelerates myocardial lineage commitment of repre-
grammed CPCs but may increase the susceptibility to contractile dysfunction.

SECONDARY CARDIOVASCULAR PREVENTION: MEDICATION AND OUTCOMES

P2587
Low-dose acetylsalicylic acid and upper gastrointestinal bleeding in primary and secondary cardiovascular disease prevention populations

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Purpose: The benefit-risk profile of low-dose acetylsalicylic acid (ASA) supports its use for secondary prevention of cardiovascular disease (CVD), but absolute benefit of its use for primary prevention is less clear. This study assessed the incidence of upper gastrointestinal bleeding (UGIB) risk associated with low-dose ASA treatment in patients with a past history of CVD (secondary prevention) versus those without (primary prevention).

Methods: A population-based nested case-control study was conducted using data from The Health Improvement Network database between 2000 and 2007. We identified 2049 cases of UGIB which were sub-divided into primary- and secondary-prevention populations (i.e. those without and with a past history of CVD, respectively). A random sample of 20 000 controls was frequency-matched to cases by age, sex and calendar year. Computerized prescription records were used to assess the use of low-dose ASA. The relative risk (RR) of UGIB associa-
ted with the use of low-dose ASA was estimated by comparing current use (within 30 days of the index date) with non-use in the previous year, using un-
conditional logistic regression, and adjusted for healthcare utilization, smoking, alcohol consumption, past history of peptic ulcer, and use of gastrointestinal toxic and protective agents.

Results: The RR of UGIB in patients taking low-dose ASA for primary preven-
tion of CVD was 1.90 (95% confidence interval [CI]: 1.59–2.26) compared with ASA non-use. The corresponding RR for secondary prevention was 1.40 (95% CI: 1.14–1.72). However, given the higher incidence of UGIB with ASA non-use in secondary prevention than in primary, the absolute risk was higher for the sec-
ondary prevention population. The resultant number needed to harm per year with use of low-dose ASA was 1916 for primary prevention and 1244 for sec-
ondary prevention. The RR for secondary prevention was 1.40 (95% CI: 1.14–1.72). However, given the higher incidence of UGIB with ASA non-use
in secondary prevention than in primary, the absolute risk was higher for the sec-
ondary prevention population. The resultant number needed to harm per year with use of low-dose ASA was 1916 for primary prevention and 1244 for sec-
ondary prevention. The RR for secondary prevention was 1.40 (95% CI: 1.14–1.72).

Conclusions: The RR of UGIB may be higher in patients taking low-dose ASA for
primary prevention of CVD rather than secondary prevention, but the absolute
risk increase is greater in secondary than in primary prevention. The risk of UGIB
when using low-dose ASA for secondary prevention may vary depending on the
indications. These observations could have implications in terms of risk-benefit estimates for low-dose ASA use in patients with different medical histories.

P2588
Change of medication in patients with Coronary Artery Disease (CAD) 2005-2011. Results from the Disease Management Programme (DMP) CAD in the North Rhine region, Germany

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Purpose: In 2004 the DMP CAD was initiated primarily to improve secondary pre-
vention among patients with CAD which was characterized as insufficient at the
DMP’s beginning. In post infarction patients of the Euroaspirin study the prescrip-
tion frequency below the recommended levels (Heidrich et al., 2000) and later observations of this study population showed significant increases (Kotseva et al., 2009). The study presented here should answer the question whether there were significant improvements of prescription of beta blockers (69.3 vs. 83.3%), ACE inhibitors (63.9 vs. 83.3%), and statins (67.3 vs. 73.7%). In both subcollections of post myocardial infarction CAD patients or CAD patients suffering from chronic heart failure these changes were even larger. In post infarction patients there were distinctive in-
creases of prescription of beta blockers (78.6 vs. 86.1%), ACE inhibitors (67.8 vs.
75.4%) and statins (76.2 vs. 83.4%). Similar trends were observed in CAD pa-
patients suffering from chronic heart failure with regard to prescription of beta
blocks (70.1 vs. 82.4%) and ACE inhibitors (71.4 vs. 78.5%).

Conclusions: In a large population of CAD patients prescribed in a DMP significant improvements of secondary preventive efforts were observed. This development coincides with the DMP’s contractual defined aims. It can be seen too in other study populations. How far these effects will reduce cardiovascular morbidity and mortality is at present an open question. The lack of a control group makes it difficult to estimate the exact influence of the DMP in contrast to secular effects. Hence for future evaluation a longitudinal analysis of a patient population with similar characteristics treated outside the DMP is an urgent requirement.

P2589
Quality of oral anticoagulation with phenprocoumon in a coagulation service compared to regular medical care - first results from the thrombEVAL study

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Purpose: Current clinical trials and studies on daily clinical practice with vitamin-
k-antagonists are predominantly performed with warfarin. Data on oral anticoa-
gulation with phenprocoumon, however, are limited. We aimed to compare the
quality of oral anticoagulation in regular medical care (RM) with a specialised
couagulation service (CS) in patients treated predominantly with phenprocoumon.

Methods: In the observational, multi-center thrombEVAL trial, we investigated
613 participants in RM and 465 participants in a CS in Rhineland-Palatinate, Germany. Data were obtained from self-reported data, computer-assisted per-
sonal interviews and INR (international normalised ratio) measurements accord-
ing to standard operating procedures with detailed quality control. The time in therapeutic range (TTR) was calculated by the linear interpolation method. Study monitoring was carried out by an independent institution.

Results: The cohorts comprised 369 men and 247 women aged 71.3±12.1 years
in RM and 250 men and 215 women aged 70.0±13.7 years in the CS. Overall,
232,469 treatment days and 22,947 INR measurements were analyzed. The me-
dian duration of phenprocoumon therapy was 35.5 (11.5/62.5) months with 38.1% of all pa-
tients achieving the therapeutic target in both CS and RM. The TTR in CS was
81.0% (64.3/90.7) for all patients as compared to 72.1% (50.6/88.8) in RM. Sub-
sequently, we observed a significant increase of TTR (p<0.001). In the subgroup of CS, TTR was 80.0% (61.7/96.8) for all patients in the CS and 96.0% (82.5/100.0)
for patients with a stable INR (p<0.001). The TTR was 80.0% (64.3/90.7) for all patients in the CS and 96.0% (82.5/100.0) for patients with a stable INR (p<0.001).

Conclusions: Despite a high TTR in regular medical care with phenprocoumon,
the couple-anticoagulation service shows substantial improvement in the quality of care; this refers to both patients with unstable and with stable INR values as well as patients with self-management. Furthermore, the profile outside the therapeutic range is optimized.
Cytokines and hs-CRP levels in individuals treated with aspirin for cardiovascular prevention: a population-based study (CoLaus Study)

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Backgrounds: Pro-inflammatory cytokines and high-sensitive C-reactive protein (hs-CRP) are associated with increased risk for cardiovascular disease. Low-dose aspirin for cardiovascular (CV) prevention is reported to have anti-inflammatory effects. The aim of this study was to determine the association between cytokines and hs-CRP levels and low-dose aspirin use for CV prevention in a population-based cohort (CoLaus Study).

Methods and Results: Blood samples were assessed in 6,085 participants (3,201 women) aged 35-75 years. Medications use and indications were recorded. Among aspirin users (n=1034; 17%), overall low-dose (351; 5.8%) and low-dose for CV prevention (304; 5.3%) users were specifically selected for analysis. IL-1-beta, IL-6 and TNF-alpha were assessed by a multiplex particle-based flow cytometric assay and hs-CRP by an immunometric assay. Cytokines and low-dose aspirin use for CV prevention were independently associated with increased levels of cytokines and hs-CRP (hs-CRP: 0.41; 95% CI 0.26, 0.63) among patients with known or suspected coronary artery disease.

Conclusions: Low-dose aspirin use for prevention of cardiovascular disease does not seem to impact plasma cytokine and hs-CRP levels in a population-based cohort.

P2592 Are angiotensin receptor blockers associated with increased cardiovascular mortality? A meta-analysis of randomized controlled trials

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Background: Two recent randomized controlled trials (RCT) suggested that angiotensin receptor blockers (ARB) are associated with increased cardiovascular death (CVD). We thus performed a meta-analysis to evaluate the impact of ARB on cardiovascular death among patients with known or suspected coronary artery disease.

Methods: MEDLINE, EMBASE, BIOSIS, Cochrane databases from inception till January 2012 for RCT that reported CVD death with ARB therapy. A total of 9 RCTs were included in this meta-analysis. A random-effect model was used and between-studies heterogeneity with I2.

Results: There were 42582 patients randomized to ARB and 42642 patients randomized to placebo or other therapies. ARB use did not impact the incidence of CVD (RR 0.99, 95% CI 0.89 – 1.10, p=0.086). There was significant heterogeneity among the included RCTs, but no evidence of publication bias (Figure 1).

Conclusions: The cumulative evidence suggests that the use of ARB is not associated with neither increase no decrease in CVD among patients with known or suspected CAD.

P2594 Relationships between chronic use of lipid-lowering drugs and type of subsequent acute coronary syndrome and 28-day mortality after a first event in patients from the French MONICA registries

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Purpose: Lipid-lowering drugs (LLD) have demonstrated their efficacy in many situations to prevent cardiovascular risk. In this work we investigated the link between chronic use of LLD and type of subsequent acute coronary syndrome
(ACS), namely ST-elevation myocardial infarction (STEMI) or unstable angina/non-ST-elevation myocardial infarction (UA/NSTEMI), in real life conditions.

**Methods:** Our study was based on 2006 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 sample consisted of 1944 hospitalised incident ACS (79 were excluded because of missing data).

Logistic regression was performed first to assess the relationship between chronic use of LLD and type of ACS and with subsequent 28-day mortality. Analyses were adjusted for patients’ characteristics (living area, age, gender, previous anti-coagulant, antihypertensive, hypoglycaemic, anti-arthymic and anti-platelet chronic treatments). Analyses on 28-day mortality were secondarily adjusted for type of ACS then for early life-threatening complications (cardiac arrest and shock).

**Results:** Before index event, the rate of LLD treated patients was 22.9% (with 78.7% being treated with a statin). The percentage of UA/NSTEMI among all hospitalised ACS was 44.9%: 55.8% in patients with previous LLD treatment and 41.7% in those without (p<0.0001). The adjusted odds ratio (OR) for UA/NSTEMI was 1.43 (95% confidence interval (CI): 1.13-1.81) for subjects with versus those without LLD. There was a significant association between LLD and early and cardiac arrest (3.6% of cardiac arrests in treated versus 6.7% in untreated patients, p=0.026) but not with shock (2.9% in treated versus 4.7% in untreated patients, p=0.096). LLD treatment prior to event was associated with a significant decrease in in-hospital mortality with a HR adjusted for patients’ characteristics equal to 0.59 (95% CI: 0.36 to 0.92) for treated versus untreated patients. The OR was no longer significant after adjustment for the type of ACS, cardiac arrest and shock.

**Conclusions:** In this large population treated with LLD, patients treated with LLD had a lower rate of 28-day mortality. This may result from a lower probability to develop STEMI, or early cardiac arrest and shock. However it remains difficult to assess from these observational data what is related to the treatment and what is the effect of the underlying dyslipidaemia and associated coronary artery disease.

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**Epidemiological characteristics of low-dose aspirin treatment and gastroprotection in France: results of a national-wide postal survey**


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**Introduction:** The prevalence, the modalities of low-dose aspirin (LLD) treatment and the concomitance with clopidogrel, anticoagulant or gastroprotective treatement are not well known

**Aims & Methods:** The aim of this study was to evaluate the prevalence and the characteristics of LDA treatment in the French population. A postal survey was conducted in July 2011 on a representative sample of 10 000 subjects aged 60 or over (TNS Sofres institute). The questionnaire consisted of 53 questions relating to subject demographics and enabling analysis of the prevalence and characteristics of LDA treatment, prevalence of concomitant treatments as well as specific questions to evaluate compliance to LDA.

**Results:** 8355 subjects responded: 136 questionnaires were discarded (blank or incomplete) so that 8219 subjects effectively participated in the survey (women: 56.1%; age: 72.5±8.1 years).

The prevalence of LDA treatment was 19% (n=1602) (23% in men and 17% in women). It was 11%, 19%, 27%, in subjects aged 61-64, 70-74 and 80-84 years respectively. Comparing to the whole French population, the number of subjects aged 60 or over treated with LDA was evaluated at 2.6 million (IC 99%: ± 150 000).

The treatment was administered at the dose of 75 mg for 63% of the population and the mean dose was 108.4±60 mg/d. Twenty seven % of the patients treated with LDA received a concomitant treatment with a NSAID, 9% with clopidogrel and 3% with an anticoagulant. Thirty % of the patients treated with LDA received a gastroprotective treatment with PPI (30%) and nine more % were prescribed a gastroprotective treatment with H2 antagonists. The prevalence of concomitant gastroprotective treatment was 39% (95% CI: 0.36 to 0.92) for treated versus untreated patients. The OR was no longer significant after adjustment for the type of ACS, cardiac arrest and shock.

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**Impact of clopidogrel on the progression of carotid atherosclerosis in the patients with vascular retinopathy**

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**Aims:** Cilostazol, a selective type III phosphodiesterase inhibitor, has antiplatelet and vasodilating effects and has been proposed to have beneficial effects on prevention of atherosclerosis. We investigated the effects of cilostazol in the progression of carotid intima-media thickness (IMT) and total plaque area (TPA) in patients with vascular retinopathy.

**Methods:** From December 2009 to April 2010, a total of 63 consecutive vascular retinopathy patients with carotid atherosclerosis who are naïve in cilostazol were enrolled. We examined the changes of carotid IMT/TPA and visual acuity/macular thickness before and after 1-year treatment of cilostazol (200 mg/di).

**Results:** Plasma hs-CRP, the total cholesterol level and microalbuminuria was significantly reduced (p<0.003) after cilostazol treatment. Mean left, mean right common carotid artery and mean left, mean right internal carotid artery IMT was significantly reduced after cilostazol treatment compared with baseline (0.60±0.16 mm, P<0.002 vs. 0.60±0.16 mm, P=0.002). We found no significant association of change in HDL-C with log risk ratio (and log of relative risk of clinical endpoint (non-fatal myocardial infarction or cardiac death) was examined by linear regression for the whole dataset and then for each drug class, weighted by the inverse of the variance.

**Conclusion:** This analysis suggests the relation between surrogate marker, assessed by relative change in HDL-C level, and clinical endpoint may be drug dependent. Alternatively, other markers of HDL function may be more relevant.
Systematic review and meta-analysis on the efficacy and safety of colchicine for pericarditis prevention

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Background: Recurrent pericarditis prevention is a major management goal that may reduce morbidity and management costs. Although empirical anti-inflammatory therapy is considered the mainstay of treatment, no specific drug has been proven to be efficacious for prevention but colchicine.

Aim: The purpose of this systematic review was to investigate the efficacy and safety of colchicine for pericarditis prevention.

Methods: Controlled clinical studies were searched in several databases and were included provided they focused on the pharmacologic primary or secondary prevention of pericarditis. We performed a meta-analysis including studies primary outcome, adverse events, and drug withdrawal.

Results: From the initial sample of 127 citations, 5 controlled clinical trials were finally included (795 patients): 3 studies were double-blind randomised controlled trials and 2 studies were open-label RCTs. Trials followed patients for a mean of 13 months. Meta-analytic pooling showed that colchicine use was associated with a reduced risk of pericarditis during follow-up (RR=0.40 [0.30-0.54], p<0.001). The meta-analysis failed to give new insights on the secondary prevention of pericarditis or any significant higher risk of adverse events compared with placebo (RR=1.24 [0.71-2.10], p=0.48, p for heterogeneity=0.42, I2=0%). Gastrointestinal intolerance is the main frequent side effect (mean incidence 8%), but no severe adverse events were recorded.

Conclusions: Available evidence suggests that colchicine is safe and efficacious for the primary and secondary prevention of pericarditis.

Adherence to guidelines in aspirin prescription in low cardiovascular risk patients

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Background: Aspirin is widely used in low risk patients (pts) with cardiovascular disease to prevent thrombosis, despite the increasing risk of bleeding. Pts with a previous episode of bleeding have a high risk of recurrence. The aim of the present study was to evaluate the adherence to guideline in aspirin prescription in pts with previous minor bleeding.

Methods and Results: The analysis is based on 2005 pts: [90 men (45.8%) and 1105 women (54.2%)], mean age 58±14 yrs±12 yrs affected by minor rectal hemorrhage. All pts have been followed for 1 year. The use of aspirin has been evaluated: dose, time, other bleeding episodes (major and minor), and we also evaluated adherence to guideline in prescription aspirin in cardiac pts with previous minor bleeding. The daily aspirin dosage ranges from 80 to 500 mg.

Results: 220 pts were treated with aspirin (10.9%): [120 men (12.5%) and 100 women (9.0%)], mean age 58±11 yrs. 210/220 (95.5%) pts were treated with aspirin according to guidelines, 10 assumed aspirin without indications. 68 pts (24.9%) that needed an aspirin or antiplatelets therapy due to their cardiovascular risk were not treated. Nevertheless, only 1 have contraindication or allergy. The recurrence of hemorrhage has been reported from 1860 pts, of which 210/220 were taking aspirin and 1650/1875 pts were not (95% vs. 88% p<0.001). The gender analysis shows that bleeding was present in 895 men (90%) vs. 965 (90%) women. In the male gender group 115 pts (12.5%) were treated with aspirin while aspirin were used by 870 (78.7%) men. In the female gender group 95 pts (9.9%) were treated with aspirin while 870 (90.1%) were not. The age median was 58 years. By comparing the prescription of aspirin with the median raises up that 23 pts down- mean were treated with aspirin vs. 197 up-mean (2% vs. 21.5%, p<0.001). By comparing men and women older than 58 that assumed aspirin (24.9% vs. 18.7%; p=0.001), the recurrence of hemorrhage is higher in men than in women (95% vs. 92.9%; p<0.05).

Conclusions: The recurrence of bleeding is more frequent in older pts with a previous hemorrhage episode. It tends to be more frequent in men than in women.

The adherence to prescription guidelines is observed even if in the case of a previous hemorrhage episode but not at all. However, the hemorrhage recurrence risk is higher in pts with no specific indication for the aspirin assumption.

After myocardial infarction - is patients treatment by the cardiologist better than by the general practitioner?

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Objective: Secondary prevention after myocardial infarction has undoubtedly a life-prolonging effect. Still it remains unclear how often a sufficient medical prevention is applied in daily routine. Furthermore it is uncertain, whether a direct cardiologic care leads to a more guideline adapted post infarction therapy and whether this may reduce future cardiovascular events.

Methods: Since September 2005, all patients with ACS were prospectively included into the Dresden myocardial infarction registry and followed after 12 month and since 2008 also after 24 month. All living patients with complete 24-month follow-up were now analyzed for the kind of ambulant care, post infarction treatment and further hospital stays.

Results: During this period 1236 consecutive patients with ACS were included into the registry. Hospital mortality was 6.8% (n=65). 972 (76.8%) patients lived after 24 month, 6 patients were lost to follow up, 968 patients entered this analysis. 703 men and 263 women. STElevation infarction occurred in 47.6%. There were: 6.1% cardiogenic shocks and 5.7% resuscitations prior to hospital admission.

After 24 month 737 patients (76.3%) were in cardiologic care. 23.7% were treated by a general practitioner. 89.1% received beta blocker, 87% statins, 88.9% ACEI or ARB. 6.6% of the patients had no anti platelet therapy 2 years after the index event. Patients in direct cardiologic care received with 75.4% vs. 60.3% significantly more often a complete guideline based medical secondary prevention with anti platelet therapy, beta blockers and ACEI/ARB when compared to patients in cardioologic care according to their report often nonsmoker (89.0%). 84.9% and took significantly more often part in heart rehabilitation programs (17.3% vs. 8.2%, p<0.001). Nevertheless, during the analyzed period there were no differences in cardiovascular rehospitalizations between the two groups (17.4% vs. 22.9%, p=0.09). Predictive for a cardiologic treatment after myocardial infarction was a STEMI as index event, an age<65 and an initial admittance out of the Dresden urban area. In contrast, patients with LV-EF<40% or a more complicated ACS (cardiogenic shock, resuscitation, ACVB required) were not more frequently in cardiologic care.

Conclusions: Patients in cardiologic care have a better awareness of their disease and follow more often a guideline adapted post infarction therapy. The question whether this knowledge is due to a better information by the cardiologist or whether motivated patients in the case more often insist on a direct cardiologic treatment remains still needs further study.
Methods: A multicenter study RELIF (REGulare Lecherie i proFilaktila) has been performed in 20 big cities of Russia: in each city were randomly selected 5 polyclinics, in each policlinic – 5 general practitioners (GPs), each GP enrolled 5 consecutive pts with AH who came for a visit. Both pts and GPs filled out questionnaires containing information on risk factors, their targets achievement, current drug regimen, adherence to treatment.

Results: A total of 2175 pts were enrolled; 1510 pts (59.99%) reported themselves to be adherent with their drug regimen which was defined as agreement with 3 statements: “I take my drugs every day”; “I take drugs strictly in doses recommended by my physician”; “I do not miss any intake of my drugs”. Angiotension-converting enzyme (ACE) inhibitors were the most frequently used class of antihypertensive drugs. They were prescribed in 73.37% of pts; almost equally in patients reporting themselves to be compliant or not compliant with their regimen (respectively 74.83% and 71.40%, p<0.1). Second most used were diuretics (61.46% of pts), which were prescribed to adherent pts more often (65.13% vs 56.36%, p<0.001). Beta-blockers were prescribed in 44.71% of pts (45.87% adherent and 42.58% not adherent, ns). 25.06% of AH pts were on calcium antagonists, which were associated with better compliance (28.13% vs 20.76%, p<0.001).

Conclusions: Present study has shown a gap between general practice and National (as well as European) standards for AH treatment. Poor adherence of patients seems to be of concern, but it may be improved by certain drug choices as well as by use of fixed-dose combinations.

Table 1. Comparison of different lipid fractions levels between the two groups

<table>
<thead>
<tr>
<th></th>
<th>HDL (m mol/L)</th>
<th>LDL (m mol/L)</th>
<th>CHOL (m mol/L)</th>
<th>TG (m mol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (all)</td>
<td>1.0±0.2</td>
<td>1.8±0.4</td>
<td>3.6±0.6</td>
<td>1.5±0.9</td>
</tr>
<tr>
<td>Male (m)</td>
<td>1.0±0.2</td>
<td>1.8±0.4</td>
<td>3.5±0.6</td>
<td>1.5±0.9</td>
</tr>
<tr>
<td>Female (f)</td>
<td>1.1±0.3</td>
<td>1.5±0.4</td>
<td>3.7±0.5</td>
<td>1.5±0.9</td>
</tr>
<tr>
<td>Group 2 (all)</td>
<td>1.2±0.3</td>
<td>3.5±1.0</td>
<td>5.2±1.1</td>
<td>2.1±0.9</td>
</tr>
<tr>
<td>Male (m)</td>
<td>1.1±0.3</td>
<td>3.3±0.6</td>
<td>5.1±1.0</td>
<td>2.1±0.8</td>
</tr>
<tr>
<td>Female (f)</td>
<td>1.3±0.3</td>
<td>3.9±1.3</td>
<td>5.7±1.2</td>
<td>2.0±1.1</td>
</tr>
<tr>
<td>p vs all</td>
<td>-0.001</td>
<td>-0.000</td>
<td>-0.001</td>
<td>-0.001</td>
</tr>
<tr>
<td>p vs Group 1</td>
<td>-0.001</td>
<td>-0.001</td>
<td>-0.001</td>
<td>-0.001</td>
</tr>
<tr>
<td>p vs Group 2</td>
<td>-0.001</td>
<td>-0.001</td>
<td>-0.001</td>
<td>-0.001</td>
</tr>
</tbody>
</table>

HDL, high-density lipoproteins; LDL, low-density lipoproteins; CHOL, total cholesterol, TG, triglycerides.

Conclusion: Patients with adequately regulated lipid levels with statins seem to have significantly lower protective HDL levels. It is necessary to determine if that has negative prognostic effect on CAD, how aggressively should we go with lipid lowering therapy and should we use HDL raising substances.

Methods: Do the elderly receive suboptimal secondary prevention post primary percutaneous coronary intervention (PCI)?

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Purpose: To evaluate the impact of age on secondary prevention following primary percutaneous coronary intervention (PCI) in a contemporary unselected cohort.

Methods: Consecutive patients (n=1100) receiving PCI from 5 UK centres formed our cohort. The use of evidence based therapy at discharge was evaluated according to age (~60, 60-75 and ~75 yrs). Follow up (6 week) prescribing practice was assessed in 40% (n=447) of these patients.

Results: See table. 19% were aged over 75 yrs. Increasing age was associated with gender and declining renal function. At discharge and follow up, fewer patients aged over 75 yrs received ACE inhibitors/ARBs. This variation was also seen in the use of statins at discharge after PCI, but to a lesser degree. There was no consistent difference in dosage of beta-blockers or ACE inhibitors according to age.

Table 1. Discharge

<table>
<thead>
<tr>
<th>Discharge</th>
<th>~60 yrs</th>
<th>60–75 years</th>
<th>~75 yrs</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>435</td>
<td>452</td>
<td>213</td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>81%</td>
<td>65%</td>
<td>60%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean Creatinine, mmol/L (SD)</td>
<td>83 (39)</td>
<td>87 (38)</td>
<td>109 (88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beta blocker (%)</td>
<td>94</td>
<td>93</td>
<td>89</td>
<td>NS</td>
</tr>
<tr>
<td>ACE(i)/ARB (%)</td>
<td>98</td>
<td>92</td>
<td>95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean Creatinine, mmol/L (SD)</td>
<td>80 (17)</td>
<td>88 (30)</td>
<td>101 (37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow up</td>
<td>1163</td>
<td>1187</td>
<td>917</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Creatinine, mmol/L (SD)</td>
<td>80 (17)</td>
<td>88 (30)</td>
<td>101 (37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beta blocker (%)</td>
<td>92</td>
<td>91</td>
<td>93</td>
<td>0.01</td>
</tr>
<tr>
<td>ACE(i)/ARB (%)</td>
<td>93</td>
<td>86</td>
<td>77</td>
<td>0.09</td>
</tr>
<tr>
<td>Statin (%)</td>
<td>99</td>
<td>99</td>
<td>95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bisoprolol equivalent dose, mg (SD)</td>
<td>3.1 (1.8)</td>
<td>3.4 (2.0)</td>
<td>3.1 (2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow up</td>
<td>3.9 (1.8)</td>
<td>3.4 (2.0)</td>
<td>3.1 (2.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: Around one fifth of patients receiving PPCI are >75 yrs. Secondary prevention following PPCI is very good, even in the elderly. By 6 weeks post PPCI a small drop off in evidence based therapy is seen, although 90% or more of those aged >75 yrs were still on beta-blockers and statins. Further evaluation is required to fully understand these associations.

Methods: Is prescription behaviour changed by a single continuing medical education (CME) report? Results from the disease management programme (DMP) coronary artery disease (CAD) in the North Rhine Region.

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Background: In 2005 29.3% of the patients with heart failure (NYHA class 2–3) in the DMP CAD received a calcium antagonist (CAA), which is not part of the guideline recommended first line therapy (beta blockers BB plus ACE inhibitors ACE-i).

Objective: Can a single CME report on use of CAA in patients with heart failure added to the regular feedback report increase the prescription rate for guideline recommended therapy?

Results: Change of prescriptions of CAA, BB and ACE-I, and time course of change of prescriptions were analyzed in CAD patients with heart failure. In 2005 428 of 3495 physicians (12%) answered the CME questionnaire. They took care of 955 patients with heart failure (NYHA 2–3), of whom follow-up documentation was available for 2017 pts were entires of physicians who did not answer CME). CAA prescription changed from 28.1-27.6% (29.9-31.2), BB from 78.9-80.5% (74.6-78.1), ACE-I from 69.9-74.6% (72.8-76.3), and BB+ACE-I from 53.9-59.5% (54.8-58.2). p for group differences 0.02-0.05. Blood pressure increased decreased from 129.1-125.8 mmHg, p<0.04 (137.1-129.9, p<0.001).

Discussion: Difference over time in prescription rates for guideline compliant medications was consistent in favour of those physicians who had participated in the CME activity. The latter did not influence prescription of heart failure medications, which showed a slow and modest increase over time (3 y) in the total group. Guideline knowledge is high, but for improvement of prescription behaviour other factors than just updating knowledge also have to be addressed.

Methods: Do the elderly receive suboptimal secondary prevention post primary percutaneous coronary intervention (PCI)?

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Purpose: Statins are beneficial in secondary prevention of myocardial infarction. However, the beneficial effect of a calcium antagonist (CAA) compared with lower doses is controversial. We studied factors impacting the prescription of a HDS at discharge after an Acute Myocardial Infarction (AMI), and assessed effects of this HDS on mortality and cardiovascular morbidity after 3 years of follow-up.
Utilization of prophylactic drug therapy after acute myocardial infarction in Abu Dhabi

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Purpose: Pharmaceutical treatments aiming to decrease blood lipids, decrease blood pressure, inhibit platelet aggregation, and control diabetes (where indicated) are the cornerstones of secondary prevention after acute myocardial infarction (AMI); there is considerable evidence on their beneficial effects on rates of re-infarction and mortality. This study describes the use of selected classes of medication during a one year period following AMI events in Abu Dhabi, and compares uptake of these drug classes between Abu Dhabi and Sweden.

Methods: In Abu Dhabi, information on medications dispensed during the first year following hospitalization with a diagnosis of AMI during January 2010 to June 2011 (n=1,326) was retrieved from the Health Authority of Abu Dhabi’s electronic monitoring system. In Sweden, both re-infarction and mortality. This study describes the use of selected classes of medication during a one year period following AMI events in Abu Dhabi, and compares uptake of these drug classes between Abu Dhabi and Sweden.

Methods: In Abu Dhabi, information on medications dispensed during the first year following hospitalization with a diagnosis of AMI during January 2010 to June 2011 (n=1,326) was retrieved from the Health Authority of Abu Dhabi’s electronic monitoring system. In Sweden, both re-infarction and mortality. This study describes the use of selected classes of medication during a one year period following AMI events in Abu Dhabi, and compares uptake of these drug classes between Abu Dhabi and Sweden.

Results: During the first three months following the AMI events, the proportions of patients in Abu Dhabi with at least one prescription of at least one anti-hypertensive (AHT) drug was 76%, statin 72%, platelet aggregator inhibitor (PAI) 76%, beta-blocker 64%, and drugs affecting the renin-angiotensin system (RAS) only 24%. Uptake of these drug classes declined rapidly over the year following the AMI event (to 36%, 34%, 34%, 28% and 28%, respectively, during month 10-12). Reductions among UAE citizens were somewhat lower than among expatriates. In Sweden, the proportions of AMI patients with prescriptions for AHT, statins, PAI, beta-blocker and RAS drugs were 90%, 82%, 89%, 83% and 83%, respectively, during months 0-3, and 78%, 69%, 76%, 65% and 55%, respectively, during months 10-12.

Conclusion: The health data systems in Abu Dhabi offer a valuable tool for monitoring adherence to drug use. There is a substantial decline in the utilisation of key classes of medication in the year following AMI; this decline is significantly greater than that seen among comparable patients in Sweden. It appears that the outcomes of AMI patients in Abu Dhabi could be substantially improved by promoting adherence to evidence-based guidelines concerning long-term secondary prevention measures.

P2608

Experiences of patients with oral anticoagulation in regular medical care compared to a coagulation service - results from the thrombEVAL study

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Purpose: Long-term oral anticoagulation (OAC) with warfarin is widely established for prevention of thrombotic and thromboembolic complications. However, only limited data are available about the experiences of patients with OAC in daily clinical practice.

Methods: Patients treated with oral anticoagulation for >4 months in regular medical care were included in an observational multi-center trial and compared with patients treated for 6 months in a coagulation service. Data were obtained from a questionnaire-based interview, medical records, and the anticoagulation pass according to standard operating procedures. The individual time in therapeutic range (tPTT) was calculated by the linear interpolation method. Data monitoring was carried out by an independent institution.

Results: Overall, 613 patients (366 men, 247 women, aged 71.3±12.1 years) in regular medical care and 120 patients (76 men, 44 women, aged 68.4±14 years) in the coagulation service were examined. The analysis covered 22,947 INR measurements. Treatment with OAC was rated as “complied” by 8.7% of the patients only. Regular INR-measurements were rated as “important” by 50.2% and as “unimportant” by 46.8% of the patients. An INR-measurement was missed at least once within the last year by 17.6%. With regard to the items “availability”, “appointments”, “waiting time”, “time for questions”, “efficiency”, the treatment physician was rated with 1.85 (grade from 1 “very good” to 6 “insufficient”) in regular medical care. In the coagulation service, there was an even better assessment with 1.41 (all p<0.001). Furthermore, patients report a better knowledge about thromboembolic disease (2.04±0.95 vs. 2.62±1.17, p<0.0001) and complications of OAC (2.33±1.10 vs. 2.98±1.31, p<0.0001) in the coagulation service. Patients with a better self-rated knowledge about the disease have a longer pTTR (p<0.005). 70.0% of patients in regular care think that a coagulation service is useful and 69.4% would like to use a coagulation service. Medical care is estimated as “good” or “very good” by 86.9% of the patients in regular care and 99.2% in the coagulation service.

Conclusion: Medical care with OAC is generally rated as good in clinical practice and even better in a coagulation service. The knowledge about the disease and complications which is associated with a longer pTTR is improved in the latter. The willingness to attend a coagulation service is high.

P2609

Effect of low dose eplerenone on endothelial function in patients with stable coronary artery disease

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Purpose: Clinical study showed as eplerenone significantly reduced all cause cardiovascular mortality in patients with left ventricular dysfunction after a recent myocardial infarction. The aim of the present study was to investigate whether low dose eplerenone (25 mg) displayed favorable effects on endothelial function. To evaluate this, we determined the parameters, the dose of eplerenone the patients received at discharge was not related to death or MACE occurrence in the following 3 years (HR = 1.04 [0.77-1.36], p > 0.087). A similar analysis using a more stringent definition for HDS (atovaroxan ≥ 40 mg or rosuvastatin ≥ 20 mg) yielded similar results.

Conclusions: The issue of long term benefit of high doses of statin therapy compared with lower ones after an AMI remains unanswered in an observational context, because in this “real life” large registry, high doses were preferentially prescribed to patients with a low risk profile, but less commonly to patients with a high risk profile.

Methods: Participants were 2420 survivors of a STEMI or NSTEMI from the French multicenter FAST-MI registry conducted in 2005, with a known statin dose at discharge. Rosuvastatin at any dose, atovaroxan ≥ 20 mg/d and Simvastatin 40 mg/d were considered as HDS. Factors related to HDS prescription were studied using logistic regression. Impact of HDS prescription on occurrence of death or major cardiovascular events [MACE] (MI, stroke or revascularisation) was studied using a Cox proportional hazards model after propensity score matching.

Results: 54.5% of the patients had a HDS prescription at discharge. In crude risk analyses, HDS prescription was associated with a lower risk of death or MACE (HR=0.84 [0.71-0.98], p<0.03). However, patients already under treatment with a HDS before the ACS, patients managed in a university hospital, located in a large city, with a younger age, a STEMI, a high blood pressure at entry (≥ 140 mm Hg) and who were discharged rapidly after their AMI were more likely to benefit from a HDS prescription at discharge. After propensity score matching using these parameters, the dose of statin the patients received at discharge was not related to death or MACE occurrence in the following 3 years (HR = 1.04 [0.77-1.36], p > 0.087). A similar analysis using a more stringent definition for HDS (atovaroxan ≥ 40 mg or rosuvastatin ≥ 20 mg) yielded similar results.

Conclusions: The issue of long term benefit of high doses of statin therapy compared with lower ones after an AMI remains unanswered in an observational context, because in this “real life” large registry, high doses were preferentially prescribed to patients with a low risk profile, but less commonly to patients with a high risk profile.
SECONDARY CARDIOVASCULAR PREVENTION: INTERVENTIONS AND OUTCOMES

P2610 Impact of home versus clinic based management of chronic heart failure: the which heart failure intervention is most cost-effective & consumer friendly in reducing hospital care (WHICH?) multicentre, S. Stewart1, M.J. Carrington1, T.H. Marwick2, P.M. Davidson3, P. Macdonald4, D. Horwitz5, P. Newton6, H. Krum7, C. Redf7, P. Scuffham7 on behalf of WHICH? Trial Investigators. 1Baker IDI Heart and Diabetes Institute, Melbourne, Australia; 2Cleveland Clinic, Cleveland, United States of America; 3University of Technology, Faculty of Nursing, Midwifery and Health, Sydney, Australia; 4St. Vincent’s Hospital, Sydney, Australia; 5University of Adelaide, Queen Elizabeth Hospital, Adelaide, Australia; 6Monash University, CRE Therapeutics, Department of Epidemiology & Preventive Medicine, Melbourne, Australia; 7Griffith University, Brisbane, Australia

Purpose: The most effective mode of post-discharge, chronic heart failure (CHF) management is unknown. We undertook a head-to-head comparison of the most common forms of face-to-face CHF management to test the hypothesis that a home-based intervention (HBI) would be more cost-effective in optimising “all-cause” outcomes than a clinic-based intervention (CBI).

Methods: The WHICH? Trial was a prospective, multi-centre randomised controlled trial with a blinded endpoint adjudicator. Overall, 280 hospitalised CHF patients (73% male, aged 71±14 years and 73% with LVEF < 45%) were randomised to outreach HBI or specialised CHF CBI. The primary endpoint was all-cause, unplanned, hospitalisation for heart failure or death during 12–18 month follow-up. Secondary endpoints included frequency, type and duration of recurrent hospitalisation with prospective economic analyses of total health care costs.

Results: During study follow-up, fewer CBI patients (124/137 [91%]) attended a specialist CHF clinic appointment compared to HBI patients (140/143 [98%]) who received a home visit (OR 0.93, 95% CI 0.87 to 0.98; p=0.008). HBI patients also tended to have more home visits than CBI patient visits to the CHF clinic (3.4±2.5 versus 2.9±2.5 visits; p=0.061). Overall, 102/143 (71%) HBI versus 104/137 (76%) CBI patients experienced the primary endpoint (adjusted HR 0.87; 95% CI 0.73 - 1.00; p=0.061): comprising fewer deaths in the HBI group (31 [21.7%] versus 38 [27.7%]; adjusted HR 0.75, 95% CI 0.45 - 1.26; p=0.350) and similar proportions were hospitalised. Similar proportions in both groups were hospitalised for CHF, a cardiovascular condition or for any reason. However, HBI patients had fewer days of recurrent unplanned hospitalisation (158±116 versus 11.6 days; p=0.059) and all-cause stay (5.78±10.2 versus 8.66±11.6 days/patient/100 days; p = 0.003); with significantly less cardiovascular (590 less days [-37%]; p=0.025) but not CHF-related stay (259 less days [-25%]; p=0.218). Consequently, HBI patients had significantly increased days out-of-hospital alive (452±158 [85% of maximal follow-up] versus 418±173 days [80%]; p=0.019). Despite more prolonged event-free survival, total cost of health care was significantly less in the HBI than CBI group (median [IQR] costs AU$3902 [1111 to 2.297] versus AU$4316 [330 to 4.105];3 month of follow-up; p=0.034).

Conclusions: Head-to-head, HBI was not superior to CBI in reducing all-cause death or hospitalisation. However, due to markedly less hospital stay, HBI was associated with more prolonged event-free survival and significantly fewer health care costs.

P2611 International differences in outcomes in stable outpatients with atherothrombosis: Results from the REACH Registry, G. Ducroux1, J. Labreuche1, R. Qiao2, E. Pancherkovski2, C.S. Liao3, Y. Ikeda4, S. Goto5, P. Amarenco6, D.L. Bhattacharya7, P.G. Steg1 on behalf of The REACH registry investigators. 1AP-H - Hospital Bichat-Claude Bernard, Paris, France; 2Cardiovascular Institute & Wu Fau Hospital, Beijing, China; 3People’s Republic of; 4Cardiology Research Center, Moscow, Russian Federation; 5National Taiwan University Hospital, Taipei, Taiwan; 6Kokura Memorial Hospital, Fukuoka, Japan; 7Tokai University, Kanagawa, Japan; 8Harvard Medical School, Brigham and Women’s Hospital, TIMI Study Group, Boston, United States of America

Purpose: We aim to describe geographical differences in outcomes in stable outpatients with atherothrombosis around the world.

Methods: The REACH registry collected data and 4-year follow-up for 45,227 patients in different countries. This population included 37,154 patients with established atherothrombotic disease (coronary artery disease, cerebrovascular disease, or peripheral artery disease) and 8073 asymptomatic patients with at least 10 years, 64.7% were men. Risk factors were as follows: diabetes mellitus 43.6%, hypercholesterolemia 70.4%, obesity 28.4%, current smokers at baseline 15.6%, hypertension 81.3%. The analyses of baseline characteristics according to geographical zone showed marked differences. The cumulative 4-year composite outcome (CV death, myocardial infarction, or stroke) of patients with prior atherothrombosis at baseline showed important variability (from 12.5% for Japan to 18.16% for Eastern Europe). Results are detailed in the figure. Marked differences in outcomes were also observed in patients with risk factors only.

P2612 Comprehensive cardiac rehabilitation program in acute phase improves long-term prognosis of arteriosclerotic myocardial ischemia in Japan, J. Tomono, H. Adachi, H. Kan, R. Kawaguchi, T. Toyama, H. Hoshizaki, S. Oshima. Gunma Prefectural Cardiovascular Center, Division of Cardiology, Maebashi, Japan

Purpose: While comprehensive cardiac rehabilitation program (CR) is known to have favorable effects in relatively acute period, it is still unknown whether it also improves long-term prognosis. Like a legacy effect shown by UKPDS, there is a possibility that earlier improvement of metabolic derangement and earlier acquisition of exercise habit would have favorable effects on subjects’ prognosis. Hereby, we studied the effect of CR on secondary prevention of ischemic heart disease patients for 10 years.

Method: Consecutive 276 stable angina pectoris patients were enrolled. They had received percutaneous coronary intervention from January to December 2006 in CR group (n=107) and non-CR group (n=158). Eleven patients could not be followed up, and 265 patients were observed. Patients were divided into two groups according to the participation of CR; CR group (n=107) and non-CR group (n=158). They were followed until December 2011 (mean observation period was 65.3 months). Event free ratios of cardiac event (target lesion revascularization (TLR), new onset of arteriosclerotic myocardial ischemic lesion (De Novo lesion), acute coronary syndrome (ACS), heart failure or death) were investigated according to the Kaplan-Meier method and were evaluated by log-lank test.

Results: Seventy one events occurred during the study period (TLR 22, De Novo 35, ACS 9, heart failure 2, death 3). Event free ratio was greater (p < 0.05) in CR group. There was no difference in TLR between two groups (n.s.) as for the onset of De Novo lesion, CR strongly prevented it as comparing with non-CR (p < 0.05).

Conclusion: Comprehensive cardiac rehabilitation program was revealed to exert a long-term effect on secondary prevention of new onset of myocardial ischemia.

P2613 Long-term impact of a nurse-led, home-based, prevention program for hospitalised cardiac patients on risk of secondary events: the multicentre young @ heart randomised controlled trial, S. Stewart1, M.J. Carrington1, Y.K. Chan1, A. Calderone1, S. Goldstein2, P. Scuffham3 on behalf of Young @ Heart Investigators. 1Baker IDI Heart and Diabetes Institute, Melbourne, Australia; 2University of New South Wales, Sydney, Australia; 3Griffith University, Brisbane, Australia

Purpose: Despite the proven benefits of short-term cardiac rehabilitation and heart failure management programs, there is a paucity of evidence to support the application of longer-term secondary prevention programs.

Methods: The Young at Heart Study was a multicentre, randomised controlled trial with blinded end-point adjudication. Analyses of major endpoints, including all-cause morbidity and mortality during 2-year follow-up will be available in mid-2012. The study compared usual post-discharge care (UC) with the nurse-led, Young at Heart (Y@H) intervention. A “sliding-scale” intervention system for patients with risk factors only.

Figure 1: Kaplan-Meier curves of De Novo lesion
Clinical prognosis of patients with acute coronary syndromes and LDL-c <70 mg/dl: first evidence of "J-curve" effect in secondary prevention

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Background: Prognosis of patients admitted for acute coronary syndromes (ACS) and low-density lipoproteins (LDL-c) <70 mg/dl has not been largely studied.

Methods: Observational study with 1-year follow-up of consecutive patients admitted for ACS in a single center.

Results: 25% of the 574 patients had baseline LDL-c <70 mg/dl and also had higher age, higher prevalence of hypertension, diabetes, previous coronary heart disease or heart failure, previous statins treatment as well as lower total cholesterol, HDL-c, triglycerides and hemoglobin. Patients with LDL-c <70 mg/dl received lower daily doses of atorvastatin (p=0.01) at discharge. During 1-year follow-up all-cause crude mortality was higher in patients with LDL-c <70 mg/dl (OR: 1.89, 95% CI 1.04-3.45; p=0.02), mainly driven by cardiovascular mortality (94% vs. 51%; p<0.05). Nonetheless, Cox regression analysis did not find independent risk of LDL-c <70 mg/dl for all-cause mortality (OR: 1.07; 95% CI 0.58-1.96; p=0.8) or cardiovascular mortality (OR: 1.12; 95% CI 0.54-2.32; p=0.7).

When patients were divided into categories of LDL-c, a "J-curve" effect was noted for all-cause mortality. Only patients with baseline LDL-c >70 mg/dl obtained clinical benefit from statin treatment in all-cause mortality (OR: 0.36; 95% CI 0.13-0.96; p=0.04); patients with LDL-c <70 mg/dl showed a non-significant trend to worst prognosis (OR: 1.6495% CI 0.21-13.05; p=0.06).

Conclusions: ACS patients with LDL-c <70 mg/dl have poorer midterm prognosis that is mainly explained by previous cardiovascular disease and nonbenefit from statins was observed. Our results suggest a "J-curve" effect of baseline LDL-c and 1-year prognosis after an ACS.
Technology based home-care model improves outcomes of uptake, adherence and health in cardiac rehabilitation

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Purpose: Cardiac rehabilitation (CR) plays a pivotal role in recovery from cardiac events such as myocardial infarction (MI). Despite the known benefits of participating in traditional centre-based CR programs, uptake and adherence remain low (14–43% after MI). The Care Assessment Platform (CAP) is a mobile and internet technology based home-care CR service model developed to improve patient uptake and adherence compared to traditional CR programs.

Methods: Post MI patients (n=120, 100 males) were randomised into hospital-based (Control, n=60) and CAP home-care (Intervention, n=60) CR programs. The CAP CR service model was aimed at improving patient empowerment and overcoming the limitations and barriers to uptake and adherence that characterise traditional CR programs. The mobile phone platform was utilised for health and exercise monitoring, delivery of motivational and educational materials and messages, with follow-up information with a case manager via a secure internet portal. The case manager provided weekly consultations over the 6 week CR program. Uptake and adherence were measured as well as health outcomes, including functional capacity (6-minute walk test (6MWT)), anthropometric and blood lipid profile, and emotional state (DASS21 Questionnaire).

Results: Patients were aged 37 to 81 (mean ± SD = 56 ± 10 y). Uptake in the Intervention group was significantly better than in the Controls (87% (n = 52) vs. 67% (n = 40)5). Adherence rate throughout the 6-week CR program was significantly higher in the Intervention group (92%) than the Control group (70%)5. There was a significant improvement in the 6MWT walk distance from baseline to 6 weeks for Control and Intervention groups ([543.8, 583.0] vs. [594.2, 74.3] and [509.9, 76.9] vs. [569.6, 80.5] m, respectively)5. Significant reductions in weight (88.3±20.4 vs. 87.3±20.7 kg) and triglyceride levels (1.26±0.75 vs. 1.11±0.68 mmol/L) were observed following the CR program 6, and the intervention group also improved significantly in the Intervention group as measured through DASS21 Depression and Anxiety scores (median2, IQR6 to median, IQR7 in both)4.

Conclusions: The technology based home-care CR model demonstrated increased uptake and completion rates compared to the traditional centre-based CR program, resulting in improvement in the over-all CR participation. The CAP CR was also effective in improving health outcome measures of functional capacity, clinical measurements and emotional state. (Statistical significance of p < 0.05 was achieved through chi squared, paired t-test, non-parametric test.)
Harvesting the benefits of a cardioprotective lifestyle after coronary angioplasty

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The benefits of adherence to a heart-healthy lifestyle in combination with evidence-based drug treatment after PCI have recently been demonstrated in the OASIS-5 study: an up to four-fold reduction of new cardiac events within 6 months post-PCI was observed among lifestyle adherent patients as compared to non-compliers. Which gains may be expected when these findings are applied to current clinical practice?

P2621

Objective: In the SPICI study (Study of Patient Information after Coronary Intervention) patients were asked to report on their lifestyle regarding the use of tobacco, physical activity and food habits. The study was based on a questionnaire sent to an unselected, consecutive post-PCI population in 28 Swedish hospitals, representing a sample of 10% of all PCI patients annually. Using the data on cardiac events 6 months post-PCI from the OASIS-5 study we estimated the event rate in the Swedish population, provided all patients were fully adherent to lifestyle recommendations.

Result: Answers were obtained from 1073 patients 26% females, 74% males, av. age 66 years (34-89). Although half of the previous smokers had quit still 16% continued to use tobacco. Using the guidelines from the 4th Joint European Societies Guidelines on Cardiovascular Prevention in Clinical Practice 55% reported adhering to all 3 recommendations and 40% had reported that they had changed dietary habits. Approximately 50% engaged in regular physical activity, mainly supported by training sessions in patient groups, 31% had increased their activity after PCI.

Annually 18.000 patients undergo PCI in Sweden. Using the findings of the OASIS-5 study over 1000 new cardiac events (myocardial infarction, stroke and cardiovascular death) might be expected within 6 months post-PCI. Applying the odds ratios for quitting smoking 0.57 and for adherence to food and physical activity 0.52 on the patient reported habits one third of the events in Sweden (300-400 events, of which 150-200 deaths) could be prevented if 100% compliance to lifestyle recommendations could be reached.

Conclusion: If the fruits of a cardioprotective lifestyle are to be harvested prevention and rehabilitation programmes after PCI need an in-depth revision of current practice: greater emphasis on lifestyle factors and on how to support patients in their long-term commitment to behavioural change.

Midregional pro-A-type natriuretic peptide strongly and independently predicts risk of recurrent coronary events in patients with stable coronary heart disease followed over 8 years

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Context: Pathophysiological studies suggest that A-type natriuretic peptides might provide valuable information about cardiac dysfunction in patients with coronary heart disease (CHD). The clinical relevance of elevated circulating midregional pro-A-type natriuretic peptide (MR-proANP) in patients with stable CHD several weeks after an acute event has not been evaluated.

Objective: To assess the predictive value of MR-proANP for recurrent cardiovascular disease (CVD) events in stable CHD patients, simultaneously controlling for the N-terminal fragment of the precursor to B-type natriuretic peptide (NT-proBNP) and a large number of potential confounders.

Design, Setting, and Participants: Plasma concentrations of MR-proANP were measured at baseline in a cohort of 1,048 patients aged 30-70 years with CHD, and participating in an in-hospital rehabilitation program between January 1999 and April 2004 in two cooperating hospitals.

Main Outcome Measure: Cardiovascular mortality, non-fatal myocardial infarction and non-fatal stroke.

Results: During a median follow-up of 8.1 years, 150 patients (incidence 21.1 per 1,000 patient years) experienced a fatal or non-fatal secondary CVD event. Elevated MR-proANP levels were associated with heart failure, higher number of affected segments and left-ventricular dysfunction in a statistically significant way. Furthermore, after adjustment for age and gender, MR-proANP was strongly correlated with NT-proBNP (R=0.72, p-value <0.0001). In a multivariate model, MR-proANP was associated with a hazard ratio (HR) of secondary CVD events of 3.00 (95% confidence interval (CI), 1.70-5.28) when the top quartile was compared to the bottom one. Further adjustment including NT-proBNP attenuated the association only slightly (HR 2.36; 95% CI, 1.29-4.32). Finally, MR-proANP clearly improved various multivariate measures of model accuracy, including the area-under-the-curve (AUC), and reclassification measures.

Conclusion: Elevated MR-proANP levels in stable CHD patients are associated with several CVD disorders and predict long-term CVD events in these patients, even after adjustment for a wide range of potential confounders including NT-proBNP.

Prevalence of silent necrosis in a cohort of patients submitted to cardiovascular magnetic resonance

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Acute coronary syndromes may appear and develop in a silent way. Patients with silent necrosis may not receive adequate therapy, and thus are more prone to short and long-term complications. Our objective was to assess the prevalence of silent necrosis in our cohort of patients submitted to a late gadolinium enhancement magnetic resonance scan (LGE-CMR) in our institution.

Methods: All patients submitted to a LGE-CMR and no previous history of acute coronary syndrome, were included. The CMR protocol included, in all patients, TrueFISP cine sequences in the usual views and late gadolinium enhancement sequences. In a percentage of cases myocardial perfusion sequences after administration of 0.4mg/kg of dipyridamole were also acquired.

Results: 1342 patients with no known previous history of acute coronary syndrome were recruited (755 males, 623.14 yrs). Reasons for referral were: 71.3% to rule out coronary artery disease (CAD), 12.4% for study of dilated cardiomyopathy (DCM), 3.7% for arrhythmogenic right ventricular cardiomyopathy, 2.6% valvular heart disease, 5.8% to rule out myocarditis, and 4% for other reasons.

Of them, 165 (132 males, 66±11 yrs), representing 12.3% of the whole group, showed myocardial necrosis. Patients with silent necrosis were older (p<0.001) and more frequently males (p<0.001). 20% of patients studied to rule out CAD and 12.4% of those studied for DCM had necrosis. None of the patients with suspicion of myocardial necrosis. Necrosis extension was usually small: necrotic mass 7.9±9.4g, percentage of necrotic to total myocardium 4.2±4.6% and number of affected segments 2.5±2.1. Nonetheless, in 17 patients (10.3%) percent of necrotic myocardium was >10% and in 20 patients (15%) the number of affected segments was >5. In 71% of cases necrosis was subendocardial, in 12% transmural and in 17% both patterns coexisted. After adjustment for age, gender and reason for referral, patients with silent necrosis were shown to have worse systolic function (left ventricular ejection fraction: 62.1±1 vs 54.3±3, P<0.01) and ventricular remodeling.

Conclusions: In this descriptive study of our series of patients referred for CMR, with no known previous history of acute coronary syndrome, prevalence of silent necrosis was 12.3%. Though in the majority of cases necrosis was small, systolic function was worse in patients with necrosis. Detection of silent necrosis is important in order to provide adequate therapy and improve prognosis.

Endothelial dysfunction in the brachial artery predicts clinical outcome in patients with coronary artery disease undergoing successful percutaneous coronary intervention

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Background: Previous studies showed that endothelial vasomotor dysfunction is a predictor of cardiovascular events; however, in the era of drug-eluting stents, the clinical relevance of endothelial dysfunction on the outcome in patients undergoing percutaneous coronary intervention (PCI) should be re-evaluated.

Methods: This study included 116 patients with stable coronary artery disease. The flow-mediated dilatation (FMD) of the brachial artery (Unex Co. Ltd., Nagoya, Japan) was examined after PCI, and then optimized therapy to reduce risk factors was performed according to American College of Cardiology/American Heart Association guidelines. Patients were followed up for 25 months or until 1 of the following events occurred: cardiac death, nonfatal myocardial infarction, recurrent and refractory angina pectoris requiring coronary revascularization, or ischemic stroke.

Results: When patients were divided into quartile, FMD in Q1, Q2, Q3 and Q4 were 1.9±0.5%, 3.1±0.4%, 4.3±0.3%, and 6.3±1.3%, respectively. There were no significant difference in age, gender, prevalence of hypertension, diabetes mellitus, and dyslipidemia among quartile. During follow-up, events occurred in 38 (32.8%) patients. Multivariable logistic analysis showed that the most impaired FMD was an independent predictor of events (hazard ratio: 3.27, 95% confidence interval: 1.00 to 10.63, p=0.04).

Multivariable logistic analysis

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History of Heart Failure 2.91 1.06 7.97 0.04
Conclusions: The impairment of endothelial vasomotor function after PCI has an adverse impact on outcome in stable coronary artery disease patients despite optimized therapy to reduce risk factors.

Correlation between low-density lipoprotein cholesterol/high-density lipoprotein cholesterol ratio and incidence of cardiovascular events after percutaneous coronary intervention

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Objectives: Several clinical studies demonstrated that the low-density lipoprotein cholesterol/high-density lipoprotein cholesterol (LDL-C/HDL-C) ratio was an excellent predictor of cardiovascular diseases. The aim of this study was to investigate whether the LDL-C/HDL-C ratio could affect the outcomes after percutaneous coronary intervention (PCI).

Methods and Results: Nine-hundred-seventy-nine patients who underwent successful PCI were divided into the following three groups: those with LDL-C/HDL-C < 1.5, 1.5 < LDL-C/HDL-C < 2, LDL-C/HDL-C ≥ 2. Among the three groups, the incidence of major adverse cardiac events (MACE) during the subsequent five years after PCI was measured. Primary endpoint was defined as cardiac death, non-fatal myocardial infarction and new stenosis. In addition, secondary endpoint was evaluated including the occurrence of restenosis. In both endpoints, Kaplan-Meier analysis demonstrated that the patients with LDL-C/HDL-C < 1.5 had significantly lower incidence of MACE than the patients with LDL-C/HDL-C ≥ 2.0 and also with 1.5 < LDL-C/HDL-C < 2 (figure: primary endpoint). Cox proportional hazards analysis indicated that the LDL-C/HDL-C ratio had a strong correlation with the incidence of MACE (P < 0.001).

Conclusion: The LDL-C/HDL-C ratio was a valuable predictor of cardiovascular events after PCI.

LDL goal achievement in 576 consecutive, unselected coronary heart disease patients; status in general practice and results of a structured follow-up program in out of hospital cardiology practice

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Purpose: LDL goal achievement (LDL≤2.5 mmol/L or ≤2.0 if feasible) is generally as low as 1/3 in patients with high risk, including those with angiographically documented coronary heart disease (CHD), attributed to insufficient effect of drugs and side effects. We sought to assess the level of goal achievement in consecutive, unselected CHD patients remitted from primary care to a cardiology practice outside hospital and to evaluate the effect of a structured follow-up (FU) program.

Methods: All patients with CHD (ICD-10 i25.1) from 2010 were retrospectively reviewed, and all patients from 2011 were prospectively followed until June 2012. LDL goals were achieved, or further trials considered futile for lack of effect, side effects or administrative reasons. As needed, statins were started, dosages increased, more potent statins prescribed and ezetimibe added. In case of side effects, statins were changed.

Results: Only 1/3 of patients had LDL levels according to guidelines when remitted, after the FU program this increased to 86%. The reasons for not achieving LDL goals were insufficient drug effect in 6 patients, side effects or contraindication in 8, administrative reasons in 8 patients, and 14 were still in FU.

Extracorporeal lipoprotein(a) elimination for coronary atherosclerosis regression in coronary heart disease patients with elevated lipoprotein(a) levels

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Purpose: To evaluate the effect of extracorporeal lipoprotein(a) [Lpa] elimination on coronary atherosclerosis progression in CHD patients with elevated Lpa levels.

Methods: A total of 55 subjects (mean age 54.8±7.4 years, 67% male) with stable CHD verified by angiography, Lpa level >50 mg/dL, and LDL-C level >2.5 mmol/L on chronic statin treatment were prospectively evaluated for 18 months. Patients were allocated to receive apheresis treatment weekly with either immunoadsorption columns (n=15, Lpa LipoPak, PCARD Ltd., Russia) or double-filtration plasmapheresis (n=40; Evolux 5A, Kaudermis Ltd., Japan) on the atorvastatin background, or atorvastatin only (n=28). The primary efficacy end-point was the nominal change in percent diameter stenosis (DS), determined by quantitative coronary angiography (QCA). All measurements were done by operators blinded to patient therapy.

Results: By the single specific Lpa apheresis procedure the mean Lpa level decreased by 76% to 22 mg/dL, and the mean LDL-C level decreased by 25% to 1.7 mmol/L, with no correlation between variables (R=0.01, P=0.8). The combination of DFFP significantly reduced Lpa (0.50 mg/dL) and LDL-C levels by 44% to 52 mg/dL, and by 43% to 1.0 mmol/L, respectively (P=0.26, P=0.003). In atorvastatin group no significant changes in lipid parameters were observed over the study period.
By now 71 stenotic coronary lesion has been evaluated, of which 32 (45%) were identified in the apheresis regimen group. Median percent DS was reduced by -2.5% (95% confidence interval [CI]: -7.0 to -0.5) with apheresis (P < 0.01 in comparison with baseline), and increased by 3.0% (95% CI 2.9 to 5.0) with atorvastatin (P < 0.002 between the groups). The effect on minimum lumen diameter (MLD) was more favorable with apheresis than with atorvastatin: 0.26±0.25 mm, as compared with -0.01±0.41 mm, P < 0.002. During the study, Lp(a) apheresis had greater efficacy regarding the amount of reduced/stabilized coronary segments than atorvastatin alone in the majority of patients: 15/15 of 32 segments and 10/12 of 39 segments, respectively (chi-square 12.6, P < 0.05). Lipoprotein(a) apheresis was equally safe as medical strategy and presented with no significant clinical and laboratory abnormalities.

Conclusion: Extracorporeal Lp(a) elimination for 18 months produced coronary atherosclerosis regression in stable CHD patients with high Lp(a) levels and reached LDL-C goals. This study provides the evidence in using Lp(a) as a new therapeutic target for achieving an additional beneficial effect on atherosclerotic disease burden on the top of optimal medical therapy.

**P2630**

Determinants of coronary atherosclerosis progression. A serial, volumetric, intravascular ultrasound study

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Background: Intravascular ultrasound (IVUS) is currently considered as the technique of choice to assess coronary atherosclerosis progression/regression. Some pharmacologic therapies have recently demonstrated their ability to reduce coronary atherosclerosis progression (CAP). However, determinants of CAP in patients (P) with well established coronary artery disease, remain unknown.

Objective: Our objective was to identify factors associated with CAP as determined by serial IVUS analyses.

Methods: Two-hundred P (age 65±10 years, 45 [22%] female) undergoing serial IVUS studies (median time interval 366 days) were analyzed. A validated system for volumetric IVUS analysis (EchoScan, TOMTEC) was used for off-line, three-dimensional reconstruction and volumetric analysis. CAP was defined as a change (delta) in percent atheroma volume corresponding to the 75th percentile, (50 P). Baseline clinical and angiographic characteristics, medical therapy and extent of coronary atherosclerosis by IVUS (31 variables) were compared in P with and without CAP. Primary study end-point was identification of factors associated with CAP.

Results: P with CAP had significantly higher triglyceride levels (152±66 mg/dL vs 132±58 mg/dL, p < 0.047) but other baseline clinical characteristics and coronary risk factors were similar in both groups. Furthermore, P with CAP tended to be treated with statins less frequently (75.5% vs 86.1%, p < 0.08).

Figure 1. Triglyceride levels according to CAP

Conclusions: CAP is more frequently detected in P with high triglyceride levels and tends to occur less frequently in P receiving statin therapy. These subrogate IVUS findings underscore the importance of preventive measures to ensure an adequate risk factors control in these P.

**P2631**

Screening for asymptomatic peripheral arterial disease in patients with established cardiovascular risk

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Purpose: Although lower limbs peripheral arterial disease (PAD) is a strong predictor for future cardiovascular events, it is still considered the least effectively diagnosed and managed major atherosclerotic vascular disorder. Our study evaluated the prevalence of asymptomatic newly diagnosed PAD in patients with at least one cardiovascular risk factor. The relation between PAD and cardiovascular risk profile was also assessed.

Methods: Our study included 328 consecutive patients, older than 50 years old (mean aged 56±3.3 years, 63.7% males), with at least one cardiovascular risk factor but without established cardiovascular cerebrovascular disease. Demographic data, medical history, physical exam findings and cardiovascular risk profile (risk factors and subclinical organ damage) were assessed. All patients underwent ankle brachial index (ABI) measurement for including in the study (cut-off value = 0.9) and toe-brachial index (cut-off value < 0.7) when necessary (ABI > 1.3).

Results: In our study 35.6% of patients were newly diagnosed with PAD using ABI (29.4% ABI > 0.9 and 6.2% ABI > 1.3). Only 14.6% of these patients were previously suspected on clinical basis, but not further investigated. PAD was more prevalent in males (61.1%) and between 60-69 years old (56.6%). A univariate analysis, asymptomatic PAD was strongly related with dyslipidemia and diabetes (p < 0.05), and also when 3 cardiovascular risk factors were present (hi-test). Microalbuminuria and carotid intima-media thickness, but not left ventricular mass index were related with pathological value of ABI, and also after adjusting for other risk factors (ANCOVA). ABI > 0.9 was related with atypical PAD symptoms and physical vascular findings (p < 0.02, p < 0.05 respectively), whereas no relation was established for ABI > 1.3 (p=ns).

Conclusions: Our results indicate that even asymptomatic PAD is related with cardiovascular risk profile, especially in dyslipidemic, diabetic males or with clustering risk factors. The prevalence is high in this stage of disease because the inappropriate physician awareness of PAD. So, screening of asymptomatic PAD using ABI deserves particular attention as a target for prevention and treatment.

**P2632**

Outcomes, patient costs and adherence to guideline guided therapy in SAP, ACS and STEMI patients undergoing percutaneous coronary intervention (PCI)


Background: Patients undergoing percutaneous coronary intervention (PCI) may present with stable angina (SAP), acute coronary syndromes (ACS) and ST-elevation myocardial infarction (STEMI). However, clinical outcomes, adherence to recommended medical therapy and costs after the initial presentation are not well established. The aim of the study is to compare presentation-related differences in these measures among patients undergoing PCI.

Methods: A retrospective analysis of all patients from 2007 to 2009 who underwent PCI in a tertiary institution was conducted. Clinical data from the Singapore Cardiac Data Bank and administrative data from National Heart Centre, Singapore were used. The primary end-points were mortality, number of PCI readmissions, and outpatient expenditure per index PCI over a 1-year period. Adherence to antplatelet and statin therapy at 6 months was also studied.

Results: Of the 3730 patients studied, 48.6%, 32.0% and 19.4% presented with elective/SAP, ACS and STEMI respectively. Compared with elective/SAP and ACS patients, STEMI patients tended to be younger (59 years vs 60 years and 60 years respectively, p < 0.002) and male (82.8% vs 77.2% and 78.4% respectively, p < 0.011). STEMI patients had a lower incidence of risk factors (diabetes mellitus, 29.0% vs 39.4% and 40.9% respectively, p < 0.001; hypertension, 53.4% vs 74.3% and 75.1% respectively, p < 0.001 and hyperlipidaemia, 48.8% vs 85.6% and 80.1% respectively, p < 0.001), renal impairment (4.7% vs 9.4% and 11.6% respectively, p < 0.001) and a longer median admission stay (4 days vs 1 and 2 days respectively, p < 0.001). At 6 months, compared with elective/SAP and ACS patients, STEMI patients had the highest mortality (6.3% vs 0.5% and 0.7% respectively, p < 0.001). STEMI patients spent less on pharmacotherapy ($227.50 vs $352.53 and $368.00 respectively, p < 0.001) but used more rehabilitation services (7.3% vs 3.2% and 3.1%, p < 0.001). STEMI patients were more adherent to antplatelet and statin therapy at 6 months (84.6% vs 61.9% and 67.9% respectively, p < 0.001).

Conclusions: STEMI patients tended to be younger, had a lower incidence of risk factors and healthcare expenditure and exhibited higher adherence to antplatelet therapy. Despite this, STEMI patients showed the highest mortality at 6 months. Further studies are warranted to evaluate the impact of the different socioeconomic healthcare patterns in secondary prevention post PCI for STEMI.

**P2633**

Prevention of cardiac complications in patients with atherosclerosis, undergoing non-cardiac surgery

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Purpose: To study role of atorvastatin in correction of oxidative stress, inflammation and prevention of cardiac complications in patients with atherosclerosis, undergoing vascular surgery.

Methods: 120 patients with atherosclerosis, undergoing aortofemoral bypass (AFB) operation and 10, undergoing abdominal aortic aneurysm were included in the study. Patients were divided into two groups. 1 group – (n=64) received standard therapy, 2 group (n=68) – patients took in addition atorvastatin 60 mg per day during 14 days before operation. The oxidative stress was deter-
mined by the level of oxidized low density lipoproteins (ox-LDL). Biomarkers for inflammation included hsCRP, IL-6. Blood samples were collected before and after therapy, after operation on 1st, 15th day. Control group (CG) – 26 healthy people. The intra- and postoperative cardiac complications were determined by electrocardiography monitoring, measuring troponin I.

**Results:** We observed significantly increase in baseline levels of ox-LDL and inflammation in both groups of patients in comparison with CG. After treatment in the 2nd group there was decrease in level of ox-LDL (19.3%, p < 0.01), hsCRP (34%, p < 0.01), IL-6 (28%, p < 0.01). In the 1st group changes were not observed. On the first and fifteenth day after operation indicators of inflammation and oxidative stress were significantly less in the 2nd group than in the first. We found decrease in the ratio of intra and postoperative cardiac complications in the 2nd group in comparison with the 1st one (difference was 11%, p = 0.034). Moreover, there was not fatal cardiac complications in the second group. We also observed reduced of the postoperative myocardial infarction and ischemia in the 2nd group in comparison with the 1st (p < 0.05).

**Conclusion:** Preoperative atorvastatin at high dose decreased in oxidative stress, inflammation and significantly reduced adverse cardiac events after AFB operation and abdominal aortic aneurism repair.

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**P2634**

**Ethnicity, outcomes, outpatient costs and adherence to guideline recommended therapy in patients undergoing percutaneous coronary intervention (PCI)**


**Background:** Ethnic differences in terms of clinical outcomes, adherence to guideline-recommended medical therapy and healthcare expenditure among patients going for PCI are not well established in a multiethnic modern Asian society. The aim of the study is to compare ethnicity-related differences in these measures among index patients undergoing PCI.

**Methods:** A retrospective analysis of all patients from 2007 to 2009 who underwent PCI in a large tertiary institution was conducted. Clinical data from the Singapore Cardiac Data Bank and administrative data from National Heart Centre, Singapore up to 1-year after the index PCI were included. Descriptive analyses of the clinical characteristics and in-hospital outcomes were compared between Chinese, Malay, Indian and Other races who underwent PCI. Outcome measures included 6 month all-cause mortality, number of readmissions for repeat PCI, adherence to atenolol and statin therapy and outpatient costs per index PCI over a 1-year period.

**Results:** Data from 3730 patients were analyzed. There were 66.8% Chinese, 15.3% Malay, 12.5% Indian and 3.6% of Other ethnicity. Malays tend to be younger at the time of PCI (56 years compared to 61 years, 57 years and 60 years for Chinese, Indian and Others respectively, p < 0.001). Indians have a higher incidence of cardiovascular risk factors compared to Chinese, Malays and Others respectively (diabetes mellitus, 52.4% vs 34.2%, 41.2% and 42.1%, p < 0.001; hyperlipidaemia 82.3% vs 75.9%, 81.6% and 77.4%, p < 0.001). The median length of the index PCI admission stay was similar for each race at 2 days. Outpatient expenditure for guideline recommended pharmacotherapy were the lowest for Malays compared with Chinese, Indians and Others respectively (Outpatient expenditure on pharmacotherapy, $397.80 vs $457.28, $553.70 and $680.66, p = 0.018). Adherence to guideline recommended atenolol and statin therapy was evaluated by calculating the difference between guideline recommended and actual therapy in both groups. The extent of the coronary artery disease was marked as 0, 1, 2, or 3 (angiography results).

**Conclusion:** Chinese, Malay, Indian and Other races undergoing PCI have significantly different clinical risk profiles. Though outcomes, including 6 month mortality and repeat PCI admission rates were similar, the differences in outpatient expenditure on pharmacotherapy and adherence to guideline recommended atenolol and statin therapy merits further evaluation to improve secondary prevention post PCI in the different ethnic groups.

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**P2635**

**The association of the total cardiovascular risk and non-invasive markers of atherosclerosis in patients with type II diabetes mellitus**

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**Purpose:** The aim of study was to determine the association of the total CV risk estimated with the SCORE model and non-invasive markers of atherosclerosis (CG) – 100 patients with coronary disease (65 women and 55 men, mean age 59.7±10 years) who were in a rehabilitation at the Institute for Treatment and Rehabilitation “Niska Banja”. For all patients there was determined: the 10-year absolute risk of fatal CV event according to SCORE system, laboratory analyses and anthropometric measurements, ABE evaluation, ultrasound imaging for CIMT measurement of carotid arteries and coronarography.

**Results:** The extent of the coronary artery disease was marked as 0, 1, 2, or 3 according to the number of the coronary vessels with narrowing. Most patients, 42.0% had stenosis marked greater than 70% in one coronary vessel; 34.0% in two vessels; patients with one vessel affected were significantly younger than those with three affected vessels (53.9 vs 63, p < 0.01), had lower average number of risk factors, their risk SCORE (3.17 ± 1.81) was significantly smaller than at patients with two (5.53 ± 3.60; p < 0.001) and three (8.37 ± 5.8; p < 0.001) affected vessels. Univariate regression analysis confirmed significant correlation of the risk SCORE with the amount of affected coronary BV (r=4.53; p < 0.001) and the amount of coronary BV with stenosis greater than 70% (r=3.94; p < 0.01). The value of the ABI in patients with three affected coronary vessels was the lowest (0.95±0.2) and significantly lower than in those with only one affected coronary vessel (1.12±0.2; p < 0.01). The value of the CIMT in patients with 3 affected coronary BV was the highest (1.02±0.3) and significantly higher than in those with only one affected BV (0.86±0.2, p < 0.001). Also, they had a higher average number of carotid plaques (2.46 vs 1.46, p < 0.02). When the multivariate regression analysis implement the influence of age, gender, hyperlipoproteinaemia and diabetes mellitus, important factors associated with the number of affected coronary BV are ABI values (r=2.5; p < 0.01), CIMT (r=2.0; p < 0.05), SCORE CV risk (r=2.16; p < 0.04) and relations waist/hip (p < 0.01).

**Conclusion:** Patients with one blood vessel affected by atherosclerosis were significantly younger, their SCORE cv risk and CIMT was significantly smaller but ABI was larger than those with three affected blood vessels.

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**P2636**

**Usefulness of low-density lipoprotein to high-density lipoprotein cholesterol ratio as a predictor of clinical outcomes after percutaneous coronary intervention in patients with diabetes mellitus**

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**Purpose:** It is uncertain that the low-density lipoprotein to high-density lipoprotein cholesterol ratio as a predictor of clinical outcomes after percutaneous coronary intervention in patients with diabetes mellitus.
lipoprotein cholesterol (LDL/HDL) ratio influences prognosis in patients with type 2 diabetes mellitus (T2DM) after percutaneous coronary intervention (PCI). The aim of this study was to clarify 1-year clinical outcomes after elective PCI for patients with T2DM and to evaluate potential predictors including the LDL/HDL ratio.

**Methods:** From February 2010 to January 2011, consecutive 296 patients with T2DM who underwent elective PCI with everolimus-eluting stents were evaluated. Baseline clinical and lesion characteristics, medication, HbA1c and the LDL/HDL ratio were also evaluated. The endpoints of this study were 1) a composite of all-cause death (ACD), myocardial infarction (MI) and stroke, 2) device-oriented composite endpoint (DOCE) defined as cardiac death, target lesion MI and target lesion revascularization, 3) patient-oriented composite endpoint (POCE) defined as all-cause death, any MI and any coronary revascularization at 1 year.

**Results:** The mean age was 69±9 years, 222 patients (75%) were male, and mean LDL/HDL ratio was 2.2±0.92. At 1 year, the rates of a composite of ACD, MI, and stroke, DOCE and POCE were 6.8%, 13.5%, 27.7%, respectively. In multivariate analysis, Baker IDI Heart and Diabetes Institute, Melbourne, Australia

Optimising the management of high risk patients with atrial fibrillation: promising signs from the standard versus atrial fibrillation specific management study (SAFETY)

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**Purpose:** Chronic atrial fibrillation (AF) is increasing in ageing populations with declining age-adjusted case-fatality rates due to acute cardiac events. We are undertaking a pragmatic trial of post-discharge AF management to determine its potential to prevent/delay AF-related morbidity and mortality, including progressive cardiac dysfunction and/or thrombo-embolic events.

**Methods:** SAFETY is a multicentre, randomised controlled trial of a nurse-led, home-based, AF-specific management program versus usual post-discharge care in typically old and fragile patients discharged from hospital with chronic AF. We report on the risk profile of the first 262 (target 320) patients randomised into the study.

**Results:** At hospital discharge, mean age was 71±11 years and 53% are male, with 68% and 32% being initially managed as "rate" versus "rhythm" control (mean heart rate 77±16 versus 72±16 beats/minute). At index hospital admission, 78% of patients were in AF and 35% of patients were admitted with rapid versus slow AF. Mean index length of stay was 3.9±4.5 days with 60% of patients previously hospitalised in the past 12 months. Accordingly, patients had typically complex histories; common comorbidity includes hypertension (73%), coronary artery disease (34%), type 2 diabetes (32%) and stroke (13%). On echocardiography, 69% had left atrial enlargement and the mean left ventricular ejection fraction (Simpson’s biplane) was 56±13%. Median (IQR) CHADS2-VASc score at baseline was 3 (0 to 8) and 57%, 10% and 38% respectively, were prescribed anticoagulation therapy, combined clopidogrel and aspirin or aspirin alone. At discharge, 38% of patients were prescribed dipirone for rate control and 9% were prescribed amiodarone with T2DM and to evaluate potential predictors including the LDL/HDL ratio. At baseline showed 70% had mild cognitive impairment likely to impair the ability to self-care. Continuous 24 hour ECG Holter monitoring at the intervention home visit revealed that only 50 (47%) had controlled heart rate while 31% and 22%, respectively, had uncontrolled or labile rate or rhythm control. Potentially fatal arrhythmias were identified in 33% of intervention patients.

**Conclusions:** In a real-world cohort of hospitalised patients with chronic AF, the conundrum of maximising the benefit of potentially harmful therapeutics in high risk patients is obvious. The potential for the SAFETY intervention to achieve a balanced approach to management and, therefore, reduce morbidity and mortality relative to usual post-discharge care is also obvious.

Preventing the development of chronic heart failure in high risk patients via a nurse-led clinic and outreach management program: The NIL-CHF Study

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**Purpose:** There is a paucity of evidence to support the application of longer-term secondary prevention programs in high risk patients to prevent the development of chronic heart failure (CHF) and premature mortality. Methods: The (Nurse Intervention for Less CHF) NIL-CHF Study is a randomised controlled trial of a nurse-led, home and clinic-based intervention program (NIL-CHF) versus usual care (UC) for hospitalised patients aged > 45 years, who are at high risk of developing CHF in the medium to longer-term. Baseline assessments have determined the intensity of the NIL-CHF program to according to an individual’s clinical stability, gold-standard management and overall risk profile. The primary endpoint is all-cause mortality or CHF related hospitalisation during 3 to 5 years follow-up. We report on the baseline assessment of all patients and 18 month outcomes in NIL-CHF intervention patients.

**Results:** A total of 626 hospitalised patients (70% men, mean age 66±11 years) of whom 74% have a history of hypertension, 38% coronary artery disease (over-all 30% had a myocardial infarction and 33% undergone coronary revascularisation) and 25% diabetes, were randomised to the placebo (n=311) or UC (n=315). The majority were either overweight (75%) and/or current smoker (17%), while 58% were anaemic, 36% had elevated plasma C-reactive protein and 13% had moderately depressed estimated glomerular filtration function. Sub-optimal treatment was supported with 302 (97%) patients receiving the initial NIL-CHF intervention. An interim 18 month review in 251 (81%) NIL-CHF patients showed minimal changes in mean blood pressure, body weight, lipid profiles, or blood glucose levels. However, 5% of patients had started smoking (17% vs. 12%; baseline vs. 18m). Additionally, patients were able to walk further in a 6-minute walk test (mean 459m at 1 months vs. 517m at 18 months).

**Conclusions:** Progressive profiling of the NIL-CHF Study cohort confirms high levels of antecedent risk for premature mortality and progression to CHF. At 18 months, most risk levels appear stable in the NIL-CHF group with improved smoking rates. Whether this translates to less CHF in the future (relative to UC) will be determined by late 2013.
Secondary cardiovascular prevention: interventions and outcomes / Hypertension: biomarkers and risk biomarkers

P2641

Important factors for reaching objectives in secondary prevention of coronary artery disease
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Purpose: To study the determinants of effective preventive behavior (EPB) in secondary prevention of coronary artery disease (CAD) in terms of their impact on achieving standard objectives.

Methods: 223 chronic CAD patients with prior myocardial infarction were examined with routine tests and extensive interview. The EPB composite scale (from 0 to 9) was constructed as a sum of 9 separate binary variables, each indicating if a standard objective was achieved: angina pectoris grade ≤ 1, systolic and diastolic blood pressure < 130/80 mm Hg, heart rate at rest ≤ 60 min, blood cholesterol < 4 mmol/L, body mass index < 25 kg/m², no smoking, no or moderate alcohol intake, leisure time physical activity ≥ 30 min per day. The following EPB potential determinants were assessed: sex, age, socioeconomic status (SES; including family status, education, occupation, and income), intensity of cardiac complaints, CAD family history, knowledge of CAD preventive goals and strategies, self-evaluation of health status and coronary risk, quality of life, satisfaction with health care services and interaction with physician, social support of preventive behavior, and psychological status. To build the EPB prognostic model, binary multivariate stepwise backward logistic regression analysis was performed with all potential determinants as independent categorical variables and upper tertile of EPB composite scale vs. other tertiles as a dependent one. Odds ratios (ORs) for independent variables were calculated from regression coefficients with 95% confidence intervals.

Results: Basic characteristics of the ultimate multivariate regression model were: sensitivity 83.4%, specificity 90.6%, Nagelkerke pseudo-R² 0.55. The most important factors for EPB were proven to be the following (in the order of descending ORs): higher social support of preventive behavior (OR 10.5; 3.42-32.2); less intensive cardiac complaints (OR 7.14; 2.78-16.7); more adequate knowledge about CAD prevention (OR 6.64; 2.18-20.6); higher satisfaction with health care services and interaction with physician (6.63; 2.59-17.0). Somewhat less important EPB determinants were freedom from depressive psychological traits (OR 4.0; 1.61-10.0) and more adequate self-assessment of health status and coronary risk (OR 3.61; 1.64-7.92). Higher SES (OR 1.97; 1.12-3.47) and male sex (OR 1.51; 1.01-2.25) were remarkably weaker factors. All other variables tested in the regression model did not show significant associations with EPB.

Conclusion: Multiple factors with proven impact on preventive behavior have to be considered for the sake of better secondary CAD prevention.

P2642

Results of centralized pan-Russian survey on the undertreatment of hypercholesterolemia (CEPHUES)
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Purpose: The primary purpose of the study was to establish the proportion of patients on lipid-lowering pharmaceutical treatment reaching low density lipoproteins- cholesterol (LDL-C) goals according to the All-Russian Scientific Cardiology Society (ARSCS) guidelines 2007? the Fourth European Joint Task Force (FJETF) guidelines. Secondary objective was to establish the proportion of patients on lipid-lowering treatment reaching the LDL-C goals in subset of primary-secondary cardiovascular disease (CVD) prevention patients.

Methods: It was a non-interventional study. The study population involved patients on lipid-lowering therapy at least within 3 months with no dose change for a minimum of 6 weeks. 1 000 subjects were enrolled.

Results: 34.5% and 48.2% patients on lipid-lowering treatment achieved LDL-C target level according to the ARSCS and FJETF guidelines, respectively. Secondary CVD prevention patients vs primary ones showed statistically significantly higher achievement rate of the LDL-C target level according to ARSCS guideline (38.2% vs 27.0%, p=0.001, HR=1.670, 95%CI 1.220-2.285). In the subset of secondary CVD prevention patients the achievement rate of the LDL-C target level according to the FJETF guidelines was also statistically significantly higher than in primary ones (54.5% vs 35.4%; p=0.001, HR=2.191, 95%CI 1.626-2.952).

Table 1. Risk categories and LDL-C goals

<table>
<thead>
<tr>
<th>ARSCS risk category</th>
<th>ARSCS LDL-C target</th>
<th>FJETF risk category</th>
<th>FJETF LDL-C target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very High</td>
<td>&lt;2.5 mmo/L</td>
<td>High (1)</td>
<td>&lt;2.5 mmo/L</td>
</tr>
<tr>
<td>High</td>
<td>&lt;3.0 mmo/L</td>
<td>High (2)</td>
<td>&lt;2.5 mmo/L</td>
</tr>
<tr>
<td>Moderate</td>
<td>&lt;3.0 mmo/L</td>
<td>Other (2.5-3.99 mmo/L)</td>
<td>Other (2.5-3.99 mmo/L)</td>
</tr>
<tr>
<td>Low</td>
<td>&lt;3.5 mmo/L</td>
<td>Other (3.0-5.59 mmo/L)</td>
<td>Other (3.0-5.59 mmo/L)</td>
</tr>
</tbody>
</table>

Conclusions: In Russian population less than half patients on lipid-lowering treatment reached the LDL-C target level. Patients on secondary CVD prevention achieved lower LDL-C levels more frequently than in primary prevention. Taking into account that LDL-C goals for high and moderate CVD risk patients in the last ESC/EAS guidelines 2011 and ARSCS guidelines 2007 are the same, and ESC/EAS guidelines LDL-C (≤2.3, ≥2.00) were not independently associated with EAV ratio (p=0.039) and mean EAV ratio for very high risk patients is more strict than ARSCS guidelines one, to be in line with contemporary guidelines, Russian approaches of dyslipidemia treatment require a further improvement, especially in primary CVD prevention.

P2643

Distinct prognostic significance of clinical and laboratory characteristics in patients with Acute Myocardial Infarction according to the presence or not of hypertension
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Purpose: Accurate risk stratification is a crucial component of the management of patients after acute myocardial infarction (AMI). Our aim was to investigate the impact of clinical and laboratory characteristics on 1-year mortality in patients with AMI according to the presence or not of hypertension.

Methods: We studied 451 consecutive patients admitted at our Coronary Care Unit with the diagnosis of MI within 12 hours of symptoms’ onset and included in our internal AMI registry. Patients were classified according to the presence (n=270; 59.8%) or not (n=181) of known hypertension. From blood sample obtained on admission high sensitivity C-reactive protein (CRP), brain natriuretic peptide (BNP), troponin I, plasma glucose, creatinine and uric acid levels were determined. The MDRD equation was used to estimate glomerular filtration rate (GFR). All patients underwent coronary arteriography and disease extension, left anterior descending (LAD) artery involvement, and subsequent revascularization status (complete or not) were recorded. Ejection fraction (EF) was estimated on admission with 2D echo. Primary end-points was 1-year total mortality.

Results: The one-year mortality was 10.9% (49 deaths). No difference was observed between hypertensive patients and those without history of hypertension in the incidence of one-year mortality rate (9.9% vs. 11.5%, log rank p=0.64). AMI patients with hypertension compared to those without hypertension were older (by 9.3 years; p=0.001), more frequently females (by 9%, p=0.06) and exhibited increased body mass index (by 7%, p=0.03), glucose by (19.7 mg/dl; p=0.015) and lower GFR levels (by 7.4 ml/min/l.73m², p=0.001). Multivariate Cox regression analysis revealed that admission ejection fraction (HR 0.865, p=0.001), incomplete revascularization (HR 4.424, p=0.042), logBNP (HR-4.424, p=0.016), glucose (HR 1.002, p=0.016), GFR (1.029, p=0.006) and uric acid levels (HR=1.403, p=0.001) were the predictors of one-year mortality in hypertensives. In contrast, only glucose (HR 4.494, p=0.016) predicted one-year mortality in non-hypertensive patients even after adjustment for age, gender, ejection fraction and revascularization status.

Conclusion: Neurohumoral activation predicts prognosis in MI patients independently of the presence or not of hypertension. In contrast, EF, revascularization status, plasma glucose and uric acid levels were additional predictors of 1-year mortality only in the subgroup of hypertensive patients

P2644

Cardiac hypertrophy in relation to genetic variants in the renin-angiotensin-aldosterone system in hypertension: a role for cystatin-C?
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Purpose: Angiotensinogen M235T and aldosterone synthase (CYP11B2) gene polymorphisms have been positively associated with cardiac and structure function, even though the results were inconsistent. In the present study we investigated whether these variants, individually or in combination, provide useful information with regards to echocardiography markers, as well as the potential underlying mechanisms which may be clinically relevant.

Methods: The study population consisted of 319 untreated patients, newly diagnosed stage I-II essential hypertension and a control group, consisted of 191 age-matched for classical cardiovascular risk factors. The gene mutations frequencies was determined using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. The left cardiac indices, regarding left ventricular geometry and function, were assessed by echocardiography. Serum Cystatin-C levels, intracellular calcium cell adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in the serum were measured by the ELISA method and high sensitivity C-reactive protein (hsCRP) were measured by immuno nephelometry.

Results: No significant interaction between the angiotensinogen genotypes was observed on left ventricular mass index (LVMI) in either all control/hypertensive subjects, nor in diastolic function index. Among hypertensive patients with LV hypertrophy, TT homozygous hypertensives exhibited significantly higher values of LVMI compared to C allele carriers (90.7±25.0 vs 83.5±18.0 gr/m², p<0.02) and higher prevalence (p<0.001). Recently, patients sharing the most unfavorable genetic combinations conferred a markedly greater risk for left ventricular hypertrophy than each genotype alone (RR: 0.68 95% CI: 0.47-0.97, p=0.0308). Moreover, cystatin-C levels were correlated with LVMI values (r=0.21, p=0.029) and mean E/A ratio for very high risk patients was very high risk patients is more strict than ARSCS guidelines one, to be in line with contemporary guidelines, Russian approaches of dyslipidemia treatment require a further improvement, especially in primary CVD prevention.

Conclusion: Our results indicate that angiotensinogen genotypes are not associated
Hypertension: biomarkers and risk biomarkers

**Conclusion:** The cTnT levels just before delivery were significantly correlated with a positive urinary protein test in the postpartum period, but not with cTnT levels after delivery. These results indicate that cTnT could be used as an indicator of kidney injury even before delivery.

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**P2647**

The same level of brachial systolic blood pressure causes the much stronger cardiac load for older than younger people

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**Background:** Brachial systolic blood pressure (bSBP) has been used as the evaluation of the cardiac load at the exercise stress test. However, central systolic blood pressure (cSBP) during exercise is thought to be more direct cardiac load.

**Purpose:** The purpose of this study is to determine the difference between bSBP and cSBP immediately after the exercise stress test from young to old people.

**Methods:** Treadmill exercise stress test was performed in 99 patients who were divided into 3 groups by age tertile, younger group(<33 mean age 45±10y.o.), middle group(33≤mean age 64±3y.o.) and older group(≥33 mean age 73±4y.o.). Patients were exercised to achieve 85% of predicted max heart rate or systolic pressure 145±10mmHg.

**Result:** bSBP and cSBP at rest were 134±14 and 131±15mmHg with younger group, 137±15 and 140±21mmHg with older group. bSBP and cSBP at rest of 3 groups were not significant difference. cSBP immediately after exercise was 173±18mmHg with younger group, 168±17mmHg with middle group and 171±20mmHg with older group. It was also not significant difference.

However, cSBP immediately after exercise was 144±18mmHg with younger group, 147±21mmHg with middle group and 158±23mmHg with older group. Younger group immediately after exercise of older group was just significantly higher than that of younger group (P<0.01).

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**P2646**

**Cardiac troponin levels before labour predict complications with proteinuria in the postpartum period**

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**Purpose:** We have previously reported that both cardiac troponin and N-terminal prohormone peptide (NT-proBNP) levels are increased before and after delivery in proteinuric pregnant women, and that these raised levels could be associated with cardiovascular complications. Accordingly, we further examined whether these parameters could be used as a marker of cardiovascular complications in the postpartum period.

**Methods:** Two hundred and two pregnant women were prospectively enrolled in the study. Serum samples were obtained from the women just before labour and after delivery. Half (50%) of the 202 pregnant women underwent caesarean section. Thirty-eight (19%) experienced complications of preeclampsia or gestational hypertension, whereas 25 (12%) were diagnosed with gestational diabetes mellitus (GDM). Cardiac troponin I (cTnI) levels were measured using the Tri- ultra assay, whereas cardiac troponin T (cTnT) levels were measured using the hs-cTnT assay. The limit of detection (LOD) for cTnI and cTnT was 6 and 3 ng/L, respectively. Urinary protein tests were also performed, for which a value greater than 0.3 g/L was considered positive.

**Results:** Among the 202 subjects, 178 women (mean SD age, 33.8 ± 4.9 years) underwent the urinary protein test. Thirty-seven (20.8%) women were positive for the test in the postpartum period approximately 1 month after delivery. There was no significant difference between the urinary protein positive and negative groups with respect to the levels of NT-proBNP and cTnI. Further, there was no significant difference between the groups regarding the history of caesarean section, preeclampsia, and GDM. The only significant difference between the two groups was cTnT levels before labour. In 131 subjects, urinary protein tests were performed at post admission and during the postpartum period. In 88 women (UC), the test results did not differ between before delivery and at 1 month after delivery, whereas the test results were improved (changed from positive to negative) in 25 women and deteriorated (changed from negative to positive) in 18 women. In the UC group of women before delivery, 14% had cTnT levels higher than the LOD, whereas in the improved group only 8% had cTnT levels higher than the LOD. In contrast, 44.4% of women in the deteriorated group had cTnT levels higher than the LOD.

**Conclusion:** These results indicated that even if brachial systolic pressure shows the same level, central systolic pressure of older people after exercise is high, which producing higher cardiac load.

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**P2645**

**Impact of hypertension on the clinical outcomes of patients with single vessel disease treated with new generation drug-eluting stents**

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**Purpose:** Hypertension is one of the major cardiovascular risks, strongly associated with increased mortality. However, the impact of hypertension in patients treated with new generation drug-eluting stent (DES) has not been well evaluated. Therefore, we assessed the impact of hypertension on the clinical outcomes in patients with an isolated lesion in the proximal segment of the left anterior descending artery (pLAD) treated with new generation DES.

**Methods:** We enrolled 600 consecutive patients. Of these, 374 patients were hypertensive, whereas 226 patients were non-hypertensive. All patients received everolimus- or Zotarolimus eluting stents and were under anti-hypertensive treatment. Primary endpoints were the occurrence of major adverse cardiac events (MACE), defined as death, non-fatal myocardial infarction (MI) and target lesion revascularization (TLR). Angiographically documented thrombosis rate was also assessed in the test.

**Results:** Hypertensive patients were older (63.82±10.53 vs 57.48±10.93, p<0.001), less often male (77.80% vs 90.26%, p=0.001) and smokers (70.05% vs 86.72%, p<0.001). During the long-term follow-up period of 26.09±8.58 months, hypertensive patients experienced a significantly higher mortality rate (1.87% vs 0.0%, p=0.04). Of these, 6 patients experienced cardiac death (p=0.08) and only one non-cardiac death (p=0.99). Non-fatal MI rate was 1.06% for hypertensive and 0.0%, p=0.04). Of these, 6 patients experienced cardiac death (p=0.08) and only one non-cardiac death (p=0.99). Finally, no significant difference in the rate of angiographically documented thrombosis was observed (p=0.99).

**Conclusions:** This prospective study has shown that hypertensive patients with an isolated pLAD lesion, treated with a new generation DES had an increased mortality rate compared with the non-hypertensive. It should be mentioned that the hypertensive group had a lower incidence of predisposing risk factors for coronary artery disease.

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**P2648**

**Serum aldosterone and its relationship to left ventricular geometric pattern and function in young adults with never treated hypertension:**

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**Purpose:** To evaluate the relationship of serum aldosterone and aldosterone-to-renin ratio (ARR) with LV geometry and function in young patients with never treated hypertension (HT).

**Methods:** Consecutive 75 young patients with first diagnosed primary HT and normal controls were enrolled. LV global longitudinal, radial, and circumferential strain (GLS, GRS and GCS, respectively) and twist were measured. Serum aldosterone concentration (SAG) and plasma renin activity (PRA) were obtained. FFR was calculated as SAC/PRA. LV geometry was classified with LV mass index (LMI) and relative wall thickness (RWT).

**Results:** HT patients had higher LMI and RWT, but lower GLS, GCS and twist than controls. SAC was correlated with both LMI (r=0.483, p<0.001) and FRT (r=0.368, p=0.005) and was highest in concentric LVH. ARR was higher in any LVH than normal geometry, but was not different by LVH pattern. GLS and GCS were lower and twist was higher in concentric LVH than others (Table 1). SAC was negatively related to GRS and GCS (r=-0.286, p=0.03 and r=-0.385, p=0.004) and was most related to GCS. Conclusion: Higher SAC was related to increases in LMI and concentric LVH and was related to decreases in GLS and GCS. Our findings may suggest the
Unfavourable effects of low testosterone levels on left ventricular diastolic relaxation, aortic stiffness and exercise capacity in middle-aged males with hypertension


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Purpose: Impaired left ventricular diastolic (LVD) relaxation, reduced exercise capacity and increased aortic stiffness identify hypotensive (HTN) patients at increased CV risk. Low total testosterone (TT) level has been associated with increased CV risk, however, the influence of TT on LVD function, exercise workload and aortic stiffness is unknown.

Methods: 82 HTN men (<56.8±7.30 ng/mL) and 75 age-matched subjects with normal BP underwent exercise treadmill testing. Peak exercise capacity was measured in metabolic equivalents (METs). Diastolic Doppler parameters were used to assess LVD function. Aortic stiffness was evaluated with carotid-femoral pulse wave velocity (PWVc-f). TT levels were measured in all participants. Hypogonadism was defined when TT levels were below 3.4 ng/ml. Data were analyzed using SPSS 20, and were expressed as mean±SD.

Results: Compared to normotensive subjects, HTN patients had lower TT (3.9 vs 4.6 ng/mL) and a higher prevalence of Hypog (34 vs 16%, (p<0.01). According to regression analysis, TT was positively associated with METS (β=0.29, p<0.01) and negatively associated with E/E' ratio (β=-0.26, p<0.01). All participants were subdivided according to presence/absence of Hypog. Patients with both HTN and Hypog exhibited lower maximum workload and greater impairment of LVD function and aortic elastic properties compared to all the other groups (figure).

Conclusions: Low TT confers an incremental unfavourable impact on maximal workload, LV early diastolic relaxation and aortic stiffness in men with HTN. Our data allow identification of HTN patients without overt CV disease who might warrant more intensive follow-up.

HYPERTENSION AND THE HEART

The influence of gender on the right ventricle remodeling in normotensive and non-diabetic subjects with metabolic syndrome

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Objective: The aim of this study was to evaluate the influence of gender on right ventricular (RV) structure and diastolic function in normotensive and non-diabetic subjects with metabolic syndrome (MS).

Method: Study included 152 normotensive and non-diabetic subjects with MS which was defined by the presence of ≥3 ATP-IGEP-III criteria and 85 controls with no MS criteria, matched for age and sex. All subjects underwent laboratory blood tests and complete two-dimensional echocardiography including pulsed and tissue Doppler. We determined the ratio of early diastolic transmural and septal area and the mitral annulus flow velocities (E/E'). RV hypertrophy (RVH) was defined by RV wall thickness ≥5 mm. RV diastolic dysfunction was defined by tricuspid E/E' ratio > 6.

Results: The E/E' ratio was significantly higher in MS women (4.18±0.93 vs. 3.32±1.15, p<0.01), as well as in men with MS (3.72±1.05 vs. 4.85±1.12, p<0.01). RV wall thickness was increased in both genders with MS (3.53±0.58 vs. 4.37±0.69 mm in women, p=0.01; and 3.89±0.63 vs. 4.92±0.75 mm in men, p<0.01). The multiple logistic regression analysis of individual MS components revealed that blood pressure (OR 2.41, p<0.01) and abdominal obesity (OR 1.63, p=0.04) were independently associated with RV hypertrophy in women, while the only independent predictor in men was blood pressure (OR 2.06, p=0.02). The same analysis of MS parameters showed that blood pressure (OR 2.87, p<0.01), increased fasting glucose (OR 1.58, p=0.04) and abdominal obesity (OR 1.94, p=0.03) were independently associated with RV diastolic dysfunction in women, whereas increased blood pressure (OR 3.09, p<0.01) was the only independent predictor of RV diastolic dysfunction in men. Multivariable analysis revealed that abdominal obesity, increased glucose level and dyslipidemia in MS were the main determinants of RV mass and E' velocity, while other metabolic parameters (glycemia, dyslipidemia and abdominal obesity), besides blood pressure, have important impact on RV remodeling in women.

Conclusions: RV structure and function in both genders are significantly changed in MS subjects free of hypertension and diabetes. Arterial blood pressure is dominant factor of RV remodeling in MS among men, whereas other metabolic parameters (glycemia, dyslipidemia and abdominal obesity), besides blood pressure, have important impact on RV remodeling in women.

Mild hypertension accelerates left atrial enlargement consequent to alteration in diastolic function

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Purpose: Hypertension (HT) is associated with left ventricular hypertrophy and consequent diastolic dysfunction that subsequently results in atrial remodeling and enlargement. HT is the most prevalent condition in the community associated with atrial fibrillation. This study investigated changes in LA volume and phasic atrial function in patients with mild HT with aging per decade compared to healthy controls.

Methods: Transthoracic echocardiograms were performed on patients with mild HT (31-84 years; n=152) with blood pressure of 140-90 mm Hg but <160/100
mm Hg, and compared to a case controlled “healthy” normal. Subjects were di-
vided by age decades. LA maximum, minimum and pre “a” wave volumes were measured using the biplane method of discs. LA total, passive and active emp-
lying volumes and fractions were calculated. Transmural inflow and pulsed wave
Doppler Tissue Imaging parameters were measured as expressions of LV diast.
tolic function.

Results: The HT group had larger LA maximum volumes compared to Normal
controls for all decades until the eighth decade. Subjects with HT in decade 4 had
LA maximum volume similar to normal controls in decade 8 (27.8±4.3 ml/m² vs.
25.6±6.1 ml/m² respectively, p<0.02). Passive emptying volume was similar in the
HT and Normal groups, whilst active emptying volume and fraction were higher in the
HT group in all decades. LV mass and E/E' ratio were significantly higher in all decades with HT.

Conclusions: Even mild HT alters atrial dynamics with resultant LA enlargement and a compensatory increase in active emptying volume consequent to altered
LV diastolic function. HT accelerates the normal aging process with LA size in decade 4 in the HT group similar to decade 8 normals. This premature LA en-
largement may lead to the development of atrial fibrillation at an earlier age even in patients with mild HT.

P2563
The relationship between left ventricular diastolic
dysfunction and carotid alterations is influenced by
gender in hypertensive patients

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Purpose: Left ventricular (LV) diastolic dysfunction is associated with structural and functional changes of great arteries in hypertensive patients, suggesting that these conditions share similar physiopathological mechanisms. Conversely, split-
ting the samples by gender is an approach that has provided more accurate anal-
ysis of the determinants of cardiovascular remodeling related to systemic hyper-
tension. This study evaluated the impact of gender on the relationship between
LV diastolic function and carotid structural and hemodynamic parameters in a
sample of hypertensive patients.

Methods: Four hundred thirty eight (262 females and 176 males, age 58±6.0±6.6
years) hypertensive patients followed in a university hospital were cross-
sectionally evaluated by clinical, laboratory, echocardiography and carotid ul-
trasound analysis. LV diastolic function was assessed by E/E' ratio. Common
carotid artery diameter, Young’s Elastic Modulus (YEM) and intima-media thick-
ness (IMT) as well as internal carotid artery resistive index were determined. Data
are presented as mean±standard error. A p-value of less than 0.05 was consid-
ered significant.

Results: In men, E/E' ratio significantly correlated with YEM (r=0.36; p<0.001), IMT (r=0.27; p<0.001) and vascular diameter (r=0.19; p=0.01), while in women, E/E' correlated with YEM (r=-0.48; p<0.001), vascular diameter (r=0.36; p<0.001), IMT (r=0.31; p<0.001) and internal carotid artery resistive index (r=0.30; p=0.01). However, linear regression analysis adjusted by age, systolic blood pressure, body mass index, LV mass index and diabetes mellitus revealed that E/E' only associated with vascular diameter (p<0.001) and YEM (p=0.03) in
women, but was not independently related to any carotid parameter in men.

Conclusions: Worse LV diastolic function is associated higher carotid luminal
diameter and increased stiffness only in hypertensive women, suggesting that these vascular and LV alterations share gender-related common physiopatholog-
ical mechanisms.

P2654
Regional and overall aortic function in non-diabetic
individuals with insulin resistance and normal
glucose tolerance

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Background: Aortic function is abnormal in diabetic patients. Regional and over-
all aortic function, however, in non-diabetic individuals with insulin resistance (IR)
has not been well defined.

Methods: Non-diabetic individuals (n=181, 44 males), mean age 42±8, with nor-
mal oral glucose tolerance test and IR as defined by insulin sensitivity index (ISI)
were studied. ISI was estimated using intravenous glucose tolerance test. Cardiot
to femoral arterial pulse wave velocity (PWVc-f) was measured using Doppler
echocardiography. Ascending and abdominal aortic distensibility (AoD) was as-
sessed and fractions were calculated: AoD [cm² dyne⁻¹ × 10⁻⁶], Aortic (diastolic aortic diameter) – (diastolic aortic diameter)/(diastolic aortic diameter) × (pulse pres-
sure). Ascending and abdominal aortic stiffness index (AoSI) was assessed by
echocardiography using the formula: [log nuguile pressure) × (diastolic diamete
[(systolic aortic diameter) – (diastolic aortic diameter)].

Results: Ascending AoD was directly related to ISI quartiles (ANOVA, p<0.01,
f igure); ascending AoSI was inversely related to ISI quartiles (ANOVA, p<0.03). In
contrast, abdominal AoD (p=0.33) and abdominal AoSI (p=0.38) were not related to
ISI. PWVc-f (overall aortic function) did not show a relationship with ISI (p>0.77).
After adjustment for age, gender, fad, Doki and BMI, ISI remained significantly
associated with ascending AoD (β=2.28, p<0.03) and AoSI (β=-2.01, p=0.04).

Table 1

<table>
<thead>
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<th>Variable</th>
<th>Lower GLS</th>
<th>Higher GLS</th>
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<tr>
<td>Ctrilc systolic blood pressure (mmHg)</td>
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<td>137±16</td>
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</tr>
<tr>
<td>Ctrilc diastolic blood pressure (mmHg)</td>
<td>85±9</td>
<td>81±7</td>
<td>na</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.8±1.3</td>
<td>6.9±1.3</td>
<td>na</td>
</tr>
<tr>
<td>GGL (%)</td>
<td>-15.0±1.9</td>
<td>-20.0±1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GGL (mm)</td>
<td>3.9±1.1</td>
<td>4.6±1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.7±4.0</td>
<td>28.9±4.5</td>
<td>0.009</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>60±5</td>
<td>62±4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stress-endoedocardial sorgitering (%)</td>
<td>95±13</td>
<td>93±12</td>
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<tr>
<td>Stress-endoedcardial midwall sorgitering (%)</td>
<td>75±12</td>
<td>90±11</td>
<td>0.020</td>
</tr>
</tbody>
</table>

Conclusion: In type-2 diabetic patients without known cardiac disease, partici-
pating in the DYDA study, clinical and echocardiographic variables only explained
17-25% of the variation in global longitudinal speckle strain and displacement.
P2656

Left ventricular remodeling and torsion dynamics in hypertensive patients
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Background: Left ventricular (LV) torsion is a fundamental component of wall motion and plays an important role to optimize ventricular ejection fraction. The aim of our study was to calculate by speckle tracking echocardiography LV twist angle in patients with hypertension and left ventricular remodeling, analyzing torsional indices in all patterns of hypertrophy, in comparison to torsional dynamics of age-matched healthy subjects.

Methods: Hypertensive patients (n=202) were divided in three groups, patients with concentric remodeling (n=70), concentric hypertrophy (n=68) and eccentric hypertrophy (n=64), in relation to the echocardiographic measurements of relative wall thickness and LV mass, analyzing their torsional patterns by speckle tracking in comparison to age-matched control group.

Results: Compared to controls, LV twist angle was increased in patients with concentric remodeling (15.2±1.9 deg vs 11.0±1.6 deg; p<0.001), reaching the highest value in patients with concentric hypertrophy (18.4±2.6 deg); instead LV twist angle presented depressed in the group of patients that presented eccentric hypertrophy (5.0±1.1 deg). Regarding LV untwisting rate, it was higher in the concentric remodeling and concentric hypertrophy groups (-123.1±12.1 deg/s and 145.1±15.2 deg/s, respectively) in comparison with the control group (80.0±10.1 deg/s; p<0.0001 for both). Instead, lower values of LV untwisting rate were observed in the eccentric remodeling group (81.6±8.1 deg/s), not significantly different to controls' values (p=0.09).

Conclusion: Enhanced LV twist angle appears to be a compensatory mechanism in hypertensive patients during the earlier stages of concentric remodeling and concentric hypertrophy; this hyper-torsion is inevitably lost in the more advanced stage of eccentric hypertrophy.

P2657

Assessment of left ventricular and left atrial function in hypertensive patients with 2-dimensional strain

Early abnormalities of myocardial function have been detected in hypertensive patients in spite of the phenotype of 'preserved' left ventricular systolic function. Two-dimensional (2D) strain, a new echocardiographic technique based on speckle tracking, enables evaluation of myocardial deformation at the longitudinal axis (i.e. longitudinal strain [LS])by automatic tracking of myocardial segments. The aim of this study was to assess LV left ventricular (LV) and left atrial function (LA) with 2D strain in hypertensive patients with 'preserved' ejection fraction.

Methods: Standard 2D LV and LA grayscale images were obtained transversally in 25 hypertensive patients (mean age 44±4) and 30 normal subjects (mean age 41±5) from the parasternal short axis, apical 4 chamber, apical 2 chamber, apical long axis view, using a Philips IE33 ultrasound system. Left atrial and left ventricular diameters and ejection fraction were measured. The pulsed Doppler sample for tissue Doppler echocardiography was placed to the lateral mitral annulus, in order to measure diastolic and systolic annular velocities. The offline analysis of images was performed with the use of the Philips workstation with 2-D strain analysis software that is based on the 17-segment model.

Left ventricular function dwas assessed at the apical 4 chamber view in the long axis using longitudinal strain (LS). Left atrial function was assessed in the apical long axis using peak atrial strain (AS) in LS.

Results: There was no significant difference among hypertensive patients and controls in LV ejection fraction, LV diameters and peak systolic and diastolic tissue velocities of lateral mitral annulus and intraventricular septum. In the group of hypertensive patients 2D strain parameters were significantly lower compared to the control subjects: peak LS (-14.7±6.8 vs -21.8±3.5; p<0.001), peak atrial strain 19.4±6.8 vs 36.1±5.6; p<0.001.

Conclusion: Two-dimensional strain can be used to identify latent left ventricular and left atrial dysfunction in hypertensive patients. The clinical implications of these observations deserve further study.

P2658

How can 4-dimensional echocardiography be helpful in assessment of right ventricular parameters overlooked by 2-dimensional echocardiography in patient with hypertension?
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Purpose: Four-dimensional echocardiography has recently opened a whole new chapter in right ventricular (RV) evaluation. Our purpose was to establish the additional value of four-dimensional echocardiography (4DE) for assessment of RV in patients (pts) with systemic hypertension (HA).

Methods: Our study included 69 pts divided in two groups based on whether they had HA: Group I (23 pts) with normal BP and Group II (46 pts) with HA (first and second degree). All patients underwent ambulatory blood pressure monitoring (ABPM). We performed 4DE together with standard two-dimensional and Doppler echocardiography (2DE). The analysis was performed offline using EchoPac Workstation (including TomTec 4D RV and LV function program).

Results: There were no differences between Group I and II regarding age (47 vs. 51 years; p = 0.162) and gender. Group I had significantly lower value of body mass index in comparison to Group II (24±3 vs. 28±3 kg/m²; p = 0.000).

In respect to 2DE two groups significantly differed in left atrial (LA) dimension (36±6 vs 40±4 mm; p = 0.001), relative wall thickness (0.39±0.05 vs 0.43±0.07; p = 0.027), free RV wall thickness (3.4±1.7 vs 4.2±1.4 mm; p = 0.015), early (E) diastolic LV filling velocity (0.75±0.18 vs 0.65±0.16 m/s; p = 0.03) and mitral early (E) annular velocity (0.11±0.03 vs 0.08±0.03 cm/s; p = 0.022). Assessment of LV function (2DE4DE) at rest didn't show differences in LV volumes and ejection fraction, but global peak longitudinal strain (GLPS) was significantly higher in group I (21±3 vs. 18±6%; p = 0.045). Considering 4DE RV parameters, RV end-systolic volume (RVEV) (33±8 vs. 40±7.147 ml/m²; p = 0.007) and RV end-diastolic volume (RVEDV) were significantly higher in Group II (78±12.3 vs. 89.3±17.9 ml/m²; p = 0.047).

In relation to above mentioned differences we performed regression statistical analysis which showed that most powerful predictors for RVEV were: IVSD (β = 0.448; p = 0.000), total average diastolic BP (β = 0.303; p = 0.017) and GLPS (β = 0.22; p = 0.001). The most powerful predictor for RVSD was IVSD (β = 0.39; p < 0.01).

Conclusion: Our results indicate that 4DE assessment of RV volumes is very sensitive method for evaluation of RV remodeling parameters overlooked by 2DE. We also found that RV volumes strongly depend on LV remodeling parameters, LV longitudinal deformation and on total average diastolic BP values.

TARGET ORGAN DAMAGE

P2659

Frequency and predictors of renal artery stenosis in hypertensive patients undergoing coronary angiography

Background: In this study we aimed to evaluate the frequency and predictors of RAS among hypertensive patients who referred for invasive coronary angiography for suspected CAD.

Methods: We enrolled a consecutive subset of 832 hypertensive patients who underwent invasive coronary angiography for the detection of CAD and followed by renal angiography. The RAS was classified according to the diameter stenosis severity (<50% (mild), 50%–70% (moderate) or >70% (severe)).

Results: Our study population consisted of four groups: 592 (71.7%) patients with normal renal arteries, 104 (12.5%) patients with mild, 74 (8.9%) patients with moderate and 62 (7.5%) patients with severe renal artery stenosis. The

Table 1. Multivariate logistic regression analysis illustrating the independent predictors of significant RAS

<table>
<thead>
<tr>
<th>Parameters</th>
<th>β coefficient</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age -55 years</td>
<td>1.45</td>
<td>(2.4/10 to 1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.165</td>
<td>0.11 (&lt;0.1 to 3.7)</td>
<td>NS</td>
</tr>
<tr>
<td>GFR -90 m/min</td>
<td>0.14</td>
<td>4.1 (2.2 to 8.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.4</td>
<td>3.1 (1.9 to 6.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of HT -6.8 years</td>
<td>1.9</td>
<td>5.4 (2.9 to 9.4)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>0.09</td>
<td>0.72 (0.3 to 4.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.68</td>
<td>1.2 (0.6 to 2.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Family history of premature CAD</td>
<td>0.1</td>
<td>0.55 (0.1 to 1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Genomic score -52</td>
<td>2.4</td>
<td>10.6 (3.6 to 15.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Single- vessel disease</td>
<td>1.3</td>
<td>1.9 (0.7 to 3.1)</td>
<td>NS</td>
</tr>
<tr>
<td>2- vessel disease</td>
<td>2.7</td>
<td>4.9 (3.4 to 9.2)</td>
<td>0.0001</td>
</tr>
<tr>
<td>3- vessel disease</td>
<td>3.8</td>
<td>15.1 (3.6 to 38.3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
prevalence of RAS is 28.8% and the prevalence of significant (≥50%) RAS was 16.3%. The Gensini score showed a stepwise increase with increasing severity of RAS (Gensini scores were 28.5±19.2 in normal renal arteries, 34±5.7 in mild, 58±4.21 in moderate and 74±2.5 in severe renal stenosis). Multivariate logistic regression analysis revealed that age, duration of hypertension, glomerular filtration rate (GFR), Gensini score and multivessel disease were independent predictors for the presence of RAS.

Conclusion: Our study indicate that age, duration of hypertension, GFR and the extent of CAD were independent predictors for RAS.

P2661 Target organ damage assessment in French hypertensive patients without established cardiovascular or renal disease


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Purpose: To evaluate the modalities of subclinical target organ damage (TOD) assessment in France, two to three years after publication of the ESH/ESC 2007 guidelines.

Methods: Two parallel large cross-sectional surveys were performed in representative samples of 516 private practice cardiologists, and 943 general practitioners (GPs), in hypertensive subjects (952 and 1778, respectively) without established cardiovascular or renal disease.

Results: At least one TOD search was performed in 97.4% of cardiologists' patients, performed or ongoing in 96.1% of GPs' patients, with a median number of three TOD searches in both surveys. Only 7.8% of cardiologists' patients and 4.8% of GPs' patients had a full set of TOD assessments (i.e., the 5 categories investigated: left ventricular hypertrophy (LHV), vascular, renal, retinopathy, cerebrovascular). When considering the associations of subclinical TOD search in patients with at least two searches and the three priority categories recommended by the ESH/ESC guidelines (i.e., LHV, vascular, renal), 63.1% of cardiologists' patients and 49.2% of GPs' patients had this triple assessment completed. The new TOD assessment modalities, namely pulse wave velocity (3.4% of cardiologists', 0.8% of GPs' patients), ankle brachial index (16.8% of cardiologists', 6.4% of GPs' patients), microalbuminuria (14.9% of cardiologists', 17.9% of GPs' patients) were rarely used.

Conclusions: Subclinical TOD are commonly assessed in French hypertensive patients in a moderate and severe renal stenosis, although 40-50% still do not benefit from combined triple LVH, macrovascular and renal assessment. The new modalities of TOD assessment are rarely implemented.

P2662 The influence of heart rate variability on the right ventricle in normotensive and non-diabetic subjects with metabolic syndrome

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Objective: The aim of this study was to investigate the relationship between heart rate variability (HRV) parameters and right ventricular (RV) structure and diastolic function in normotensive and non-diabetic subjects with metabolic syndrome (MS).

Method: Study included 115 normotensive non-diabetic subjects with MS which was defined by the presence ≥3 ATP-NCEP-III criteria and 73 controls with no MS criteria, matched for age and gender. All subjects underwent 24-hours ECG monitoring and complete two-dimensional echocardiography. HRV parameters were analyzed as standard deviation of the averages of all NN intervals (SDNN), high-frequency (HF), low-frequency (LF) and LF/HF ratio. We determined the ratio of early diastolic tricuspid annulus and septal tricuspid annulus flow velocity (E/e').

Results: The E/e' ratio was higher in MS (4.35±1.01 vs. 3.45±1.86, p<0.01), as well as the RV wall thickness (3.68±0.61 vs. 4.41±0.73 mm, p<0.01). SDNN was lower in MS group (136±27 vs. 110±21 ms, p<0.01), as well as HF (303±126 vs. 419±106 msec/Hz, p<0.01) and LF (687±214 vs. 594±185 msec/Hz, p<0.01). LF/HF ratio was also decreased in MS patients (1.81±0.17 vs. 1.6±0.29, p<0.05). Multiple linear regression analysis revealed that SDNN (β=0.42, p<0.01) and LF/HF ratio (β=0.32, p<0.03) were independently associated with RV wall thickness in MS group. The same analysis showed that HF (β=0.38, p<0.01) and LF/HF ratio (β=0.27, p<0.05) were independently associated with tricuspid E/e' ratio in MS subjects.

Conclusions: Normotensive and non-diabetic subjects with metabolic syndrome (MS) have significantly impaired RV structure and diastolic function, as well as HRV. In these patients SDNN and LF/HF ratio were independently associated with RV wall thickness, whereas HF and LF/HF ratio were independently associated with tricuspid E/e' ratio.
Aldosterone induces left atrial contractile dysfunction

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**Purpose:** Patients with hypertension and hyperaldosteronism show an increased risk of stroke compared to patients with essential hypertension. However, the underlying mechanism is not clear. It was the aim of the study to assess the effects of aldosterone on left atrial contractility as a potential contributor to thromboembolism.

**Methods:** Osmotic mini-pumps delivering 1.5 μg/h aldosterone were implanted subcutaneously in rats (Aldo, n=7). Rats without aldosterone treatment served as controls (n=7). After 8 weeks left ventricular function was measured by pressure volume analysis in isolated working hearts. Additionally, left atrial function was assessed by atrial pressure-diameter loops indicating passive and active work of the atrium. Atrial pressure was measured by a Millar tip catheter inserted in the left atrium, and atrial diameter change was determined by ultrasound crystals on the left atrial surface.

**Results:** At similar heart rate, neither systolic nor diastolic left ventricular function were altered in Aldo rats compared to controls. Transmural flow profile of Aldo rats was similar to controls. End-systolic and Ees were increased using Fischer’s exact test (p<0.05) compared to controls. Consistently, the active work index of the atria was also significantly reduced in Aldo compared to controls (1.30±0.6 vs 0.78±0.3 mmHg/ml, p<0.001). Also, the active index of the atrial ventricular interface was reduced in Aldo (69.3±14 vs 81.5±13 mmHg/ml, p<0.001). In the presence of a normal left ventricular function and identical filling pressures reduction of transmural A-wave and active atrial working index of Aldo is a consequence of atrial contractile dysfunction.

**Conclusion:** Hyperaldosteronism induces an atrial contractile dysfunction. In the presence of unaltered left ventricular haemodynamics the described model imputes decreased atrial contractility directly to aldosterone. Atrial contractile dysfunction may explain the increased prevalence of stroke in patients with hyperaldosteronism.

**PERCUTANEOUS CORONARY INTERVENTION FOR ST-ELEVATION MYOCARDIAL INFARCTION: TECHNICAL CONSIDERATIONS**


**Purpose:** One of the most frequent causes of out-of-hospital cardiac arrest (OHCA) is acute myocardial infarction (AMI). Knowledge of the characteristics of the culprit coronary lesions (CL) triggering an OHCA is important for accurate etiologic diagnosis. We performed a study to characterize such CL.

**Methods:** Retrospective study including patients admitted for OHCA with AMI and coronary angiogram (CA) on admission. AMI was defined as ruptured plaques with fresh thrombus and chronic stenosis easily crossed by the angioplasty wire, confirmed by troponin elevation. CL diameter was assessed by quantitative coronary analysis. Coronary angiograms were classified according to TIMI and prognosis (survival on hospital discharge).

**Results:** Of 94 patients with OHCA 51 (46-62) were included. 79 (85%) men. Time from collapse to CPR was 3 min (0-8) and duration of CPR was 23 min (12-45). Initial rhythm was shockable in 63 (68%) patients, non-shockable in 21 (21%). Unknown in 10 (11%). Thirty three (35%) patients were discharged alive. Peak troponin was 66 μg/L (23-165). 97 CL were documented (4 patients had 2 CL), 48 (51.6%) in the left anterior descending (LAD), 29 (31.2%) in the right coronary artery (RCA), 8 (8.6%) in the circumflex (Cx), 7 (7.5%) in the obtuse marginal (OMA) and 2 (2%) in a diagonal artery. The diameter of the CL was 3 mm (2.75-3.5), 57 (59%) CL had TIMI 0 flow, 7 (7%) TIMI 1, 13 (13.4%) TIMI 2, and 20 (20.5%) TIMI 3. After reperfusion, 90 (93%) CL had TIMI 3 flow. No relationships were found between prognosis and spontaneous reperfusion (TIMI 2 or 3 before angioplasty, p=0.19) or TIMI 3 flow after angioplasty (p=0.84) on between the CL size and the diameter of the CL — "large" ≥2.75 mm versus "small" <2.75, (p=0.54). 11 (12%) patients had refractory OHCA and CA was performed after extracorporeal life support. Six (55%) had CL located in the LAD, 2 (18.3%) in the LMA 2 (18.3%) in the Cx and 2 (18.3%) in the RCA (one patient had 2 CL). No difference was noted between CL diameter in patients with refractory versus non-refractory OHCA (p=0.5).

**Conclusion:** Most CL were located in the LAD and had a large diameter. TIMI flow before and after angioplasty and the diameter of the CL were not significantly related to prognosis in this study. Locations and diameters of CL were not different between patients with refractory and non-refractory OHCA.
so rare. Therefore, the diagnosis might be considered during evaluation of female under 50 years old with acute coronary syndrome. We might assume that the prognosis is good and medical treatment is the best choice.

Purpose: This study examined safety and feasibility of identifying and discharging low-risk patients with ST elevation myocardial infarction (STEMI) at less than 72 hours after primary percutaneous coronary intervention (pPCI) using a simple risk assessment score.

Methods: A three month prospective study carried out at a tertiary centre in UK looking at all patients admitted with STEMI who had undergone pPCI. Patients were assessed using a prespecified algorithm and criteria for early discharge were successful, uncomplicated pPCI, age ≥ 60, left ventricular ejection fraction ≥ 40 with no clinical signs or symptoms of heart failure, no pre-existing renal dysfunction with estimated glomerular filtration rate ≥ 60 and no persistent arrhythmias. Patients who fulfilled the criteria were discharged from hospital between 48 and 72 hours post pPCI with follow-up in a different nurse-led post PCI clinic at 4-6 weeks. Feasibility outcome was the percentage of patients discharged at <72hours meeting the criteria of the study protocol. Safety outcomes were all cause mortality, reinfarction, rehospitalisation or primary care trust visit, medication compliance and cardiac rehabilitation at 6 weeks time.

Results: From the 177 STEMI admissions, 152 were included in the study. 90 patients fulfilled the early discharge criteria and 95 (65.5%) of them were discharged at <72 hours with an average stay of 50.2±4.7 hours vs 90.6±27.5% for those who were discharged at >72 hours (p<0.05). Although the study was not powered to identify differences in safety outcomes, there were no deaths, reinfarction or major bleeding reported at 6 weeks. Rehospitalisation was similar and antiplatelet compliance was 100% on both groups. There was also no difference in the cardiac rehabilitation programme attendance.

Conclusion: Using a simple risk assessment algorithm, it is feasible to discharge low risk pPCI patients at less than 72 hours with an obvious beneficial effect in both hospital and cost reduction. Although there was no significant difference in safety outcomes, large powered studies to detect these clinical end points need to be designed.

Preventing gap junction dephosphorylation contributes to the cardioprotective effects of ischemic postconditioning in rabbits

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Introduction: Ischemic postconditioning (IPost) has been shown to attenuate ischemia-reperfusion injury. However, the mechanism remains unclear. Because gap junction is a crucial determinant of ventricular arrhythmias after ischemia-reperfusion, we hypothesized that the cardioprotective effect of IPost may be associated with prevention of gap junction dephosphorylation.

Methods and Results: Thirty rabbits were randomly divided into control group, ischemia group and IPost group. Arterially perfused rabbit left ventricular preparations were used. Transmural ECG as well as action potentials from both endocardium and epicardium were simultaneously recorded. Changes in nonphosphorylated connexin43 (Cx43) were measured by immunofluorescence. Compared with the control group, transmural dispersion of repolarization (TDR) and arrhythmia increased sharply with augmented nonphosphorylated Cx43 in the ischemia group (P < 0.05 for both). Interestingly, compared with the ischemia group, IPost reduced TDR (57.4±0 vs 39.5±1.7 P < 0.05) and prevented arrhythmia (8/10 vs 1/10, P < 0.05) with a parallel decrease in nonphosphorylated Cx43 in the IPost group (P < 0.05).

Conclusion: These data indicate that IPost is capable of reducing TDR and suppressing arrhythmia by preventing dephosphorylation of Cx43 in rabbit model.

Evolution of left ventricular ejection fraction in patients with multivessel coronary heart disease submitted to 3 therapeutic strategies: 10 years follow-up

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Background: Coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) are assumed assestheapeutic options for the protection of the ischemic myocardium. However, it is not established if those procedures are mandatory for leftventricular ejection fraction (LVEF) preservation. In this setting, weevaluated the evolution of LVEF in patients with chronic multivessel coronary-
PCI for ST-elevation myocardial infarction: technical considerations

grade flow, myocardial blush grade, ST-segment resolution) and major adverse cardiovascular outcomes (death, reinfarction, revascularization, stroke) during early in-hospital period and at long-term follow-up were recorded.

Results: First TIMI grade 3 flow (96% vs 86%) and flow (92% vs 87%) were significantly more frequent in DS group (for all p<0.001). In-hospital (1.2% vs 4.6%, p<0.001) and long-term all cause mortality rates (5.1% vs 12.7%, p<0.001) were significantly lower in the DS group. The incidences of stroke, target vessel revascularization, reinfarction and stent thrombosis of the two groups were not significantly different (for all p>0.05). At multivariate analysis (Hazard ratio [HR] 0.67, 95% confidence interval [CI] 0.52 – 0.76, p<0.023) and propensity-score based analysis (HR 0.86, 95% CI 0.76 – 0.93, p=0.40), DS was not an independent predictor of all-cause mortality at long-term follow-up.

Conclusion: Direct stenting is associated with better myocardial perfusion and lower short- and long-term mortality in selected cases of STEMI. However, direct stenting is not an independent predictor for long-term mortality.

4 years follow up after one-stage PCI of left main stenosis and infarct-related left anterior descending or circumflex arteries in STEMI patients

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Aims: The purpose of this study was to determine immediate and long-term results of safety and efficacy of one-stage PCI of left main stenosis (LMCA) and infarct-related left anterior descending (LAD) or circumflex (LCX) arteries in ST elevation myocardial infarction (STEMI). Even though STEMI guidelines recommend the procedure to infarcted artery without interventions in other segments of coronary vessels, there are often cases when it’s impossible to complete the PCI of the infarct-related LAD or LCX without affecting LMCA. Appropriateness of one-phase endovascular treatment in such cases needs to be investigated.

Methods and results: 281 PCI of LMCA were performed in our cathlab during the last 5 years. There were 57 stable and 224 ACS patients among them. LMCA lesion as the reason of ACS was registered in 19 patients, they were not included into the study. In other 205 cases LAD or LCX were symptom-related accompanying significant LMCA lesions. The ACS subgroup (205 patients) contained 108 non-ST-elevation patients and 97 STEMI patients. These 97 STEMI patients with LMCA stenosis and infarct-related LAD or LCX were of major interest and were followed up for approximately 4 years. LAD was infarct-related in 65% of cases and in 35% the reason of the ACS was LCX. 7 patients were admitted with cardiogenic shock. Concomitant RCA lesion was in 60% of cases. Most procedures were performed using transradial approach (81%), IABP was used in 41% of patients. IVUS was made in 27% of cases. All patients were treated with drug eluting stents (DES). 4 patients died during the procedure, 2 more patients died during hospitalization, so hospital mortality was 6.2%. There were no repeated myocardial infarctions or target vessel revascularizations during hospitalization. Recurrent angina symptoms due to untreated lesions occurred in 38 patients (39%). 10 patients (10.3%) died during the follow up period. Therefore 4 year mortality was 16.5%. Target lesion revascularization was performed in 11 patients (11%). Among them there were 3 cases of repeated PCI of LMCA. Myocardial infarction occurred in 8 patients. PCI of untreated lesions was performed in 14 patients (14%). MACCE-free survival was 55.1%.

Conclusions: According to the short- and long-term result of our study, we assume that PCI of LMCA and infarct-related LAD or LCX arteries in STEMI patients is effective and safe. With growing confidence we can confirm that PCI of LMCA is a method of treatment. Certainly, further large randomized trials with adequate follow up periods are required.
Influence of gender on one-year clinical outcomes after drug eluting stent implantation compared to bare metal stent

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Background: Women with coronary artery disease have a higher mortality rate than men especially after percutaneous coronary intervention (PCI). The impact of drug-eluting stent (DES) vs. bare metal stent (BMS) on this finding is unknown.

Aim: To compare one year safety and effectiveness of DES vs. BMS in all comers PCI according to sex.

Methods: Patients were divided in 4 groups, according to stent used (DES vs. BMS) and sex. Clinical and angiographic data were prospectively entered into our database. The occurrence of cardiovascular (CV) death, Major Adverse Clinical Event (MACE), TLR and stent thrombosis (ST) was recorded at one year follow-up.

Results: 2794 patients underwent PCI with stent implantation. 21.1% were women, and 47.6% of stents were DES. Women were older (68.9±12.9 year vs. 64.0±12.1 year; p<0.0001), had more renal dysfunction (42.8% vs. 22.5%, p<0.0001), a trend for more hypertension (65.4% vs. 56.4%), Women presented more frequently cardiogenic shock than men (4.8% vs. 2.7%, p=0.01), less frequent non-cardiac shock (10.3% vs. 9.8%, p>0.01), similar findings were found for all cause of death (17.3% vs. 14.6%, p=0.7) and for MACE (19% vs. 15.2%, p=0.6). There are benefits of DES in every group (3.6% vs. 2.2%); similar findings were found for all cause of death (11.1% vs. 9.6%, p=0.08) and MACE (13.1% vs. 11.5%, p=0.03). There is no difference between genders in CV death in the BMS group (13.7% vs. 10.7%, ns), nor in the DES group (20.0% vs. 18.2%, p>0.01); similar findings were found for all cause of death (17.7% vs. 14.6%, p=0.7) and for MACE (19%/v15.2%, p=0.06). There are benefits of DES over BMS implantation, but no difference between male and female.

Figure 1. One year clinical event rates. *p<0.0001.

Conclusions: Mortality is higher in women when compared to men after PCI. DES implantation showed best results than BMS for male and female and there is no difference between gender.

Clinical features and outcome of emergency percutaneous coronary intervention on left main coronary artery in acute myocardial infarction

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Purpose: Acute myocardial infarction, due to left main coronary artery (LMCA) occlusion carries a grave prognosis. Large series of primary percutaneous coronary interventions (pPCI) on LMCA culprit lesions are scare. We sought to identify, the clinical presentation and outcome of this group of patients, and to identify, the clinical presentation and outcome of this group of patients, and to identify factors that may influence the outcome during and after pPCI.

Method: For a period of five years, from January 2006 until January 2012, through CardioBase query search we identified 4334 patients treated with pPCI for AMI in our center. Unprotected LMCA lesion, as acuipetal lesion, was present in 32 pts (1.0%). These patients became the subjects of our study. Data on demographics, clinical and angiographical features and outcome was collected from all in-hospital and clinical notes. Mortality was assessed as in-hospital and on long-term clinical follow-up (FU).

Results: Average age of study group was 63.5±15.2 years, and 16 (50%) were male. TIMI 1-0 pre-procedural flow was present in 15 (47%), Killip class 3-4 class in 19 (59.3%), mean pain-to-balloon time was 214±203 minutes. IABP was used in 3 pts (9%), and 27 pts (84%) had angiographic evidence of thrombus presence in LMCA. Rentrop gradus 2-3 retro-collaterals from RCA, were present in 3 pts (9.7%) patients only, RCA was dominant in 30 pts (94%), while occluded RCA was in 7 pts (22%). Angiographic successes was accomplished in 26 pts (81%), stenting of LMCA was performed in 29 pts (94%) and TIMI 2-3 flow after procedure was achieved in 25 pts (78%). Overall patient mortality was 15.3±2 pts (46.9%), 8 patients died during pPCI procedure, 5 died during hospital stay, and 2 deaths occurred after discharge (mean duration of follow-up 14.6±12.1 months). Independent predictors of in-hospital mortality were low systolic blood pressure (SBP) on admission (82.1±11.8 vs 100±12.3, mmHg; p<0.021), TIMI flow 1-0 pre-procedurally (9/13 vs 6/19 p=0.035) and Killip class 3-4 presenta-

Conclusions: Mortality is no difference between gender.

Impact of time delay to treatment on microvascular obstruction and in-hospital fatal cardiac complications in patients with ST-Segment Elevation Myocardial Infarction

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Background: Primary percutaneous coronary intervention (PCI) is more effective than thrombolytic therapy for the treatment of ST-segment elevation myocardial infarction (STEMI) when delivered by an experienced team soon after the onset of symptoms. However, data from experimental studies suggest that the extent of microvascular damage is worsened by longer durations of ischemia. The purpose of this study was to examine the effects of early recanalization on the coronary microvascular integrity and in-hospital event rate.

Methods: One hundred and ninety-three consecutive patients with first anterior STEMI who underwent PCI were subjected to coronary flow measurement with a Doppler guidewire. The coronary flow velocity spectrum provided the following parameters: systolic peak velocity (SPV) and diastolic deceleration time (DDT). We defined the presence of microvascular obstruction (MVO-CFV) as DDT of ≤ 600 ms and the presence of systolic flow reversal. We classified the patients into three categories according to time from symptom onset to first balloon inflation: ≤ 120 min (group 1), > 120 to 240 min (group 2), > 240 min (group 3). The in-hospital event rate was compared among the 3 groups.

Table 1. In-hospital complications in each group

<table>
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<tr>
<th></th>
<th>≤ 120 min (group 1; n=73)</th>
<th>&gt; 120 to 240 min (group 2; n=73)</th>
<th>&gt; 240 min (group 3; n=60)</th>
<th>p-value</th>
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<tr>
<td>MVO-CFV (%)</td>
<td>0% (0/73)</td>
<td>0% (0/73)</td>
<td>0% (0/60)</td>
<td>0.01</td>
</tr>
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<td>Cardiogenic shock (%)</td>
<td>0% (0/73)</td>
<td>7% (5/73)</td>
<td>31 (20/63)</td>
<td>0.01</td>
</tr>
<tr>
<td>De novo ischemia (%)</td>
<td>0% (0/73)</td>
<td>14% (10/73)</td>
<td>46 (27/60)</td>
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<tr>
<td>In-hospital death (%)</td>
<td>0% (0/73)</td>
<td>0% (0/73)</td>
<td>6% (3/60)</td>
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</tbody>
</table>

Note: p-value indicates statistical significance of the comparison among the 3 groups.
Is primary PCI feasible in nonagenarians? 

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Aim: The reperfusion strategy requiring primary percutaneous coronary intervention (PCI) for ST-segment elevation acute myocardial infarction (STEMI) in nonagenarian patients remains controversial. The purpose of this study was to evaluate the outcomes and the result of primary PCI in patients aged 90 years old or more with STEMI.

Methods and Results: We conducted a monocentric retrospective study and focused on nonagenarians treated with primary PCI for acute myocardial infarction. A retrospective analysis over the past 8 years identified 35 patients > 90 years of age having been treated with primary PCI in our institution. We enrolled 35 patients with acute myocardial infarction who were treated with primary PCI. Mean age 92.7±2.5 years, 74.3% were women. In these patients, 20% were suffering from diabetes mellitus and 23% had previous myocardial infarction. Cardiogenic shock was present at admission in 9 (25.7%) of these patients. The primary PCI was successfully performed in 10 (28.6%) patients (primary PCI failure in 9 patients; mean delay in PCI of 5.7 hours) due to severe conduction disorders. Mean delay between symptom onset and balloon was 92±12.7 hours and 29 patients (82.9%) underwent PCI through transluminal approach. Among these patients, 16 (45.7%) had multivessel coronary artery disease and 31 (88.6%) had single-vessel PCI (3 LAD, 53% LAD, 15% CX and 29% RCA). Revascularization of the culprit vessel was obtained in 100% of the cases and 88% were successful procedures (TIMI flow of 2 or 3). Bare-metal stents were implanted in 30 cases (85.7%) versus 1 case (2.8%) for drug-eluting stents. Distal embolization occurred in 2 patients (5.7%) and acute coronary dissection occurred in 2 other cases (5.7%) but only one patient (2.8%) had severe bleeding during the use of clopidogrel in 31 cases (88.6%) and anti-GpIIb-IIIa in 17 cases (48.6%). Mean cardiac troponine Ic was 90 ng/ml and mean cardiac troponine Ic post-PCI was measured at 43 ng/ml. Mean hospital stay was 4.8±4 days and in-hospital mortality rate was 25.7%. Survival rate after 6 months was 51.4%, and was 40.6% after 1 year.

Conclusion: In our study, primary PCI in nonagenarians with STEMI is successful and feasible through a transradial approach. It is associated with high rate of successful percutaneous reperfusion of the infarct-related artery. These results suggest that primary PCI should be offered in selected nonagenarians with acute myocardial infarction, as shown by the survival rate at one year.

Comparison of reperfusion efficacy of thrombus aspiration with and without distal protection during primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction

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Purpose: A recent randomized trial showed better coronary reperfusion and clinical outcomes by primary percutaneous coronary intervention (PCI) with thrombus aspiration than by conventional PCI in patients with acute ST-segment elevation myocardial infarction (STEMI). On the other hand, beneficial effects of distal protection in primary PCI are still controversial. We tested a hypothesis that thrombus aspiration with distal protection is superior to simple thrombus aspiration in primary PCI.

Methods: Consecutive 176 STEMI patients were enrolled prospectively and were assigned to thrombus aspiration group (A, n=104) or thrombus aspiration with distal protection group using a filter-device system (A+DP, n=72). We compared angiographic reperfusion grades, left ventricular (LV) function, and clinical outcomes between the two groups. Results: The TIMI flow grade-3 in the A+DP group was 77(74) versus 69 (54) in the A group (P=0.005). The mean cardiac troponine Ic was 75.1±51.7 vs. 65.4±53.4 in the A and A+DP group (P=0.066). All patients were successfully operated only in daylight hours and was dispatched after the PCI-centre had accepted the patient. System delay was defined as time from first medical contact (print time on triage ECG) to arrival in the catheterization laboratory. We also determined 30-day mortality for those who underwent PCI.

Results: A total of 450 patients; 38% with STEMI and 114 STEMI patients. Inter-hospital transport patients comprised 38% in the ambulance group and 18% in the STEMI group (p<0.001) and the median transport distance were 94 (64-172, median, 5-95% range) vs. 97 (62-162, 5-95% range); respectively (p=0.01). The median time from ECG to arrival in the CL was 104 minutes (63-225, 5-95% range) with GT and 84 minutes (60-160, 5-95% range) with PSH (p=0.001). The 30-day mortality was 7% (18/262) for STEMI patients and 2% (2/91) for PSH patients (p=0.095).

Conclusion: Air transportation by a helicopter significantly reduced time to PCI-centre arrival as compared to ground transport. This study indicates that helicopters can reduce system delays when the estimated ground transportation exceeds only 30 min, and therefore has potential benefit in most regions.
The impact of stenting on coronary blood flow in STEMI

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Introduction: In patients with STElevation acute myocardial infarction (STEMI), primary percutaneous coronary intervention (PCI) has been shown to be superior to thrombolysis for the restoration of normal coronary blood flow. However, depending on the technique used, no-reflow phenomenon is seen in some of these patients.

Materials and methods: Data from 385 consecutive patients with STEMI who underwent primary primary PCI were evaluated. Coronary angiograms of the patients were reviewed. TIMI flow grades, corrected TIMI frame count (CTFC) values and degree of stenosis were measured at the beginning by QCA, after angioplasty and after stenting. According to the degrees of residual stenoses (RS) and CTFC values after angioplasty, patients were divided to four groups. In group I (n=82), RS < 50% and CTFC < 28. In group II (n=50), RS > 50% and CTFC < 28. In group III (n=40), RS > 50% and CTFC > 28. In group IV (n=46), RS > 50% and CTFC > 28.

Results: In group I, CTFC values were significantly higher after stenting than after angioplasty (21.8±4.9 frames vs. 16.6±4.9 frames; p=0.02); on the other hand in group IV, CTFC values were significantly lower after stenting than after angioplasty (49.3±3.4 frames vs. 63.8±27.4 frames; p=0.037). CTFC values were similar after angioplasty and after stenting in groups II and III (19.6±5.0 frames vs. 20.4±11.3 frames; p=0.37 and 57.8±26.9 frames vs. 55.5±31.6 frames; p=0.433, respectively).

Conclusion: Routine stent implantation during primary PCI is an effective way to reduce residual stenosis in patients with STEMI. However, it has a negative effect on coronary flow in patients with minimal residual stenosis and with TIMI grade 3 flow.

Conclusion: In patients treated with PCI CX-related NSTEMIs were less often associated with total vessel occlusions or haemodynamic instability. After adjustment for age in-hospital was significantly higher in patients with CX-related STEMI.

P2688 Anticoagulation, arterial access and bleeding in primary PCI: an analysis of the randomized ATOLL trial

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AIM: We sought to determine the incidence of major bleeding complications in the randomized ATOLL trial that used predominantly transradial access (67%). We examined whether these bleedings had an impact on mortality.

Methods: In the international multicenter ATOLL study, 910 patients presenting with ST elevation myocardial infarction were randomly assigned to receive an intravenous bolus of 0.5 mg/kg of eptoxanopin or unfractionated heparin before primary PCI. The use of eptoxanopin compared with unfractionated heparin was associated with a reduction of clinical ischaemic events. The present analysis evaluated the occurrence of major bleeding complications and their association with mortality at 1 month.

Results: Patients were treated with intense antiplatelet therapy as 63% received high-dose clopidogrel (600 mg or more) and 80% of patients received glycoprotein IIb/IIIa inhibitors. During the first 30 days non-CABG related bleeding complications (STEEPLE definition) occurred in 42 patients (4.6%), with transfusion in 18 patients (2%). Major bleeding rates did not differ between eptoxanopin and unfractionated heparin group (4.4% vs 4.8%, p=0.79). There was numerically, a reduction of major bleeding in patients undergoing radial primary PCI as compared with femoral primary PCI (3.6% vs 6.5%, p=0.06). The two most common overt bleeding complications were gastrointestinal and access-site bleedings. Major bleeding was strongly associated with 30-day mortality (OR 6.5, 95% CI 2.8 to 14.6, p<0.001).

Conclusion: In a predominantly radial primary PCI study major bleeding was strongly related to 1-month mortality. GI bleeding being a frequent complication.

P2689 Comparison of BARC and GUSTO bleeding classifications as predictors of one-year mortality after primary PCI in the real-world population


Purpose: GUSTO bleeding classification was shown superior to TIMI bleeding classification in stratifying patients with bleeding complications according to one-year mortality after primary PCI. Our aim was to compare GUSTO with the new BARC classification in this respect.

Methods: We examined 1672 patients undergoing primary PCI, from a register of a high volume catheterization laboratory from September 2009 to December 2010. Bleeding complication was defined as any intra-hospital bleeding that could satisfy criteria for GUSTO and/or BARC classification. Separate Cox regression
models were created for GUSTO and BARC bleeding classifications to assess mortality hazard for different levels of bleeding.

### Results:

Bleeding complications were documented in 6.8% of patients. Bleeding patients had significantly higher one-year mortality rate than non-bleeding patients (32% vs 12%, p<0.001). Patients classified as GUSTO major and moderate were at significantly higher risk for one-year mortality compared to non-bleeding patients, but had similar hazard ratios (see the figure). The HR=5.76, CI95=3.210-10.337, p<0.001 and HR=5.194, CI95=2.748-9.816, p<0.001. Unlike with GUSTO, mortality hazard increased proportionally with the higher grade of bleeding when classified to BARC (see the figure) (BARC 3a: HR=2.340, CI=1.49-3.67, p<0.001 and BARC 3b: HR=4.875, CI95=2.83-8.397, p<0.001). Patients classified as mild GUSTO or BARC -3a were not at higher risk of one-year mortality than non-bleeding patients (mild GUSTO: HR 1.613, CI95=0.937-2.776, p=0.084; BARC -3a: HR=1.180, CI95=0.165-6.419, p=0.869).

### Conclusions:

BARC classification seems more efficient than GUSTO in differentiating between patients with high and very high risk of one-year mortality due to bleeding complications after primary PCI.

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### P2690

#### 1-Year prognosis after unprotected left main coronary artery occlusion treated with primary angioplasty


**Purpose:** ST-segment elevation myocardial infarction (STEMI) due to unprotected left main coronary artery occlusion (ULMCO) is a dramatic and catastrophic entity with high risk of out-of-hospital sudden death. Therefore very few data have been published regarding mid-term outcomes after primary percutaneous coronary intervention (PCI) in this group of patients. The purpose of this study was to determine the frequency and predictors of 1-year mortality in patients with STEMI due to ULMCO referred to our institution for primary PCI.

**Methods:** Single-center retrospective study of consecutive patients who underwent primary PCI for STEMI from January 2006 to February 2011. Among 1963 patients admitted for primary PCI, 37 (1.88%) had acute ULMCO.

**Results:** In the ULMCO subgroup, mean age was 63±15 years and 29 (78%) were male. Diabetes was present in 23% of patients, 47% were hypertensive, 41% had hyperlipidemia and 58% were smokers. Cardiogenic shock at admission or during PCI was present in 54% of patients. Distal segment was the most frequent ULMCO location (27, 73%) and 13 patients (35%) had basal TIMI flow grade 0 or 1. Multivessel disease was present in 20 patients (54%) and total occlusion of right coronary artery in 5 cases (13%). Stents were used in most cases (76%) and 65% of stents deployed were drug-eluting stents. Intracoronary balloon was implanted in 43% of cases and 17 patients (46%) required emergent endotracheal intubation and mechanical ventilation before or during PCI. Overall mortality was 49% at 1-year follow-up. Most of deaths occurred in hospital (17) and only 1 patient died after discharge. Mortality in patients with cardiogenic shock (p<0.001) occurred in 75% of the patients at 1-year follow-up. Patients with basal TIMI flow grade 0-1 and patients needing endotracheal intubation had 77% (p=0.001) and 82% (p<0.001) mortality at 1-year follow-up, respectively. Multivariate analysis identified as independent predictors of 1-year mortality the cardiogenic shock (RR 6.18 [95% CI 4.26-8.11]) and the need for endotracheal intubation (RR 5.78 [95% CI 1.63-20.42]).

**Conclusions:** Primary PCI can be successfully performed in patients with STEMI due to ULMCO. However, in our experience, 1-year mortality in this subgroup of patients was remarkably high. Cardiogenic shock and need for intubation before or during PCI were the most important determinants of mid-term mortality.

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### P2691

#### Prognostic impact of nonculprit lesions PCI during primary PCI for STEMI


**Background:** Percutaneous coronary intervention (PCI) of the culprit vessel is the conventional treatment in STEMI. However, pts often have significant coronary lesions in other vessels. In patients with STEMI and multivessel disease, it is unknown whether it is safe or even desirable to also treat the nonculprit vessel during primary PCI procedure.

**Aims:** This study aimed to test the safety of the culprit and nonculprit lesions PCI with PCI of only the culprit lesion in STEMI during primary PCI.

**Method and Results:** We used our Database of all pts treated using primary PCI for STEMI. Excluded pts were those with cardiogenic shock and one vessel disease. Patients were allocated into 2 groups: culprit vessel PCI and nonculprit PCI. Of note, “one time” multivessel PCI was used in only 6.4% of our STEMI patients.

<table>
<thead>
<tr>
<th>Culpit PCI (N=926)</th>
<th>Nonculprit PCI (N=64)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63±12</td>
<td>63±14</td>
</tr>
<tr>
<td>Male</td>
<td>85%</td>
<td>81%</td>
</tr>
<tr>
<td>Anterior AMI</td>
<td>40%</td>
<td>59%</td>
</tr>
<tr>
<td>DM</td>
<td>29%</td>
<td>33%</td>
</tr>
<tr>
<td>Successful culprit PCI</td>
<td>95%</td>
<td>98%</td>
</tr>
<tr>
<td>Successful Non culprit PCI</td>
<td>93%</td>
<td>N/A</td>
</tr>
<tr>
<td>Killip Score</td>
<td>4.9±3.7</td>
<td>5.1±3.9</td>
</tr>
<tr>
<td>Contrast (ml)</td>
<td>174±68</td>
<td>278±59</td>
</tr>
<tr>
<td>One year mortality</td>
<td>Death</td>
<td>6.5%</td>
</tr>
<tr>
<td></td>
<td>Re-MI</td>
<td>5.5%</td>
</tr>
<tr>
<td></td>
<td>STEMI Thrombosis</td>
<td>2.5%</td>
</tr>
<tr>
<td></td>
<td>TVR</td>
<td>13.6%</td>
</tr>
<tr>
<td></td>
<td>CABG</td>
<td>6.1%</td>
</tr>
<tr>
<td></td>
<td>MACE</td>
<td>22%</td>
</tr>
</tbody>
</table>

**Conclusion:** Nonculprit PCI strategy is not advisable in non-shock patients with multivessel coronary disease in patients with STEMI undergoing primary PCI.

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### P2692

#### Comparison of one-year clinical outcomes between early invasive and conservative strategy in elderly ST-elevation myocardial infarction complicating cardiogenic shock: data from KAMIR

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**Background:** The benefit from early invasive strategy for elderly (>75-year-old) patients with acute myocardial infarction (AMI) complicating cardiogenic shock was recently reported.

**Methods:** We collected and analyzed data of 356 elderly (>75-year-old) patients with cardiogenic shock among the enrolled total 8970 acute ST-segment elevation myocardial infarction (STEMI) (6623 male, age 64±13 years) from Korea Acute Myocardial Infarction Registry (KAMIR) between Jan 2008 and June 2011. In-hospital and one-year survival rate free from major adverse cardiac event (MACE) defined as cardiac death, myocardial infarction and target vessel revascularization were compared between early invasive (n=226) and conservative (n=130) strategy during one year of follow-up.

**Results:** Left ventricular ejection fraction was different between early invasive and conservative (49% vs. 43%, p=0.028). Other baseline clinical characteristics were not significantly different between two groups. In-hospital survival rate of early invasive strategy was higher than conservative strategy (87.4% vs. 75.3%, p=0.013). However, 30-day and one-year MACE-free survival rate were similar between early invasive and conservative strategy (62.8% vs. 62.3%, p=0.512; 60.6% vs. 60.0%, p=0.513).

**Conclusion:** Nonculprit PCI strategy is not advisable in non-shock patients with multivessel coronary disease in patients with STEMI undergoing primary PCI.
Predictors of in-hospital mortality in patients with acute myocardial infarction complicating cardiogenic shock in the contemporary era of primary percutaneous coronary intervention


Purpose: Primary percutaneous coronary intervention (PCI) is currently the preferred reperfusion therapy for patients presenting with acute myocardial infarction (AMI). About 5–10% of all AMIs are complicated by cardiogenic shock which is associated with a high in-hospital mortality. There is limited data on the clinical outcomes of this group of patients in the contemporary era of PCI.

Methods: We sought to evaluate the survival rate and predictors of in-hospital mortality in our cohort of Asian patients (n=145) with AMI and cardiogenic shock who underwent PCI at our institution from January 2009 to December 2010. Clinical data was collected retrospectively on demographic characteristics, presenting signs and symptoms, blood investigation, hospital course and in-hospital mortality.

Results: The mean age at presentation was 63.1 ± 12.1 years with male predominance (88%). The majority of patients (73%) presented with anterior MI with 54% found to have multi-vessel disease on coronary angiography. Occlusive left main disease was present in 16 patients (11%). The majority of patients received bare metal stent implantation (65%) during PCI with post-procedural Thrombolysis in Myocardial Infarction (TIMI) 3 flow achieved in 77% of patients. The average door-to-balloon time was 69 ± 29.6 minutes. Multi-PCI vessel was performed in 26 patients (18%).

The mean ejection fraction was 34.4 ± 12.3%. For hemodynamic support, 141 patients (97.9%) used inotropic support, 100 patients (65%) received intra-aortic balloon counterpulsation and 5 patients (3.4%) received extracorporeal membrane oxygenation. The overall in-hospital mortality was 28% (40 patients). Factors associated with in-hospital mortality were older age at presentation, history of cardiac arrest during hospitalization, occlusive left main disease, post-procedural TIMI 3 flow, severe heart failure and renal failure. By multivariate analysis, independent predictors of in-hospital mortality were cardiac arrest and renal failure (hazard ratio 4.43, 95% CI: 1.25-15.8, p=0.02 and hazard ratio 7.8, 95% CI: 1.78-33.9, p=0.006 respectively). All 7 patients (4.8%) who developed >1 episode of cardiac arrest did not survive the index hospitalization.

Conclusion: In the contemporary era of PCI, the in-hospital mortality of patients with AMI and cardiogenic shock remained relatively high. History of cardiac arrest during hospitalization and renal failure were independent predictors of in-hospital mortality. Novel treatment options are certainly needed to improve the prognosis of this group of patients.

Interhospital transfer due to failed prehospital triage for primary percutaneous coronary intervention: incidence, predictors, and clinical impact in contemporary practice

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Purpose: For patients with ST-elevation myocardial infarction (STEMI), guidelines recommend prehospital triage and direct referral to a percutaneous coronary intervention (PCI)-capable center as the preferred strategy to minimize ischemic time. However, little is known about the incidence and impact of failed prehospital triage. We assessed the incidence, predictors, and clinical impact of interhospital transfer for primary PCI after initial referral to a non-PCI-capable center due to a failed prehospital STEMI diagnosis.

Methods: Our 12-lead electrocardiogram (ECG) based prehospital triage system consists of a single PCI-capable center and 5 non-PCI-capable referral centers. Primary PCI was the preferred reperfusion strategy for all STEMI patients and interhospital transfer, if required, was performed by ambulance. Data were obtained from a prospectively collected registry STEMI.

Results: Between January 2008 and January 2010, 609 patients (73%) with STEMI undergoing primary PCI were directly admitted through prehospital triage and 127 patients (15%) required interhospital transfer after failed prehospital triage. Other patients were emergency department admissions and self-referrals. Door-to-balloon times <90 minutes were achieved in 96% of patients in the prehospital triage group and 14% in the interhospital transfer group (P < 0.001). These rates were 98% and 55% for door-to-balloon times <120 minutes (P < 0.001). In the interhospital transfer group, the first available ECG could be considered diagnostic for STEMI in 77% of cases. Predictors of interhospital transfer were diabetes, prior myocardial infarction, and greater distance from event location to PCI-capable center. Interhospital transfer independently accounted for a 44% increase in ischemic time (95% confidence interval [CI] +32% to +66%; P < 0.001). Although 1-year mortality was higher in the interhospital transfer group (10% vs. 5.3%; P=0.036), no independent relationship with mortality was found (hazard ratio 1.42; 95%CI, 0.70-2.88; P=0.335).

Conclusion: In a fully operational prehospital triage system, failed prehospital triage and subsequent interhospital transfer occurred in 15% of STEMI patients undergoing primary PCI despite an often diagnostic ECG. Interhospital transfer was a major predictor of ischemic time, although no independent association with mortality was found. Continuing efforts to optimize prehospital triage and direct referral for primary PCI in patients with STEMI are warranted, especially for patients with onset of STEMI at greater distance from a PCI-capable center, diabetics, and patients with prior myocardial infarction.

Reperfusion delay in patients treated with primary percutaneous coronary intervention: insight from a real world danish STEMI population in the era of telemedicine

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Background: Reperfusion delay in STEMI is associated to adverse outcome. We evaluated time from alarm call (system delay) and from first medical contact (PCI related delay), where fibrinolysis could be initiated, to balloon inflation in a prehospital organization with tele-transmitted ECM, field triage and direct transfer to PCI or primary PCI.

Methods: Single center cohort study in 472 patients. The PCI center registry was linked by person identification number to emergency medical services (EMS) data. The Danish Board of Health databases in the period of 2005-08. Patients were stratified according to transfer distances into zone 1 (<25 km), zone 2 (65-100 km), zone 3 (101-185 km) and according to referral by pre-hospital triage. We evaluated delays according to ESC guidelines, pre-hospital fibrinolysis (PHF) (120 min acceptable PCI delay +30 min needle time) and in-hospital fibrinolysis time limits (PHF + transfer time to local hospital) (Figure 1).

Results: System delay was 86 min (IQR 72-113) in zone 1, 133 (116-180) in zone 2 and 179 (149-215) in zone 3 (p<0.001). PCI related delay in directly referred patients was 109 (92-121) min in zone 2, but exceeded recommendations in zone 3 (139 [121-160]) and for patients admitted via the local hospital (219 [171-250]).

Conclusions: In spite of pre-hospital triage in 73% of STEMI patients, PCI was delayed beyond ESC guidelines for patients >100 km away and non-directly referred patients. System delay predicts mortality, therefore EMS personnel education should ensure pre-hospital triage as admission via local hospitals delays optimal care. Geographical zone stratification identifies patients with long delays. Options are pharmacoinvasive regiments, research in early ischemia detection and airborne transfer.
Early outcome and prognostic factors among elderly patients with ST-segment elevation myocardial infarction treated with primary coronary angioplasty

Background: Elderly patients are at high risk of mortality when they present with STEMI. In-hospital mortality in a multivariate analysis was independently associated with increased risk of mortality at 30 days. There was a trend toward higher PCI success rate in male patients (13.2% vs 23.8%, p=0.08).

Methods: The study included 587 consecutive patients undergoing PCI between January 2009 and September 2011. The median SXs was 15.5. We divided the patients into tertiles: SXs≤10; SXs>10 and ≤18; SXs>18.

Results: The median patient age was 75 years, 73.6% were men, 51.3% had hypertension, and 25% had diabetes. Percutaneous access was via the radial approach in 84.1% of the patients. The culprit artery was the left anterior descending artery in 44.1% of the patients. 31% had a three-vessel disease, and a stent was implanted in 90% of the patients. The median duration of follow-up was 2.1 years, and 10.9% of the patients died: 5.1% in SXs≤10, 9.1% in SXs>10, and 19.1% in SXs>18 (p=0.000) (See Image). The incidence of major adverse cardiovascular events (MACE) at the end of the follow-up was 21.9%, 15.3% in SXs≤10, 19.7% in SXs>10, and 31.8% in SXs>18 (p=0.000). The SXs levels were an independent determinant of mortality in a multivariate analysis [HR IC 95%: 1.021 (1.010-1.032), p=0.000], and of MACE [HR IC 95%: 1.010 (1.008-1.028), p=0.000].

Conclusions: The SXs provides important prognostic information regarding mortality and major adverse cardiovascular events in a cohort of patients with STEMI who were undergoing PCI.

P2698

Prognostic value of the syntax score in patients undergoing primary Percutaneous Coronary Intervention


Purpose: The SYNTAX score (SXs), designed to stratify outcomes in multivessel PCI and CABG, has been validated in unselected populations undergoing elective PCI. Patients with ST-segment elevation infarction (STEMI) were excluded from the original SXs algorithm, the utility of using the SXs in this patient group remains undefined. The aim of this study was to evaluate the prognosis value of the SXs in a contemporary cohort of patients admitted to our hospital with STEMI who were undergoing primary percutaneous coronary intervention (PPCI).

Methods: We evaluated 116 patients (aged 86.3±4.2 years), 49 (42.2%) males, admitted to our hospital between August 2008 and December 2011, with diagnosis of STEMI who underwent urgent PCI.

Results: There were no gender differences in cardiovascular risk factors, left ventricular ejection fraction (LVEF) at admission, Killip class, infarct related artery or TIMI flow (3) was 3 in 94 (81%) patients. At univariate analysis, older age (p=0.01), LVEF ≤40% (p=0.005), failure of PCI (TIMI flow≤3, p=0.001), systolic blood pressure <100 mmHg (p=0.016), and no history of myocardial revascularization (p=0.027) were associated with higher mortality at 30 days. Multivariate Cox proportional hazards analysis identified impaired LVEF (HR 2.40, 95% CI 1.01-5.69, p=0.047), age (1 year step, HR 1.14, 95% CI 1.05-1.24, p=0.002) and failure of PCI (HR 3.93, 95% CI 1.68-9.1, p=0.002) to be independently associated with increased risk of mortality at 30 days. There was a trend toward higher PCI success rate in male patients (13.2% vs 23.8%, p=0.08).

Conclusions: The SXs STEMI PCI for predicting in-hospital mortality was validated in our cohort of patients. The SXs is easy to implement in clinical practice and is very useful for the stratification of this group of patients.

P2699

ST-elevation myocardial infarction complicated by cardiogenic shock: risk factors and outcome after primary percutaneous coronary intervention

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Purpose: Prognosis of patients with ST-elevation myocardial infarction (STEMI) complicated by cardiogenic shock is generally poor. Early recognition may be beneficial for outcome. We sought to investigate predictors of cardiogenic shock and to evaluate long term outcomes.

Methods: In 3 Dutch tertiary centers, all patients treated with primary percutaneous coronary intervention were enrolled in a prospective registry. Patients were stratified retrospectively according to development of peri-procedural shock defined as a systolic blood pressure lower than 90 mmHg with signs of tissue hypoperfusion requiring treatment in form of resuscitation, inotropic agents or assistant devices. Predictors of cardiogenic shock were assessed using multivariable logistic regression. Mortality rates were obtained through municipality records.

Results: In total, 190 patients (5.7%) suffered STEMI complicated by cardiogenic shock, while 3156 patients did not develop shock. Patients suffering from shock were older (65.9±12.3 vs. 63.1±12.4, p=0.003), more often female (32.1% vs. 24.7%, p=0.022), suffered more often from insulin-dependent diabetes (6.7% vs. 2.4%, p=0.001), renal insufficiency (8.4% vs. 3.5%, p=0.001) and more frequently had a history of myocardial infarction (17.2% vs. 10.5%, p=0.004) or by-pass surgery (5.4% vs. 2.3%, p=0.008). Presentation with out of hospital cardiac arrest was more common in shock patients (34.2% vs. 4.7%, p=0.001). Furthermore, diagnosis-to-balloon time was longer (median 86 min. vs. 79 min, p=0.009); although symptom- and door-to-balloon times were comparable. Culprit lesion was more frequently the left main artery (11.1% vs. 0.8%, p=0.001) and less often the right coronary artery (26.8% vs. 41.7%, p<0.001). Multivessel disease was present in 66.3% vs. 52.3% in non-shock patients, p=0.001. Post-procedural TIMI flow 3 was present in 78.4% of shock patients vs. 92.0%, p<0.001. Mortality was significantly higher at 7 days (30.0% vs. 2.1%), 30 days (37.4% vs. 2.7%) and 1 year (45.3 vs. 5.2%). Independent multivariable predictors of developing cardiogenic shock were included presentation with out of hospital cardiac arrest (HR
Additive prognostic value of SYNTAX score over Clinical risk scores and the SYNTAX score predicts the upper tertile for 3 or 4 scores (45% and 75%, respectively). All scores distinguish patients in the lowest tertile, in 5 pts (7%) in the intermediate, and in 15 pts (23%) versus cardiovascular events in the long-term follow-up.

**Conclusion:**

PAMI scores, but did not improve the CADILLAC risk score for prediction of adverse cardiovascular events at 12 months.

**Methods:**

This observational study included 209 consecutive patients with STEMI undergoing pPCI. The primary endpoint was the major adverse cardiovascular event (MACE) defined as a composite of cardiovascular mortality, non-fatal myocardial infarction and non-fatal stroke. To test whether the addition of SYNTAX score to each of the five studied clinical scoring systems in STEMI improves the regression model significantly, the omnibus test of model coefficients was used.

**Results:**

Survival status and follow-up could not be obtained in 3 patients (1.4%). Thus, the final number of patients included in our analysis was 206 (163 (79%) male, 58±13 years old). Patients were stratified by tertiles of the SYNTAX score (lowest tertile: <12; second tertile: 12-<19.5; highest tertile: ≥19.5). The median follow-up for the studied patients was 614±106 days (20.4±4 months) after pPCI. Primary endpoint occurred in 4 pts (2%) in the lowest, in 5 pts (7%) in the intermediate, and in 15 pts (23%) in the highest SYNTAX score tertile. All studied scoring systems were good univariable predictors for long-term MACE in our population (p<0.001). SYNTAX score was independent predictor of MACE and improved the models significantly when added to GRACE (p=0.011), TIMI (p=0.008), ZWOLLE (p=0.009), and PAMI (p=0.012) risk scores. On the contrary, SYNTAX score did not improve the model of PAMI prediction when added to CADILLAC score (p=ns).

**Conclusion:**

In the population of STEMI patients treated with pPCI, SYNTAX score significantly improved prognostic value of GRACE, TIMI, ZWOLLE and PAMI scores, but did not improve the CADILLAC risk score for prediction of adverse cardiovascular events in the long-term follow-up.

**P2703**

In-hospital and long-term mortality after primary PCI for ST-segment elevation myocardial infarction during on- versus off-hours

**Purpose:**

Some of the previous studies have reported higher in-hospital and long-term mortality rates in patients with STEMI undergoing primary percutaneous coronary intervention (pPCI) during Off-Hours. Our aim was to compare in-hospital and long-term mortality in STEMI patients treated with pPCI during On- versus Off-Hours in a high volume catheterization laboratory.

**Methods:**

The study included 784 consecutive STEMI patients treated with pPCI during 2008. The patients were categorized by their admission time to the cath-lab during On-Hours (work days from 7 a.m. to 7 p.m., 367 patients) versus Off-Hours (work days from 7 p.m. to 7 a.m. and weekends, from Friday 7 p.m. to Monday 7 a.m., 417 patients). The follow-up period was at least 24 months for each patient.

**Results:**

Baseline demographic, clinical and angiography characteristics were similar in both patient groups. Time-to-primary PCI delay between the first medical contact and the first balloon inflation was 148 min vs. 128 min, p=0.05, thus longer in the on-hours group. No significant difference was found in in-hospital mortality (3.8% during On- versus 2.9% during Off-Hours, p=0.251), whereas mortality rate after 24 months was significantly higher in the On-hours group (10.6% vs. 6.3%, p=0.037). The survival curve is presented in figure.

**Conclusion:**

In a large contemporary registry STEMI presentation during Off-
Ten years of cardiogenic shock complicating acute myocardial infarction: patient characteristics, treatment and outcome at a single interventional centre

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Background: Cardiogenic shock complicating acute myocardial infarction (AMI) remains to be associated with high in-hospital mortality even today. Data on incidence, patient characteristics, treatment and outcome during the last 10 years are very scarce.

Methods: We analysed retrospectively all patients with AMI admitted to our tertiary care hospital between 2000 and 2009 (MIRLU-Registry).

Results: Between 6/2000 and 12/2009 5053 patients (pts) with AMI were treated at our hospital. The proportion of pts with cardiogenic shock was 7.5% (range: 3.4-11.5%/year, p for trend= 0.59); 11.4% in pts with ST elevation AMI (STEMI). Mean age of shock pts was 66.8±13.1 years; 67.6% were male; acute invasive diagnosis was performed in 96.5%, among those 78.3% were treated with PCI and 10.1% with CABG. Mean pre-hospital delay (symptom onset to admission) was 94.7±604.1 minutes and mean in-hospital delay (admission to start of angiography) was 221.2±445.6 minutes (mean in-hospital delay for cardiogenic shock patients with STEMI only: 78.2±103.0 minutes). Total hospital mortality during these ten years was 29.9%.

Conclusions: In the course of the last 10 years of current clinical practice at an interventional centre the rate of cardiogenic shock complicating AMI was 7.5% (STEMI 11.4%, NSTEMI 3.6%). During this period of time significant trends in pre-hospital and in-hospital delays or in in-hospital mortality could not be observed.

Culprit lesion revascularization versus complete revascularization in acute myocardial infarction patients with multivessel disease undergoing percutaneous coronary interventions

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Background: The impact of culprit Lesion Revascularization (CLR) versus Complete Revascularization(CR) in Acute Myocardial Infarction (AMI) patients(pts) with Multivessel Disease(MVD) Undergoing Percutaneous Coronary Interventions (PCI) with Drug-eluting Stents(DES) is still in debate in the DES era.

Methods: A total of 374 consecutive AMI pts with MVD underwent PCI with DESs by either CLR(n=239) or CR (n=135) strategy were retrospectively analyzed from Livalo Acute Myocardial Infarction Study (LAMIS). We were evaluated major clinical outcomes up to 12months outcomes

Results: Baseline clinical-characteristics were similar between the two groups except Previous MI (3.7% vs 0.8%, p=0.019), Diabetes (40.7% vs 29.7%, p=0.030), and triple-antiplatelet therapy (57% vs 31.7%, < 0.001) were higher incidence in CR group. CLR group had more Current-smoker (39.2% vs 56.8%, p=0.004). Procedural success rate (85.9% vs 86.1%, p=0.538) and in hospital outcomes were similar between the two groups. At 12 clinical outcomes (follow-up rate:89.8%) were not significantly different in two groups (table).

Table: Cumulative 12-month clinical outcomes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
<th>CLR(n=239)</th>
<th>CR(n=135)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>374</td>
<td>374</td>
<td>374</td>
<td>1.00</td>
</tr>
<tr>
<td>Death</td>
<td>47(13)</td>
<td>35(14.6)</td>
<td>12(8.8)</td>
<td>0.053</td>
</tr>
<tr>
<td>Cardiac</td>
<td>7(2)</td>
<td>4(1.7)</td>
<td>3(2.2)</td>
<td>0.60</td>
</tr>
<tr>
<td>Non Cardiac</td>
<td>38(16)</td>
<td>37(15.9)</td>
<td>1(0.7)</td>
<td>0.053</td>
</tr>
<tr>
<td>CABG (%)</td>
<td>11.1</td>
<td>11.1</td>
<td>8.5</td>
<td>0.46</td>
</tr>
<tr>
<td>PCI (%)</td>
<td>79.4</td>
<td>77.8</td>
<td>78.3</td>
<td>0.74</td>
</tr>
<tr>
<td>CABG (%)</td>
<td>11.1</td>
<td>11.1</td>
<td>8.5</td>
<td>0.46</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>43.3</td>
<td>43.3</td>
<td>43.3</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Conclusion: In AMI pts with MVD undergoing PCI with DESs, CR strategy seems to be safe and effective similar as the CLR strategy at cumulative clinical outcomes up to 12 months.

Unjustified age and gender differences in discharge treatment after acute ST elevation myocardial infarction. A French nationwide assessment of quality of care

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Background: Women & older patients receive fewer effective treatments at discharge after acute myocardial infarction (AMI) but it is unclear whether this is justified by contra-indications.

Methods: Three consecutive nationwide campaigns evaluating quality of discharge prescription after AMI were performed by the French National Authority for Health (HAS) in 2008, 2009 and 2010. In all centres admitting >10 AMI pts and who participated in all 3 campaigns, pt records were randomly selected. Contra-indications and prescriptions were recorded. Appropriate prescription (AP) of aspirin, clopidogrel, beta blockers, statins and ACEI was considered if drug was prescribed in absence of a contra-indication, or not prescribed in the presence of a contra-indication. A composite indicator was calculated ("all or none" method). Adjusted odds ratios (OR) for the composite indicator were calculated by gender and age class (quartiles).

Results: In total, 39777 records were examined from 291 centres in 2008 (n=14644), 2009 (n=11638) and 2010 (n=13495). Average AP rates were 97.9% for aspirin, 94.2% clopidogrel, 89.3% beta-blockers, 89.4% ACEI, 93.3% statins, 72.9% for the composite with a significant increase from 2008 to 2010. After adjustment for center volume of activity (>50 AMI/year), center type (university, non-university public, non profit private, private) and year, failure of AP for all secondary prevention treatments was 26.6% higher in women, and 2.7 times higher in patients >80 years vs those >55 years. No sex-age interaction was found, except for beta blockers, where gender difference disappeared with older age.

Conclusion: In this nationwide quality assessment program, women and older patients received suboptimal secondary prevention treatment that was not explained by contra-indications.
Female gender as independent predictor for early mortality in patients treated with primary percutaneous coronary intervention: influence of treatment delays

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Purpose: Women have shown inferior outcomes after acute myocardial infarction compared to male counterparts. Risk factor clustering, diffuse microvascular disease and higher rates of bleeding complications are among possible explanations for this. The connection between gender and mortality after primary percutaneous coronary intervention (PCI) has not been fully elucidated. We sought to evaluate influence of gender on outcome after primary PCI for ST-elevation myocardial infarction (STEMI).

Methods: In 3 tertiary centers in the Netherlands, all patients treated with primary PCI for STEMI were enrolled in a prospective registry. In a retrospective analysis, patients were stratified according to gender. Predictors of mortality were assessed univariately with Cox proportional hazards models. Significant predictors (p<0.01) were added to multivariable models. Mortality rates were obtained through municipality records.

Results: In total, 840 (25.1%) women underwent primary PCI compared to 2506 men. Women were older (67.5 yrs vs. 61.8 yrs, p<0.001) and showed more insulin-dependent diabetes, hypertension, history of malignancy and cardiogenic shock on presentation. Men were more often smokers and more frequently had a previous infarction, coronary intervention, bypass surgery or peripheral vascular disease. Women showed higher symptom-to-ballon (median 193 min. vs. 176 min., p=0.002) and diagnosis-to-balloon times (median 81 vs. 78 min., p=0.046) while door-to-balloon times were balanced (median 47 min). Culprit location, number of vessel disease and TIMI flow post-procedure were comparable. All-cause 7 day mortality was 5.8% in women vs. 3.0% in men, p<0.001; 30 day mortality 7.5% vs. 3.8%, p<0.001 and 1 year mortality 9.9% in women and 6.7% in men. Landmark analysis (at 30 days) showed stable mortality rates until 1 year follow-up between men and women. Multivariable cox model, corrected for univariate predictors of mortality including age; diabetes; previous MI; peripheral vascular disease; previous stroke; renal disease; previous malignancy; cardiogenic shock; out-of-hospital cardiac arrest; showed that female gender is predictive for 30 day mortality (HR 1.48, 1.02-2.14, p=0.039). Adding durations of treatment delay did not influence the model.

Conclusions: Female gender is independently predictive for 30 day mortality. After initial higher mortality, rates between men and women stabilize up to one year follow-up. Cause of early mortality in women is likely multifactorial. Lowering treatment delays may prove beneficial, although an effect on mortality through modeling was not observed.
with STEMI, and also examined variables accountable for any differential findings that early post-menopausal females have a relatively lower risk of adverse events in comparison to pre-menopausal or elderly women deserves further investigation.
PPCI in STEMI patients: the impact of female gender

Methods: 316 female and 998 male patients presented to our haemodynamic center with STEMI and treated with primary percutaneous coronary intervention (PCI) were consecutively enrolled from December 2001 to June 2011. CIN was defined as an increase of > 0.5 mg/dl compared with baseline creatinine.

Results: The incidence of CIN was 13.8% (181/1314). There were no significant differences regarding baseline creatinine, volume of contrast injected, percentage of patients with anterior AMI and with multivessel coronary artery disease. However, mean age was significantly higher in female (71.1±13.1 vs. 62.5±12.8 years; p<0.001), while pre-procedural ejection fraction (43.3±11.2 vs. 44.9±9.8%; p=0.03) and pre-procedural haemoglobin (12.6±1 vs. 14.1±1.9 g/dl; p<0.001) were significantly lower in women than in men. Diabetes was more represented in female (20.2 vs. 15.1%; p=0.036) and even patients presenting with shock were significantly more in women than in men (14.5 vs. 9.2%; p=0.006). A multivariable logistic regression analysis demonstrated that the independent factors able to influence CIN incidence were: the value of Mehran risk score (OR 1.05; 95%CI: 1.03 to 1.08; p=0.006); female gender (OR 1.62;95%CI: 1.12 to 2.34; p=0.011) and the absence of a pre-medication with a double antiplatelet therapy (OR 1.71; 95%CI: 2.51 to 2.39; p=0.002).

Conclusions: Our results are in line with the hypothesis that female gender was an independent prognostic factor able to significantly influence the development of CIN in patients with STEMI treated with primary PCI.

PHARMACOLOGIC MANIPULATIONS DURING PERCUTANEOUS CORONARY INTERVENTION FOR ST-ELEVATION MYOCARDIAL INFARCTION

Lower SYNTAX score is a risk of slow-flow phenomenon in patients with acute coronary syndrome

Methods: Subjects were 90 consecutive patients with acute coronary syndrome who underwent emergent PCI from July 2010 to February 2012. Coronary lesion complexity was evaluated by the SYNTAX score. Slow-flow phenomenon was defined as thrombolysis in myocardial infarction (TIMI) grade 0, 1 or 2 flow on angiography during PCI with no evidence of mechanical vessel obstruction.

Results: Slow-flow during PCI was observed in 18 patients (20.0%). Patients with slow-flow presented significantly lower SYNTAX score than patients without slow-flow (12.2±8.3 vs 21.1±12.1; p=0.019). According to logistic regression analysis, the SYNTAX score was an independent negative predictor of slow-flow phenomenon (Odds ratio 0.926, 95%CI 0.865-0.990; p=0.025).

Conclusions: The SYNTAX score may be useful in predicting high risk subset of slow-flow among patients with acute coronary syndrome.

Reperfusion in acute miocardial infarction with ST elevation more than 12 hours after the onset of symptoms

Methods: The data from 789 patients hospitalized with STEMI in 2010 were analyzed retrospectively. Among the 101 patients (12.8% of the total) admitted more than 12 hours from symptom onset (excluding those with cardiogenic shock or/and prior thrombolysis), 41 underwent PCI with stenting (the invasive group) and 60 were treated conservatively (the conservative group). The groups were comparable in baseline clinical and infarct characteristics.

Results: Hospital mortality was lower in the invasive group (7.3% vs. 11.7%), but this difference was not significant. There was no recurrence of infarction in either group. The incidence of post-infarction angina was significantly lower in the invasive group (0% vs 41.7%; p<0.01). The total of in-hospital cardiovascular events (death, post-infarction angina, recurrence of infarction) was also lower in the invasive group (7.3% vs. 53.3%; p<0.01).

Conclusion: Revascularization (PCI) in patients with STEMI admitted more than 12 hours after the onset of symptoms may lead to improved in-hospital outcomes, first of all due to reduction in the rate of post infarction angina.
and management of AMI patients treated with prasugrel in a real world context, and to determine compliance with the recommended indications.

Methods: FAST-MI 2010 is a nationwide French registry that included 4168 patients with AMI in 213 centres. Appropriate prescription was defined as prescription of prasugrel in patients submitted to PCI, and in patients < 75 years of age and ≤ 60 kg body weight, with no history of stroke or transient ischemic attack (TIA). We noted whether prasugrel was administered pre- or post-coronary angiography (CAG).

Results: In total, 4115 received thienopyridines, of whom 1259 received prasugrel (31%). Among those treated with prasugrel, 96.6% underwent CAG, 94% underwent PCI; 0.8% underwent CABG; 4% were ≥ 75 years and 3% were < 60 kg: prior stroke/TIA was present in 1%. Overall, 92% of prasugrel prescriptions were appropriate.

In 1040 pts in whom timing of first prasugrel dose was known, 44% received it before CAG. Compared with post-CAG administration, pre-CAG administration was associated with a 9.6% increase in cardiovascular complications (9.3% vs 4.9%, p = 0.006) and a trend towards increased major bleeding (0.9% vs 0.2%, p = 0.10); a trend towards less stent thrombosis (0.4% vs 1.4%, p = 0.13) and recurrent MI (0.7% vs 2.0%, p = 0.06). There was no difference in inhospital death (0.4% vs 0.5%, p = NS).

In-hospital death was 0.3% in those with appropriate prescription of prasugrel vs 2.0% in those with non-appropriate prescription (p = 0.009); recurrent MI was also less frequent (0.6% vs 1.7%, p = 0.03), as was stroke (0.4% vs 2.0%, p = 0.009). TIMI major bleeding (0.3% vs 2.0%, p = 0.009) and a trend towards minor bleeding (1.4% vs 3.0%). Stent thrombosis did not differ (1.1% vs 1.0% in appropriate vs non-appropriate prescription).

Conclusion: Over 90% of prasugrel prescriptions were appropriate, although >40% received the first dose before CAG. Major cardiac events were more frequent in patients with non-appropriate prescription. Pre-angiography prescription was associated with more bleeding complications, and trends to lower risk of ischemic events, with no difference in mortality.

Transportation to primary percutaneous coronary intervention is a strong independent predictor of functional status after myocardial infarction

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Aim: Subjective symptoms represent significant criteria of a patient's health condition; thus, we focused on long-term prevalence of heart failure symptoms and angina pectoris after myocardial infarction between two groups of patients, in which two different therapeutic strategies were used during the acute phase of a ST elevation myocardial infarction (STEMI).

Methods: The PRAGUE 2 study enrolled 850 patients with STEMI. The patients were randomized into two groups – transport to a primary percutaneous coronary intervention center (pPCI) (n = 429) vs. fibrinolysis in community hospitals (n = 421). The data was collected from primary hospitals and PCI centers or with questionnaires.

Results: The mean follow-up was 58 months. At 5 years, 45.4% of patients after primary PCI presented symptoms of angina pectoris vs. 58% of those treated with fibrinolysis (OR 0.47, 95% CI 0.29-0.76, p < 0.001). At 5 years, 83.6% of patients after invasive therapy had no symptoms of angina pectoris vs. 58% of those treated with fibrinolysis (OR 4.47, 95% CI 2.79 - 7.18, p < 0.001).

Conclusions: The symptoms of angina pectoris and heart failure were significantly lower in patients assigned to pPCI in the acute stage of myocardial infarction compared with patients treated with fibrinolysis at the 5-year follow-up.

Efficacy of modified release trimetazidine in the real clinical practice in the Russian study “perspective”

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Aim: To investigate the dynamic of angina attacks (AA), left ventricular ejection fraction (LVEF), erec tissue dysfunction (ED), clinical complications after one year trimetazidine MR (TMZ MR) consumption in stable angina (SA) patients (pts) of Canadian Cardiovascular Society (CCS) functional class II-II in real clinical practice. Results: 981 pts with SA (mean age 57.8±0.2) and heart failure (HF) of NYHA functional class II-II or type 2 diabetes, or chronic obstructive pulmonary disease from 40 Russian cities were randomized into two groups: a group of active treatment (n=838) receiving TMZ MR 36 mg twice daily on top of standard therapy, and a control group receiving only standard treatment (n=143). Clinical examination and questionnaire survey of patients were performed at 2, 6 and 12 months.

Results: Treatment with TMZ MR was associated with a reduction in the frequency of AA and nitroglycerin tablets consumption (TNT) by 42% and 41%, respectively, at 2 months and by 70% and 68%, respectively at 12 months (p < 0.0001). It resulted in a 1.6 fold reduction in the number of functional class III/IV pts and a 7 fold increase in the number of functional class I/II pts. In the control group there were no significant changes in the frequency of AA and TNT after 12 months of treatment. Treatment with TMZ MR was also associated with a reduction in the corrected QT interval of ECG from 0.39±0.05 to 0.34±0.14 sec (p = 0.05) at 12 months.

LVEF significantly increased by 4.6% (p = 0.05) in the TMZ MR group after 12 months. Among those treated with the control group, the International Index of Erectile Function (IIEF) Questionnaire revealed a decrease in the severity of ED after 12 months in the TMZ MR group. The proportion of pts hospitalized with cardiovascular complications during 12 months of follow-up was lower in the TMZ MR group (13.9%) than in the control group (25.29%, p<0.007). The proportion of pts registered as a disabled person was 5.7% vs 12.6%, p=0.017, respectively. Overall, there was an improvement in clinical status in 77.2% of pts of the TMZ MR group vs 12.6% of patients of the control group (p<0.017).

Conclusion: Treatment with trimetazidine MR in SA pts with concomitant diseases and syndromes in real clinical practice settings in different regions of Russia resulted in an improvement of clinical status of pts, which was accompanied by a lower number of cardiovascular complications and hospital admissions.

Anxiolitics decrease cardiovascular events during upper gastrointestinal endoscopy (UE) in patients with coronary artery disease

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Background: Although UE is usually considered to be a safe procedure, arrhythmias and ischemic events occur in 38.5% to 75% of cases, especially in elderly people with coronary artery disease (CAD). Cardiovascular events occurring during UE have been attributed to fear, anxiety and catecholamine secretion.

Aim: To observe if giving anxiolitics prior to UE in elderly patients with CAD protects against arrhythmias and/or ischemic events.

Method: 80 patients aged over 60’s, matched by sex, BMI, severity of cardiac disturbances and ECG features were randomized in 2 groups: patients from the first group (n=45) received lorazepam 1mg, and patients from the second group (n=45) received placebo 1 hour before UE. We compared the frequency of ECG changes occurred during and immediately after UE, ECG recordings were made starting 1 hour prior to the procedure, during UE and within 1 hour after the procedure, using the continuous Holter ECG recorder.

Results: Arrhythmias and ischemic ST-T changes were significantly less frequent in patients with CAD pre-treated with anxiolitics (p<0.0023, CI 95% 34.99-105.49, respectively p<0.0044, CI 95% 25.12-78.102).

Conclusion: Our study results suggest that the sympathetic nervous system activated by fear and anxiety triggering arrhythmia and underlying ischemia can be counteracted by anxiolitics given 1 hour before UE in patients with CAD.

Bibliography:

Risks and benefits of thrombolytic, antiplatelet and anticoagulant therapies in acute coronary syndromes with ST segment elevation: systematic review and meta-analysis


Introduction: ST-elevation myocardial infarction (STEMI) is responsible for high morbidity and mortality, and new classes of drugs are being added to its treatment over time. The real benefit versus the bleeding risk of the associations is not yet known, given the large diversity of regimens and doses.

Objectives: Assess, by systematic review, the impact of the progressive addition of thrombolytics, anticoagulants, antiplatelets and primary PCI on 30-day outcomes: death, reinfarction (AMI) and major bleeding (MB) in patients with STEMI.

Methods: A Medline search with the words “acute”, “myocardial infarction/therapy” was performed, to identify randomized trials comparing these combinations of drugs in adults with STEMI, at least 500 patients. The study should provide death, AMI and MB rates. Similar arms were grouped, and the correlation between progressive addition of drugs, number of drugs and primary PCI and the outcomes were evaluated by Spearman coefficient and multivariate regression analysis as well as the correlation between the year and era of the study and the outcomes.

Results: The search resulted in 2313 articles; 59 remained after exclusions. 404.556 patients, with mean follow up time of 23.3 days, were divided into 35
groups of treatment arms. There was a trend towards the correlation between gradual introduction of drugs (12 groups) and death (r = -0.564, p = 0.056) and MB (r = -0.571, p = 0.053). There was significant correlation between the number of drugs and the rates of death (r = -0.466, p = 0.009) and MB (r = -0.403, p = 0.016), confirmed by multivariate regression model. This model also showed that primary PCI had additional benefit over mortality compared to the number of drugs, as well as increased MI risk. The results of the study had significant correlation with the 3 outcomes assessed: death (r = -0.380, <0.001), MB (r = -0.212, p = 0.014) and AMI (r = -0.231, p = 0.009), as well as the era of accomplishment.

Conclusion: The increasing complexity of STEMI treatment resulted in significant reduction in mortality and increased rates of MB, that does not nullify the net clinical benefit. There is correlation between the year and the age of the study and reduction of mortality and AMI, with a concomitant increase in MB.

P2724
Primary PCI in the elderly: a comparison of intravenous enoxaparin versus unfractionated heparin in the randomized atoll trial
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Background: Anticoagulation of elderly patients (>75y) remains poorly evaluated in primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI). Intravenous (IV) enoxaparin does not need adjustment or monitoring in the elderly.

Objectives: To evaluate the efficacy and safety of enoxaparin versus unfractionated heparin (UFH) in the elderly group of patients of the ATOLL international randomized trial.

Methods: 165 elderly STEMI patients, received an IV bolus of 0.5 mg/kg of enoxaparin (n=85) or UFH (n=80) before primary PCI. The primary end point (EP) was the 30-day incidence of death, complications of myocardial infarction (MI), procedure failure, or major bleeding. The secondary EP was the composite EP of death, recurrent ACS or urgent revascularation.

Findings: Mean age was 80.1 y/o, with 47.3% (n=76) of women. Radial access was used in 62.4%, of and Ilibilla inhibitors were used in 73.9%. The primary end point occurred in 37.6% (n=32) of patients with enoxaparin vs. 47.5% (n=38) with UFH (RR 0.79; 95% CI, 0.55 to 1.33; P=0.20). Enoxaparin resulted in a significantly lower rate of the main secondary EP (RR 0.42; 95% CI 0.21 to 0.87; P=0.015). The net clinical benefit combining death, complications of MI or major bleeding (RR 0.55; 95% CI 0.31 to 0.98; P=0.04) was reduced with enoxaparin as well as other ischemic EP (figure). Major bleedings did not differ between the 2 groups but minor bleeding was lower on enoxaparin (p=0.002).

Interpretation: In ATOLL, elderly patients were at high risk of death (15.5%) and still had primary PCI performed predominantly through a radial access (62.4%). The results are consistent with the main findings of the study, IV enoxaparin being superior to UFH in reducing all ischaemic events.

P2725
The benefit of beta-blocker therapy in hospital survivors receiving primary percutaneous coronary intervention after ST-elevation myocardial infarction from the Korea Acute Myocardial Infarction Registries
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Purpose: Beta-blockers (BBs) has been long been recommended for the treatment of ST-elevation myocardial infarction (STEMI) in the current guidelines. However, the efficacy of BBs therapy in STEMI patients who underwent primary percutaneous coronary intervention (PCI) is controversial. Moreover, the benefit of BBs therapy in hospital survivors who underwent primary PCI has not been fully investigated.

Methods: Between November 2005 and January 2008, 2,688 hospital survivors (2,049 men; mean age = 60.6±12.5 years-old) who had an STEMI with a symptom-to-door time of 12 hours and underwent primary PCI were analyzed from the Korean AMI registry. Patients who received BBs therapy before hospitalization were excluded from this study. The 12-month MACE was defined as a composite of death, non-fatal MI, and repeat revascularization.

Results: Of these patients, BBs were used in 2,042 (76.0%) hospital survivors. Patients receiving BBs were younger with less dyspnea at presentation, higher body mass index, longer symptom-to-door time, higher systolic and diastolic blood pressure, higher left ventricular ejection fraction, and higher serum levels of glucose, total cholesterol, and triglyceride. Ventricular arrhythmia during hospitalization was less frequently observed in BBs patients. In Cox proportional-hazards model, there was no significant difference in the 12-month MACE between BBs patients and no-BBs patients (9.9% versus 11.1%; crude hazard ratio [HR] 0.864, 95% confidence interval [CI] 0.660–1.131; p=0.627). The 12-month mortality was significantly lower in BBs patients compared with no-BBs patients (2.5% versus 3.3%; crude HR 0.498, 95% CI 0.302–0.820; p=0.006). Propensity scores (PS) for BBs use was calculated for each of the patients, and was used to match 604 patients not receiving BBs with 604 patients receiving BBs. During the follow-up, 126 (10.4%) MACEs and 37 (3.1%) deaths from any cause occurred in the matched cohort. In Cox proportional-hazards model, there were no significant differences in the rate of 12-month MACE (10.6% versus 10.3%; HR 1.030, 95%CI 0.726–1.460; p=0.869) and mortality (2.8% versus 3.3%; HR 0.850, 95%CI 0.445–1.622; p=0.621) between BBs and no-BBs patients.

Conclusions: The benefit of BBs therapy might be less cardioprotective in hospital survivors with STEMI who underwent primary PCI. Further studies are required in these patients.

P2726
Bolus injection of sodium bicarbonate improves clinical outcomes in patients with chronic kidney disease undergoing an emergent coronary procedure
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Background: Bolus injection of sodium bicarbonate (SB) has been suggested as a possible strategy for prevention of contrast-induced nephropathy (CIN) in patients with chronic kidney disease (CKD) undergoing emergency coronary procedure. However, there is no information available on the effect of SB bolus injection on long-term clinical outcomes in CKD pts with emergency coronary procedure.

Method: We enrolled 59 CKD pts (eGFR=60ml/min/1.732) with an emergent coronary procedure. These patients were randomized to receive a bolus of 154 mEq/L SB (n=30) or sodium chloride (SC=n=29) at the dose of 0.5ml/kg for 6 hours in both groups. Serum creatinine (Cr) levels were measured at baseline, 3 days after the contrast administration and repeated every several month.

Results: Baseline characteristics were similar between SB and SC groups. In SC group, Cr significantly increased 3 days after the contrast administration and remained higher at the last follow-up day, whereas SB group had no significant increase in Cr level. During the follow-up period of 14±11 months, the incidence of renal replacement therapy and death was significantly lower in SB than SC groups (10% vs 33%, p=0.014, HR:0.31, 95% CI 0.09 to 0.99).

Conclusion: SB Bolus injection would preserve not only short- and long-term renal function but also would reduce the risk of death and renal replacement therapy in CKD pts undergoing an emergent coronary procedure.

P2727
Comparison of primary versus percutaneous coronary intervention in patients with very early acute myocardial infarction

Background: Recent studies reported that facilitated percutaneous coronary intervention (PCI) with tissue-type plasminogen activator (tPA) for acute myocardial
infarction (AMI) did not improve the clinical outcomes. However, majority of previous trials targeted patients treated within 6 or 12hrs from onset. Furthermore, in those studies,facilitated PCI results in a relatively lower rate of initial Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow. Pamiteplase, one of mutant t-PAs widely used in Japan, is known to have lower risk of bleeding complication than other t-PAs, because of superior fibrin affinity. We conducted this study to elucidate the safety and efficacy of pamiteplase-facilitated PCI in very early, first-anterior-AMI patients.

Methods: We randomly assigned 81 patients with first-anterior ST-elevation AMI (STEMI) treated within 3-hours from onset, to receive primary PCI (primary group, n=41) or PCI preceded by intravenous administration of half to full dose pamiteplase; facilitated PCI (pamiteplase group, n=40). The clinical outcomes were then evaluated.

Results: Clinical characteristics were similar between the two groups, including onset to balloon time, pre-infarction angina, Killip class, and the risk factors. Pamiteplase group achieved significantly higher rate of TIMI grade 2 flow or more at the first angiography (73% vs 24%, P < 0.001) and complete ST-resolution (80 vs 59%, P = 0.05). Peak CK-MB was significantly lower in pamiteplase group (329 ± 294 vs 377 ± 285, P < 0.001). Major or minor bleeding complications in hospital stay and major adverse cardiac events(MACE) within 6-months were comparable between the two groups(pamiteplase group vs primary group,5 vs 12%, 3 vs 12% respectively). Additionally, 29 patients who obtained initial TIMI≤2 grade in Pamiteplase group showed significantly better left ventricular ejection fraction (LVEF) after 6-weeks (57 ± 11 vs 51 ± 15, P < 0.001), and lower MACE within 6-months (0 vs 13%, P < 0.05), compared with primary group.

Conclusions: In early first-anterior-AMI patients, pamiteplase-facilitated PCI did not increase bleeding complication, and was associated with higher incidence of initial TIMI grade 2 or more flow, preservation of LVEF, and lower MACE. It might be useful in such high-risk early ST-elevation AMI patients.
in Sao Paulo STEMI mortality is still around 15%. In a 10 million inhabitants metropolis it is difficult to have immediate primary PCI as recommended by guidelines; alternatives should be looked for.

**Aims:** To define if a specific program of training health personnel for recognizing STEMI and providing tenecteplase (TNK) and immediate transfer to a tertiary care general hospital would decrease 30-day and follow-up mortality in STEMI patients originating from public emergency rooms (ERs) from the outskirts of town.

**Methods:** From February 2010 to January 2012 STEMI patients with less than 12 hours of symptoms from five public ERs on the outskirts of town or from SAMU ambulances received either TNK or, depending on traffic conditions, were transferred for primary PCI. After TNK there was immediate transfer in all cases to a tertiary care general hospital for rescue or systemic elective coronary angiography (cath) 6-24 hours after fibrinolytic therapy (pharmacoinvasive approach – PIA).

**Results:** In the study period 320 patients, ranging from 32 to 89 years-old, were treated as per protocol with 79% utilizing PIA route and 21% undergoing primary PCI; angiography was performed in 95% of the sample, TIMI 3 flow occurred in 59% of TNK cases and rescue angioplasty was necessary in 18% and major bleeding in 14% of those patients.

**Conclusions:** This initial experience with PIA, treating patients with low-income and from the periphery of a large city, seems to provide adequate immediate and short-term follow-up results, most of all considering previous recent experience in this population. Training to improve fast recognition of STEMI, use of TNK, rapid cath and systemic 6-24 hours catheterization contributed to improve results. Expansion of the program is ongoing.

**Effect of nicorandil on clinical outcomes in patients with ST-segment elevation myocardial infarction: analysis from the Korea Acute Myocardial Infarction Registry**


**Background:** Nicorandil has cardioprotective effect in the ischemic myocardium because of ischemic preconditioning, reduced myocardial necrosis and improved coronary artery reperfusion. There are rare large studies whether nicorandil is effective in patient with ST segment elevation myocardial infarction (STEMI) and non ST segment elevation myocardial infarction (NSTEMI).

**Method:** 6370 patients with STEMI in Korean Acute Myocardial Infarction Registry (KAMIR) were divided to two groups: a group with nicorandil (n=1,313, Group N) and a group without nicorandil (n=5,057, Group C). We analyzed for death and myocardial infarction and composite of major adverse cardiac events (MACE) at 1, 6 and 12 month.

**Results:** There are no differences of baseline characteristics, angiographic finding and medication between each group. At 1 month, Group N is significant low incidence of MACCE, compared to Group C. (Composite MACE: 2.2% vs. 4.1%, p<0.001, Cardiac death: 1.1 vs. 1.8, p=0.068, MI: 0.1 vs. 0.5 p=0.019). At 6 month, Group N shows a significant low incidence of MACE, compared to Group C (Composite MACE: 8.1% vs. 10.1%, p=0.047, Cardiac death: 1.7 vs. 2.7, p=0.054, MI: 0.1 vs. 0.9 p=0.002). However, at 12 month, Group M is not significant difference in incidence of MACCE, compared to Group C. MI is low in Group N (Composite MACE: 13.8% vs. 15.1%, p=0.374, Cardiac death: 2.8 vs. 3.8, p=0.163, MACE in: 0.4 vs. 1.2 p=0.046). In patients with NSTEMI do not show difference of clinical outcomes at 1, 6 and 12 month.

**Conclusion:** Administration of nicorandil in patients with STEMI reduced MACE, cardiac death and MI. Nicorandil mainly improved short-term clinical outcome on the STEMI. But, Nicorandil didn’t have an effect on clinical outcome on the NSTEMI.

**Use of bivalirudin during primary PCI in clinical practice: results from the PCI registry of ALKK**

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**Background:** In randomized controlled trials treatment with bivalirudin compared with unfractioned heparin (UFH) and a glycoprotein (GP) IIb/IIIa receptor blocker resulted in a significant reduction in major bleeding with similar rates of ischaemic events in patients with ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). So far, little is known about its use and effectiveness in clinical practice.

**Methods:** We analyzed data from the German PCI registry of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausarzte (ALKK) from 2010. A total of 4,271 primary PCIs conducted in 38 hospitals were prospectively enrolled into the ALKK-PCI registry. In 218 procedures (5.0%) patients were treated with bivalirudin. 13 out of 36 hospitals (34.2%) used bivalirudin (range: 6%–47%). In 2010 an increase in the use of bivalirudin could be seen, blood samples: 2006: 0.7%, 2007: 0.4%, 2008: 0.2%, 2009: 0.4%, 2010: 5.0%). Patient and intervention characteristics as well as hospital outcome are displayed in the table below.

**Conclusion:** In clinical practice only a minority of STEMI patients treated with primary PCI received bivalirudin. However, in comparison to previous years its use has markedly increased. Patients treated with bivalirudin were more likely to be treated with prasugrel and less likely with clopidogrel, UFH and GP IIb/IIIa receptor blockers. Patients characteristics and in-hospital outcome did not significantly differ between those with and without bivalirudin.
group experienced nausea (58% v 20%, p = 0.015), no decrease or cessation of exenatide was required. Infarct size, cardiac function and myocardial salvage at 4 months did not differ significantly. However, a trend towards a lower infarct size as a percentage of the area at risk was seen in patients with TIMI 0 and 1 flow receiving exenatide (0.35±0.14 vs 0.47±0.17 (n=11), p=0.09).

**Conclusions:** We demonstrated that administering exenatide in patients with acute MI undergoing primary PCI is feasible and safe. Although not powered for this analysis, EXAMI phase I seems to show a trend towards a higher myocardial salvage in the exenatide group. A large randomized placebo controlled study is required to assess the efficacy of exenatide on myocardial salvage.

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**P2735**

**Safety and efficacy of the radial approach for emergency percutaneous coronary intervention in ST-segment elevation acute myocardial infarction**


Transradial approach (TRA) to percutaneous coronary intervention (PCI) offers several advantages over the traditionally used transfemoral approach (TFA). It is particularly attractive for patients undergoing emergency PCI (E-PCI) for ST-segment elevation acute myocardial infarction (STEMI-AMI), since bleedings are the most common complications and a relevant cause of associated morbidity and mortality. Nevertheless, its safety and efficacy in this setting is controversial. To evaluate this fact, 641 STEMI-AMI patients undergoing E-PCI were analysed: primary PCI in 493 (76.9%) and rescue PCI for failed thrombolysis in 148 (23.1%). The analysis was performed in 398 patients (48.2%). Mean age was 63±12.5 years. Women were more prevalent in the TFA group (22 vs 15.9%; p=0.04) without differences in the other basal clinical variables. Abaximab, use, number of diseased vessels, contrast volume, fluoroscopy and procedure time were similar. Access-site crossover was infrequent and similar in both groups. Percutaneous closure device was used in 62.8% of patients in TFA group. Procedural success rate (defined as final TIMI flow grade 2-3 in the infarct related artery) was higher in the TFA group. PCI was deferred for significant residual no in infarct related lesions more frequently in TFA group. Despite this fact, hospital stay of the TFA group was longer. Incidente of in-hospital complications was lower in the TFA group, mainly due to vascular access site complications.

**Use of TRA for E-PCI in patients with STEMI-AMI was associated with fewer inhospital complications and a shorter length of hospital stay, with a similar success rate than TFA. So, TRA could become the preferred approach in this setting.**

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**P2737**

**Effectiveness of upstream use of prasugrel in ST-segment elevation myocardial infarction**

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**Background:** Prasugrel is a potent and rapid P2Y12 inhibitor. However, very little is known about the biological effectiveness of upstream prasugrel (P2Y12) use in STEMI-AMI. The aim of this study is to evaluate the efficacy of upstream use of prasugrel in STEMI-AMI patients at the time of primary percutaneous coronary intervention (PCI).

**Objective:** Using the P2Y12 point-of-care assay, we assessed prasugrel responsiveness at the beginning of PCI.

**Methods:** We conducted a prospective, single-center, observational study and compared the effects of intracoronary administration of prasugrel for upstream STEMI-AMI patients operated during first two days and those operated after first two days after onset of rupture. STEMI-AMI patients were included in the analysis. The mean time between symptom onset and prasugrel ingestion was 196±191 min and between prasugrel ingestion and platelet reactivity measurement was 103±129 min. The mean P2U was 244±114 in 17 patients (36%) exhibiting low residual platelet reactivity at start PCI. Presenting TIMI-3 flow of the IRA was observed in 14.1% of the patients. TIMI-2 flow in 7.0%, TIMI-1 flow in 14.3% and TIMI-0 flow in 65.1%.

**Conclusion:** In STEMI patients undergoing PCI with contemporary antiaggregation regimens, platelet responsiveness to upstream prasugrel was only sufficient in approximately 40% at the beginning of intervention. These findings support the use of glycoprotein IIb/IIIa inhibitors during PCI.

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**P7238**

**Surgical repair of interventricular septal defect in acute myocardial infarction: clinical characteristics and main determinants of early survival**

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**Object:** Despite great progress in cardiology, mortality of patients in whom rupture of interventricular septal defect is accompanied by complex of acute myocardial infarction, is still very high. Our aim was to analyze clinical characteristics and main determinants of early survival in patients in whom surgical repair of ventricular septal defect in acute myocardial infarction was performed.

**Methods:** In our work we analyzed group of consecutive patients diagnosed with rupture of interventricular septum in acute myocardial infarction in the period of 20 years (January 1989 – June 2009) From 74 patients with this complication 32 underwent surgical repair (Male 20, 62, 1±7.8 years old).

**Results:** Mean systolic arterial pressure on admission was 111±32.06 and before surgical treatment 98.8±31.4 (p 0.0001). Poorer prognosis was observed in patients who received thrombolytic therapy in myocardial infarction (p 0.005). In 62.5% of patients coronary angiography showed multivessel coronary artery disease. Surgical treatment of rupture of interventricular septum was performed in the course of first seven days in 16 patients (50%) and most of them were operated on the 4th day after onset of rupture. There was significant difference in early mortality for patients operated during first two days and those operated after 2nd day of rupture of interventricular septum (24.1% and 75.86% respectively, p=0.002). In 16 patients myocardial revascularization with one or more coronary artery bypass grafts was performed. There was no significant difference in early survival comparing with patients with only isolated repair of interventricular septal defect. In half of surgically treated patients extracorporeal circulation time was longer than 100 minutes and mean aortic clamp time was 77.1±3.7. 21, Early, 30th day mortality was 4.6%.

**Conclusions:** Early operative treatment of rupture of interventricular septum tends to increase 30th day survival. Hemodynamic state oh admission was main independent predictor of early survival.
Right ventricular strain analysis is a stronger predictor of outcome than left ventricular analysis in patients with advanced heart failure referred for heart transplantation.

Background: The incremental value of left atrial (LA) deformation analysis by speckle tracking echocardiography (STE) has not been evaluated prospectively.

Methods: This prospective study included 312 adults (mean age 71±6 years, 56% males) in sinus rhythm who were followed for development of first AF, conge...
Reduced right ventricular longitudinal strain in patients with preserved right ventricular function and left ventricular dysfunction: a study using conventional and strain imaging method

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Background: The right ventricle (RV) plays an important role in patients with cardiopulmonary disease. Patients with left ventricle (LV) dysfunction secondary to myocardial infarction or heart failure are at increased risk for both RV dilatation and dysfunction. Indeed, RV dysfunction is one of the most powerful independent predictors of mortality in patients with chronic heart failure. It is known that longitudinal strain measurement of the left ventricle detects abnormal longitudinal function of the subendocardial level at an earlier stage. There are no data about longitudinal strain of the RV. We therefore examined RV function examined RV function using conventional echocardiographic and strain imaging techniques.

Methods and Results: We examined 30 patients with conventional echocardiography, according the recently published guidelines of the assessment of the right heart in adults, and strain imaging using the speckle tracking method. There were 2 groups of 15 patients each, group 1 with reduced LV ejection fraction (LVEF) and group 2 with normal LVEF. The aim of the study was to delineate parameters of RV function in patients with versus without LV dysfunction. There was no significant statistical difference between groups in terms of age (59 ± 12 vs. 58 ± 12), gender (20% vs. 27% female) and septal wall thickness (11.3 ± 0.8 mm vs. 10.6 ± 1.3 mm). Patients in group 1 had a significantly lower LVEF (mean 31 ± 9%, vs. 65 ± 5%, p < 0.01), LVEDV and LVESV in group one was significantly larger (LVEDV 154 ± 72 ml vs. 110 ± 27 ml, p < 0.01; LVESV 77 ± 18 ml vs. 27 ± 8 ml, p < 0.01). The RV was larger (RV base diameter 38 ± 7 mm vs. 32 ± 3 mm, p < 0.01) and thicker (RV thickness 5.9 ± 1.3 mm vs. 4.6 ± 0.8 mm, p < 0.01) in group one. RV function in both groups was not statistically different: mean RIMP 0.41 ± 0.09 vs. 0.38 ± 0.07 (p < 0.02), mean TAPSE 18.3 ± 4.1 vs. 20.6 ± 2.2 (p = 0.06). Despite the normal RV systolic function, the longitudinal strain of the RV free wall was statistically lower in group 1 (mean 16 ± 3.6% vs. 23.6 ± 3.9%, p < 0.01).

Conclusion: In patients with reduced LVEF and preserved RV function, according to conventional parameters (RIMP and TAPSE), there was a significant reduction of the longitudinal strain of the RV free wall compared to the control group with normal LVEF. RV longitudinal strain measurement may detect RV abnormalities at an earlier stage before the RV dysfunction is visible from conventional parameters.

Impact of arterial stiffness on left ventricular longitudinal function in healthy subjects: A speckle-strain imaging study

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Background: An increase in arterial stiffness is an important marker of increased left ventricular (LV) load and worse cardiovascular outcomes. The interaction between arterial stiffness and LV performance is well-known as “ventriculo-arterial coupling”. Myocardial strain is a sensitive parameter of global ventricular function over conventional echocardiographic parameters. However, the impact of arterial stiffness on the LV global strain profiles has not been fully studied. The aim of this study was to investigate the relationship between arterial stiffness and the LV global strain and strain rate (SR) in healthy subjects.

Methods: One hundred male subjects (mean age, 48 ± 12 years, male 59) without atherosclerotic risk factors such as hypertension, dyslipidemia and diabetes mellitus were analyzed. Using speckle tracking analysis, we measured the LV global longitudinal strain (LS), systolic SR and diastolic SR from apical 3 views, and global circumferential strain and systolic and early diastolic SR from the short axis view at the papillary muscle level. We also measured brachial ankle pulse wave velocity (baPWV) as the arterial stiffness parameter immediately after the echocardiographic examination.

Results: The LV global longitudinal strain and systolic and early diastolic SR were significantly correlated with baPWV (r=0.267, p=0.044) and LV mass index (r=0.205, p=0.038) were independent predictors of LV global longitudinal strain. On the other hand, age (beta=0.260, p=0.007) and gender (beta=0.204, p=0.022) were independent predictors of LV global longitudinal early diastolic SR. The baPWV showed a tendency to be a significant predictor of global longitudinal early diastolic SR (beta=0.198, p=0.089).

Conclusion: Our results addressed that arterial stiffening was closely associated with the deteriorated LV global longitudinal systolic function in healthy individuals. In addition, aging and gender mainly affected the LV longitudinal diastolic function.
Conclusion: When image quality is optimal, 3D STE seems to be a rapid and promising approach to assess global and regional LV function and mechanical dyssynchrony.

Impact of septal curvature on regional strain in patients with hypertrophic cardiomyopathy

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A unique shape of the interventricular septum in hypertrophic cardiomyopathy (HC) is characterized by the convex toward the left ventricle (LV). The impact of the shape on regional myocardial function has not, however, been documented. This study was aimed to examine the relationship between curvature of LV wall and myocardial strain.

Methods: Fifty-six patients with HC (age, 55±12 yrs) and 20 age- and sex-matched control subjects were enrolled. The curvature (1/R) was measured by drawing a matching curve in the endocardial surface from the apical 4-chamber view (Fig.1A). Peak values of longitudinal systolic strain (ΔL) and transverse systolic strain (ΔT) were calculated in the septal and lateral wall by the two-dimensional speckle tracking echocardiography.

Conclusion: In heart failure patients, contractile reserve on exercise is a strong independent predictor for death and hospital admissions.

End-systolic pressure-volume relation predicts cardiac events in patients with abnormal ejection fraction and negative stress echocardiography

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Background: A maximal negative stress echo identifies a low risk subset for subsequent events. However, the potentially prognostically relevant information on global contractile reserve of the left ventricle is unsettled.

Aim: To assess the prognostic value of the stress-induced variation in the left ventricular end-systolic pressure-volume ratio (ESPVR) in patients with abnormal (<50%) left ventricular ejection fraction (LVEF) and negative stress echocardiography.

Methods: We enrolled 400 patients (dilated cardiomyopathy, n = 225; ischaemic dilated cardiomyopathy, n = 139; suspected coronary artery disease, n = 36; 306 males, mean age 63±12, ejection fraction 30±9%, with negative (exercise 57, diprydamole 165, dobutamine 160, non-invasive pacing 18) stress echocardio-
graphy result. In all, the ESPVR was determined at rest and at peak stress. Main outcome measures: combined death and heart failure (HF) related hospitalization.

Results: During a median follow-up of 19 months (interquartile range 6-48), 53 deaths (49 cardiac, 4 non-cardiac), and 83 HF-related hospitalization occurred. Event-free survival was higher (p < 0.001) in patients with ΔESPVR (the difference between peak and rest ESPVR) > 0.4 mmHg/mL/m². Multivariable indica-

tors of event-free survival were rest EF (HR 0.955), ACE-inhibitor therapy (HR 0.543), Wall Motion Score Index stress improvement (HR 0.367), and ΔESPVR (HR 0.551). All incremental analysis, ΔESPVR ≥ 0.4 mmHg/mL/m² added prognostic information.

Conclusion: Patients with < 50% rest LVEF despite no inducible ischemia may still experience an adverse outcome related to abnormal contractile reserve, which can be identified by ΔESPVR > 0.4 mmHg/mL/m².

P2751 Prognostic value of the extent of mitral annulus longitudinal excursion in AL amyloidosis

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Introduction and aim: Primary (AL) amyloidosis is a systemic disease caused by the extracellular deposition of insoluble fibrils derived from amyloidogenic immunoglobulin light chains (LC), that are synthesized by clonal plasma cell prolif-
eration in the bone marrow. Although clinical presentation is extremely variable, depending on the organ(s) that are involved by amyloid deposition, cardiac in-
volvement represents the most common cause of death. Despite extensive cardiac involvement, global systolic function is preserved until the later stages of the disease, characterizing a picture of diastolic heart failure with normal ejection fraction. Since regional systolic function may be easily measured by longitudi-
nal excursion of the mitral annulus, aim of the present study was to assess this parameter in AL amyloidosis and to evaluate its prognostic value.

Methods: We enrolled 295 consecutive never-treated subjects, in whom a first diagnosis of primary AL amyloidosis was concluded between 2008 and 2009, according to the International Society of Amyloidosis criteria. Patients in whom cardiac involvement was excluded served as controls (n=121). Systolic function was evaluated as: left ventricular (LV) EF, longitudinal mitral annulus lateral (LAPSE) and septal (MAPSE) excursion. When compared with patients without cardiac involvement, in patients with cardiac AL septal MAPSE was 7.3 ± 2.3 vs 12.4 ± 2.1 mm (p < 0.001), lateral MAPSE 9.3 ± 1.9 vs 14.9 ± 2.4 mm (p < 0.001), whereas tissue Doppler E'-ratio was 0.5 ± 0.1 vs 0.4 ± 0.1 (p < 0.001). Dilated end-diastolic LV volumes (p < 0.001). As expected, diastolic dysfunc-
tion was evident in all cardiac AL patients, as evident by increased E/E' ratio (p < 0.001). Despite preserved global systolic function (i.e. EF > 50%), both M-
Mode and TDI-derived indices of systolic regional function were markedly de-
pressed. When compared with AL patients without myocardial in-
volvement, cardiac AL was characterized by increased wall thickness (p < 0.001) and reduced end-diastolic LV volumes (p < 0.001). As expected, diastolic dysfunc-
tion was evident in all cardiac AL patients, as evident by increased E/E' ratio (p < 0.001). Despite preserved global systolic function (i.e. EF > 50%), both M-

Results: Cardiac AL amyloidosis was associated with marked diastolic dysfunction and preserved ejection fraction. When compared with patients without myocardial involvement, cardiac AL patients showed a marked depression of both MAPSE and LAPSE (7.2 ± 2.3 vs 12.3 ± 2.1 mm, and 9.5 ± 1.9 vs 14.7 ± 2.2 mm, respec-
tively; p < 0.001 for both). After receptor-operated curve analysis to identify the best cutoff value for the diagnosis of cardiac involvement, survival analyses were per-
formed. After a median follow-up of 477 days, Kaplan-Meier survival analysis re-
vealed a significantly higher mortality in the groups with depressed MAPSE and LAPSE (p < 0.001 for both).

Conclusion: Despite preserved ejection fraction, regional systolic function is de-
pressed in cardiac AL amyloidosis. This abnormality can be identified by the sim-
plicity of M-Mode analysis of longitudinal excursion of the mitral annulus. Notably, the extent of longitudinal systolic dysfunction has a profound impact on patients' prog-

P2752 Systolic dysfunction in diastolic heart failure with preserved ejection fraction: the case of cardiac amyloidosis

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Cardiac amyloidosis represents an archetypal form of restrictive heart disease, characterized by profound diastolic dysfunction. Ejection fraction (EF) is usually preserved until the late stage of the disease. Therefore, the majority of patients with cardiac AL amyloidosis do fulfill the definition of diastolic heart failure, i.e. heart failure with preserved ejection fraction. However, systolic regional dysfunc-
tion is well evident when performing echocardiographic or nuclear magnetic reso-
nance studies. To analyze different indexes of echo-derived diastolic and systolic function in a large cohort of cardiac AL amyloidosis patients with preserved ejec-
tion fraction, we enrolled 221 consecutive never-treated subjects, in whom a first diagnosis of cardiac AL amyloidosis was concluded between 2006 and 2009, according to the International Society of Amyloidosis criteria. Patients in whom cardiac involvement was excluded served as controls (n=121). Systolic function was evaluated as: left ventricular (LV) EF, longitudinal mitral annulus lateral (LAPSE) and septal (MAPSE) excursion, isovolumic (IVVm) and systolic (Sm) tissue Doppler peak velocity (E'). Diastolic dysfunction was characterized in terms of: transmitral Doppler early (E) and atrial (A) velocities, E deacceleration time, pulmonary venous flow velocity, early diastolic tissue Doppler peak velocity (E') and E/A ratio. Patients with sig-
ificant valve disease, previous myocardial infarction, atrial fibrillation, or chronic obstructive lung disease were excluded. All patients with EF below 50% (n=20) were also excluded. When compared with AL patients without myocardial in-
volvement, cardiac AL was characterized by increased wall thickness (p < 0.001) and reduced end-diastolic LV volumes (p < 0.001). As expected, diastolic dysfunc-
tion was evident in all cardiac AL patients, as evident by increased E/A ratio (p < 0.001). Despite preserved global systolic function (i.e. EF > 50%), both M-
Mode and TDI-derived indices of systolic regional function were markedly de-
pressed. When compared with AL patients without cardiac involvement, in patients with cardiac AL septal MAPSE was 7.3 ± 2.3 vs 12.4 ± 2.1 mm (p < 0.001), lateral MAPSE 9.3 ± 1.9 vs 14.9 ± 2.4 mm (p < 0.001), whereas tissue Doppler E'/Vann was 10.9 ± 2.6 vs 7.0 ± 2.6 mm/sec (p < 0.001), and Sm 11.5 ± 2.9 vs 8.1 ± 2.5 mm/sec (p < 0.001). All these parameters of systolic regional function were correlated with the severity of cardiac damage, as expressed by NT-proBNP serum levels.

Conclusions: In cardiac AL amyloidosis, diastolic heart failure is characterised by marked regional systolic dysfunction despite preserved ejection fraction.

P2753 Novel continuous monitoring system of cardiac output with use of aortic peak flow velocity and peripheral arterial pressure profile

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Purpose: In managing patients with unstable hemodynamics, monitoring cardiac output (CO) in addition to the arterial pressure is strongly required. However, conventional methods to monitor CO such as the thermodilution pulmonary artery catheter are inaccurate, intermittent, and invasive. The purpose of this study was to validate our newly developed continuous (i.e. automatic) low invasive CO monitoring system, and compare its performance to that of a conventional low invasive CO monitor, the FloTrac/Vigileo system.

Methods: Our system automatically determines peak velocity of the ascending aorta using continuous-wave Doppler transthoracic echocardiography, and car-
diac ejection time and aortic cross sectional area using the pulse contour of the radial arterial pressure. These parameters are continuously processed to esti-
mate CO (COfv). In 8 anesthetized closed-chest dogs instrumented with aortic flow probe to measure “gold standard” reference CO (COref), hemodynamic con-
ditions were varied over wide ranges (heart rate, 66-179 bpm; mean arterial pres-
sure, 66-179 mmHg). COref was obtained by using cardiovascular agents, or by electrical pacing. In each condition, COfv and COref were measured by the FloTrac/Vigileo system and compared.

Results: Overall analysis of pooled data (1490 data sets) indicated that COfv correlated with COref more strongly than with COref in absolute values (Figure A vs B) as well as in percentage changes from baseline values (Figure C vs D).

Conclusions: Our system enables continuous, accurate, and low invasive mon-

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Cardiac remodeling and changes in left ventricular function after cardiac decompensation in systolic heart failure

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Background and aims: Left ventricular end-diastolic diameter (LVDD) and ejection fraction (LVEF) are commonly used to describe heterogeneous systolic heart failure (SHF) populations. In the present study, we aimed to describe and predict the changes in left ventricular size and function after an event of cardiac decompensation in SHF.

Methods: Patients with SHF hospitalised for cardiac decompensation were eligible if LV EF was still ≤40% prior to discharge. Standardised clinical interrogation, examination and echocardiography were performed in all patients prior to discharge and after six months on guideline-adjusted therapy. LVDD was measured in the parasternal long axis view. LV EF was quantified using the Simpson biplane method from apical two- and four-chamber view. Tricuspid valve gradient as a surrogate of systolic pulmonary artery pressure (sPAP) was measured using the apical four-chamber view.

Results: We included 846 patients; 97 of those died during the 6 months after discharge (11%) and 209 were unavailable for follow-up. Hence, 540 patients completed the study. Mean age was 67±12 years, and 75% were male. Prior to discharge, LVDD and LVEF were 62±9mm and 28±7%, respectively. After 6 months, LVDD had decreased from 65±8 to 57±8mm in 269 patients and increased from 59±8 to 65±8mm in 271 patients. LV EF had improved about >5% in 380 patients (70%), and about >20% in 202 patients (37%). In multivariable regression analysis, LVDD measured 6 months after discharge depended on LVDD, sPAP, pulse pressure and sPAP measured prior to discharge, as well as ischemic etiology and the duration of the disease. LVDD 6 months after discharge additionally depended on left bundle branch block but was not related to initial sPAP. The predictors for favourable and unfavourable remodeling were a disease history <1 year and ischemic etiology, respectively.

Conclusion: Profound changes of cardiac size and function occur in the majority of patients with SHF after cardiac decompensation over the course of 6 months. Neither large LVDD nor low LVEF reliably predict remodeling. Rather, the main predictors of LVDD and LVEF at 6 months are duration and aetiology of SHF.

P2754 How reliable are dysynchrony measurements in the presence of infarct scar?

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Background: Assessment of mechanical dysynchrony to predict response to cardiac resynchronization therapy (CRT) is the main goal of the echocardiographic screening of CRT candidates. However, the impact of infarct scar on this assessment remains controversial. In this study, we investigated the impact of the extent and localization on conventional dysynchrony parameters and the new parameter of apical rocking.

Methods: We studied data of 36 infarct patients with normal GRS duration and 480 non-ischemic DCM patients (31% ischemic cardiomyopathy). Infarct scar localization and extend was defined by contrast-enhanced MRI. Influence of infarct scar on the motion pattern of the LV was examined by measuring direction and amplitude of apical rocking. Results were compared with conventional dysynchrony measurements, i.e. the standard deviation of time to peak velocity in 12 mid and basal segments (SD-Ts12), the direction of time to peak velocity between anteroseptal and posterior wall (AP-Del) and septal to lateral delay in time to peak velocity (SL-Del).

Results: Infarct patients showed relevant apical rocking in 61% while the apex moved regularly away from the infarct during systole. Scar extend correlated inversely with apical rocking (r = -0.36, P < 0.05). Conventional dysynchrony parameters were positive in 20% – 35% of infarct patients. In CRT candidates without scar, apex motion is dominated by the conduction delay (systolic motion towards lateral). In CRT candidates with ischemic CMP this pattern is modulated by the scar. Again, apical rocking was inversely related to scar extend (r=-0.62, P < 0.05). In all CRT candidates apical rocking showed higher sensitivity, specificity and accuracy to predict response to CRT compared to conventional dysynchrony measurements.

Conclusion: LV motion patterns are dominated by conduction delays but modulated by infarct scar. Higher scar burden results in less pronounced apical rocking. Apical rocking has a higher accuracy for the prediction of CRT response than conventional echo parameters. We therefore propose apical rocking as useful screening parameter for CRT candidates.

P2755 A blunted heart rate response during dobutamine stress echocardiography is associated with impaired myocardial contractile reserve in nonischemic dilated cardiomyopathy

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Background: Heart failure patients may have desensitization of myocardial β-adrenergic responsiveness. Pressure-volume relationship (PVR) is a robust method to evaluate myocardial contractility during dobutamine stress echocardiography (DSE). We evaluated the relationship between heart rate change (ΔHR) and the presence of myocardial contracture reserve during DSE in nonischemic dilated cardiomyopathy.

Methods: We studied 60 HF patients (age 66±11 years; ejection fraction 29±8%) having high-dose DSE (up to 40 mcg/kg/min). PVR was defined as systolic cuff pressure/end-systolic volume index difference between rest and peak DSE. All patients were on optimal and maximally tolerated β-blockers therapy.

Results: Resting HR was comparable in patients with and without contracture reserve (69±15 vs 72±10 bpm; p=NS), however HR at peak stress (112±20 vs 103±18 bpm; p=0.04) and ΔHR (70±39 vs 41±25% p=0.04) were significantly higher in the former. Using C statistics, ΔHR of >38% was the best cut-off for predicting myocardial contractile reserve (sensitivity 80%, specificity 70%). Patients with higher ΔHR showed lower end-systolic volume at rest (108±50 vs 142±79 ml; p=0.046) and at peak stress (71±82 vs 113±90 ml; p=0.014), higher resting (30±4 vs 26±3% p=0.015) and peak stress LV ejection fraction (59±15% vs 38±14% p=0.005), no difference in WMSI at rest (2.1±0.32 vs 2.19±0.28; p=0.015) with significant difference in WMSI at peak DSE (1.63±0.49 vs 1.86±0.44, p=0.015) and in ΔWMSI (0.51±0.29 vs -0.31±0.22, p=0.035) and lower E/e’ (12±7 vs 17±6; p=0.002).

Conclusion: In patients with nonischemic dilated cardiomyopathy a blunted heart rate change during DSE is associated with impaired contractile reserve as well as echocardiographic indicators of more advanced disease.

P2756 LV functional recovery from Tako-Tsubo cardiomyopathy is incomplete after 3 months: evidence from 2D speckle-tracking echocardiography

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Introduction: Tako-Tsubo cardiomyopathy (TTC) is a unique disorder of myocardial function, generally considered self-limiting and fully reversible. Although obvious hypokinesia resolves, data which challenge this view include abnormal natriuretic peptide concentrations after 3 months and late persistence of inflammatory cells on LV biopsy.

Hypothesis: To assess the null hypothesis that, at 3 months after TTC, LV function is identical to that of controls, we quantitated LV functional recovery, via 2D speckle-tracking (2DS) echocardiography.

Methods: 33 consecutive TTC patients [mean age 66±11 (SD, all females) were compared with 16 normal controls (mean age 64±11 years, all female). In addition to an acute study, echocardiography was performed at 10 days and 3 months thereafter, for 2DS analysis. Prespecified indices were global longitudinal strain (GLS) and strain rate (LSR), as well as peak apical rotation. Peak plasma norepinephrine and NT-proBNP were determined in the acute phase, while NT-proBNP was repeated after 3 months.

Results: All patients demonstrated serial improvement in prespecified 2DS indices (one-way ANOVA, P<0.005). At 3 months, patients exhibited lower GLS than controls (mean 17.9±3%, versus 20.3±1.6%, P<0.005, see figure), but did not differ significantly in LSR or apical twist. There was no significant correlation between 2DS indices and biomarkers of acute severity. However, 3 month GLS correlated directly with simultaneous NT-pro-BNP (r=0.38, P=0.04; see Figure 1).

Figure 1.
patients with other patients (p=0.03). The correlation between GPSLS value and apnea-hypopnea index (AHI) were stronger than the correlation of AHI with other echocardiographic parameters (r= -0.741; p=0.001).

Table 1. Peak Systolic Strain values of the patients and the control group

<table>
<thead>
<tr>
<th>Group</th>
<th>Healthy</th>
<th>Mild OSA</th>
<th>Moderate OSA</th>
<th>Severe OSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>28</td>
<td>28</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>GPSLS (%)</td>
<td>-25.58±2.16</td>
<td>-23.93±3.96</td>
<td>-21.27±2.60†</td>
<td>-16.94±2.66‡</td>
</tr>
<tr>
<td>PSSLS (%)</td>
<td>-21.37±1.9</td>
<td>-19.87±2.44</td>
<td>-18.37±2.64‡</td>
<td>-15.29±2.92‡</td>
</tr>
<tr>
<td>PSSLS (%)</td>
<td>-23.26±2.1</td>
<td>-21.57±2.39</td>
<td>-19.72±2.57†</td>
<td>-16.93±2.93‡</td>
</tr>
<tr>
<td>vGPSLS (%)</td>
<td>-27.37±3.7</td>
<td>-24.65±2.93</td>
<td>-23.45±3.91</td>
<td>-19.23±3.97‡</td>
</tr>
</tbody>
</table>

vGPSLS: global peak systolic longitudinal strain; OSA: obstructive sleep apnea; PSSLS: BMA; peak systolic longitudinal basal, mid, apical segments.

Conclusion: Longitudinal LV mechanics in OSA patients with normal UVEF have been deteriorated in the subclinical stage associated with the severity of disease. AFI can be used as an effective and safe method in determination of subclinical myocardial dysfunction in OSA patients, because it is semi-automated, and easy to use with short analysis time.

**P2770**

**Anemia has significant impacts for adaptive servo ventilation therapy on heart failure patients with Cheyne-Stokes respiration**

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**Background:** Cheyne-Stokes respiration (CSR) and anemia influence the progression of chronic heart failure (CHF). Adaptive servo ventilation (ASV) is a new effective therapeutic device for CSR, but the prognostic effect of ASV for CHF patients with or without anemia is not clear.

**Methods:** One hundred five patients with CHF and CSR were divided into two groups: treated with ASV (n=39) and without ASV (n=66). Patients with home nocturnal oxygen therapy or continuous positive airway pressure therapy during night were included in non-ASV group. All patients were prospectively followed after discharge during a mean follow-up period of 506 days with the end points of cardiac death or progressive heart failure requiring rehospitalization. Anemia was defined as hemoglobin level <12.1 g/dl for men and <11.6 g/dl for women.

**Results:** There were 59 patients (56.2%) with anemia in all subjects. Apnea-hypopnea index was similarly improved after ASV (P=0.001) in CHF patients with or without anemia. In anemia group, ASV decreased plasma BNP level (P=0.005), but this decrease was not observed in patients without anemia (P=0.095). The Kaplan-Meier survival curve demonstrated that cardiac event free rate was significantly higher in CHF patients treated with ASV than those without ASV (62.6% vs 19.4%; P<0.005) in anemia group, but this improvement was not obtained in anemia group (60.2% vs. 64.4%; P=0.372).

Conclusion: Longitudinal LV mechanics in OSA patients with normal UVEF have been deteriorated in the subclinical stage associated with the severity of disease. AFI can be used as an effective and safe method in determination of subclinical myocardial dysfunction in OSA patients, because it is semi-automated, and easy to use with short analysis time.

**P2758**

**Strong inter-relationship between hemodynamic state and serum parathyroid hormone in patients with chronic heart failure**

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**Background:** Both serum intact parathyroid hormone (PTH) and plasma brain natriuretic peptide (BNP) levels are important prognostic predictors of chronic heart failure (CHF). We evaluated the impact of serum PTH on hemodynamic state and their relations by comparing plasma BNP levels.

**Methods:** We prospectively studied 105 patients with CHF (63±13yr, 64% male, NYHA class I/II/III/IV: 20/34/45/6, left ventricular ejection fraction; UVEF 43±20%, estimated glomerular filtration rate: eGFR 60±16 ml/min/1.73m²). Patients with advanced kidney disease with an estimated eGFR <30 ml/min/1.73m² were excluded. Serum intact PTH and plasma BNP levels were assessed simultaneously in all patients with or without anemia is not clear.

**Results:** Although serum PTH level was within the normal range (<65 pg/ml) in 87% of patients, log-transformed PTH levels had significant correlation with pulmonary capillary wedge pressure (PCWP: 15.5±9 mmHg), stroke volume index (SVI: 38±11 ml/m²), heart rate (HR: 73±14/min), and cardiac index (CI: 2.6±0.7 L/min/m²) in all patients (r=0.55, r= -0.52, r=0.40, and r= -0.41, p<0.05, respectively). After adjusting for clinical variables associated with PTH (eGFR, corrected calcium levels, inorganic phosphate levels, and therapeutic use of loop diuretics), PCWP and SVI were independent determinants of log-transformed PTH levels. Conversely, after adjusting for clinical variables associated with CHF (eGFR, BNP levels, left atrial diameter, LV end-diastolic volume index, and UVEF), PTH level was an independent predictor of PCWP, SVI, HR, and CI (r=0.37, 0.31, 0.29 and -0.23, p<0.05, respectively), and was defined as a superior predictor of SVI, HR, and CI compared with log-transformed BNP levels on stepwise multivariable Cox proportional hazards regression analyses.

**Conclusions:** Serum PTH level has strong inter-relationship with hemodynamic state and was a superior independent predictor of hemodynamic insufficiency compared with plasma BNP level in patients with CHF.

**P2759**

**Evaluation of subclinical left ventricular systolic dysfunction in patients with obstructive sleep apnea by automated function imaging method**

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**Purpose:** We aimed to evaluate the left ventricular function with the automated function imaging method (AFI) based on speckle tracking echocardiography (STE) in obstructive sleep apnea patients (OSA) with normal left ventricular ejection fraction (LVEF) and without any confounding disease that can cause myocardial dysfunction.

**Methods:** 21 healthy individuals and 59 OSA patients were included in the study. According to severity of the disease, OSA patients were examined in three groups; mild, moderate and severe OSA. Apical 2, 3 and 4 chamber images were obtained for AFI evaluation. The global peak systolic longitudinal strain (GPSLS) values were determined for each view, and averages of these were used in comparison of the patient groups.

**Results:** The GPSLS values of the OSA patients were lower than the healthy individuals and these values were in decreasing trend in OSA patients correlated with the disease severity (25.58±2.16 vs. 23.93±3.96 vs. 21.27±2.60 vs. 16.94±2.66 respectively), and the difference was significant in comparisons of the moderate OSA patients and healthy individuals and in comparisons of severe OSA patients with other patients (p=0.03). The correlation between GPSLS value and apnea-hypopnea index (AHI) were stronger than the correlation of AHI with other echocardiographic parameters (r= -0.741; p=0.001).

**Conclusion:** Longitudinal LV mechanics in OSA patients with normal UVEF have been deteriorated in the subclinical stage associated with the severity of disease. AFI can be used as an effective and safe method in determination of subclinical myocardial dysfunction in OSA patients, because it is semi-automated, and easy to use with short analysis time.

**P2761**

**Prognostic role of the complication of both sleep-disordered breathing and chronic kidney disease in patients with idiopathic dilated cardiomyopathy**


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**Purpose:** Sleep-disordered breathing (SDB) is associated with activation of the sympathetic nervous system, whereas chronic kidney disease (CKD) is related to impairment of the renin-angiotensin-aldosterone system. Little information is available on the relation of these conditions to heart failure. The aim of this study was to investigate that both SDB and CKD are associated with poor prognosis in patients with idiopathic dilated cardiomyopathy (IDCM).

**Methods:** A total of 133 consecutive patients with IDCM were screened for SDB, evaluated for estimated glomerular filtration rate (eGFR), and subjected to car-
Long term survival of patients with congestive heart failure receiving ICD/CRT-D devices in a district general hospital

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Background: There is a shortage of outcome data for patients with congestive heart failure (CHF) receiving implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy-defibrillator (CRT-D) devices treated outside of clinical trials.

Methods and results: We report the survival status of 180 CHF patients implanted with ICD and CRT devices in a District General Hospital between January 2001 and December 2011. In the study period 108 ICDs and 72 CRT-Ds were implanted. The mean follow-up time was 31±24 months. Females were 11.4%. Median age was 71 years (range 32-86 years). In 65% of patients there was an ischemic substrate. A primary prevention indication was present in 53.8%. Risk factors consisted of: hypertension 50.6%; active cigarette smoking 7.2%; hypercholesterolemia 61%; diabetes 28.9%. Past cardiovascular history included previous PCI 31.3%; previous CABG 21.7%, previous stroke 7.8%. Mean EF was 27±5.6%. NYHA class III was present in 44.4% of cases and 5% of patients were in class IV. Medical therapy consisted of beta-blockers 86.1%; RAAS inhibitors 85.5%; Vitamin K antagonists 30.7%. Hb was 12±1.5 mg/dL; Sodium 137.5±4.2 mEq/L; Potassium 4±0.4 mEq/L. Mean QRS was 139±33.9 msec. AF was present in 25.9% of patients. The 10-year survival rate was 31.4%. No difference in mortality was observed between primary and secondary prevention groups. The 10-year appropriate therapy rate was 32.2%. Freedom from hospitalization was 90.1% at one year, 69.5% at 5 years and 38.6% at ten years. Freedom from death or HF hospitalization was 14.1% at 10 years (Fig. 1).

Conclusions: Congestive heart failure treated by optimal medical therapy and ICD/CRT devices retains a poor long-term prognosis in patients treated outside of clinical trials.

Volumetric response to cardiac resynchronization therapy assessed by echocardiography predicts benefits in long-term prognosis of patients with severe heart failure

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Study aim: To analyze the long-term outcome of heart failure (HF) patients (pts) treated with cardiac resynchronization therapy (CRT) and to evaluate predisposing factors for therapeutic response.

Methods: 519 HF pts were included in our study. Within the first 12 months of follow-up pts were classified as volumetric responders (R); LV volume reduction of >10% vs. volumetric non-responders (NR). Pts were then followed by clinical examination and echocardiography. The end-point was defined as all-cause mortality, heart transplantation, or assist device implantation.

Results: At baseline, clinical data were comparable in R vs. NR (age, BMI, NYHA class: n.s.). Mean follow-up time was 62±32.6 months. End-point data were available in 189 R and 171 NR pts at their respective last follow-up. From these, 58 R (31%) and 125 NR (73%; p < 0.001) reached the end-point. In R vs. NR pts, non-ischemic cardiomyopathy (70 vs. 42%, p < 0.001) and sinus rhythm were more frequent (85 vs. 72%, p < 0.001). Furthermore, the QRS complex was wider (171±43 vs. 144±72 ms, p < 0.001), and Tissue-Doppler Imaging (TDI) more often showed dyssynchrony defined as a regional electromechanical delay >40ms (98 vs. 50% in p < 0.001).

P2763 Positive early response to CRT in patients optimized by SonR: results from the CLEAR study

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Introduction: The CLEAR study aimed to compare patients’ (pts) clinical benefits resulting from CRT optimization performed either automatically through a data-based procedure using the hemodynamic SonR signal or with standard clinical practice (STD) clinical practice during a 12-months follow up (FU). This sub-analysis focused on the evolution throughout time of the CRT response in the two randomized study groups.

Methods: Data from 268 HF pts in sinus rhythm implanted with a CRT pacemaker according to applicable guidelines were gathered. Within 7 days after implant, pts were randomly assigned to SonR or STD optimization and followed up to 12M: i) SonR arm pts underwent SonR optimization of VV configuration and AVO, at discharge, 3M, 6M FUs and on a weekly basis; ii) STD arm pts were optimized according to each center’s clinical practice. CRT response was assessed based on a composite criterion including all-cause deaths, HF-related hospitalizations, NYHA class and Quality of Life (QoL) scores. CRT response was analyzed at 3M, 6M and 12M FUs, as well as the contribution of each criterion.

Results: On an intention-to-treat approach, data from 199 pts (73.4±9.7 years, 63% male, NYHA class: 3±1.3, LVEF: 26.9±8.2) were available for final analysis, equally balanced in SonR (n=100) and STD (n=99) arms. A trend towards significant better CRT response was observed in the SonR vs. STD group as early as 3M FU (table 1). This response was mainly driven by NYHA class improvement.

Conclusions: The automatic SonR based optimization procedure ensured a higher clinical CRT response rate as compared to standard clinical practice not only on long term, but also on a short-term FU basis. These results further highlight the potential role of SonR based CRT optimization in increasing pts’ clinical response.

P2764 Volumetric response to cardiac resynchronization therapy assessed by echocardiography predicts benefits in long-term prognosis of patients with severe heart failure

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Study aim: To analyze the long-term outcome of heart failure (HF) patients (pts) treated with cardiac resynchronization therapy (CRT) and to evaluate predisposing factors for therapeutic response.

Methods: 519 HF pts were included in our study. Within the first 12 months of follow-up pts were classified as volumetric responders (R); LV volume reduction of >10% vs. volumetric non-responders (NR). Pts were then followed by clinical examination and echocardiography. The end-point was defined as all-cause mortality, heart transplantation, or assist device implantation.

Results: At baseline, clinical data were comparable in R vs. NR (age, BMI, NYHA class: n.s.). Mean follow-up time was 62±32.6 months. End-point data were available in 189 R and 171 NR pts at their respective last follow-up. From these, 58 R (31%) and 125 NR (73%; p < 0.001) reached the end-point. In R vs. NR pts, non-ischemic cardiomyopathy (70 vs. 42%, p < 0.001) and sinus rhythm were more frequent (85 vs. 72%, p < 0.001). Furthermore, the QRS complex was wider (171±43 vs. 144±72 ms, p < 0.001), and Tissue-Doppler Imaging (TDI) more often showed dyssynchrony defined as a regional electromechanical delay >40ms (98 vs. 50% in p < 0.001).
Factor influencing functional improvement in patients with idiopathic dilated cardiomyopathy treated with intracoronary infusion of autologous mononuclear bone-marrow cells

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Purpose: Different studies have shown clinical improvement and a mild benefit in left ventricular function in patients with idiopathic dilated cardiomyopathy (DC) treated with cell therapy. However, the degree of functional improvement varies among patients, and factors influencing such a response are not well known. This study investigates factors influencing the 6-month gain in left ventricular ejection fraction in 27 patients with DC included in a trial (Clinical Trials, Gov NCT00629096) on intracoronary cell therapy.

Methods: Patients were studied at baseline and 6 months after intracoronary infusion of autologous bone-marrow mononuclear cells, suggesting that the amount of very immature cell forms infused bears a significant inverse correlation (r=-0.41; P<0.003) between the gain in ejection fraction and baseline HLD level, suggesting higher gain with low HLD levels. In fact, HLD was significantly lower in those patients with higher gain in ejection fraction (<10%) (30.0±8 vs 40.10; p<0.01). The 24-hour migratory capability of the infused cells (100) was significantly reduced in the responders group compared to non-responders (5.4±1.7 vs 8.1±2.3; p<0.009 for vegf and 5.8±1.7 vs 8±2.9; p<0.002 for sfd1). Additionally, in the gain in hypoxenic radii correlated directly (r=0.52; p<0.02) with the % of cd34+HDL-DR negative immature cells, suggesting that the amount of very immature cell forms infused bears a favourable influence.

Conclusions: Younger patients with DC and lower plasma levels of HDL benefit more from intracoronary cell therapy. Functional gain also seems to be enhanced by a lower migratory capacity and a higher % of immature infused cells.

Heart rate reduction and improvement of NYHA class during uptitration of beta-blockers for heart failure independently predict mortality


Background: Beta-blocker (BB) treatment is associated with outcome in heart failure (HF). Recently published results of the Cardiac Insufficiency Bisoprolol Study in Elderly (CIBIS-ELD) indicate superiority of using heart rate, not maximum dose, as a titration target.

Methods: We invited elderly HF patients enrolled in CIBIS-ELD to participate in an observational follow-up 1.5 to 5.6 years after the end of uptitration with BB.

Results: 720 patients (269 women, 37% mean age 72.6±6) were followed up. 134 patients (19%) died. Follow-up included 2268 patient-years at risk. Baseline heart rate of patients who died was 74.3±14.1 bpm compared to 72.6±13.9 bpm of patients who survived (P<0.019). NYHA classes improved from baseline 2.9±0.55 to 2.25±0.53, respectively (P<0.01). Three months after the start of uptitration, heart rates lowered to 69.3±13.3 vs 65.6±12.1 bpm, respectively (difference adjusted for baseline, 2.7 bpm, 95% CI 0.7 to 4.7, P=0.007), NYHA classes improved to 2.19±0.58 vs 1.98±0.56 (adjusted difference, 0.14, 0.05 to 0.24, P=0.002). In multiple Cox regression adjusting for age, sex, BB pretreatment, ventricular function, heart rate and NYHA class at baseline, reduction of heart rate by 10 bpm during uptitration was associated with a subsequent mortality HR of 0.85 (95% CI 0.73 to 0.98; P=0.03), improvement by one NYHA class was associated with mortality HR of 0.64 (0.44 to 0.93; P=0.02), and achieved dose level was not significantly associated with mortality (P=0.49).

Conclusion: Our data confirm that reduction of heart rate and NYHA class during BB uptitration but not achieved dose predict mortality in HF.

Therapeutic patient education and all-cause mortality in patients with chronic heart failure: a propensity analysis from a large, multicenter, prospective French cohort (ODIN)

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Purpose: Meta-analyses of disease management programs have shown favorable effects in chronic heart failure (CHF). Therapeutic patient education (TPE) forms an integral part of these programs and may influence mortality per se. In order to determine the relationship between TPE and long-term mortality in CHF, CHF patients were prospectively enrolled from 2007 to 2010 in a multicenter French cohort (ODIN) by 61 centers previously trained in a TPE program in CHF.

Methods: In the “real-world” setting of the study, patients either received (“educated”) or did not receive (”non-educated”) TPE in addition to routine CHF management. Comparisons between groups used 1-way ANOVA and unpaired t tests for continuous variables and χ2 tests for categorical variables. The Kaplan-Meier method was used to calculate survival curves, and Cox regression analysis was used to assess predictors of 24-month outcome, entering TPE as a co-variable. All collected variables were included in the multivariable model. Propensity analyses were then performed for the application of TPE using a multivariate logistic regression model, and matched cohorts of 1 educated patient for each non-educated patient were developed. First, a propensity score was calculated, including all of the collected variables except for classes of cardiovascular medication (model 1: 825 pairs). A second propensity analysis was then performed including all variables except for model 2: 818 pairs. For all tests, P>0.05 was considered significant.

Results: From the 3257 participants who were included in the study (mean age: 67.5 years; 69.5% men), 2347 were educated (72.5%) and 890 were not educated (27.5%). All-cause mortality (median FU: 27.2 months; lost to FU: 158 patients (4.9%)) was 17.7% (n=446) in the educated group vs. 21.0% (n=276) in the non-educated group (unadjusted HR: 0.84; 95% CI 0.40-0.57; P<0.001; adjusted HR: 0.70, 95% CI 0.58-0.84, P<0.001). This association remained in paired groups after adjustment for all baseline covariates excluding (model 1) or including (model 2) cardiovascular medications and propensity score (HR: 0.72, 95% CI 0.58-0.90, P<0.003, and HR: 0.73, 95% CI 0.59-0.90, P<0.004, respectively).

Conclusion: In CHF, TPE by trained healthcare professionals appears associated with lower all-cause mortality. These findings obtained in an observational registry in routine care need to be confirmed in prospective randomized studies.

Medical anticipatory care plans in advanced heart failure prevent hospital re-admissions

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Purpose: Recurrent prolonged hospital admissions in advanced heart failure (HF) are a significant financial burden on the NHS. Anticipatory care plans (ACP) are traditionally patient-led and patient-held documents specifying patients’ wishes with respect to their care. Medical anticipatory care plans (MACP) comprise patient specifications in addition to detailed direction of acute and chronic management for medical professionals involved in the patient’s care. MACP may reduce hospital re-admissions in advanced HF and improve matching between preferred and actual place of care/death.

Method: A retrospective audit of the first 100 advanced HF patients referred to a large Scottish city-centre HF and palliative care out-patient service between November 2009 and February 2011 was performed.

Results: Of 100 consecutively referred advanced HF patients 65 (65%) were men and average age was 74 years. Seventy-nine patients (79%) had HF with reduced ejection fraction (HFREF) where the most common aetiology was ischaemic heart disease (84%) and 21 patients (21%) had HF with preserved ejection fraction (HFPEF) where the most common aetiology was valvular heart disease (76%). By February 2012 a total of 58 patients (58%) had died. Of the patients dying, 46 (79%) had HFREF and 12 (21%) had HFPEF. Thirty-two of the patients who died (55%) had a MACP created in the months preceding death. For those advanced HF patients with a MACP there were no further hospital admissions. Conversely for the 26 patients (45%) who died without prior creation of a MACP there were 90 hospital re-admissions altogether incurring 892 hospital-bed days. For those patients with a MACP the majority’s preferred place of care (PPC) and preferred place of death (PPD) was home. PPC matched actual place of death (APD) for all patients (100%) with a MACP PPD matched actual place of death (APD) in 31 patients (97%) with a MACP. Of the 26 patients without a MACP 20 patients (76%) died in hospital.

Conclusions: Volumetric CRT response translates into a significant mortality benefit in CRT recipients. In our population non-ischemic origin of HF, presence of sinus rhythm, duration of the QRS-complex, and TDI-defined dysynchrony were associated a better long-term prognosis.
Conclusion: Medical anticipatory care plans for patients with advanced HF substantially reduce hospital readmissions and markedly increase matching of preferred place of care/death to actual place of care/death.

ACUTE HEART FAILURE

Baseline characteristics and hospital mortality in the acute heart failure database (AHEAD) main registry

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Aims: The objectives of the Acute Heart Failure Database (AHEAD) registry are to assess patient characteristics, aetiology, treatment and outcome of acute heart failure (AHF) in districts with centralised care of patients with acute coronary syndromes. The registry was set up in seven centers with Cath Lab facilities.

Methods and Results: Of 4,153 patients, 12.7% patients died during hospitalisation. The median length of hospitalisation was 7.1 days. Mean age of patients was 71.5±12.4 years; males were younger (68.6±12.4 years) compared with females (73.1±11.5 years) (p<0.001). De novo heart failure was seen in 55.9% of patients. According to the classification of heart failure syndromes, acute decompensated heart failure (ADHF) was reported in 50.8%, hypertensive AHF in 4.8%, coronary syndrome in 28.9%, cardiacogenic shock in 14.7%, high output failure in 3.3%, and right heart failure in 3.8%. The mortality of cardiacogenic shock was 62.6%, of right HF 16.6%, of pulmonary oedema 71.0%, of high output HF 6.1%, 1.1% of the mortality of hypertensive HF or ADHF was <2.5%.

The highest mortality we found during the first month. Total 1 year, resp. 3 years survival since 30th day after the admission was 79.7% at 1 year, resp. 64.5% after 3 years. We did not found statistical significant difference in survival since 30th day after admission among the syndromes. According to multivariate analysis we defined independent predictors of worse prognosis - age, 70 years, comorbidities, mild renal insufficiency, anaemia, diabetes mellitus, previous stroke or MI, COPD, severe left ventricular dysfunction (ejection fraction <30%). The better prognosis had patients with de-novo AHF and patients with ACE inhibitors at discharge. Levels of natriuretic peptides were the most powerful predictors of high risk of mortality in long-term follow-up.

Conclusion: According to multivariate analyses, low systolic blood pressure, low cholesterol level, hypotension, hypokalemia and the use of inotropic agents were predictive parameters for in-hospital mortality in patients with cardiacogenic shock. Severe left ventricle dysfunction and renal insufficiency were predictive parameters for morality in patients with cardiacogenic shock. Invasive ventilation and age over 70 years were the most important predictive factors of mortality for both genders with or without cardiacogenic shock. Age and comorbidities were the most predictive parameters for long term prognosis.

QRS and QTc interval in prediction of short- and long-term outcomes of patients with acute decompensated heart failure

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Aims: The objective of this study was to evaluate the prognostic value of prolonged QRS and QTc interval in patients hospitalized for acute decompensated heart failure (ADHF).

Methods: The Korean Heart Failure (KorHF) registry is a nationwide registry including 3300 consecutive patients who presented with ADHF at 24 centers in South Korea between June 2004 and April 2009. Electrocardiogram data obtained on admission for 2634 patients were analyzed.

Results: During a mean observation period of 1.7 years, patients with QRS prolongation reached the composite endpoint, defined as all-cause death or heart failure (HF) hospitalization, more frequently than patients with normal QRS interval (47.4% vs. 37.3%, p<0.001). All-cause death, cardiac death, heart transplantation, and HF hospitalization also occurred more frequently in the prolonged QRS group (all-cause death 23% vs. 18%, p=0.006; cardiac death and heart transplantation 8% vs. 5%, p=0.007; HF hospitalization 32% vs. 24%, p<0.001). QRS prolongation independently predicted an adverse outcome (HR 1.28, 95% CI 1.08-1.53, p=0.005). On the other hand, QTc prolongation was not associated with worse outcome.

Conclusion: Prolongation of QRS interval, but not of the QTc interval, predicted unfavorable outcomes in patients hospitalized with ADHF. Therefore, QRS prolongation, which is easy to measure on presentation, may be used to identify high risk patients with ADHF.

A half of acute heart failure patients with cavity lead ST-elevation is related to ongoing ischemic heart disease

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Background: It has been widely recognized that ST-segment elevation in Cavity Lead (Lead aVR) is strongly associated with pan-coronary ischemia. Such conditions has recently named as Clinical Scenario 4, however, the prevalence of acute heart failure (AHF) with Cavity Lead ST-elevation (CaL-STE) related to ongoing multi vessel ischemia is unknown.

Methods and Results: This study enrolled consecutive 180 AHF patients admitted with pulmonary congestion. Patients were divided into two groups by the findings in the admission electrocardiogram. (1) CaL-STE-group; Cavity Lead ST-elevation ≥0.1mV (n=31, 17.2%), (2) non-CaL-STE-group; without significant ST-elevation in Cavity Lead (n=149, 82.8%). Ongoing ischemic with angiographic multi-vessel disease was presented more frequently in CaL-STE-group (n=17 (55%) vs. n=16 (11%), p<0.0001). The other 14 patients with CaL-STE, the ST-elevation was mainly due to severe left ventricular hypertrophy. In hospital mortality was significantly higher in CaL-STE-group (19.4 ±6.5%, p<0.02). The rate of intra-aortic balloon pumping (16.1% vs. 5.37%, p=0.04) and continuous positive pressure ventilation (41.9% vs. 17.6%, p=0.003) use was also higher in CaL-STE-group. The prevalence of diabetes (64.5% vs. 28.2%, p<0.001) and dyslipidemia (58.1% vs. 26.9%, p=0.0007) was higher in CaL-STE-group.

Conclusions: The elevation of ST-segment in Cavity Lead is responsible for ongoing ischemia and it has relations with multiple coronary risk factor. It is also a predictor of in-hospital death in patients with AHF. Early intensive treatment is needed for patients with CaL-STE.

Short and long-term prognosis of patients hospitalised with acute myocardial infarction and/or acute heart failure

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Background: The registry included all patient hospitalized on the Cardiology department of one University hospital from October 2004 to March 2009. 13 895 patients were hospitalised and 3 179 of them were hospitalised more than once, so the registry includes 17 074 hospitalizations. This analysis compares the in-hospital differences an prognosis of patients hospitalised with acute myocardial infarction (AMI) and/or acute heart failure (AHF) during December 2011.

Results: 1 611 patients were hospitalized with AMI and without AHF (group A), 4 769 with AMI with AHF (group B) and 1 006 with AHF and without AMI (group C). Patients in group A were younger 69.1 years (A) versus 70.1 years (B) or 70.4 years (C) (p <0.001) and were less frequently female 29.4% (A), 36.8% (B) and 41.4% (C) (p <0.001). Angiography (mostly with PTCA and/or stent) was performed in 88.6% in group A and in 79.8% in group B and in 33.6% in group C. The admission blood pressure was highest in group A 144/81 mmHg and lowest in group B 136/79 mmHg (p <0.001).

Patients with heart failure had more frequently atrial fibrillation (AF) (43.1% group C, 23.9% group B and 10.4% group A) and diabetes mellitus (DM) (39.5% A, 40.5% B and 28.7% A).

The in hospital mortality was 0.7% in group A, 10.7% in group B and 8.6% in group C (p <0.001), the lengths of hospital stay in patients who died was only 2 days in group B, but 4 days in groups A and C, the lengths of hospital stay in patients who were discharged alive was 5 days in group A, but 7 days in groups B and C. The incidence of AF and/or DM did not influence the in-hospital mortality.

The strongest predictor of mortality was low blood pressure at admission. The one year mortality was 6.4% vs 22.1% vs 20.2% (p <0.001) and the three year mortality was 10.7% vs 32.2% vs 33.6% (p <0.001). Renal insufficiency and diabeties mellitus were strong predictors of poor prognosis in all three groups.

Conclusion: AMI without AHF has hospital mortality below 1%, but AHF with or without AMI nearly 10%. Most of the deaths appear within the first 3 days. The long term mortality after discharge was 11% in AMI without AHF, but 33% in AHF and was slightly lower in men than in women, but women were significantly older (from 5 to 7 years in each group), so if adjusted to age the prognosis of both sexes was similar.
ECG in patients with acute heart failure can predict in-hospital and long-term mortality


Purpose: Initial risk stratification in patients with acute heart failure (AHF) is poorly validated. Previous studies tended to evaluate the prognostic significance of only one or two selected ECG parameters. The aim of this study was to evaluate the impact of multiple ECG parameters on mortality in AHF.

Methods: The Acute Heart Failure Database (AHEAD) registry collected data from 4135 patients admitted for AHF to seven hospitals with Cath Lab facilities. Clinical variables, heart rate, duration of QRS, QT and QTC intervals, type of rhythm and ST segment changes on admission were collected in a web based database. The Acute Heart Failure Database (AHEAD) registry collected data from 4135 patients admitted for AHF to seven hospitals with Cath Lab facilities. Clinical variables, heart rate, duration of QRS, QT and QTC intervals, type of rhythm and ST segment changes on admission were collected in a web based database.

Results: 17.2% of patients died during hospitalisation, the remainder were discharged and followed for a median of 16.2 months. The most important parameters were prolonged QRS and junctional rhythm, which independently predicted both in-hospital mortality (QRS > 100 ms, odds ratio [OR] 1.329, 95% CI 1.052-1.680; junctional rhythm, OR 3.715, 95% CI 1.748-7.896) and long-term mortality (QRS > 120 ms, OR 1.428, 95% CI 1.160-1.757; junctional rhythm, OR 2.629, 95% CI 1.538-4.496). Increased hospitalisation mortality was predicted by ST segment elevation (OR 1.771, 95% CI 1.383-2.269) and prolonged QTc interval (> 475 ms; OR 1.483, 95% CI 1.016-2.164). Presence of atrial fibrillation and bundle branch block was associated with increased unadjusted long-term mortality, but mostly reflected more advanced heart disease, and their predictive significance was attenuated in the multivariate analysis.

Conclusion: ECG in patients admitted for acute heart failure carries significant short- and long-term prognostic information and should be carefully evaluated.

Hydration status by BIVA and mortality following admission for acute heart failure

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Aims: Volume overload is a crucial mechanism related to progression and worse outcomes in heart failure (HF). The estimation of volume status is of critical importance in the management of patients with HF; nevertheless, fluid overload estimation in clinical practice remains largely empirical. Bioimpedance vector analysis (BIVA) has emerged as a potential easy and accurate method for assessing fluid status. The aim of this study was to assess the association between hydration by BIVA and the risk of all-cause mortality following admission for acute heart failure (AHF).

Methods: We analyzed 286 consecutive patients admitted for AHF. We prospectively assessed hydration status after initial stabilization (median 72 hours after admission). The independent association between hydration status and mortality was assessed with Cox regression analysis.

Results: During a median follow-up of 8 months (IQR 2.5-11 months), 52 (18.2%) deaths were identified. An stepped increase of risk was observed when moving from Q1 (<73.2%) to Q3 (74.2%) (Figure 1). After adjusting for established risk factors (including natriuretic peptides, patients with hyperhydration (>74.2%) showed an increased risk of death (HR=2.37, CI 95%:1.10-5.15; p=0.029) when compared to Q1.

Conclusion: Hyperhydration by BIVA after initial stabilization was related to a higher risk of death in a non-selected population admitted for AHF. Further studies are warranted to establish the definitive role of this easy method for risk stratification and guiding therapy in patients with AHF.

Heart type fatty acid binding protein (hfABP) in patients with acute congestive heart failure


Purpose: Heart type fatty acid binding protein (hfABP) is a small cytoplasmatic protein being involved in cellular energy homeostasis. During ongoing myocardial damage hfABP is supposed to transport fatty acids from the cell membrane to mitochondria for oxidation. HFABP has been discussed as an early diagnostic marker in patients suffering from acute coronary syndromes. However, the role of hfABP in the diagnosis and prognosis of patients suffering from acute congestive heart failure (aCHF) has rarely been investigated. This study investigated serum levels of hfABP in patients suffering from acute congestive heart failure (aCHF).

Patients and Methods: 356 patients presenting to the emergency department with symptoms of acute dyspnea and/or peripheral edema were evaluated for this analysis. Patients were followed up to five years. Serum blood samples for measurement of hfABP (nfABP ELISA, Signosis, Inc) were collected immediately after the initial clinical presentation of the aCHF patients in the emergency department.
Results: Median hFABP levels were significantly higher in patients with a history of aCHF (31.8 ng/ml, n=121) compared to patients without (19.0 ng/ml, n=235) (P<0.001). Median hFABP levels were significantly higher in patients being classified to functional NYHA class III/IV (31.0 ng/ml, n=125) compared to those of NYHA class I/II (20.3 ng/ml, n=56) (P<0.001). Accordingly, median hFABP levels were significantly higher in patients being classified to structural ACC/AHA class C/D (22.2 ng/ml, n=193) compared to those of class A/B (19.2 ng/ml, n=115) (P<0.001). Patients with a left ventricular dysfunction had significantly higher median hFABP levels (30.9 ng/ml, n=88) than those without (20.6 ng/ml, n=118) (P<0.001). Mortality rates of all patients were 14% (51/356) at 1 year and 33% (119/356) at 5 years. Median hFABP levels were significantly higher in patients who died during clinical follow-up (1 year: 31.14 ng/ml vs. 20.37 ng/ml, P<0.001; 5 years: 28.94 ng/ml vs. 18.15 ng/ml; P<0.001).

Conclusions: It was demonstrated that hFABP serum levels were increased in patients suffering from aCHF. hFABP was associated with functional NYHA, structural AHA/ACC classification and left ventricular dysfunction. Increased levels of hFABP might indicate patients with aCHF at higher functional or structural disease stages and might predict 1- and 5-year mortality in high risk aCHF patients.

P2778
The predictive value of transaminases at admission in patients hospitalized for acute heart failure syndromes: findings from the RO-AHFS registry
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Purpose: Transaminases are commonly elevated in the both the inpatient and ambulatory settings in heart failure (HF). It is presently unclear if transaminase levels at admission are predictive of in-hospital morbidity and mortality in patients hospitalized for HF.

Methods: Over a 12 month period, the RO-AHFS registry enrolled 3224 consecutive patients admitted with a primary diagnosis of AHFS at 13 medical centers. A post-hoc analysis of the 489 patients (15.2%) with alanine transaminase (ALT) and aspartate transaminase (AST) was conducted. Patients were stratified by median ALT and AST values. Multivariate Cox regression models were used to assess the hazard ratios for ALT and AST.

Results: The mean age of the study population was 68.5±12.9 years and 60% were men. An ischemic etiology of HF was reported in 61% of patients and the mean LVEF was 38.6±12.4%. At admission, the prevalence of elevated ALT and AST, respectively, were 28% and 24% and the median (IQR) ALT and AST were 41.0 (22.9-64.0) and 28.0 (15.5-51.0) U/L, respectively. Multivariate Cox regression models adjusted for age, gender, BMI, EF, SBP, serum Na, serum BUN, serum Cr, hemoglobin, QRS duration, atrial fibrillation/flutter on baseline EKG, and medication utilization (β-blockers, ACE/ARBs, and mineralocorticoid receptor antagonists).

Conclusions: The changes of ALT levels during admission are shown in Figure A. G1 were characterized by higher prevalence of Nohria profile C. On the other hand, G3 had higher systolic blood pressure on admission. During a mean follow-up of 2.1 years, Kaplan-Meier curve showed G1 and G3 had poorer prognosis compared with G2 (Figure B). Furthermore, 3-year mortality of G3 was about 150% higher compared with that of G1. Compared with G2, multivariable Cox model including glomerular filtration rate (GFR) decline during admission showed that the hazard ratios for all-cause death were 1.38 (95% CI 0.75-2.53; P=0.30) and 2.60 (1.55-4.38; P<0.001) for G1 and G3, respectively.

P2779
Prognostic impact of blood urea nitrogen increase during admission in patients with acute heart failure syndrome
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Purpose: Higher blood urea nitrogen (BUN) level on admission due to acute heart failure syndrome (AHFS) is associated with higher in-hospital mortality. However, the prognostic importance of the changes in BUN level during admission on long-term survival has not been fully elucidated. The purpose of the study was to examine the impact of the increase in BUN level during admission on long-term survival.

Methods: The Tohoku Acute Heart Failure Registry (N=498) is a multicenter retrospective cohort study involving AHFS patients who were admitted to 4 collaborating hospitals in 2007. The present study subjects were 337 survivors in this cohort with sufficient data. We divided them into 3 groups according to the tertiles of the BUN change (mg/dl), during admission as follows: G1 (BUN before discharge (BUNdis) – BUN on admission (BUNad) ≤ -1.63 and ≤ -5.73, N=113), G2 (BUNdis - BUNad > -1.63 and ≤ -5.73, N=113), G3 (BUNdis - BUNad > -5.73, N=112).

Results: The changes of BUN levels during admission are shown in Figure A. Figure B. Furthermore, 3-year mortality of G3 was about 150% higher compared with that of G1. Compared with G2, multivariable Cox model including glomerular filtration rate (GFR) decline during admission showed that the hazard ratios for all-cause death were 1.38 (95% CI 0.75-2.53; P=0.30) and 2.60 (1.55-4.38; P<0.001) for G1 and G3, respectively.
Short and long-term outcome of impedance-guided preemptive therapy to prevent pulmonary congestion-edema in the course of acute myocardial infarction

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Background: Patients sustaining an acute myocardial infarction (AMI) frequently develop pulmonary congestion-edema (PEd) during their hospitalization. Currently, treatment is initiated after the appearance signs of lung fluid overload. Ongoing monitoring of the status of lung fluid content (LFC) in AMI patients may enable the prediction of impending PEd and preemptive therapy, thus precluding PEd and improving outcomes.

Aims: We sought to find out whether non-invasive lung impedance (Li) guided preemptive diuretic treatment of AMI patients developing PEd improves clinical outcomes.

Methods: Li was determined by using a new noninvasive method to measure the electrical resistance of the lungs. Any increase in LFC results in Li decrease. Previously we have found that a decrease of 12-14% from normal Li value reflects the beginning transition from interstitial to alveolar edema. In the present study we prospectively randomized 222 patients (2:1 ratio) admitted for their first AMI without known chronic heart failure (CHF) and signs of PEd at admission and who expressed a >12% Li decrease to conventional therapy or Li-guided preemptive diuretic treatment.

Results: 148 patients were treated conventionally (Gr1) and 74 preemptively according Li (Gr2). Groups were well matched with regard to clinical, instrumental and laboratory parameters. In Gr1 all patients developed different stages of PEd. Treatment was begun only at symptom onset. In Gr2 Li-guided preemptive treatment was started immedi- ately after randomization at asymptomatic stage of evolving PEd and halted its development in 89% of patients. Unadjusted analysis showed that hospital stay, 1-year re-hospitalization rate after discharge, 6-years development new CHF and survival rate was better in Gr2 patients (p<0.001). Adjustment for such parameters as age, LVEF, maximal CK, diabetes, hyperten- sion, hyperlipidemia, smoking, level of creatinine and hemoglobin at admission showed that Li-guided preemptive treatment improved clinical outcome. Length of hospital stay reduced (OR=3.5, CI: 2.9-4.1, p<0.0001), 1-year re-hospitalization rate reduced (OR=3.7, CI:2.2-6.1, p<0.001), 6-years occurrence of new CHF reduced (OR=3.5, CI:1.3-7.5, p=0.002) and 6-years survival rate was better (OR=3.2, CI:1.9-9.1, p=0.027). Off different clinical and laboratory parameters the major influence on clinical outcome had age, diabetes mellitus, LVEF >30% and maximal CK (>2200 mg/dl). (p<0.001).

Conclusions: Li-guided preemptive therapy halts progression to PEd in 89% of patients, and significantly reduces hospital stay, recurrent admissions, evolution of CHF and mortality.

Relation of left ventricular ejection fraction to short- and long-term outcome in patients with non-ST-segment elevation myocardial infarction (NSTEMI) - analysis from the PL-ACS Registry

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The aim of the analysis was the analyze the relation of EF to treatment strategy and 12-month mortality in patients with non-ST-segment elevation myocardial infarction (NSTEMI).

Methods: All patients with NSTEMI with known EF (N = 45205) who were registered in the prospective Polish Registry of Acute Coronary Syndromes (PL-ACS) between 10.2003 and 11.2009 were included in the analysis. Follow-up mortality was obtained from the government database.

Results (table): Left ventricle ejection fraction was strongly correlated with the baseline risk profile of the NSTEMI patients. As the EF was lower, patients were less frequently treated invasively. However, bypass surgery was more frequent in patients with low EF. Early and 12-month outcomes were strongly related to the EF, being significantly worse in patients with lower left ventricle ejection fraction.

Conclusions: The rate of revascularization by PCI in NSTEMI decline as the left ventricle ejection fraction is lower. Patients with low EF have significantly worse early and 12-month outcomes.

Endomyocardial biopsy in unexplained new-onset heart failure: time matters

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Background: The role of endomyocardial biopsy (EMB) in the evaluation of patients with non-ischemic cardiomyopathy (CMP) is still under debate. A recent AHA/EAC consensus document suggests to perform EMB in "unexplained new-onset heart failure of 2 weeks to 3 months duration", although the scientific evidence for this recommendation is scarce. The objective of this retrospective study was to evaluate the impact of this time frame and to identify prognostic parameters in patients with suspected inflammatory cardiomyopathy.

Methods: 272 patients (mean age 45±13 years), who underwent EMB between March 2001 and November 2010 at our Department of Cardiology at Medical University, were enrolled in this study. Patients with a history of heart transplantation and those suffering from systemic diseases (amyloidosis, sarcoidosis) were excluded. Workup of biopsy specimens included immunohistochemistry for the assessment of myocardial inflammation and PCR for the detection of virus persistence. The combined endpoint was defined as death for any reason, heart transplantation, assist device implantation or hospitalization for acute heart failure. Mean follow-up was 32±26 months.

Results: Time from diagnosis of CMP to EMB was significantly higher in patients with events compared to those without (18 months vs. 6 months, p<0.001). Patients with NYHA-class III and IV suffered significantly more often from a cardiovascular event compared to those in NYHA-class I and II (33% vs 16%; p=0.007). Presence of bundle branch block (rate of events 32% vs 19%; p=0.047) and un-specific ST segment changes at time of first presentation (80% vs 93%; p=0.016) were associated with poor outcome. In multivariate analyses evidence of inflammation alone (p=0.008) or in combination with viral persistence (p=0.025) was associated with worse outcome only in patients presented within 3 months of unexplained new-onset heart failure. On contrast, EMB results did not impact on outcome in patients who presented after 3 months of new-onset heart failure.

Conclusion: Our data suggest, that time from diagnosis to EMB, NYHA class as well as ECG changes are associated with worse outcome. In multivariate analyses we found that EMB-results had only an impact on prognosis if patients underwent biopsy within 3 months after new-onset of heart failure symptoms. Consequently, our study supports the time frame suggested by the AHA/EAC consensus statement on EMB.

Assessment of left ventricular remodeling after myocardial infarction by speckle tracking echocardiography

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Background: Left ventricular remodeling (LVR) is the most prognostically important consequence of acute myocardial infarction (AMI) that develops several months after percutaneous coronary revascularization (PCI).

Aim: The purpose of the study was to evaluate changes in left ventricular (LV)
systolic function after acute myocardial infarction (AMI) using speckle tracking echocardiography (STE).

**Methods:** The study population consisted of 66 patients with AMI treated with primary PCI. STE was performed during the infarct-related artery was re-established. Patients were divided into 3 groups based on the presence of LVR (increase of LV end-diastolic and end-systolic volume: >20%) at 3 months follow-up.

**Results:** At initial presentation 3-5 days after AMI, longitudinal strain (9.4±3.7% vs 11.6±3.6% p<0.05) and transversal strain (10.4±8.2% vs 15.6±8.2% p<0.0001) were lower in remodeling group (R+) than in non-remodeling group (R-). LV wall motion score index did not differ between both groups. After 30 days, circumferential strain decreased in both groups (15.6±9.8% vs 25.5±8.8% p<0.001), radiaal strain (14.0±8% vs 14.1±5.5%p<0.001), longitudinal strain (−8.7±6.8% vs −13.5±4.5%p<0.005) and transversal strain (10.5±8.1% vs 16.7±8.3%p<0.003) remained lower in R+ group in comparison to R-group. On multivariate analysis, LVEF, GLS assessed by speckle tracking echocardiography during first 30 days after AMI were determinants of LVR. According to ROC analysis, circumferential apical strain smaller at baseline, longitudinal and circumferential strain 30 days after AMI were decreased in R+ group in comparison to R-group. On multivariate analysis, LVEF at baseline, longitudinal and circumferential strain 30 days after AMI were determinants of LVR. According to ROC analysis, circumferential apical strain smaller than 15.92% sensitivity, 93%, specificity, 59%, positive predictive value 80%) was the most powerful predictor of remodeling after primary PCI.

**Conclusion:** Impaired indexes of LV deformation, especially circumferential apical strain, detected by speckle tracking echocardiography during first 30 days after AMI, can be predictors of LVR.

**P2785**

**Relationship between left ventricular longitudinal deformation and clinical heart failure during admission for acute myocardial infarction - a two dimensional speckle tracking study**

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**Background:** Congestive heart failure (CHF) during hospitalization for acute myocardial infarction (MI) predicts poor outcome. LV ejection fraction (LVEF) does not always reflect the clinical signs of heart failure. We hypothesized that LV longitudinal strain is a stronger marker of heart failure as assessed by in-hospital clinical CHF than traditional echocardiographic indices.

**Methods and results:** We consecutively studied 611 patients (mean age 63.2±11.7 years, 71.6% male) with acute myocardial infarction admitted to a tertiary centre. Within 48 hours of admission a comprehensive 2-dimensional and Doppler echocardiography including 2-dimensional speckle tracking with assessment of global longitudinal myocardial strain (GLS) was performed along with measurements of plasma NT-proBNP. A total of 89 patients (16.2%) had in-hospital CHF assessed by Killip class >1 where GLS was significantly impaired compared to patients without in-hospital CHF (Killip class 1, 8±3.4 vs 13.8±4.3; p<0.0001). In stepwise multiple logistic regression analysis adjusting for age, known CHF,3-vessel disease, LAD involvement, episodes of atrial fibrillation, renal function, NT-proBNP, TNT, LVEF, wall motion index and diastolic dysfunction, GLS remained as the strongest marker of clinical CHF (Odds ratio 1.16, 95% CI unit increase 1.05-1.28; p=0.001). Internal validation by bootstrapping confirmed minimal optimism of the model (C-statistics: 0.85 vs. 0.83).

**Conclusion:** Global Longitudinal function assessed by GLS is significantly impaired in MI patients in in-hospital CHF and multivariable analysis suggests that reduced GLS is the single most powerful marker of manifest LV hemodynamic deterioration in the acute phase of MI.

**P2786**

**Influence of late exercise training on myostatin and follistatin expression in soleus muscle of rats with chronic heart failure**

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**Introduction:** Physical exercise can play a role in heart failure (HF) treatment. However, the mechanisms involved in exercise-induced improvement of functional capacity are not clear. Myostatin, a member of the transforming growth factor-β family, is a myoblast differentiation factor known to modulate muscle growth and function in infarcted rats prevented myostatin changes in skeletal muscle. This study evaluated the effects of late exercise training on myostatin expression in soleus muscle from rats with myocardial infarction-induced heart failure. As follistatin is one of the most commonly studied myostatin antagonists, we also analysed its expression.

**Methods:** Myocardial infarction (MI) was induced by left coronary occlusion. Sham-operated animals were used as controls. Three months later, rats were randomized into four groups: Sham (Sh-Sed, n=12), Sham exercised (Sh-Ex, n=12), MI sedentary (MI-Sed, n=11), and MI exercised (MI-Ex, n=10). Physical exercise was performed on a treadmill with 4 cycles of 50 min/day, 5 days/week, and 16 min/mi for 12 weeks. Cardiac structures and left ventricular function were assessed by transthoracic echocardiogram before and after training period. Infarct size was measured by left ventricular histological analysis. Myostatin and myostatin protein levels were analysed by Western blot. Fiber cross-sectional area and splitting frequency were evaluated in histological sections. Statistical analysis: ANOVA and Bonferroni test.

**Results:** MI size did not differ between MI-Ex (49.8±5.1%) and MI-Ex (48.4±9.8%; p=0.69). Exercise training improved systolic function in MI-Ex compared to MI-Sed (p<0.05), which was characterized by increased left ventricular fractional area change (Sh-Ex 70±1.6% vs. Sh-Ex 70.0±5.6%; MI-Ex 72±7.8; MI-Ex 29.5±7.51%). Soleus muscle cross-sectional area did not differ between groups. The frequency of splitting fibers was higher in exercise compared to sedentary groups and higher in MI-Ex than Sh-Ex (Sh-Ex 0.1%; Sh-Ex 2.2%; MI-Ex 0.5%; MI-Ex 6.1%; n=6 each group). Myostatin protein levels were lower in MI-Sed than Sh-And MI-Ex (Sh-Ex 1.00±0.35; Sh-Ex 1.02±0.37; MI-Ex 0.66±0.18; IM-Ex 1.77±0.48 arbitrary units; n=9 each group). Follistatin protein levels did not differ between groups.

**Conclusion:** Late exercise training increases the frequency of splitting skeletal fibers and prevents changes in myostatin and follistatin protein expression in skeletal muscle of infarcted rats.

**P2787**

**Mitochondrial function as a potential mediator of metabolic remodeling in the heart**

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**Purpose:** We previously reported that left ventricular hypertrophy (LVH) and congestive heart failure (CHF) are associated with a distinct change in the metabolic profile of the heart, in which glucose uptake increased at the LVH stage, and glucose uptake further increased and fatty acid uptake decreased at the CHF stage, associated with decreased gene expression related to mitochondrial function in a rat model of heart failure. The purpose of the study was to clarify the link between the changes in substrate utilization and mitochondrial function.

**Methods:** Carboxyl cyanide m-chlorophenylhydrazone (CCCP; 5 mg/kg), a compound known to reduce the mitochondrial membrane potential, was injected intraperitoneally into Sprague-Dawley rats. We assessed the cardiac function of the rats with CCCP or vehicle, cardiac metabolic state of the rats on in situ 31P magnetic resonance spectroscopy, and their mitochondrial membrane potential assessed by two-photon laser microscopy using ex vivo perfused hearts. Second, we examined whether CCCP caused a change in the myocardial uptake of glucose and fatty acids using 18F-deoxyglucose (FDG) and 125I-15-(p-iodophenyl)-9,8,5-methylpentadecanoic acid (BMFA), respectively.

**Results:** The rats administrated CCCP showed a transiently decreased systolic function on echocardiography (fractical shortening: CCCP: 45.6±1.1% vs. vehicle: 51.6±2.2%; p<0.05) and a 0.60-fold decrease in cardiac phosphorylase content (p<0.05) and a 0.59-fold decrease of cardiac ATP on in situ 31P magnetic resonance spectroscopy. Since ATP was mainly produced by mitochondrial membrane potentials, decreased ATP caused by CCCP injection means dispersion of the mitochondrial function. In ex vivo perfused hearts, CCCP decreased the mitochondrial membrane potential assessed by two-photon laser microscopy. The glucose uptake increased 1.96 fold compared to the vehicle group (p<0.05) and the fatty acid uptake increased 5.48 fold compared to the vehicle group 90 minutes after CCCP administration, indicating that mitochondrial dysfunction caused the changes in substrate uptake.

**Conclusions:** This rat model using CCCP could be used as a model of mitochondrial dysfunction. Mitochondrial dysfunction may be closely associated with metabolic remodeling in the heart, especially in the failing heart.

**P2788**

**Influence of N-acetylcycteine on NADPH oxidation complex in skeletal muscle of rats with heart failure**

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**Introduction:** There is substantial evidence that increased oxidative stress in heart failure contributes to skeletal muscle changes. However, the sources of reactive oxygen species (ROS) generated in skeletal muscle during heart failure are still unclear. The NADPH oxidation complex is an important ROS source in skeletal muscle. This study aimed to evaluate the influence of antioxidant N-acetylcycteine on NADPH oxidation activity and gene expression in soleus muscle of rats with myocardial infarction-induced heart failure.

**Methods:** Myocardial infarction (MI) was induced by left coronary occlusion. Sham-operated animals were used as controls. Four months later, rats were assigned to three groups: Sham (n=8), MI-C (MI without treatment, n=8), and...
Body composition assessment by Bio impedance in relation to the gold standard method DXA. Data from the SICA-HF study

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Background: Fat-free mass (FFM) is increasingly recognized as determining factor for survival of patients with chronic heart failure (CHF). It is therefore a promising target for physiologic and pharmacologic interventions to improve functional status and potential outcome. In clinical and ambulatory settings, however, assessment of fat free mass is rarely performed and applicable methods are poorly established. The aim of this study is to compare two methods for measurement of FFM in patients with CHF.

Methods: A total of 100 patients with CHF were enrolled [mean age 69±8 years, 22% female, NYHA (I/II/III/IV) 64/36, BMI 26.3±3.2 kg/m²]. Additionally we measured 20 healthy controls of similar age and BMI [age 66±9 years, 55% female, BMI 25.0±2.7 kg/m²]. Body composition was measured with the gold standard method of dual-energy-X-ray absorptiometry (DXA). Tissue distribution for fat tissue, fat-free (lean) tissue and bone tissue was assessed for total body and separately for arms, legs, and appendicular mass (arms plus legs). In comparison to this reference method, FFM was assessed by Bioelectrical impedance analysis (BIA). Presence of peripheral oedema was meticulously recorded and taken into account.

Results: In CHF patients FFM measured by BIA (FMFBIA=SD 53.7±11.1 kg) were strongly correlated to FFM measured by DXA of total regional FFM (FMFDXA=r=0.93, FMFMAMDXA=r=0.84, FMFFDXA=r=0.83 FMFAppar diculaDXA=r=0.86, all p<0.0001). In controls we found the same correlation between FMFBIA and FFM measured by DXA of total regional FFM (FMFDXA=r=0.94, FMFMAMDXA=r=0.92, FMFFDXA=r= 0.91 FMFAppar diculaDXA=r=0.93, all p<0.0001). A total of 52 patients with CHF had oedema, but FMFBIA correlated with FMFDXIA in patients with and without oedema (FMFDXIA total patients with oedema r=0.9 and FMFDXIA total in patients without oedema r=0.97, both p<0.0001). Comparison of Allman plots confirmed a good concordance between both methods in both patient sets (SD 11.4) and controls (SD 9.7) although an increasing difference between methods in very high FFM values was observed.

Conclusion: BIA assessment provides reasonable good measure of fat free mass in comparison to the gold standard method (DXA) clinical stable heart failure patients regardless of the presence or absence of oedema. BIA is, in comparison to DXA, much more suitable for fast and routine clinical application due to mobility, simple and affordable technical application without use of radiation. More consequent application of BIA seems a suitable tool to assess and monitor fat free mass.

Iron deficiency is a key determinant of health-related quality of life in patients with chronic heart failure regardless the anaemia status

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Purpose: Recent evidence suggests that iron deficiency (ID) in CHF is associated with impaired exercise capacity and poorer outcomes. The influence of ID with or without anaemia on health-related quality of life (HRQoL) in these patients has not been explored. This study aimed to evaluate the influence of ID and anaemia on HRQoL in patients with CHF.

Methods: 759 consecutive stable CHF patients with either reduced or preserved LVEF were included. At inclusion, clinical variables were recorded and blood samples were obtained for evaluation of iron status. HbQoL was measured using the Minnesota Living with Heart Failure Questionnaire (MLWHQF) (higher scores meaning worse QoL). Anaemia was defined as haemoglobin <12 g/dL. ID was defined as ferritin<100 ng/mL or %transferrin saturation (TSAT)<19%. As an additional marker of ID, the ferritin index (ratio of soluble transferrin receptor/log10[ferritin]) was evaluated (higher values indicate more pronounced iron deficiency). ID was not significantly different between anaemic and non-anaemic patients (p=0.59). Anaemia was associated with HRQoL (MLWHQF overall score: ID=44.6±25.03 vs. non-ID=9.8±26.1; p=0.005).

Results: Baseline characteristics were: Mean age 72±11 years, 45.2% were in NYHA class III-IV, 41.6% of patients had preserved LVEF. ID patients compared to non-ID patients had lower levels of ferritin and TSAT (p<0.0001). Blood free fatty acid levels were increased by 53% (p<0.005) and triglyceride (TG) levels were increased 2.0-fold (p<0.005). Analysis of the levels of Hb showed liver incorporated more glucose, the expression of genes related to gluconeogenesis was decreased, the expression of genes and proteins related to lipogenesis was increased, and TG content was increased 1.8-fold (p<0.005). Gene expressions of sterol regulatory element binding protein (SREBP)-1c and SREBP-2 increased, key enzymes of lipogenesis, were strongly correlated to FFM measured by DXA of total and regional FFM (FFM-MVX, NOX4, and NOX2 subunits did not differ between SREBP-1c and SREBP-2 also increased. The paradoxical production of triglycerides synthesis in failing hearts was associated with a proinflammatory response in liver.

Conclusions: The Dalt salt-sensitive rat can be used as a model of cardiac cachexia. The cachexia was associated with abnormal hepatic metabolism that might work as a maladaptive response during the progression of HF when the body is losing weight and peripheral tissues are substrate to maintain tissue homeostasis.
Background and Objective: In adult bone marrow and other tissues the number and function of stem cells decline with aging. Myocardin (MyC) and telomerase (TeM), two nuclear proteins, may synergize to promote cardiovascular myogenic-ness of adult mesenchymal cells. MyC acts as a transcription cofactor for myogenin, while TeM prevents senescence. This study examined the impact of enhanced expression of MyC and TeM on survival, growth, and differentiation of mesenchymal stromal cells (MSC) from old bone marrow and adipose tissues, as well as the therapeutic efficacy of transplantation of TeM+MyC+ MSCs in murine hindlimbs with ischemic injury.

Methods and Results: MSCs from adipose or bone marrow tissues of young mice (2 months old) and old (12 months old) male C57Bl/6 mice and apolipoprotein E deficient (ApoE−/−) mice were efficiently transduced or co-transduced with the 3rd generation lentiviral vectors (SFFV-LTR WPRE) carrying the cDNAs coding for TeM+FP (yellow fluorescence protein) or MyC-V5 epitope fusion proteins. Flow cytometry demonstrated that transduction with TeM, and to a lesser extent, MyC, but not empty vectors (mock), elevated MSC viability and BrdU uptake (p < 0.05 vs mock). In addition, increased numbers of MSCs were identified in the transduced cells, while apoptosis of the cells in response to Fas stimulation was inhibited (Table). Western blot showed increased expression of endogenous MyC. Cardiac and smooth muscle α-actin occurred in the cells with MyC+TeM cDNA delivery.

Conclusions: UMS-mediated transplantation of TeM+MyC+ MSCs to ischemic hindlimbs improves blood flow and tissue repair.

Table 1. The effect of TeM and MyC transduction on cell death and apoptosis of murine bone marrow-mesenchymal stem cells

<table>
<thead>
<tr>
<th></th>
<th>Mock</th>
<th>MyC + TeM</th>
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<tbody>
<tr>
<td>% dead cells</td>
<td>22 ± 3</td>
<td>17 ± 3</td>
</tr>
<tr>
<td>% necrotic cells</td>
<td>4 ± 0.2</td>
<td>3 ± 0.2</td>
</tr>
<tr>
<td>% apoptotic cells</td>
<td>9 ± 1.1</td>
<td>6 ± 0.7</td>
</tr>
<tr>
<td>Caspase-3</td>
<td>9 ± 1.3</td>
<td>4 ± 0.3</td>
</tr>
<tr>
<td>% dead cells</td>
<td>37 ± 7</td>
<td>8 ± 1.0</td>
</tr>
<tr>
<td>% necrotic cells</td>
<td>3 ± 0.1</td>
<td>5 ± 0.7</td>
</tr>
<tr>
<td>% apoptotic cells</td>
<td>97 ± 1.7</td>
<td>39 ± 4.0</td>
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Values are mean ± SD of percentage of positive cells for Annexin V and/or propidium iodide.

Conclusions: The simultaneous delivery of the TeM and MyC genes rescues MSCs from old adipose and bone marrow tissues by increasing their capacity of survival, proliferation, and differentiation. TeM+MyC+ MSCs possess the potential of repairing ischemic tissues and, when transplanted into the ischemic hindlimb, improve blood flow and revascularization.
thigh cuff inflation and plasma miRNA changes were analysed at baseline, at 10 min, 1h, 5h, 2 days and 7 days. Computational analysis using the temporal clustering by affinity propagation algorithm identified six distinct miRNA clusters. One cluster included all miRNAs associated with risk of future myocardial infarction. It was characterized by early (1h) and sustained activation (7 days) post ischaemia-reperfusion injury and consisted of miRNAs predominantly expressed in platelets.

**Conclusions:** In subjects with subsequent myocardial infarction differential co-expression patterns of circulating miRNAs occur around endothelial-enriched miR-126 with platelets being a major contributor to this miRNA signature.

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**The calcineurin splicing variant CnAβ1 induces recovery from myocardial infarction and reduces cardiac hypertrophy and fibrosis**

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**Purpose:** Calcineurin regulates cardiac development and maladaptive hypertrophy. CnAβ1 is a naturally occurring splicing variant of the calcineurin A beta gene. It has a unique C-terminal region not found in any other known protein. We have recently shown that transgenic mice overexpressing CnAβ1 in the heart (aMHC-CnAβ1) have improved cardiac function after myocardial infarction. However, this model did not allow us to discriminate between a protective and a reparative effect. Also, the effect of CnAβ1 in non-ischaemic heart disease was not explored in these mice.

**Methods:** Inducible cardiomyocyte-specific transgenic mice that overexpress CnAβ1 upon administration of doxycycline in the diet (Tet-On) underwent myocardial infarction by ligation of the left coronary artery for 30' followed by reperfusion. We established three experimental groups that received no doxycycline, doxycycline-rich diet either 3 weeks before or 1 week after establishment of CnAβ1 transgenic mice. Pre- or post-infarction also reduced the expression of heart failure markers and fibrosis. In addition, using aMHC-CnAβ1 mice we observed that constitutive cardiomyocyte-specific overexpression of CnAβ1 reduced cardiac hypertrophy after transaortic banding. These mice showed improved function and reduced fibrosis compared to wild type, suggesting that CnAβ1 has beneficial effects both on ischaemic and non-ischaemic hearts.

**Conclusions:** Whereas other calcineurin isoforms have a strong detrimental effect on the adult heart, CnAβ1 induces cardiac recovery after myocardial infarction and reduces hypertrophy and fibrosis following aortic stenosis. These results make CnAβ1 an interesting candidate for gene therapy in the heart.

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**MicroRNA-434a is a pivotal age-induced regulator of cardiac apoptosis, telomere maintenance and contractile function: Implications for therapeutic inhibition**

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**Background:** Aging is the major risk factor for developing complications like acute myocardial infarction (AMI) and chronic heart failure. The mechanisms involved in cardiovascular aging are poorly understood, but microRNAs (miRNAs) are emerging as key biological regulators.

**Results:** We investigated the changes in mRNA and miRNA expression in hearts of aged mice (18 months old) compared to young mice (6 weeks old) by microarray profiling. Amongst the significantly upregulated miRNAs in aged hearts was the entire miR-34 family. MiR-34a is highly expressed and significantly correlates with age in human hearts as well (p<0.004). Inhibition of miR-34a in 18 month old mice using specific antagonists against miR-34a (Anti-34a) reduced apoptosis in the heart (41±15.5%, P<0.05). Consistently, progenitor-derived cardiomyocyte dysfunction in KU80-/- mice was also ameliorated by miR-34a inhibition (Absolute ejection fraction (EF) increase: 17.7±2.1%). Moreover, 18 month old miR-34a-/- mice displayed superior cardiac contractile function (EF: 63.5±2.7%) and reduction in apoptosis and hypertrophy, compared to wild littermates (EF: 52.3±2.2%).

**Conclusions:** Furthermore, we found that Anti-miR induces miR-34a in the heart and that silencing of miR-34a improves recovery after AMI. This is evidenced by an improvement in EF and wall motion score index (WMSI) 14 days after AMI in mice treated with Anti-34a (EF: Anti-34a: 29±6.9% vs. 36.8±3.7%, P<0.005; WMSI: Anti-34a: 2.1±0.16 vs. Anti-34a: 1.5±0.12, P<0.05), as well as a reduction in apoptosis and fibrosis (74.0±15.4% and 68.1±10% inhibition, p<0.05, resp). One of the established targets of miR-34a is SIRT1, but mice experiments with SIRT1 +/- showed that the beneficial effect of Anti-miR is solely rely on SIRT1.

Next, we identified several novel potential targets of miR-34a, of which PNUTS (PPP1R10) is most strongly downregulated in aged hearts (89.4±4.2% inhibi-
LIPID LOWERING THERAPY: NEW CHALLENGES

2934 Statin use in patients undergoing hemodialysis

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Background: The effects of statins in patients undergoing hemodialysis (HD) were controversial. Our study aimed to determine whether statin use was beneficial in HD patients by using the Taiwan National Health Insurance database.

Methods: The statin cohort included HD patients with statin use. The age, gender-matched comparison cohort was selected from HD patients without any statin use. The endpoints of the study included acute myocardial infarction, ischamic stroke, hospitalization due to unstable angina, deep vein thrombosis, pulmonary embolism, cardiovascular mortality, and all cause mortality.

Results: The statin cohort included a total of 4,074 HD patients (mean age 53.3±13.5 years, male 34.9%), and the comparison cohort included 8,116 HD patients. During a maximum 7 years’ follow-up, there were totally 220 patients with acute myocardial infarction, 333 patients with ischamic stroke, 406 patients with hospitalization due to unstable angina, 76 patients with deep vein thrombosis, 10 patients with pulmonary embolism, 126 cardiovascular mortality, and 693 all cause mortality. Statin use was associated with the lower risk of ischamic stroke (hazard ratio [HR], 0.46; 95% confidence interval [CI], 0.36-0.60, p < 0.001), hospitalization for unstable angina (HR 0.59; 95% CI, 0.40-0.83, p < 0.001), deep vein thrombosis (HR, 0.10; 95% CI, 0.00-0.26, p < 0.001), cardiovascular mortality (HR, 0.27; 95% CI, 0.17-0.43, p < 0.001), and all cause mortality (HR, 0.45; 95% CI, 0.38-0.54, p < 0.001).

Conclusion: Statin use was associated with lower incidence of arterial and venous thromboembolism in patients undergoing HD.

2935 Long-term effect of statins on the risk of new onset dementia- a retrospective cohort study

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Purpose: To investigate the association between statins and new onset dementia (NOD).

Methods: This was a retrospective cohort study performed using data from claim forms from January 2001 to March 2011. Prescriptions for statins before the index date were retrieved from a prescription database. Baseline characteristics were compared and hazards ratios (HRs) calculated for statin user versus statin non-user for NOD follow-up of up to 10 years.

Results: A total of 214 NOD cases were identified in 3,992 dyslipidemic patients during the study period, including 1,068 statin users and 2,624 non-users. There were more women in the statin user group (56.3% vs. 41.7%), and statin users were more likely to have a history of cardiovascular disease (61.2% vs. 22.7%), diabetes (35.3% vs. 11.5%), and stroke (30.5% vs. 7.8%) than statin non-users (p < 0.001). The risk of NOD after adjusting sex, age, history of cardiovascular disease, diabetes, and stroke was lower among users of statins (HR, 0.90; 95% confidence interval, 0.82-0.99).

Conclusions: The results of this study suggest that dyslipidemic patients who take statins are at lower risk of NOD, irrespective of a past history of cardiovascular disease, diabetes, and stroke.

2936 Genetic variations in the PCSK9 gene in relation to lipid levels, cognitive function and clinical events in an elderly population

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Purpose: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a protein involved in the LDL cholesterol metabolism. Since PCSK9 has high affinity to the LDL receptor, inhibiting PCSK9 may be a promising therapeutic target for lipid lowering therapy. PCSK9 may be involved in processes associated with neurodegenerative disorders like Alzheimer’s disease. In this study we investigated the association between genetic variation within the PCSK9 gene and cognitive function and clinical events within the PROSPERpective Study of Pravastatin in the Elderly at Risk (PROSPER).

Methods: We performed a secondary analysis of the PROSPER study, which consisted of 4,927 participants randomly assigned to pravastatin or placebo and followed for a mean of 6.6 years. We included all participants with complete cognitive function data and used linear mixed models adjusted for age, sex, and baseline cognition in analysis. We genotyped 6 single nucleotide polymorphisms (SNPs) in the PCSK9 gene.

Results: We found only one haplotype associated with both lipid levels and clinical events. No haplotypes or individual SNPs were associated with cognitive function or clinical events.

Conclusions: Our findings suggest that therapy with PCSK9 inhibitors in addition of statin therapy will have no adverse effects on cognitive performance.
a high incidence of sudden cardiac death despite optimal pharmacologic therapy. Hospitalization frequency is actually increasing. Observational studies, prospec-
tive studies and post-hoc analyses of randomised clinical trials have suggested that statins could be beneficial in patients with chronic heart failure. Recent stud-
ies have explored the prognostic role of TDI-derived parameters in major cardiac diseases, such as heart failure. In heart failure non-invasive assessment of LV di-
astolic pressure by transmitral to mitral annular early diastolic velocity ratio (E/E') is a strong prognosticator, especially when E/E' is > or =15. This study sought to
determine whether treatment with atorvastatin affects left ventricular dysfunction and outcome in patients with chronic heart failure.

Methods and Results: A total of 191 patients with ischemic heart failure were randomized to either administration of atorvastatin (73 patients: aged 65.3±11.9; male 86%; UVEF: 39.04±11.41%) or no atorvastatin therapy (118 patients: aged 66.68±14.98; male 73%; UVEF: 35.52±11.99%) for 12 months. Conventional echocardiography Doppler was used to assess left ventricular (LV) ejection fraction and transmural systolic and diastolic filling. Patients with heart failure status) and ancillary for coronary artery calcium (CAC)-score. The HDL-C raising activity of dalcetrapib (CETP modulator) in sub-
group showed lower E/E' ratio (12.48±0.87 vs 22.01, P: 0.01) and higher late (A') diastolic TDI velocity of the mitral annulus at septal annulus (8.11±0.93 vs 4.37±1.76, P < 0.001), compared with placebo group. Cardiac dehiscence (P: 0.003), unplanned revascularization (P: 0.04), sustained ventricular tachycardia (0.002), recurrent heart failure (New York Heart Association class III or IV) were significantly increased in no atorvastatin therapy.

Conclusions: One year of atorvastatin treatment improved LV function and out-
come in patients with chronic heart failure.

2948 Body mass index is a strong predictor of myocardial infarction and stroke in fertile women, a nationwide study
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Purpose: Further knowledge of risk factors for atherosclerotic heart disease in young women is on the priority list for the American Heart Association. Therefore we examined the risk of myocardial infarction (MI) and stroke in women who had given birth and where risk factors are registered on a nationwide basis.

Methods: Women giving birth in the period 2004-2009 with no history of acute coronary syndrome or renal insufficiency were identified by cross-
linkage of nationwide registers. The women were grouped into four BMI-groups according to the World Health Organization classification, i.e., underweight (BMI<18.5 kg/m²), normal weight (BMI 18.5-24.9 kg/m²), overweight (BMI 25.0-29.9 kg/m²) and obese (BMI ≥30.0 kg/m²). We assessed the risk of MI and stroke by use of proportional hazard regression (adjusted for age, prior dia-
abetes and smoking during pregnancy) using normal weight women as the refer-
ence.

Results: We included 273,878 women with a median age of 30.5 years (in-
terquartile range 27.2-33.9 years). Median follow-up was 4.4 years (interquartile range 3.0-5.8 years). In total, 67 women experienced a MI, whereas 218 women were stroke by follow-up. The adjusted hazard ratios (HRs) of MI were 2.58 (95% confidence interval [CI] 1.00-6.70) in the overweight, 1.60 (CI 0.87-2.93) in the overweight, and 2.44 (CI 1.28-4.64) in the obese women, re-
spectively. With regard to stroke, the adjusted HRs were 1.03 (0.50-2.11) in the underweight, 1.15 (CI 0.82-1.62) in the overweight, and 1.54 (CI 1.02-2.66) in the obese women, respectively.

2949 Association of pericardial fat with incident myocardial infarction in the general population: the Heinz Nixdorf Recall study
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Purpose: Pericardial fat (PF) is associated with cardiovascular risk factors and prevalent coronary artery disease. We aimed to investigate, whether PF volume is associated with incident myocardial infarction in a general population cohort without known coronary artery disease.

Methods: Participants from the community based Heinz Nixdorf Recall Study were included in this analysis. PF volume was defined as fat inside the per-
cardial sac and quantified from non-contrast enhanced electron beam computed tomography. Cox regression analysis was used to determine the association of pericardial fat with incident fatal or non-fatal myocardial infarction during follow-
up. Adjustment was performed for traditional cardiovascular risk factors (including age, gender, waist circumference, systolic blood pressure, hypertensive medica-
tion, LDL- and HDL-cholesterol, lipid lowering medication, diabetes, and smoking status) and ancillary for coronary artery calcium (CAC)-score.

Results: Overall, 4093 participants without known coronary artery disease (59.4 years, 47% male) were included in this analysis. Median (Q1; Q3) pericardial fat volume was 85.9 ml (61.4-120.9). Age, waist circumference, systolic and diastolic blood pressure, cholesterol levels, and CAC-score as well as frequency of di-
betes, smoking and antihypertensive or lipid-lowering medication increased with quartiles of PF (p < 0.03 for all). During a mean follow-up period of 8.0±1.5 years, 130 subjects developed a fatal or non-fatal coronary event. Subjects in the high-
est quartile of PF had 5-fold increased incidence of coronary events compared to subjects in the lowest quartile (0.9 vs. 4.7%, p <0.001). In unadjusted mod-

2939 Effect of dalcetrapib on non-cholesterol sterol markers of cholesterol absorption in patients with familial hyperlipidaemia
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Purpose: The HDL-C raising activity of dalcetrapib (CEPT modulator) in sub-
jects with normal HDL-C is accompanied by an increase in non-cholesterol sterol markers of cholesterol absorption. Mechanistically, the latter may reflect ABCA1-
mediated lipidation of nascent HDL by ABCA1 from enterocytes. In the present study, we evaluated sterol markers in patients with low HDL-C due to familial hyper-
hyperlipoproteinaemia or familial combined hyperlipidaemia (FCH).

Methods: Single-centre, randomised, double-blind, two period, crossover study in which each patient received treatment with dalcepcipib 600 mg once daily on two occasions for 4 weeks. Lipids, apolipoproteins, CETP activity and CETP mass were measured using standard methodologies. Lathosterol (cholesterol synthe-
sis marker) and campesterol (cholesterol absorption marker) were measured by gas-liquid chromatography.

Results: Dalcetrapib increased HDL-C and ApoA-I similarly in patients with FHA (HDL-C +22.8%, ApoA-I +13.9%) and FCH (HDL-C +18.4%, ApoA-I +12.1%), all p <0.001 versus placebo. Changes in CETP activity and in CETP mass were also similar for patients with FHA (CETP activity −31.5%, CETP mass +120.9%) and with FCH (CETP activity -26.6%, CETP mass +111.9%); all p <0.001 versus placebo. There was no significant change seen in plasma lathosterol level ei-
ther in patients with FHA or with FCH (+3.0% and +9.4%, respectively). Whereas plasma campesterol level was unchanged in dalcetrapib-treated patients with FHA (+3.8%, NS), a striking increase was observed in patients with FCH (+25.0%, p <0.001 versus placebo).

Conclusions: Plant-sterol markers of absorption increase only in patients with-
out primary hypercholesterolaemia; notwithstanding comparable HDL-C and ApoA-I increases in both FHA and FCH patients following dalcetrapib treatment. These findings imply that, in the absence of ApoA-I and/or ABCA1 mutations, an increase in HDL-C coincides with increased pre-HDL lipidation by ABCA1 from enterocytes with concomitantly increased uptake of plant sterols.


OBESEITY AND CARDIOVASCULAR RISK: FOCUS ON BAD FAT

493 Lipid lowering therapy: new challenges / Obesity and cardiovascular risk: focus on bad fat

L. Kober, E. Sager (Editors) Lipid lowering therapy: new challenges / Obesity and cardiovascular risk: focus on bad fat


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els, doubling of PB was associated with a more than 2-fold increase in hazard ratio (HR) for coronary events (HR: 95% CI [1.74-2.88], p=0.001). Associations remained significant after adjustment for traditional cardiovascular risk factors (HR: 1.54 [1.09-2.19], p=0.05) with hazard ratios remaining unchanged when further adjusting for CAC-score (HR: 1.50 [1.07-2.11], p=0.02).

Conclusion: Pericardial fat is associated with incident coronary events independent of traditional cardiovascular risk factors and CAC-score in the general population and may help to improve risk prediction of first myocardial infarction.

2950 Long-term mortality in patients undergoing bariatric surgery compared to patients managed non-operatively for morbid obesity


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Purpose: Bariatric surgery improves cardiovascular risk but its effect on mortality has not been compared to non-operative strategies. We compared long-term, all-cause mortality after bariatric surgery (BSx) with mortality after non-operative management of morbid obesity.

Methods: This retrospective cohort included 2,020 patients undergoing BSxs at the Mayo Clinic (Rochester, MN, USA) and 2,907 non-operatively managed obese patients seen at our Nutrition Clinic between 1990-2009. Exclusion criteria were: age <18 years, body mass index (BMI) <35kg/m², and previous BSx. Non-operative patients did not undergo BSxs for various reasons (vollounarily declined, third-party payer denial, or lack of medical necessity). Most recent vital signs at the time of the BSxs/nutrition consult were abstracted from the medical records. Seventeen comorbidities assessed at baseline were used to calculate the Charlson comorbidity index, and patients were then divided in 4 groups according to their indices (0, 1-2, 3-4, ≥5). The Mayo Clinic registration system and Accurint, an electronically approved location service, allowed complete ascertainment of mortality status. We created a propensity score and performed multivariate logistic regression analysis accounting for age, sex, BMI, Charlson index, systolic and diastolic blood pressures, and year of the surgery. We used multivariate Cox-proportional hazard models to determine the association of BSx with all-cause mortality.

Results: Roux-en-Y gastric bypass accounted for 95% of the bariatric procedures. Mean age was 54±11 years (75% female) in the BSx group, and 58±14 years (67% female) in the non-operative group. BMIxs were 49±9 and 45±8 kg/m² respectively. More BSxs patients had a Charlson index of ≥1 (53.2% vs 44%, p<0.001), but indices >5 had similar frequencies in both groups (2.5% vs 2.6%, respectively). Mean follow up period was 7.4±4.9 years. Our final model using the propensity score yielded a hazard ratio of 0.76 (95% CI: 0.60-0.96) for mortality in the BSx group.

Conclusion: BSxs is associated with 24% decrease in long-term, all-cause mortality compared to non-operative management for morbid obesity.

2951 Normal-weight central obesity and cardiovascular mortality risk in the US population

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Purpose: Little is known if central obesity is related to worse survival in people with normal body mass index (BMI). We hypothesized that people with normal BMI but who are highly obese, would have a higher cardiovascular (CV) mortality as compared with people who do not have a central fat distribution.

Methods: We analyzed 12785 people ≥18 years of age from the National Health and Nutrition Examination Surveys III, a representative sample of the adult US population. We stratified subjects into 3 categories of BMI: normal (18.5-24.9 kg/m²), overweight; 25-29.9 kg/m² and obesity; ≥30 kg/m² and 2 categories of waist to hip ratio (WHR) (< vs ≥0.85 in women and < vs ≥0.90 in men). Subjects with COPD and cancer were excluded. We used multivariate Cox-proportional hazard models to evaluate the relationship of adiposity patterns and all-cause and cardiovascular mortality. Analyses were weighted and adjusted for age, sex, race, smoking, hypertension, diabetes, dyslipidemia and BMI.

Results: Mean age was 44 years, 47.4% were men. Median follow-up was 14.3 years and there were 2562 deaths, of which 1138 were CV. Subjects with normal BMI/WHR had the worst CV mortality among the 6 subgroups (unadjusted HR 3.79; adjusted HR 2.75, both p<0.0001). (Figure 1). Total and CV mortality in this normal BMI/highest WHR subgroup was even higher than in subjects with obesity by BMI (HR 1.98 and 1.20, respectively, both p<0.0001). Our results remained significant after excluding people with history of heart failure, CAD and stroke at baseline.

Conclusions: Normal weight central obesity yields the highest mortality risk of all the combinations using BMI and fat distribution categories. This pattern of obesity is associated with levels of risk higher than nearly any previously reported anthropometric measure.

2952 Waist circumference versus other obesity indices as determinants of coronary artery disease in essential hypertensive patients: A 6-year-follow-up study


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Purpose: There is still controversy over which obesity parameter has the strongest cardiovascular predictive value. The aim of the present study was to worsen and the predictive role of body mass index (BMI), waist circumference (WC), waist to hip ratio (WHR) for the incidence of coronary artery disease (CAD) in a cohort of essential hypertensive patients.

Methods: We followed up 1755 essential hypertensives (mean age 58.3 years, 965 males, office blood pressure (BP)>143/91 mmHg) free of cardiovascular disease for a mean period of 6 years. All subjects had at least one annual visit and at baseline underwent comprehensive echocardiographic study for determination of left ventricular mass index (LVMI) and blood sampling for assessment of metabolic profile. Moreover, weight and height were measured by standard techniques and waist circumference was estimated at the midpoint between the low rib margin and the iliac crest. LV hypertrophy (LVH) was defined as LVMI ≥125 g/m² in males and LVMI ≥110 g/m² in females, while CAD was defined as the history of myocardial infarction or significant coronary artery stenosis revealed by angiography or coronary revascularization procedure.

Results: The incidence of CAD over the follow-up period was 2.56%. Hypertensives who developed CAD (n=45) compared to those without CAD at follow-up (n=1710) had at baseline greater waist circumference (102.1±11.4 vs 96.6±11.9 cm, p=0.001), LVMI (116.6±28 vs 104.6±27.2 g/m², p=0.002) and prevalence of LVH (43% vs 26%, p=0.02). No difference was observed between hypertensives with CAD and those without CAD with respect to baseline office BP, BMI and WHR values (p=NS for all). In successive multivariate Cox regression models waist circumference (HR 1.036, p=0.005) and LVMI (HR 1.011, p=0.042) turned out to be independent predictors of CAD.

Conclusions: In essential hypertensive patients baseline waist circumference predicts future development of CAD, whereas BMI and WHR have no independent prognostic value. These findings suggest that among obesity indices waist circumference constitutes the easy clinical tool to assess risk in hypertensives.

2953 The impact of central obesity on mortality in patients with non-ST segment elevation myocardial infarction


Purpose: Central obesity has the positive correlation with advanced coronary artery disease. However, there exists “obesity paradox” meaning once one has acute myocardial infarction, obesity seems to be associated with unexpected beneficial effect on mortality. Till now, little is known about the correlation of central obesity and mortality in patients with acute coronary syndrome.

Methods: In patients registered in the Korean Acute Myocardial Infarction Registry(KORMI) between December 2007 and December 2010, 6560 NSTEMI patients were divided into 4 groups according to BMI: underweight (<18.5kg/m²), normal (18.5-23.0kg/m²), overweight (23.0-27.5kg/m²) and obesity (≥27.5kg/m²). They were then divided into 2 groups according to waist to hip ratio (WHR): normal(<0.8 in women and <0.9 in men) and abnormal(≥0.8 in women and ≥0.9 in men). Additionally, patients were defined with paradox 1 if they had BMI≥23.0kg/m² and abnormal WHR, and with paradox 2 BMI≥23.0kg/m² and normal WHR to evaluate the effect of post acute central obesity. In hospital mortality, 1 month mortality were mortality were analyzed.

Results: Obese group had significantly lower in hospital mortality, overall mortality at 1 month and 1 year in our study. Abnormal WHR group showed significantly higher 1 month mortality but in hospital mortality and 1 year mortality were similar with normal WHR group. Paradox 1 group revealed significantly higher in-hospital mortality, and 1 month year mortality compared with paradox 2 and normal group.
SAFETY OF ANTITHROMBOTIC DRUGS: FROM BENCH TO PRACTICE

Cardiovascular and gastrointestinal consequences of discontinuation with low-dose acetylsalicylic acid therapy in patients with cardiovascular disease

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Purpose: To estimate the risk of coronary, cerebrovascular and upper gastrointestinal bleeding (UGIB) events associated with the discontinuation of low dose acetylsalicylic acid (ASA).

Methods: The Health Improvement Network primary care database was used to identify a cohort of patients aged 50–84 years between 2000 and 2007 with a first prescription for low-dose ASA (75–300 mg/day) for the secondary prevention of coronary or cerebrovascular events (N = 38 513). Patients were followed-up between the first prescription for low-dose ASA (75–300 mg/day) for the secondary prevention of coronary or cerebrovascular events (N = 38 513) and new cases of coronary events (non-fatal myocardial infarction (MI)/coronary heart disease (CHD) death; n = 1222), cerebrovascular events (ischaemic stroke (IS)/transient ischaemic attack (TIA); n = 673) and UGIB (n = 169) were identified after a mean of 3.2, 3.4 and 4.0 years, respectively. Controls were selected (n = 5000 each for coronary and cerebrovascular events, and n = 2000 for UGIB) and frequency matched to cases by age, sex and calendar year. Individuals who discontinued low-dose ASA before the index date (index date for cases and a random date for controls) were identified. Recent discontinuation was defined as when the last prescription for low-dose ASA ended 31–180 days before the index date. Logistic regression analyses were performed to estimate the risks of the three outcomes among recent discontinuers of low-dose ASA therapy compared with those who continued therapy.

Results: The incidence of coronary, cerebrovascular events, and UGIB was 9.58 (95% CI: 9.06–10.14), 4.98 (95% CI: 4.62–5.37) and 1.12 (95% CI: 0.96–1.30) per 1000 person-years, respectively. Compared with current users, recent discontinuers of low-dose ASA had statistically significant increases in the risk of coronary events (relative risk [RR]: 1.43; 95% confidence interval [CI]: 1.12–1.84) and cerebrovascular events (RR: 1.40; 95% CI: 1.03–1.82), but had a non-significant reduced risk of UGIB (RR: 0.78; 95% CI: 0.42–1.43). Among 10 000 low-dose ASA users, an extra 40 cases of non-fatal MI/CHD death and an extra 20 cases of UGIB would be prevented, upon discontinuation with low-dose ASA therapy.

Conclusion: Individuals who discontinue with low-dose ASA therapy are at a significantly increased risk (~40%) of coronary and cerebrovascular events compared with those who continue treatment. By preventing low-dose ASA users discontinuing with therapy, for every 10 000 patients receiving low-dose ASA therapy, 60 ischaemic coronary and cerebrovascular cases could be prevented, at the cost of a small increase in the number of UGIB cases.
dine at randomization. Median duration of thienopyridine treatment was 360 days (IQR, 189–512), similar to the median duration of vorapaxar treatment (379 days; IQR, 231–585). During the on-treatment period, the hazard for bleeding with vorapaxar tended to be less in patients not on a thienopyridine across all bleeding assessments (Figure). Only 5 patients not on thienopyridine had an intracranial hemorrhage (1.02% placebo vs 4.08% vorapaxar). In patients not on a thienopyridine, vorapaxar was associated with 22% reduction in the hazard of primary endpoint (HR, 0.77; 95%CI, 0.60–0.99) and 26% in the hazard of CV death, MI, and stroke (HR, 0.74; 95%CI, 0.57–0.97), but interactions with study treatment were statistically significant.

Conclusion: In patients not on a thienopyridine, vorapaxar tended to have less hazard of bleeding and more pronounced efficacy. Future research will be helpful in defining the efficacy and safety of vorapaxar with different concomitant antiplatelet regimens.

2961 Predicted thromboembolic risk not associated with use of dual-antplatelet therapy plus warfarin relative to dual-antplatelet therapy alone in older patients with atrial fibrillation and NSTEMI

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Background: Selecting a safe and effective antithrombotic strategy for NSTEMI patients with atrial fibrillation (AF) poses a unique challenge especially among stented patients, yet little is known about which factors are associated with starting dual antiplatelet therapy [DAPT] (aspirin+clopidogrel) plus warfarin relative to DAPT alone.

Methods: We linked NSTEMI patients aged ≥65 years in the GRUSADE registry 2003-2006 to Medicare claims data and examined those with AF who received coronary stenting and either DAPT or DAPT-warfarin on discharge. Excluding in-hospital deaths, we used multivariable logistic regression analysis with backward selection to examine patient level factors associated with DAPT+warfarin vs. DAPT at discharge.

Results: Among 7,619 NSTEMI patients with AF, 1,200 (16%) were stented and received DAPT and 448 (6%) were stented and received DAPT+warfarin. Only few key factors traditionally determining bleeding risk (Table) were, after adjusting, associated with the choice to use DAPT+warfarin vs. DAPT: current smoking, odds ratio (OR) 0.59, 95% CI 0.37-0.96; creatinine clearance, OR 1.05, 95% CI 1.01-1.08 per 5 unit increments in creatinine clearance; and warfarin use, OR 15.62, 95% CI 11.89-20.52. CHADS2 score was not associated with DAPT+warfarin.

Baseline characteristics among groups

<table>
<thead>
<tr>
<th></th>
<th>DAPT (n=1200)</th>
<th>DAPT+warfarin (n=448)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y (IQR)</td>
<td>75 (71-82)</td>
<td>77 (71-82)</td>
<td>0.14</td>
</tr>
<tr>
<td>Female, %</td>
<td>43.9</td>
<td>35.7</td>
<td>0.003</td>
</tr>
<tr>
<td>Smoking (current/never), %</td>
<td>12.7</td>
<td>7.14</td>
<td>0.0014</td>
</tr>
<tr>
<td>Median Creatinine (IQR)</td>
<td>21 (19-23)</td>
<td>20 (19-23)</td>
<td>0.23</td>
</tr>
<tr>
<td>Home warfarin, %</td>
<td>33.0</td>
<td>66.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>79.4</td>
<td>80.1</td>
<td>0.09</td>
</tr>
<tr>
<td>Baseline hematocrit, %</td>
<td>39.9</td>
<td>39.8</td>
<td>0.86</td>
</tr>
<tr>
<td>Baseline systolic BP, mmHg</td>
<td>140 (120-160)</td>
<td>140 (124-159)</td>
<td>0.39</td>
</tr>
<tr>
<td>Baseline Creatinine clearance, mL/min</td>
<td>43.2 (32.5-75.7)</td>
<td>45.3 (34.7-59.0)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Conclusion: Approximately 1/3 of older NSTEMI patients with AF treated with coronary stenting were treated with DAPT-warfarin. The decision to treat with DAPT+warfarin relative to DAPT seemingly unrelated to predicted risk of bleeding and thromboembolic events.

2963 Evaluation of recombinant activated factor VII, prothrombin complex concentrate and fibrinogen concentrate to reverse apixaban in a rabbit model

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Background: As a potent anticoagulant agent, apixaban exposes to a risk of bleeding. An effective way to reverse its effects is needed. Objectives were to study efficacy and safety of recombinant activated factor VII (rFVIIa), prothrombin complex concentrate (PCC) and fibrinogen concentrate to reverse the anticoagulant effect of apixaban in a rabbit model of bleeding and thrombosis.

Methods: First, a dose ranging study assessed the minimal apixaban dose that increased bleeding. Then, 63 anesthetized and ventilated rabbits were randomized into five groups: control (saline), apixaban (apixaban and saline), rFVIIa (apixaban and rFVIIa), PCC (apixaban and PCC) and fibrinogen (apixaban and fibrinogen). TheFolllow model was applied: a stenosis and an injury were carried out on the carotid artery, inducing thrombosis, detected as cyclic flow reductions, which were recorded over 20 minutes. Then the following were measured: ear immersion bleeding time, clotting times, anti-Xa activity, thromboplastin parameter and thrombin generation test (TGT). Ultimately, a hepatosplenic section was performed and the total amount of blood loss after 15 min was evaluated as aspirin end point.

Results: Apixaban increased blood loss (129±14g vs. 85±11g) for control (measured range); p<0.0003), lengthened ear bleeding time, ProthrombinTime (PT), thrombelastographic clotting time and decreased thrombin generation rFVIIa decreased ear bleeding time (87±100g vs. 118±165g; p<0.05), but without efficacy on bloodloss. PCC and rFVIIa decreased PT as well as thrombelastographic clotting time shortened the lag time in TGT. Fibrinogen concentrate, surprisingly, increased blood loss and BT whereas it improved thromboelastographic clotting time and increased fibrinogen concentration to supraphysiological level.Es. Regarding safety, neither rFVIIa, PCC nor fibrinogen concentrate increased-cyclic flow reductions.

Conclusion: rFVIIa, PCC and fibrinogen concentrate improved laboratory parameters, but did not reverse apixaban induced bleeding.

INTERVENTIONS TO PROTECT THE HEART

2980 Long-term results after cardiac resynchronization therapy with or without surgical revascularization in patients with ischemic heart failure and left ventricle dysynchrony


Introduction: We have tested the hypothesis whether epicardial cardiac resynchronization therapy (CRT) concomitantly with surgical revascularization is superior to CRT and medical therapy in patients with ischemic heart failure, LVEF<35% and LV dysynchrony, who were eligible for coronary artery bypass surgery. The patients were randomly assigned to endocardial CRT implantation plus medical therapy (n=48) or epicardial CRT implantation plus CABG (n=48). The primary end point was the reduction in left ventricular systolic volumes (LVEV) by 15% according to echocardiography. The major secondary endpoint included the all cause death. The patients were followed up during 24 months.

Results: At 24 months, the mean LVEV was significantly lower in epicardial CRT

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The magnitude of preoperative low-grade inflammation predicts the development of acute heart failure and the need for inotropic support after elective coronary artery bypass surgery

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Background: Coronary bypass grafting operation (CABG) is a major operation that frequently requires prolonged hospitalization, due to complications that include acute failure of the left ventricle. It is therefore important to identify the key mechanisms triggering left ventricular failure post-CABG, in order to identify novel therapeutic targets. Monocyte chemoattractant protein-1 (MCP-1) is a cytokine with a key role in immune cell chemotaxis and may regulate the cellular infiltration of the myocardium post CABG. We examined the effect of circulating MCP-1 on the development of acute heart failure and the need for inotropic support after CABG.

Methods: We recruited 245 patients undergoing elective CABG. Left ventricular systolic function was evaluated preoperatively. The morning before the operation, after 6h of fasting, blood samples were obtained and the levels of MCP-1, IL-6 and hsCRP were determined. The patients were followed-up until their discharge from the hospital. The use of inotropes was recorded during their stay in the hospital. Results: Patients that required inotropic support post-operatively had significantly higher preoperative levels of MCP-1 (A), IL-6 (B) and hsCRP (C). In multiple regression analysis, MCP-1 and IL-6 were also independent predictors of the use of inotropes in the post-operative period (P<0.05 for both), independently of risk profile and preoperative left ventricular systolic function.

Conclusions: Preoperative levels of MCP-1, IL-6 and hsCRP are independent predictors of the need of post-operative inotropic support independently of preoperative left ventricular systolic function in patients undergoing CABG. Our findings identify these biomarkers as potential therapeutic targets for the prevention of post-operative complications after cardiac surgery.

The hemodynamic effect of right ventricle, real-time three-dimensional echocardiography targeted left ventricle and biventricular pacing in the early postoperative period after cardiac surgery

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Purpose: Congestive heart failure negatively impacts the prognosis in patients after cardiac surgery. The aim of our study was to assess the value of targeted cardiac resynchronization therapy (CRT) within 72 hours after cardiac surgery in patients with mechanical dysynchrony who had an EF < 35%, QRS >150 ms or between 120 and 150 ms.

Methods: A prospective randomized trial based on 3D echocardiography (RT3DE) and optimized sequential (DDD) pacing in patients after cardiac surgery. DDD epicardial pacing (Medtronic coxial epicardial leads 6495) was provided by a modified Medtronic INSYNQ III Pacemaker. Invasive measurements at individual pacing modes were performed postoperatively using Swan-Ganz thermomodiﬁer catheter.

Results: The study included 21 patients with ischemic HD or valvular HD (16 men, 5 women, average age 69 years) with LV dysfunction after cardiac surgery. Patients with biventricular (BIV) (CO 6.7 ±1.7 l/min, CI 3.5 ±0.8 l/m²/min) and left ventricular (LV) (CO 6.2 ±1.5 l/min, CI 3.2 ±0.7 l/m²/min) pacing had statistically signiﬁcantly higher CO and CI than patients with right ventricular (RV) (CO 5.4 ±1.4 l/min, CI 2.8 ±0.6 l/m²/min) pacing (BIV v.s. RV p<0.001; LV v.s. RV p<0.05; BIV v.s. LV p<0.05).

Conclusion: Daptomycin targeted and optimized CRT in the early post-operative period after cardiac surgery provided better hemodynamic results than RV pacing.

Surgical treatment for ischemic heart failure (STICH) trial: mode of death results

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Background: Mode of death (MOD) analysis has enhanced the understanding of outcomes in heart failure and led to new therapeutic approaches. However, limited adjudicated MOD data exists for coronary artery bypass graft (CABG) therapy, and there is no MOD data for this therapy in ischemic cardiomyopathy (IsCM) patients. The STICH trial compared the strategy of CABG and medical therapy (MED) to MED alone in 1212 IsCM patients. There were 462 deaths (median follow-up of 56 months); all-cause (AC) and cardiovascular (CV) mortality results have been previously reported. We analyzed the deaths in STICH to assess the effect of CABG on MOD.

Methods: A clinical events committee consisting of cardiologists and surgeons adjudicated deaths within the randomized treatment groups using pre-specified definitions for MOD. Statistical comparisons utilized Kaplan-Meier (K-M) estimates and Cox model analysis.

Results: Adjudicated results appear in Figure 1. Sudden deaths (SD) were the major MOD in both CABG (74 events) and MED (99 events) treatment groups, followed by pump failure (PF) events (33 vs. 49). CABG therapy signiﬁcantly reduced SD (p=0.040) events with a similar effect on PF events (p=0.030). Deaths post CV procedures were increased in CABG patients (38 vs. 9), but fatal myocardial infarction (MI) deaths were markedly reduced (1 vs.13). Non CV deaths were infrequent and did not differ between groups (37 vs. 33 respectively).

Conclusion: Sudden deaths were the leading cause of death in both the CABG and MED groups, and the addition of CABG to MED signiﬁcantly reduced these
events. The concomitant reduction in MI related deaths suggests that a CABG effect on SD events may relate to an anti-ischemic mechanism. PF deaths were less common but were also reduced by revascularization.

**Alternative access transcatheter aortic valve implantation: clinical characteristics and early outcome**

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**Purpose:** Transcatheter Aortic Valve Implantation (TAVI) is now considered the standard of care in extreme risk patients with severe aortic stenosis and as an alternative to surgery in those considered high risk. When the transfemoral approach was not possible, alternative vascular access was used. We compared baseline characteristics and short-term outcomes in patients undergoing TAVI with CoreValve (CV) via the transfemoral (TF) approach and left or right subclavian (SC) approach in patients implanted in a large multicenter study.

**Methods:** The CoreValve ADVANCE study evaluated the clinical effects of CV in a fully monitored, single-arm trial performed in 44 centers in 12 countries in Western Europe, Asia and South America. Extreme and high risk patients with severe aortic stenosis (n=1015, mean age 81±6 years, 51% female, mean Logis- tic EuroSCORE 20±13%) were included. The study included all consecutive patients undergoing PCI for CTO in a multicentre Japanese registry. The aim of this study was to assess whether the J-CTO score is useful for the prediction of procedural failure of PCI for CTO in a different cohort of patients.

**Results:** The study included all consecutive patients undergoing PCI for CTO at 3 tertiary PCI centres between January 2004 and December 2011. The J-CTO score assigns 1 point to each of the following: calcification, bending, blunt stump, occlusion length ≥20 mm, and previously failed lesion and classifies lesions into 4 categories (CTO) remains relatively infrequent partly due to the uncertainty and paucity of data on the likelihood of successful TAVI of these lesions. We sought to examine factors that may predict successful PCI of CTO in order to improve patient selection and optimisation of conditions for success.

**Conclusion:** TAVI with CV via the DA approach appears to be a safe and feasible alternative in a very high risk subset of TAVI patients, with very good early outcomes. It can be performed in patients with severe native and calcified aortic stenosis, and in this small subset early outcomes are encouraging.

**DIAGNOSTIC AND THERAPEUTIC CONTROVERSIES IN PERCUTANEOUS CORONARY INTERVENTIONS**

**Predictive value of the J-CTO score in percutaneous coronary interventions for chronic total occlusions**

G. Ferrante1, Y. Louvard1, T. Harb1, T. Unterseer2, T. Hovasse1, M. C. Morice1, B. Chevaller1, T. Lefevre1, P. Garot1, ICPS - Institute Hospital Jacques Cartier, Massy, France; 2Institut Cardiovasculaire Paris Sud, Quincy, France

**Purpose:** The J-CTO score has been shown to predict successful guidewire passage. The aim of the present study was to investigate whether the J-CTO score predicts procedural success or failure of PCI for chronic total occlusions (CTO) in a multicentre Japanese registry. The aim of this study was to assess whether the J-CTO score is useful for the prediction of procedural failure of PCI for CTO in a different cohort of patients.

**Methods:** The study included all consecutive patients undergoing PCI for CTO at 3 tertiary PCI centres between January 2004 and December 2011. The J-CTO score assigns 1 point to each of the following: calcification, bending, blunt stump, occlusion length ≥20 mm, and previously failed lesion and classifies lesions into 4 categories (CTO) remains relatively infrequent partly due to the uncertainty and paucity of data on the likelihood of successful TAVI of these lesions. We sought to examine factors that may predict successful PCI of CTO in order to improve patient selection and optimisation of conditions for success.

**Results:** Of 1,509 consecutive PCI of CTO in our institution performed between 2004 and 2011, the median age was 63 and 86% were male. The success rate of PCI of CTO was 71%. Significant univariate correlations to successful PCI were operator experience (r=0.08, p=0.002), and tapered morphology (r=0.1, p<0.0001), while factors that contributed to failure were age (r=0.06, p=0.02), lesion length (r=0.2, p<0.0001), no visible stump (r=0.08, p=0.001), calcification (r=-0.15, p=0.04), any tortuosity (r=-0.55, p=0.04), previous MI (r=0.1, p=0.001) and previous CABG (r=-0.12, p=0.001). Table 1 shows the significant predictors in terms of their odds ratios of successful PCI of CTO in a multivariable logistic model which also adjusted for age, sex, radial access, femoral access, operator experience, lesion length, stump visualization, tortuosity and previous CABG. Radial access was as good as femoral access in terms of successful PCI of CTO (OR 1.1, p=0.7 vs OR 1.0, p=0.8).

**Conclusion:** In this contemporary series, age, lesion length, operator experi-
Estimating organs cancer incidence related to patient radiation exposure following PCI for acute and chronic coronary total occlusion

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Background: Minimal data exists on the number of additional cancer cases related to radiation exposure following percutaneous coronary intervention (PCI).

Aim: To better understand the lifetime attributable risk (LAR) of cancer incidence for individual organs following radiation exposure during PCI in the context of two opposite sides of angiographic spectrum of coronary occlusive disease: ST-elevation myocardial infarction (STEMI) and chronic coronary total occlusion (CTO).

Methods and Results: We identified all consecutive patients treated with PCI for STEMI (n=555) and for CTO (n=543) in a tertiary care center in 6 years. The equivalent dose (HT) of ten critical organs/tissues were derived from HT/dose-area product conversion factors for different projections calculated by Monte Carlo method. The LARs of cancer incidence for six organs (colon, liver, lung, red bone marrow, stomach and thyroid) were estimated using the Biological Effects of Ionizing Radiation (BEIR)-VII model. On average, the HT applied to individual organs during PCI for CTO were almost twice the HT applied during PCI for STEMI.

In both groups, the highest HT was observed for the lung. The estimated LARs of cancer incidence for individual organs was found to markedly increase as the age of the patient decreases and was significantly higher for the lung (additional risk up to 18/100.000 person’s lifetime exposure in CTO and 9/100.000 in STEMI patients, respectively, p<0.0001) and for the red bone marrow (up to 3.5/100.000). In both groups, the estimated LAR of cancer incidence for stomach, colon, liver and thyroid was similar and very low.

Conclusions: The HT applied to individual organs during PCI for CTO were considerably higher than that applied during PCI for STEMI. In both groups, the lung was the organ with the highest radiation. According to BEIR-VII model, the number of additional cancer cases associated with better long-term clinical outcome than that observed in patients undergoing Angio-guided PCI.

Table 1: Selected significant predictors from multivariable model

<table>
<thead>
<tr>
<th>OR of Successful PCI of CTO</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year increase)</td>
<td>0.98</td>
<td>0.98, 0.99</td>
</tr>
<tr>
<td>Lesion length (per 1 mm increase)</td>
<td>0.97</td>
<td>0.97, 0.98</td>
</tr>
<tr>
<td>Operator experience (per 50 cases increase)</td>
<td>1.13</td>
<td>1.06, 1.19</td>
</tr>
<tr>
<td>Stump visible</td>
<td>1.51</td>
<td>1.12, 2.06</td>
</tr>
<tr>
<td>Target vessel morphology</td>
<td>1.36</td>
<td>1.03, 1.78</td>
</tr>
<tr>
<td>Calcification</td>
<td>0.74</td>
<td>0.65, 0.84</td>
</tr>
<tr>
<td>Art Tortuosity</td>
<td>0.72</td>
<td>0.53, 0.98</td>
</tr>
<tr>
<td>Previous MI</td>
<td>0.67</td>
<td>0.50, 0.88</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>0.44</td>
<td>0.29, 0.68</td>
</tr>
</tbody>
</table>

Discussion:

Exence, stump visibility, tapered morphology, calcification, tortuosity, previous MI and previous CABG affect successful PCI of CTO. The baseline clinical characteristics were similar between the two groups except left ventricular ejection fraction (LVEF) was lower in the angiography-guided group (47.5±12.9 vs. 54.0±9.47%, p<0.001). Six-month angiographic outcomes were similar between the two groups (table). At 2-year follow-up, the incidence of total death, cardiac death, major adverse cardiac events up of 56 months (31-84), FFR-guided group was associated with a significantly lower MACE rate as compared with Angio-guided group [23 (38%) vs. 65 (54%), p<0.02]. This difference was mostly driven by lower TVR [10 (18%) vs. 32 (33%), p=0.04], and by strong trend towards lower CACS [3 (5%) vs. 14 (15%), p=0.08], while no significant difference was found in terms of Death [15 (25%) vs. 29 (24%), p=0.77].

Conclusions: FFR-Guided PCI of coronary artery by-pass graft is safe and associated with better long-term clinical outcome than that observed in patients undergoing Angio-guided PCI.
Diagnosis and therapeutic controversies in PCIs / Risk assessment and long-term outcome after PCI

(MACCEs) were lower in the IVUS-guided group as compared with the angiography
guided group. Further, multivariate analysis adjusted by age, gender, dyslipidemia,
LVEF and Left vent classification showed that cardiac death, target lesion
revascularization (TLR), MACCE and target vessel revascularization (TVR)-MACCE
remained significantly lower in the IVUS-guided group (table).

RISK ASSESSMENT AND LONG-TERM OUTCOME
AFTER PERCUTANEOUS CORONARY INTERVENTION

Final five-year follow-up of the SYNTAX trial: optimal
revascularisation strategy in patients with three-vessel
disease and/or left main disease

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P.W. Serruya9 on behalf of SYNTAX Investigators. 1University of Leipzig, Heart
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Evaston, United States of America; 5Uppsala University Hospital, Uppsala,
Sweden; 6Baylor University Medical Center, Dallas, United States of America;
7San Raffaele Hospital (IRCCS), Interventional Cardiology Unit, Milan, Italy;
8Mayo Clinic, Rochester, United States of America; 9Boston Scientific, Natik,
United States of America

Purpose: To compare the 5-year outcomes in patients with de novo three-vessel
3VD) and/or left main coronary disease (LM) treated with percutaneous coronary
intervention (PCI) versus coronary artery bypass surgery (CABG).

Methods: SYNTAX is an 85 centre, randomised clinical trial (PCI n=903, CABG
n=897) with nested registries. A cardiac surgeon and interventional cardiologist
collected screening consecutive patients with de novo 3VD and/or LM disease. If amenable
for both revascularisation treatments, they were randomised to PCI or CABG. If
suitable for only 1 treatment option, they were entered into the PCI registry if
ineligible for CABG or the CABG registry if unsuitable for PCI.

Results: After 4-years, MACCE, all-cause death, MI and repeat revascularisation
were similar between the PCI arm versus CABG (Table). The rates of death/stroke/MI
and stroke were similar between CABG- and PCI-treated patients. In patients with
low SYNTAX Scores (<22), the rate of MACCE was similar between the 2
groups; however, in patients with intermediate or high SYNTAX Scores, MACCE
was significantly increased in the PCI cohort (Tables). Five-year outcomes will be
available at the time of the presentation.

Event rates at 4 years

<table>
<thead>
<tr>
<th></th>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACCE</td>
<td>23.6%</td>
<td>23.5%</td>
</tr>
<tr>
<td>Death/Stroke/MI</td>
<td>18.0%</td>
<td>18.0%</td>
</tr>
<tr>
<td>Death</td>
<td>8.8%</td>
<td>11.7%</td>
</tr>
</tbody>
</table>

MACCE: All-cause death, stroke, MI, repeat revascularization. Time-to-event rates at 4 years.

**P<0.05 from log-rank or chi-square test.

Subgroup comparison of outcome based on SYNTAX

<table>
<thead>
<tr>
<th>MACCE</th>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with SYNTAX score ≤22</td>
<td>26.1%</td>
<td>28.6%</td>
</tr>
<tr>
<td>Patients with SYNTAX score ≥33</td>
<td>23.6%</td>
<td>46.1%</td>
</tr>
</tbody>
</table>

MACCE: All-cause death, stroke, MI, repeat revascularization. Time-to-event rates at 4 years.

**P<0.05 from log-rank or chi-square test.

Conclusions: The clinical outcomes in the randomised three-vessel and LM SYNTAX patient population. Previous results suggest that CABG remains the standard care for patients with complex lesions (high/intermediate SYNTAX Scores), which was reinforced in the CABG registry. With less complex disease (low SYNTAX Scores), PCI may be an acceptable revascularisation alternative and should be discussed in the heart team.

The long term (4-year) prognostic significance of abnormal cardiac enzyme rises in patients treated with surgical or percutaneous revascularisation: a substudy from the SYNTAX trial

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and Thoracic Anaesthesia and Surgery, Uppsala, Sweden

Aims: The aim of the present investigation was to determine the long-term (4-
year) prognostic association of abnormal cardiac enzyme rises within the
randomised SYNTAX population.

Methods: In the SYNTAX trial, 1800 patients with left main or three-vessel coro-
nary artery disease were randomised on a 1:1 basis to undergo coronary artery
bypass graft (CABG) surgery or percutaneous coronary intervention (PCI). Per
protocol patients underwent blood sampling with creatine kinase (CK) pre and
post CABG or PCI; the cardiac specific MB iso-enzyme (MB-CABG) was undertaken
only if the CK >2 upper limit of normal (ULN). Blood samples and the SYNTAX
Score (SXscore) were evaluated by an independent core-laboratory. Incidences
of cardiac enzyme levels and associations with 4-year mortality (Kaplan-Meier
curves) and tertiles of the SXscore were determined.

Results: CK analyses were available in 1293 of 1800 (90.5%) randomised pa-
tients. A significantly greater number of patients with a CK ratio ≥2 underwent
prior CABG compared to PCI (CABG: n=491, 27.3%; PCI n=61, 3.4%; p<0.001).
CK-MB ratios were undertaken in 96.5% (CABG) and 86.9% (PCI) of patients
with a CK ratio ≥2. Within the CABG arm CK ratios of ≥2 and ≥3 demonstrated no significant
differences in all-cause Death at 4 years (CK ratio <2: 6.8%, CK ratio ≥2: 7.4%,
p=0.36); subsequently a CK-MB ratio cut-off of 3 separated 4-year mortality out-
comes into low and high risk groups (CK-MB ratio <3: 2.3%, CK-MB ratio ≥3
9.5%, p=0.00). Furthermore a CK-MB ratio ≥3 was significantly associated with
a greater occurrence of a high SXscore tertile (low 29.5%, intermediate 31.0%,
high 39.5%, p=0.02).

Conversely within the PCI arm, a CK ratio of ≥2 was associated with early (0-6
month) and 4-year (CK ratio <2: 10.8%, CK ratio ≥2: 23.3%, p<0.001) mortality.
Further analyses demonstrated a significantly increased 4-year all-cause Death
with higher CK-MB ratios.

Conclusion: Small amounts of CK-MB elevation post CABG are associated with
a high SXscore and had a detrimental impact on long-term prognosis. Significant
cardiac enzyme elevation post PCI are associated with early (0-6 month) and late
(4 year) mortality.

Impact of glycosylated hemoglobin level on two-year clinical outcomes in non-diabetic patients undergoing elective percutaneous coronary intervention

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C.G. Park4, H.S. Seo2, D.J. Oh2, S.H. Kim4, 1Kookkuk University
School of Medicine Chungju Hospital, Chungju, Korea, Republic of; 2Korea
University Guro Hospital, Seoul, Korea, Republic of; 3Background: In non-diabetic patients (pts) with ST-segment-elevation myocar-
dial infarction, elevated HbA1c levels is known to be associated with adverse
outcome. However, there have been limited data whether there are association
between high HbA1c level and long-term adverse clinical outcomes in non-
diabetes pts undergoing elective percutaneous coronary intervention (PCI) with
drug-eluting stents (DES).

Methods: The study population consisted of 655 consecutive non-diabetic pts
who underwent elective PCI between April 2007 and November 2010. Two-year
cumulative major clinical outcomes of non diabetic pts with high HbA1c group (>6.5,
<103 mmol/L, 16%) were compared with those of the control group (<6.5, n=552
pts, 84%).

Results: Baseline clinical and angiographic characteristics were similar between

Table: Major Clinical Outcomes at 2 year

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
<th>high HbA1c group (n=163)</th>
<th>normal group (n=552)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death</td>
<td>51 (31%)</td>
<td>12 (7.3%)</td>
<td>39 (7.0%)</td>
<td>0.608</td>
</tr>
<tr>
<td>Q-MI</td>
<td>11 (6.8)</td>
<td>10 (1.8)</td>
<td>0.783</td>
<td></td>
</tr>
<tr>
<td>Non Q-MI</td>
<td>10 (6.2)</td>
<td>10 (1.8)</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>TLR</td>
<td>9 (5.6)</td>
<td>10 (1.8)</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>TVR</td>
<td>15 (9.3)</td>
<td>27 (4.9)</td>
<td>0.041</td>
<td></td>
</tr>
<tr>
<td>Total MACC</td>
<td>32 (20.0)</td>
<td>68 (12.3)</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>TLR-MACC</td>
<td>17 (10.4)</td>
<td>37 (6.7)</td>
<td>0.314</td>
<td></td>
</tr>
<tr>
<td>TVR-MACC</td>
<td>15 (9.2)</td>
<td>31 (5.6)</td>
<td>0.906</td>
<td></td>
</tr>
</tbody>
</table>

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/339/430794 by guest on 04 November 2018
Prognostic models for cardiovascular events after successful primary percutaneous coronary intervention


Purpose: Several prognostic models exist for the outcome after primary PCI. However, the impact of combined clinical and angiographic risk scores on the long-term outcome of patients with successful primary percutaneous coronary intervention (PCI) has not been thoroughly investigated. The aim of this study was: 1) to validate and compare the performance of the Global Risk Score (GRS) and the Clinical Syntax Score (CSS) in patients undergoing successful primary PCI, and 2) to evaluate whether the combined risk models provide additive prognostic information to the Clinical Syntax Score, the EuroSCORE, and the SYNTAX score (SXscore).

Methods: We calculated the CSS score, the EuroSCORE, the ACEF score, the ACS score, and the SYNTAX score (SXscore) for 8,099 patients treated by PCI. The primary endpoint was the 2-year incidence of cardiac events. Secondary end points were: target lesion failure (TLF), repeat revascularisation (RR), stent thrombosis (ST) and major adverse cardiac event (MACE).

Results: GRS was higher in patients with CTO, TLF, ST, RR and MACE as compared with patients with no event. CSS score was higher in patients who had a CTO, TLF, RR, MACE, as well as in those who died, as compared with those who did not experience an event. The corresponding C-statistics for the CSS, GRS, SXscore, ACEF, EUROscore for 2-year CVD mortality were 0.781, 0.658, 0.665, 0.783, and 0.635 and for 2-year MACE were 0.703, 0.646, 0.638, 0.639 and 0.673 respectively. C-statistics revealed that the CSS score better classified event free patients, as compared with all other scores.

Conclusion: Clinical Syntax Score is the best model for the prediction of the incidence of cardiovascular death and/or MACE after successful primary PCI for the treatment of STEMI.


CHADS2 and CHA2DS2-VASc scores predict risk of stroke and death in patients with sick sinus syndrome treated with single lead atrial or dual chamber pacing


Abstract 2998 – Figure 1

**Purpose:** The risk of stroke in patients with atrial fibrillation can be addressed by use of the CHADS2 and CHA2DS2-VASc score systems. We hypothesized that these risk score systems could also be applied to patients with sick sinus syndrome randomized to AAIR or DDDR pacing to evaluate risk of stroke and death.

**Methods:** Data from 1,415 patients participating in the DANPACE trial were analyzed. Prior to pacemaker implantation risk factors were recorded. Development of stroke was assessed at follow-up visits and after evaluation of patient charts and hospital diagnoses. Mortality was assessed by information from the civil registration system.

**Results:** Patients were randomized to AAIR (N=707) or DDDR pacing (N=708). Mean follow-up was 5.4±2.6 years. In the AAIR group, 49/707 (6.9%) patients developed stroke vs. 43/708 (6.1%) in the DDDR group.

Applying the CHADS2 score (range from 0 to maximum score of 6) a significant association between score and risk of stroke was seen (HR 1.41; 95% CI: 1.22-1.64; p<0.001). However, among the 5 variables in CHADS2 only age and previous stroke or TCI significantly affected risk of stroke.

Applying the CHA2DS2-VASc score (range from 0 to a maximum score of 9) there was a significant association between score and risk of stroke (HR 1.25; 95% CI: 1.12-1.40; p<0.001). Only age and previous stroke, TCI or arterial embolism and age according to the CHADS2-VASc score (0-4 points) was included in the model a significant association with stroke was observed (HR 1.49; 95% CI: 1.25-1.78; p<0.001).

The CHADS2 score predicted mortality (HR 1.46; 95% CI: 1.36-1.56; p<0.001). In a multivariate analysis age (<75 [HR 1.75], heart failure (HR 1.70) and diabetes (HR 1.87) were significantly associated with mortality. Similarly, the CHA2DS2-VASc score was associated with mortality (HR 1.39; 95% CI: 1.31-1.46; p<0.001).

Occurrence of atrial fibrillation at follow-up visits showed no relation to stroke incidence (unadjusted HR 0.70; 95% CI:0.32-1.53; p=0.37).

**Conclusions:** In patients with sick sinus syndrome treated with pacemaker the risk of stroke and death could be predicted by use of either the CHADS2 or the CHA2DS2-VASc score. Age and previous stroke are the most important risk factors for stroke. Despite they were originally constructed for patients with atrial fibrillation these scores can also be applied to patients with sick sinus syndrome. Atrial fibrillation at follow-up did not add predictive information to the occurrence of stroke.

**3000**

**Warfarin vs aspirin in patients with chronic heart failure: pooled analysis**

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**Purpose:** Heart failure (HF) is an important contributor to thromboembolic risk. Whether patients with HF benefit with the use of warfarin rather than aspirin is not well established. To analyse risks and benefits of referred interventions we aimed to analyse randomized controlled trials (RCTs) comparing warfarin with aspirin in patients with heart failure.

**Methods:** We used recently released data from WARCEF study and searched Medline database for published RCTs comparing warfarin with aspirin treatment in patients with chronic heart failure. Analysed outcomes were mortality, stroke, myocardial infarction, worsening heart failure and major bleeding. Meta-analysis was performed using Mantel-Haenszel random effects method and relative risk (RR) and 95% confidence interval (95%CI) was calculated. Heterogeneity was assessed using I² test.

**Results:** We identified four RCTs with a total of 3663 patients with heart failure randomized to warfarin and aspirin. Mortality [RR 1.01; 95%CI: 0.86-1.16; 4 studies] and myocardial infarction risks [RR 0.99; 95%CI: 0.95-0.99; 4 studies] were similar between both antithrombotic treatments. Warfarin significantly reduced stroke risk relative by 50% [RR 0.50; 95%CI: 0.33-0.54, p<0.001] and decreased the HF worsening relative risk by 28% [RR 0.72; 95%CI: 0.57-0.90, p<0.004; 3 studies]. However major bleeding risk was significantly increased in patients treated with warfarin [RR 1.67; 95%CI: 1.00-2.70, p=0.05; 4 studies].

**Conclusions:** Patients with heart failure have decreased risk of stroke and HF worsening but major bleeding risk is increased. Tailoring antithrombotic therapy by determining the bleeding risk may be useful to define patients who will benefit most with warfarin treatment.

**3002**

**Genetic determinants of acenocoumarol and warfarin maintenance dose requirements in Polish population: a potential role of CYP4F2 polymorphism**

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**Purpose:** Vitamin K antagonists (VKAs) are highly effective in the prevention and treatment of thrombotic complications. Vitamin K episide reductase-oxidase complex subunit I (VKORC1) and cytochrome P450 (CYP) 2C9 genetic variants contribute largely to inter-individual variations in VKAs dose requirements. Polymorphisms of cytochrome P450 4F2 isoform (CYP4F2) and apolipoprotein E (APOE) have been suggested to be of minor significance. The aim of current study was to assess the impact of the above polymorphisms on dose requirements in a cohort of patients on VKAs.

**Conclusion:** Long-term antithrombotic therapy in AF patients with stable CAD should include VKA for stroke prevention and the benefit of additional antiplatelet therapy is questionable.
Methods: Genotypes of VKORC1, CYP2C9 (‘2’ and ‘3’), CYP4F2 (V433M) and APOE (rs429358 and rs7412) were determined in 233 consecutive white patients on oral anticoagulation (50% men, mean age 46.9 years, range 15-79) receiving acenocoumarol (n=149) or warfarin (n=84). Exclusion criteria were: cancer, chronic inflammatory diseases, valve replacement, use of any drugs known to interfere with VKA metabolism.

Results: The allele frequencies were 0.6 for VKORC1, 0.2 for CYP2C9‘2, 0.13 for CYP2C9‘3, 0.45 for CYP4F2‘2, 0.19 for APOE rs429358 and 0.17 for APOE rs7412. The mean weekly maintenance dose was 38.2±1.6 mg for aceno- coumarol and 41.3±2.1 mg for warfarin. There were no significant differences between the acenocoumarol and warfarin groups with regard to the gender, age, body mass index, INR and genotype distributions. The VKORC1 -1639A allele carriers required a lower dose of acenocoumarol or warfarin than the non-carriers (31.4±1.9 vs. 48.6±2.9 mg/week, p<0.001; 35.7±2.5 vs. 48.7±2.9 mg/week, p=0.001, respectively). Interestingly, carriers of CYP4F2 1347T allele required a higher dose of acenocoumarol or warfarin than non-carriers (44.8±2.8 vs. 36.9±2.4 mg/week, p=0.03). These differences remained significant after adjustment for age, sex and weight. No associations with VKAs dose requirements for other polymorphisms were observed.

Conclusions: To our knowledge, this is the largest study analyzing the influence of polymorphisms in vitamin K metabolism-related genes on VKAs dosage in central European population. We confirmed that the VKORC1 -1639A allele is associated with lower acenocoumarol and warfarin dose requirements. Higher acenocoumarol dose seems to be dependent on CYP4F2 polymorphism, which has been recently found in Swedish and Italian populations.

Ischaemic stroke: new insights on risk assessment and treatment / Challenges in treating the aorta in Marfan syndrome

Conclusions: Only a minority (36%) of Marfan patients responded to losartan therapy with reduction of plasma TGF-β. These patients had higher baseline TGF-β levels and more severe aortic disease. Plasma TGF-β might serve as a prognostic and therapeutic marker in Marfan syndrome.

Conclusions: In this randomized prospective study 99 adult Marfan patients were included receiving no other cardiovascular medication than β-blockers. Patients were randomized to receive 100 mg losartan (n=42) or no additional treatment (n=57). Aortic root diameters were measured by means of echocardiography. Plasma TGF-β levels were measured at baseline and after 1 month losartan therapy in Marfan patients and in 22 healthy controls.

Results: At baseline Marfan patients had significantly higher TGF-β levels as compared to healthy controls (126 vs 53.6 pg/ml, p=0.002). High TGF-β levels (>35 pg/ml) correlated with larger aortic root diameter (p=0.05). Losartan treat- ment reduced TGF-β levels in 36% of losartan-treated Marfan patients (respon- ders) to levels observed in healthy controls (p=0.31). Other 64% losartan-treated Marfan patients showed no change or even an increase of plasma TGF-β (non-responders). At baseline, responders had higher TGF-β levels (p=0.05) and more severe aortic disease as compared to non-responders. Baseline TGF-β levels and response to losartan treatment were independent of additional β-blocker ther- apy.

Type B aortic dissection in Marfan syndrome occurring at normal aortic dimensions

Methods: In this randomized prospective study 99 adult Marfan patients were included receiving no other cardiovascular medication than β-blockers. Patients were randomized to receive 100 mg losartan (n=42) or no additional treatment (n=57). Aortic root diameters were measured by means of echocardiography. Plasma TGF-β levels were measured at baseline and after 1 month losartan therapy in Marfan patients and in 22 healthy controls.
Individualised external support of the Marfan aortic root using computer aided design and rapid prototyping to manufacture a customised implant: characteristics and follow-up of the first 30 recipients

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Purpose: Health Technology Appraisal of an innovative procedure to prevent dilatation of the ascending aorta has allowed it to enter the phase of dissemination. As additional surgeons and institutions adopt this technology it is timely to report early clinical outcomes in the first 30 patients to have received a bespoke aortic root support.

Methods: Images from MRI or CT are used for computer aided design and rapid prototyping to create a physical replica of the individual's aortic root on which a fabric mesh support is manufactured. This is positioned around the aorta from the aortic ventricular junction to beyond the brachiocephalic artery without the necessity for cardopulmonary bypass.

Results: Age and aortic root size are given in the table. After 102 patient-years of follow up there have been no valve, aortic, or device related events.

Data and follow up for first 30 patients

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>IQR</th>
</tr>
</thead>
</table>
| Age, aortic diameter, postoperative stay and duration of follow up for the first consecutive 30 patients. IQR: interquartile range.

Figure 1. MRI before and after 7 years surgery.

Conclusions: As the aortic root size threshold for intervention has been progressively reduced, the number needed to treat to prevent a dissection is inevitably increasing. To balance benefit to harm, this less ablative form of surgery merits consideration.

Stent repair of complex coarctation of aorta: immediate and late results


Stent repair of coarctation of the aorta is an alternative to surgical correction. However, severe adverse anatomic conditions may be challenging for both, surgical or percutaneous treatment. This study retrospectively analyzes the immediate and late findings obtained from a group of 53 patients (pts) (mean age 23±16 years) who were considered to have a complex coarctation of aorta and were treated by stent repair. Complex coarctation was defined as having one or more of the following conditions: 1) related aneurysm (n=12), 2) hypoplastic coarctation (n=7), 3) complete interruption of the aorta (n=8), 4) tortuous unfavourable coarctation (n=17), 5) long diffuse stenosis (n=3), 6) heaist stent placement at early age after failed surgery or balloon angioplasty (n=10), 7) unusual location (n=10) and 8) need for a substitutian approach (n=3). The mean peak gradient before treatment was 42±18 mmHg. Related aneurysm had been developed after previous surgery in 4 instances and after percutaneous treatment in 4; in another 4 pts, the aneurysm was native. Hypoplastic coaractation involved the aortic arch in 7 pts and all of them had had previous treatment (3 surgery and 4 percutaneous treatment). In 8 pts with complete interruption, the mean length of the occluded segment was 11±11 mm. The unusual location of coarctation was the transverse arch in 6 pts and the abdominal aorta in 2. Thirteen pts received a covered stent and 40 a conventional stent. In 3 pts the aneurysm was obliterated with jailed coils. The mean stented length was 46±26 mm. Ten pts had stent re-expansion to accommodate the stent diameter to the aortic growth 5±2 years after first treatment; in 5 of them a new stent was implanted. After the mean peak gradient decreased to 5±7 mmHg (p<0.01). All related aneurysms became occluded after covered stent implantation or coil obliteration. One pt had a talaric ictus after treatment that mostly recovered. There were no other major complications during the procedure. However, a 55 years old patient with a long diffuse coarctation had a sudden death 3 hours after stent treatment. After a mean follow-up time of 10±6 years, one 66 year-old pt died of a non-cardiac cause. The remaining 51 pts remain alive and symptom free, without hypertension or significant residual Doppler gradient.

Conclusions: Several adverse anatomic conditions may complicate the treatment of pts with complex coarctation of aorta. Although challenging, stent repair is a good alternative for the treatment of these pts. The immediate relief is maintained at late follow-up.

Improvement in hypertension following primary endovascular stenting of aortic coarctation: Evidence and clinical outcomes

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Introduction: Endovascular stenting is a recognised treatment strategy for treatment of coarctation in adults.

Objective: 1) To assess the blood pressure control and the need for antihypertensive therapy following stenting of aortic coarctation in adults.

Methods: Data was collected prospectively for 39 patients with aortic Coarctation (COA) undergoing primary endovascular stenting either with covered or uncovered stents over a 4-year period. Follow up was done as part of an observational protocol. Patients underwent clinical examination and investigations including right arm Blood pressure, and 24-hour ambulatory blood pressure monitoring (ABPM) at baseline, 8-12 weeks and between 6-12 months.

Results: Twenty three patients had native Coarctation and 16 had re-Coarctation (re-COA). 26 (67%) were males. Mean age was 34±15 years (range15-72). Covered stents were implanted in 30 patients (77%). Peak gradient across the coarctation dropped from 27±11 mmHg to 5±4 mmHg post stent implantation (p<0.0001). Patients were followed for 21±17 (range4-65, median 17) months. Right arm systolic blood pressures fell from 155±15mmHg to 136±16 (p<0.0001) at 8-12 weeks and was 141±15 mmHg (p<0.009) compared to baseline) at 6-12 Months. Ambulatory 24 hour systolic blood pressures fell from 142±13 mmHg to 131±15 at 8-12 weeks (p=0.002) and to 130±14 mmHg (p=0.05 compared to baseline) at 6-12 months. There was no procedural mortality and 1 patient required surgical repair of a femoral artery false aneurysm. One patient required re-dilatation at 28 months post procedure; 1 patient had stent fractures, which was re-stented with a covered stent. Twenty-six patients were on anti-hypertensive pre-stenting and this was unchanged on follow up. Mean number of anti-hypertensive medications pre and post stent were 1.9±0.7 and1.7±0.6 (p=0.08) respectively. There was 1 non-cardiac death in the follow-up period.

Conclusion: Primary stenting of native and re-coarctation of the aorta results in significant reduction in clinical and ABP blood pressures at 6-8 weeks post procedure, which is sustained at 1 year.
Utility of comprehensive dobutamine stress MRI in the assessment of patients with left bundle branch block and suspected coronary artery disease

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Purpose: Patients with left bundle branch block (LBBB) have high prevalence of underlying coronary artery disease (CAD). However, assessing the likelihood of CAD in those patients is challenging. Employing some cardiac imaging tests can lead to unacceptably high false positive results thus diminishing diagnostic accuracy and ultimately directing these patients to alternative invasive tests in order to better characterise their coronary anatomy.

Hypothesis
We hypothesised that comprehensive dobutamine stress MRI (DSCMR) which involves the combination of cine, stress perfusion and late gadolinium enhancement could confidently predict the presence of CAD in those patients and directly compare to dobutamine stress stress contrast echocardiography (DSCE).

Methods: We evaluated 97 consecutive patients (mean age 63±7) with LBBB and suspected CAD referred for outpatient assessment. All patients underwent DSCE, comprehensive DSMCR and invasive coronary angiography (all tests performed by observers blinded to previous tests and within 14±6 days).

Results: Forty patients (40%) had evidence of underlying CAD as assessed by ICA (a luminal diameter more than 70% (Table 1)). Overall DSCE had 85% specificity and 82% sensitivity to detect CAD, referenced by ICA. Cine stress CMR alone provided an overall 87% and 83% specificity and sensitivity respectively in detecting CAD. In contrast, the combination of cine images, stress perfusion and late gadolinium enhancement boosted the overall sensitivity and specificity to 94% and 93% respectively, thus increasing diagnostic confidence. There were no complications during both DSCE and DSE.

Conclusions: Our findings suggest that comprehensive DSMCR is a robust, safe and versatile diagnostic imaging tool in assessing CAD in patients with LBBB and suspected angina.

Reperfusion injury according to reperfusion strategy Assessment with cardiovascular magnetic resonance imaging

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1University of Valencia, Valencia, Spain; 2Faculty of Medicine, Department of Internal Medicine II-Cardiology, University of Valencia, Spain.

Purpose: In ST-segment elevation myocardial infarction (STEMI) timely reperfusion is the primary therapeutic goal but may cause reperfusion injury (RI) including microvascular obstruction (MVO) and intramyocardial hemorrhage (IMH). Different reperfusion strategies exist for achieving reperfusion and some patients do not undergo timely reperfusion. Cardiovascular magnetic resonance (CMR) allows for detection of both MVO and IMH. Data on the incidence of RI assessed with CMR following to reperfusion strategy is scarce.

Methods: We stratified STEMI patients according to reperfusion therapy: no reperfusion within 12 hours after symptom onset, primary PCI (percutaneous coronary intervention), thrombolyis plus early PCI and rescue PCI. Using CMR, the incidence of RI (defined as MVO and MVO in >1 segment) was determined in T2 and late enhancement sequences.

Results: 379 patients were included in the study. Reperfusion mode was: no reperfusion, n=44, primary PCI, n=147, thrombolyis, n=142 and rescue PCI, n=46. Overall incidence of both IMH and MVO was 34%. The incidence of RI according to reperfusion strategy is displayed in the figure. In the no reperfusion group, the incidence of RI was significantly lower compared to all other groups, while the contrary was the case for rescue PCI. There was a non-significant trend towards less RI in patients treated with thrombolysis compared to primary PCI.

Oxygen-sensitive T2-prepared steady-state free-precession magnetic resonance imaging correlates to fractional flow reserve in coronary artery disease

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Background: Oxygen-sensitive T2-prepared steady-state free-precession (T2prep SSFP) cardiac magnetic resonance imaging (CMR) has the potential to evaluate myocardial perfusion due to different T2 and T2* relaxations of oxyhemoglobin and deoxyhemoglobin. Aim of our prospective study was to evaluate its diagnostic ability in comparison to invasively measured fractional flow reserve (FFR) in coronary artery disease.

Methods: T2prep SSFP sequences were acquired in three short axes (apical, midventricular and basal) at rest and after three minutes of adenosine-infusion at a constant rate of 140 μg/kg/min in a 1.5T whole-body CMR scanner. In each patient 16 myocardial segments were analyzed for relative BOLD signal intensity increase during adenosine in comparison to rest. Invasive FFR measurements were performed in all patients in the major three coronary arteries during adenosine infusion (140 μg/kg/min for three minutes). A FFR <0.8 was regarded significant. FFR was compared to CMR results.

Results: Thirty-four patients were included into the study. BOLD signal intensity increase was significantly lower in myocardial segment supplied by coronary arteries with a FFR ≤0.8 (1.1±0.22% vs. 1.5±0.4±2%, p=0.05). Sensitivity yielded 88.2%, specificity 89.5%.

Conclusion: Oxygen-sensitive T2prep SSFP CMR reliably detects hemodynamic significant coronary artery disease and offers an alternative to contrast-enhanced perfusion studies.

Stress myocardial perfusion MRI and fractional flow reserve in patients with three- vessel coronary artery disease

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Purpose: A recent study demonstrated that visual analysis of stress myocardial perfusion MRI can detect flow limiting coronary artery disease (CAD) defined by fractional flow reserve (FFR). However, the agreement between visual assessment of stress perfusion MRI and FFR has not been evaluated in patients with multivessel CAD. The purpose of this study was to evaluate the accuracy of qualitative assessment of stress myocardial perfusion MRI for predicting reduced FFR in patients with three-vessel coronary disease (3VD).

Methods: Twenty-nine patients (19 men, 70±9.8 years) with known or suspected CAD underwent 1.5T stress perfusion MRI and FFR measurements in 36 coronary vessels. Myocardial perfusion MRI images were visually analyzed by two blinded observers. FFR<0.8 was considered hemodynamically significant CAD.

Results: Nine of 29 patients had FFR <0.8. In 30 patients without 3VD, visual assessment of stress perfusion MRI yielded high diagnostic accuracy for predicting flow limiting CAD defined by FFR, with the area under ROC curve of 0.86. However, in 9 patients with 3VD, stress perfusion MRI under-
estimated flow limiting CAD defined by FFR in 6 of 12 lesions (50%), resulting in the reduced area under ROC curve of 0.61.

Conclusions: Visual analysis of stress perfusion MRI has limited concordance with FFR in patients with 3VD, which may indicate the necessity of quantitative analysis of stress-rest perfusion MRI in patients with diffuse myocardial ischemia.

Differences in dynamic kinetics of Gadolinium contrast enhancement: acute versus chronic infarct size


In acute myocardial infarctions (MI), contrast hyperenhancement includes infarcted myocardium (late enhancement), and area at risk (early enhancement). Little is known about the optimal timing to differentiate these 2 time periods and also if contrast kinetics occurs not only in acute but also in chronic MI.

Aims: To determine whether the time after contrast injection influences the size of hyperenhancement in acute and chronic MI, and the time that better predicts infarct size.

Methods: Subjects were evaluated using CMR the first week (n= 60) and 3 months (n=47) after an STEMI percutaneously revascularized. Inversion-recovery single-shot true fast imaging with steady-state precession (ss-IR) and segmented inversion-recovery gradient-echo (seg-IR) sequences were used. SS-IR were acquired starting at 10 min after contrast injection, while seg-IR were acquired starting at 10 min after contrast injection and used for comparison to ss-IR. Inversion time was properly adjusted to null normal myocardium. All images were blinded, randomized, and measured for hyperenhancement volumes.

Results: In acute MI, there was a significant decrease in infarct volume over time (p<0.01). Hyperenhancement volume was maximum 3 min after contrast injection and stable after 20 min. Nevertheless, infarct size remained constant over time in chronic MI (Figure 1). Mean infarct size in acute and chronic MI by seg-IR was 24.1±6.2 g and 12.3±8 g respectively with excellent correlation to ss-IR (r=0.96 and r=0.96 p<0.001).

Conclusions: There is a change in infarct size over time in acute but not in chronic MI, with a maximum volume 3 min after contrast injection. It is important to wait 20 min to ensure accurate determination of infarct size in acute but not in chronic MI.

3037 Modeling incremental cost-effectiveness of stress cardiac magnetic resonance imaging guided catheterization in comparison to coronary angiography based on clinical assessment

E. Welinholer, S. Kern, G. Petrov, E. Fleck, S. Kelle. German Heart Center Berlin, Berlin, Germany

Purpose: In 2003 to 2004 a decision on coronary angiography (CA) was based on clinical judgment and optional stress cardiac magnetic resonance imaging (CMR). Introduction of cost controlling by diagnose related groups (DRGs) in 2003 provided cost data and long-term follow-up allowed retrospective assessment of effectiveness.

Methods: We constructed a decision tree model that compares a group of patients with CMR plus CA (CMR CA) or with CMR plus ambulatory follow-up CMR FU to a control group of patients with CA. Cost data were derived from DRG calculation. Running costs per MRI were estimated as 750.00 € per test. Costs were modeled by linear regression and effectiveness was modeled by binary logistic regression with the death as dependent variable. Cost-effectiveness (CER) was calculated for each path as mean costs per survival and incremental CER (ICER) was determined as difference between CER in the arms with and without CMR.

Results: Mean age of patients (60% male) ranged between 59±10 years (CMR FU) and 64±10 years (CMR CA). DRG calculations were available for 38 CMR CA (median 3387 €, mean 4702€ ± 3870 €) and 29 CMR FU (median 3394 €, mean 5487 € ± 5612 € ) patients. Events were available in 579 CA (71 deaths), 73 CMR CA (3 deaths) and 199 CMR FU (13 deaths) cases. Estimated costs of different paths are given in the figure. ICER was calculated as 822 € per survival assuming 750 € expenditure per CMR procedure. Sensitivity analysis and non-parametric statistics demonstrated that 750 e largely compensate for the difference between the two main paths.

Conclusion: CMR guided coronary angiography is at least equally cost effective as the conventional approach, if a reimbursement of 750 € is calculated.
compared to six weeks; in the pump group V90 decreased (V90=86.4±14.5 mL; Ees 2.3±1.4 mmHg/mL and V0 32.5±8 mL) with p<0.02 compared to six weeks. At baseline, V15 was 103.4±14 mL; p=0.17 compared to six weeks. At twelve weeks, V15 increased in both groups: 124.3±14.5 mL and 126.8±15.2 mL in the sham and pump group, respectively (p<NS). At twelve weeks, V15 increased further in the sham group (V15=136.3±19.5 mL, p<0.05 compared to six weeks) but did not significantly change in the pump group (V15=123.1±14 mL; p<NS compared to six weeks).

Conclusion: Partial unloading improves systolic function and halts the remodeling process.

One-year survival after continuous-flow left ventricular assist device (LVAD) implantation versus heart transplantation (HTx): an Italian single-centre experience

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Background: There is a paucity of data about mid-term outcome of patients with advanced heart failure (HF) treated with LVAD in Italy, where donor shortage and their ageing limit the availability and the probability of success of HTx. On the other hand the results of continuous-flow LVAD therapy are improving remarkably. Aim of this study was to compare one-year survival rates in prospective outcome patients treated with LVAD versus HTx in one among Italian centres with greater national experience in LVAD therapy.

Methods: We evaluated a total of 200 consecutive patients with advanced HF who underwent continuous-flow LVAD implantation or HTx from 1/2000 to 11/2011 in our Hospital, with a median follow-up of 12 (7 to 12) months. We compared one-year survival rates in patients who received a LVAD (n=45) versus those who underwent HTx (n=155). LVAD patients were censored at the last follow up visit or at the time of subsequent HTx in the survival analyses.

Results: Patients that were treated with LVAD compared with patients who underwent HTx were significantly older with a median of 54 years (interquartile [IQR] 48 to 62) vs 51 (38 to 59; p=0.02), whereas the proportion of women was lower in LVAD than in HTx recipients (11% vs. 31%; p<0.01). LVAD group had an augmented profile of risk in comparison with HTx patients due to higher mean pulmonary artery pressure (37±10 vs. 23±10 mmHg; p<0.0001), higher pulmonary capillary wedge pressure (27±8 vs. 16±8; p<0.0001), larger use of intravenous inotropic agents (40% vs. 20%, p<0.01) and longer pre-surgical stay in hospital (20 days (7 to 31) vs. 1 (1 to 20); p<0.0001). A total of 36 deaths occurred: 12 among LVAD patients and 24 among HTx patients. Kaplan Meier survival curves estimated a one-year survival of 73.3% in the LVAD vs. 84.5% in HTx that was not statistically significant different (unadjusted p=0.07, adjusted for age and gender p=0.17: adjusted hazard ratio for death was 1.67; 95% confidence interval 0.80-3.76 for LVAD vs. HTx). The thirty-day peri-operative mortality was 8 (17.8%) vs. 13 (8.4%), p=0.05 in LVAD vs. HTx. Four patients in the LVAD group were subse-quently transplanted within the first year after implant.

Conclusions: Despite worse preoperative conditions, survival is non-significantly lower after LVAD than after HTx. Thus, LVAD therapy with continuous-flow devices represents a valid option, given the scarce number of donors for HTx, also in our country.

Continuous flow centrifugal left ventricular assist devices in patients with hypertrophic cardiomyopathy


Background: Left ventricular assist device (LVAD) therapy has been pri-marily used in patients with end-stage dilated cardiomyopathy. Hypertrophic cardiomy-opathy (HCM) is usually considered a contraindication for LVAD therapy. We re-viewed patient characteristics and outcomes in HCM patients implanted with the continuous-flow centrifugal LVAD.

Methods: A retrospective analysis of 39 patients implanted with the centrifugal flow LVAD was performed (VentriAssist = 20, Heartware = 19). 36 patients had di-lated cardiomyopathy (non-ischae mia dilated/ischaemic dilated cardiomyopathy) and 3 patients had hypertrophic cardiomyopathy. Echocardiographic parameters, pump flow data and outcomes were analysed.

Results: The average pump flows for the 2 groups were 5360±1276 (DCM) and 5058±1276 (HCM) (p=0.71). Mean left ventricular end-diastolic dimensions were 65.13±10.68 and 47.3±20.10, (p<0.002). All 3 patients with hypertrophic cardiomyopathy showed a marked improvement in their mean pulmonary arterial pressures at 5 months (43.4±3.9 vs 22.9±4.4 mmHg). All three patients in the HCM group were alive at 3 months.

Table 1. Outcomes in HCM patients with continuous flow centrifugal LVAD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HCM (n=36)</th>
<th>DCM (n=38)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECMO (V/PA)</td>
<td>4</td>
<td>0</td>
<td>0.54</td>
</tr>
<tr>
<td>LVEGO</td>
<td>47.3±2.10</td>
<td>65.13±10.68</td>
<td>0.02</td>
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<tr>
<td>Mean PA</td>
<td>22.3±2.8</td>
<td>22.9±4.8</td>
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</tr>
<tr>
<td>Mean RA</td>
<td>11.3±5.1</td>
<td>12.2±5.7</td>
<td>0.80</td>
</tr>
<tr>
<td>CI</td>
<td>4.5±1.1</td>
<td>4.5±1.4</td>
<td>0.68</td>
</tr>
<tr>
<td>CI</td>
<td>2.4±0.17</td>
<td>2.3±0.76</td>
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<tr>
<td>Pump Speed</td>
<td>2686±100</td>
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<tr>
<td>Alive at 3 months</td>
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</tr>
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Table 1. Outcomes in HCM patients with continuous flow centrifugal LVAD

Conclusions: Our data, the first analysis to show that patients with end-stage heart failure due to hypertrophic cardiomyopathy do benefit from continuous flow centrifugal LVAD therapy in the short to medium term.

Blood transfusion and the risk of Acute Kidney Injury following Transcatheter Aortic Valve Implantation

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Purpose: Transcatheter aortic valve implantation (TAVI) is invariably associated with the risk of acute kidney Injury (AKI) and forecasted by peri-operative blood transfusion. Whether AKI occurs due to a direct effect of the transfusion itself or because of its underlying clinical indication (i.e. baseline anaemia or bleeding) remains uncertain and is poorly understood. This study investigated the incidence, predictors and prognosis of AKI after TAVI, with special focus on the effects of peri-operative anaemia, blood loss and transfusion.

Methods: A total of 995 patients with aortic stenosis underwent TAVI with the Medtronic CoreValve or the Edwards valve. AKI was defined according to the following criteria: a urine creatinine of ≥0.3 mg/dl (≥26.4 μmol/l) or a percentage increase ≥ 50% within 72 hr following TAVI.

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Severe calcification of aortic arch is an independent predictor for stroke in patients undergoing transcatheter aortic valve implantation


1Kerckhoff Clinic, Department of Cardiology, Bad Nauheim, Germany; 2Kerckhoff Clinic, Department of Cardiac Surgery, Bad Nauheim, Germany; 3Kerckhoff Heart Center & Brain Research Group, Bad Nauheim, Germany

Background: Embolic cerebral lesions occur in up to 84% after transcatheter aortic valve implantation (TAVI), leading to a clinical manifest stroke in 0-10%. The existence of aortic arch atheroma > 4 mm is known as a risk factor for spontaneous stroke. Our objective was to assess the relationship between the incidence of clinical manifest neurological deficits after TAVI and severity of calcification of the aortic valve and the thoracic aorta when characterized by a quantitative approach.

Methods: 140 patients with severe aortic stenosis underwent TAVI and were examined with Multi Slice Computed Tomography of the thoracic aorta. We performed quantitative analysis of calcification of the aortic valve and arch and descending aorta using the Agatston score and also measured the maximum plaque size in the ascending aorta and arch.

Results: Mean age was 81.7±6.4, 62.9% of the patients were female. Mean Agatston score was 25.8±13.5% and STRS PROM was 8.1±5.7%. Major stroke occurred in 4/140 (2.8%), minor stroke in 4/140 (2.8%) and TIA in 1/140 (0.7%). Patients suffering of stroke/TIA had significantly higher values of Agatston Score in the aortic arch (9309±6048 vs. 391±3335, p = 0.01) and a trend for higher values in the descending aorta (633±4834 vs. 317±2910; p = 0.06). There was no difference between the groups neither at the aortic valve (2868±2177 vs. 2272±1518; ns) nor at the ascending aorta (1569±1486 vs. 1673±2492; ns).

In congruence, maximum plaque protrusion in the aortic arch was significantly higher than 3.1±1.7 mm vs. 3.4±1.2 mm; p<0.006), but not in the ascending aorta (3.1±1.6 mm vs. 3.1±1.6 mm; p=0.25). Multivariate regression analysis identified Agatston Score of the arch, maximum plaque protrusion of the arch, reduced left ventricular ejection fraction and fluoroscopy time as independent risk factors for stroke.

Conclusion: This study confirms that the extent and the protrusion of calcifications at the aortic arch are significantly related to an adverse neurological outcome after TAVI. Precise preoperative screening may lead to optimized clinical solutions in these patients, for example use of protection devices.

Vorapaxor in ACS patients undergoing CABG surgery: results from the TRACER trial

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Purpose: The Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome (TRACER) trial provided an opportunity to assess the effects of vorapaxor compared with placebo among TRACER participants undergoing CABG surgery in patients with NSTE ACS undergoing CABG surgery.

Methods: This prespecified, post-randomization subgroup analysis evaluated the effects of vorapaxor compared with placebo among TRACER participants undergoing CABG surgery during their index hospitalization, from discharge to end of study. CABG-related TIMI major bleeding (adjudicated independently) was evaluated among treatment groups.

Results: Among 12,944 TRACER patients, 1312 (10.1%) underwent CABG during the index hospitalization. The median age was 64 years and 78% of patients were male. The median time from loading dose to CABG was 120h with effect of single dose of vorapaxor lasting >2 weeks. CABG patients treated with vorapaxor had a 45% reduction in the primary endpoint (composite of CV death, MI, stroke, recurrent ischemia with rehospitalization, or urgent coronary revascularization) compared with placebo (HR, 0.55; 95% CI, 0.35–0.87; p=0.001). The interaction between treatment and CABG during the index hospitalization was statistically significant (interaction p<0.02). CABG-related TIMI major bleeding was not statistically significantly different between vorapaxor and placebo (9.7 vs 7.3%; HR, 1.34; 95% CI, 0.92–1.95; p=0.13), with no excess in fatal bleeding or need for re-operation.
Conclusions: In this unadjusted post-randomization subgroup analysis, NSTE ACS patients undergoing CABG and treated with vorapaxar had a 45% reduction in subsequent ischemic events. These findings are exploratory but support the opportunity for randomized trials of P2Y1 antagonism following CABG.

UNEXPECTED CULPRITS IN CARDIOVASCULAR RISK

P3053 
Prevalence and extent of subclinical atherosclerosis in patients with psoriasis


Introduction: Psoriasis is one of the most common chronic inflammatory skin disease that affects up to 2-3% of the general population. Recent studies showed that patients with psoriasis are prone to premature atherosclerosis; nonetheless the prevalence and extent of atherosclerosis in the coronary and carotid arteries are unknown.

Methods: The prevalence and extent of coronary and carotid arterial atherosclerosis in 76 patients with psoriasis (46±9 years, 71% male) without known cardiovascular diseases were compared with 51 age- and gender-matched controls (45±7 years, 71% male). Coronary arterial atherosclerosis was determined by the coronary calcium score (CCS) measured by multi-detector computed tomography. Carotid intima-media thickness (cIMT) was assessed by high-resolution ultrasound derived carotid intima media thickness (cIMT).

Results: Patients with psoriasis had a mean duration of disease of 16±4 years and a mean CCS area and seven-indices (PASI) of 14±2±1.0. Among them, 39 (56%) received methotrexate therapy as psoriasis treatment. Patients with psoriasis had a significantly higher prevalence of CCS >0 as compared to controls (28.5% vs. 3.9%, P<0.001). Moreover, the extent of coronary atherosclerosis estimated by mean CCS was more severe in patients with psoriasis (87±4.39±2 vs. 0.5±3.0, P<0.05). Carotid atherosclerosis as measured by cIMT was also significantly greater in patients with psoriasis (0.73±0.11mm vs. 0.67±0.08mm, P<0.05). Importantly, patients with psoriasis was associated with a 10-fold risk of coronary atherosclerosis defined by CCS >0, independent of age, conventional cardiovascular risk factors, disease duration and PASI. In contrast, only age was independent of carotid atherosclerosis.

Conclusion: The present results demonstrated that patients with psoriasis had early onset, diffuse arterial atherosclerosis over coronary and carotid arteries as compared to age- and gender-matched controls. Importantly, patients with psoriasis had a high risk of subclinical coronary atherosclerosis, independent of conventional cardiovascular risk factors and disease characteristics.

P3054 
Anemia is an independently risk factor for bleeding in atrial fibrillation patients on oral anticoagulation

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The risk of bleeding associated with the use of vitamin K antagonist therapy may be a barrier to prescribing warfarin, as despite the clear net clinical benefit of oral anticoagulation (OAC) in atrial fibrillation (AF) patients at risk for stroke. Indeed, the risk of major bleeding events may be devastating when they do occur. So physicians, concerns about bleeding complications and tend to override about the risk of stroke in untreated AF patients. Several risk stratification schemes have been developed in order to evaluate the hemorrhagic risk of patients on oral anticoagulation. Anemia and prior bleeding episode are common variables included in all stratification schemes. By the other way, experienced patients on OAC seem to suffer less hemorrhagic episodes than naïve patients. The aim of our study was to analyze the prognostic role of basal value of hemoglobin (Hb) in two AF population: patients OAC naïve vs experienced.

Methods: In 2009 we included all the patients with paroxysmal or permanent AF who initiated OAC in our anticoagulation outpatient clinic (naïve cohort). This population was compared with another cohort of consecutive patients with permanent AF who initiated OAC in our anticoagulation outpatient clinic (naïve cohort). Patients with paroxysmal or permanent AF on OAC from the same outpatient anticoagulation. Anemia and prior bleeding episode are common variables included in all stratification schemes. By the other way, experienced patients on OAC seem to suffer less hemorrhagic episodes than naïve patients. The aim of our study was to analyze the prognostic role of basal value of hemoglobin (Hb) in two AF population: patients OAC naïve vs experienced.

Methods: During 2009 we included all the patients with paroxysmal or permanent AF who initiated OAC in our anticoagulation outpatient clinic (naïve cohort). This population was compared with another cohort of consecutive patients with permanent AF who initiated OAC in our anticoagulation outpatient clinic (naïve cohort). Patients with paroxysmal or permanent AF on OAC from the same outpatient anticoagulation.

Results: We included 529 naïve and 930 experienced patients, age and sex were unknown. The prevalence of anemia was 31% and 50% in naïve and experienced patients respectively. The prevalence of prior bleeding events was 21% and 35% in naïve and experienced patients respectively.

Conclusions: In our analysis anemia appeared to be an independent predictor of bleeding in AF patients on OAC irrespectively of the initiation of therapy.

P3055 
Serum 25-hydroxyvitamin D relationships to carotid intima-media thickness (cIMT) and cIMT progression in a European high-risk population

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Purpose: Vitamin D deficiency has been implicated in cardiovascular disease (CVD) as well as in promoting multiple cardiovascular risk factors such as obesity, dyslipoproteinemia, type-2 diabetes and hypertension. We investigated the relations of serum 25-hydroxyvitamin D (25(OH)D) concentration to established and emerging cardiovascular risk markers, including carotid intima-media thickness and emerging cardiovascular risk markers, including carotid intima-media thickness.

Methods: IMPROVE is a European, multicentre, longitudinal cohort study, which enrolled individuals aged 54 to 80 years with at least three cardiovascular risk factors and no history of CVD from 7 centers in Finland, Sweden, the Netherlands, France, Italy, Austria, and Portugal. Baseline carotid ultrasound examination at baseline, month 15 and month 30. Blood samples, clinical data and information about lifestyle factors collected at baseline from a total 3430 subjects were used in the present sub-study of 25(OH)D.

Results: Serum 25(OH)D levels were positively correlated with latitude. Subjects having deficient levels of vitamin D (defined as serum 25(OH)D below 25 nmol/l) were more often women, smokers and diabetics, were more obese, had higher blood pressure, triglyceride, blood glucose and CRP levels, had lower HDL, and were less physically active. Waist circumference, diastolic blood pressure, triglycerides, HDL, LDL, current smoking and high physical activity showed significant and independent associations with increased cIMT.

Conclusion: Overall, there were no consistent independent relationships between 25(OH)D and segment-specific or composite IMT measures (baseline or progression) where age, sex, latitude and other cardiovascular risk factors were considered. The latter (subsequently selected by subset analysis) were included in multivariable linear regression models.

Conclusions: Levels of 25(OH)D differed across Europe, showed multiple associations with established and emerging cardiovascular risk factors but were not independently related to cIMT or cIMT progression. This argues against an independent causal role of vitamin D in early subclinical atherosclerosis in high-risk individuals.

P3056 
Relation of positive T wave in lead AVR to risk of cardiovascular mortality

I.J.T. Anttila1, K.C. Niks2, T. Nieminen3, M. Kahonen1, 1Division of Internal Medicine, Department of Cardiology, Seinäjoki Central Hospital, Finland; 2Department of Clinical Physiology, Tampere University Hospital, Heart Center, Tampere, Finland; 3University of Tampere, Medical School, Department of Pharmacological Sciences, Tampere, Finland; 4Department of Clinical Physiology, Tampere University Hospital, Tampere, Finland

Traverse abnormalities are among the most frequently encountered pathologic electrocardiographic (ECG) findings in apparently healthy population. Even minor ST-T abnormalities are associated with increased long-term cardiovascular (CV) and total mortalities. Prevalence of a positive T wave in lead aVR (aVRT+) in the general population is not known. Neither is it known whether there are differences in prevalence between women and men. There is no population-based data on the impact of aVRT+ on mortality. Therefore, the aim of the present study was to determine the prevalence and prognostic impact of aVRT+ on standard electrocardiogram at rest in a population-based cohort.

Data were collected from a large nationally representative (random sample) health examination survey conducted in Finland from 2000 through 2001. The survey consisted of 6,354 subjects (2,876 men and 3,478 women) >30 years who participated in the field health examination including standard electrocardiographic (ECG) recording at rest. The prevalence and isoelectric T wave in lead aVR was 2.2%. During the median follow-up of 98.5 months (interquartile range 96.6 to 99.8), there were 214 (3.5%) cardiovascular (CV) deaths. In Cox regression analysis, adjustment for age and gender, relative risks for CV and total mortalities associated with aVRT+ were 3.24 (95% confidence interval [CI] 2.32 to 4.54, p<0.001) and 1.91 (95% CI 1.47 to 2.49, p<0.001), respectively. In the fully adjusted model controlling for other risk factors, such as smoking, morbidity, and ECG findings, the relative risk for CV mortality associated with aVRT+ was 2.94 (95% CI 2.07 to 4.18, p<0.001). In conclusion, aVRT+, an easily recognized ECG finding, predicts risk for CV mortality in the general population. This finding could aid in screening for risk of total and CV mortalities.
Plasma dimethylglycine is an independent risk factor of acute myocardial infarction in patients with stable angina pectoris

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Purpose: Dimethylglycine (DMG) is produced during the remethylation of homocysteine from betaine. This reaction is catalyzed by the enzyme betaine-homocysteine methyltransferase (BHMT), the regulation of which seems to be connected to both carbohydrate and lipid metabolism. DMG is catabolized inside the mitochondrion, and mitochondrial dysfunction is associated with cardiovascular disease (CVD). The BHMT 742 G→A polymorphism predicts circulating DMG levels and has been related to the extent of coronary artery disease. We sought to investigate the association of plasma DMG levels to incident cardiac events.

Methods: In 6154 patients with suspected stable angina pectoris (SAP), we evaluated the associations between plasma DMG levels and clinical baseline characteristics and explored the predictive role of plasma DMG for subsequent acute myocardial infarction (AMI) during extended follow-up. Results: (83%) patients experienced an AMI during a median (5th. 95th percentile) follow-up time of 4.6 (1.6, 6.8) years. In a Cox model adjusted for age, gender and time since last meal, plasma DMG predicted future AMI (HR [95% confidence interval (CI)]: 1.97 (1.43, 2.70), p<0.001 for the 4th vs. the 1st quartile). Adjustment for established CVD risk factors (diabetes mellitus, hypertension, smoking, apolipoprotein B (apo B) and apolipoprotein A-I) in an intermediate multivariate model only slightly attenuated the estimate [HR (95% CI): 1.84 (1.33, 2.54), p=0.001 for the 4th vs. the 1st quartile]. In an extended model, also including C-reactive protein, estimated glomerular filtration rate, left ventricular ejection fraction and baseline treatment, plasma DMG was still rendered a predictor of AMI (HR [95% CI]: 1.60 (1.14, 2.24), p=0.001 for the 4th vs. the 1st quartile). The predictive ability of plasma DMG was not present in smokers or in subjects with serum triglycerides (TG) > median (p for interaction = 0.003 and 0.002, respectively). Adding plasma DMG to the intermediate multivariate model led to significant increases in C-statistics in the total population, males, ex-/non-smokers, non-diabetics and subjects with either apo B or TG below median values.

Conclusions: Plasma DMG predicts subsequent AMI in patients with SAP and the effect seems particularly strong in several subgroups at presumably lower risk. Our findings prompt further investigation into possible mechanisms between DMG, mitochondrial function and atherosclerosis.

Plasma dimethylglycine in the coronary circulation may be associated with the future cardiovascular events in patients with coronary artery disease

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Background: Adiponectin has anti-atherosclerotic properties and is also produced in the local coronary circulation. We previously reported that significantly lower adiponectin was produced in the coronary circulation of patients with than without coronary artery disease (CAD). The goal of this study was to determine whether adiponectin in the coronary circulation could predict future cardiovascular events in patients with CAD.

Methods: A total of 48 consecutive CAD patients who underwent percutaneous coronary intervention (PCI) were enrolled. The adiponectin in the coronary circulation was defined as the plasma adiponectin level at the great cardiac vein minus that at the orifice of the left coronary artery. When a adiponectin in the coronary circulation was positive or negative, it was defined as the amount of adiponectin production or that of adiponectin consumption in the coronary circulation, respectively. All patients were followed up for 61±27 months. The primary endpoint was the combined occurrence of major adverse cardiovascular events (MACE), including rehospitalization due to unstable angina, heart failure, nonfatal myocardial infarction, revascularization with PCI or coronary artery bypass grafting (CABG), ischemic stroke and cardiovascular death.

Results: A total of 15 MACE occurred, including one case of cardiovascular death, one case of unstable angina, one case of heart failure, 4 cases of PCI, one case of CABG, one case of nonfatal MI and 6 cases of ischemic stroke. Patients with MACE had higher body mass index (P=0.017) and lower adiponectin in the coronary circulation (P=0.002). In multivariate analysis, adiponectin in the coronary circulation and body mass index were independent predictors of future MACE in patients with CAD. All patients were divided into adiponectin production group (>ΔA/Δmin) and adiponectin consumption group (< ΔA/Δmin). The incidence of MACE was significantly reduced in the adiponectin production group (P=0.0046). Kaplan-Meier analysis revealed higher MACE-free survival rates in the adiponectin production group than those in the adiponectin consumption group (P=0.011).

Conclusion: Adiponectin plays an important role in cardiovascular protection and its production or consumption in the local coronary circulation of patients with CAD may be associated with the future cardiovascular events.

Does the clinical spectrum of cardiovascular disease differ between men and women?

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Purpose: To evaluate gender differences in the clinical presentation of incident (first) cardiovascular event.

Methods: We used pooled data of the population-based National FINRISK Surveys from the years 1992, 1997, 2002, 2007. Persons with prevalent cardiovascular disease at baseline were excluded and 27,900 participants (53.2% women) aged 25-74 years were included in prospective analyses. The median follow-up time was 7.9 (IQR 7.7) years. Incident major cardiovascular events (MACE) were identified from the National Hospital Discharge Register and Causes-of-Death Register. MACE were further divided to non-fatal and fatal coronary heart disease (CHD) events, ischemic stroke (IS) and heart failure (HF). Incident rates are reported per 100 000 persons per year and age adjusted to the European standard population.

Results: During 267 986 person-years of follow-up, 1 431 MACE were identified in men and 852 in women. Incident MACE were significantly more frequent among men than women (128; 95% CI 1219-1360 in men vs. 708; 656-763 in women). Men had 4 times more fatal CHD events (152; 1218-1360 vs. 37; 656-763) and 3 times more non-fatal CHD events (502; 461-548 vs. 157; 134-184) than women. Older men than women (263; 232-299 vs. 170; 144-199). Interestingly, the incidence of HF did not differ between the genders. The relative proportions of MACE categories differed substantially between the genders. HF was clearly the most common type of incident MACE among women (49% of all MACE in women), whereas among men it constituted only 29% of all MACE. The proportion of strokes was also higher in women than in men (24% vs. 20%). CHD events constituted the largest proportion of MACE among men but played a smaller role among women (91% vs. 28%).

Conclusions: Incident MACE were more common among men than among women. HF was the dominant type of MACE among women, whereas CHD dominated among men. In cardiovascular prevention among women, more attention should be paid on risk factors of HF.

Prevalence and factors associated with depressive symptoms in partner of patients with chronic heart failure

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Background: Care and support from a partner is important for the well-being of patients with heart failure and may potentially delay disease progression. Partners play an important role in providing both practical and emotional support. However, caregiving may be associated with burden, stress and mental strain and can negatively affect the partners' livesituation and lead to symptoms of depression. It is therefore important to understand what influences the well-being of the partner.

Purpose: The aim was to determine the prevalence of depressive symptoms and investigate factors associated with depressive symptoms in partners with chronic heart failure.

Methods: Data for this cross sectional study was recruited from two nurse-led heart failure clinics in Sweden. Inclusion criteria were to be a partner living in the same household as a patient diagnosed with chronic heart failure. Exclusion criteria were dementia, or other severe psychiatric illnesses, difficulties in understanding or reading the Swedish language. Linear regression analysis with symptoms of depression measured by the Beck Depression Inventory (BDI) as the dependent variable was performed. Socio-demographic and clinical characteristics, health-related quality of life (SF-36), perceived control (Control Attitude Scale), and care burden (Caregiver Burden Scale) were included to determine independent factors associated with depression.

Results: The sample consists of 155 partners, 38 men and 117 women. The mean age was 71.3 years (SD=11.5). The majority of the patients were in NYHA II or III (52% and 53% respectively). A total of 85% of the partners had no symptom of depression, 10% had minor depressive symptom, 3% moderate and 2% had major depressive symptoms. The analysis showed that depressive symptoms were significantly associated with lower perceived control in the partner (β=0.37, t = -4.81, p<0.001) and lower perceived control in the physical dimension of quality of life (β=0.17, t = -2.19, p=0.03) and these variables explained 17% of the variance of depressive symptom measured by BDI.

Conclusions: Findings from the present study show that a decrease in perceived control as well as in the physical dimension of quality of life were associated with depressive symptom in partners with heart failure. Fifteen percent of the partners had depressive symptoms, most of them minor. Before stronger conclusions can be drawn, larger samples and prospective studies are needed.
Gene therapy for recessive catecholaminergic polymorphic ventricular tachycardia

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Purpose: Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited disease that predisposes to cardiac arrest and sudden death. Reces- sive CPVT is associated with mutations in the cardiac caveolin-3 (CASQ2). Mutations cause CASQ2 absence and are also associated with a reduction in the density of triadin and junctin, two proteins that form, with CASQ2 and RyR2, a macromolecular complex devoted to control of calcium release from the sar- coplasmic reticulum. We intended to evaluate whether viral gene transfer of wild-type CASQ2 may rescue the broad spectrum of abnormalities caused by absence of CASQ2.

Methods and Results: We used an adenov-associated serotype 9 viral vector to express wild type CASQ2 in CPVT CASQ2 knock-out mice. 20 weeks after injec- tion, we observed normalization of CASQ2, triadin, and junctin. By means of con- focal immunostaining imaging and electron microscopy we observed complete rescue of ultrastructural abnormalities. Infection efficiency was 50-60% based on end- point signal. In vitro and in vivo electrophysiology demonstrated a reduction of delayed afterdepolarizations (KO: 75%; INF: 15%, p < 0.001), triggered activity (KO: 70%, INF: 5%, p < 0.001) and a dramatic reduction of bidirectional ventricular tachycardia induced by beta-adrenergic stimul (KO: 100%; INF: 10%, p < 0.001).

Conclusions: We have proven the concept that induction of CASQ2 expression in knock-out mice reverts the molecular, structural, and electrical abnormalities and prevents life-threatening arrhythmias in CPVT2-defective catecholaminergic polymorphic ventricular tachycardia mice. These data support the view that development of CASQ2 viral gene transfer could have clinical application.

Lentivirus-mediated SERCA2a gene transfer improves left ventricular function in doxorubicin-induced heart failure

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Purpose: Doxorubicin remains among the most effective anticancer drugs ever developed. The major limitation to its use is the induction of dose-dependent car- diomyopathy leading to congestive heart failure. It has been shown that the sar- coplasmic reticulum Ca2+ ATPase pump (SERCA2a) expression and activity is decreased in cardiac dysfunction leading to diminished calcium uptake and re- lease by sarcoplasmic reticulum, thus providing a rationale for SERCA2a-based gene therapy for doxorubicin-induced heart failure.

Methods: Lentiviral vector LV-SERCA2a-GFP expressing human SERCA2a gene and GFP reporter gene was constructed. A GFP expressing vector LV-GFP was used as a control. Heart failure was induced by administrating doxorubicin (15mg/kg) intraperitoneally to adult C57Bl/6j male mice. LV-SERCA2a-GFP, LV-GFP or saline was delivered by ultra-sound guided direct intramyocardial injection into the anterior wall of the left ventricle (7 mice per group). Several functional pa- rameters were measured by echocardiography 7 and 28 days after injection, after which the mice were sacrificed. RNA and protein were extracted for Western blot and RT-PCR, and tissue sections were prepared for immunohistochemical analy- sis.

Results: The in vivo method was shown to be feasible and intramyocardial in- jections were well tolerated. Reporter gene analysis from frozen tissue samples exhibited robust GFP expression confirming that cardiomyocytes had been trans-duced by the viral vector. Western blot analyses demonstrated SERCA2a expres- sion in LV-SERCA2a-GFP injected samples. Echocardiography analyses demon- strated a significant change in the ejection fraction (EF), end-diastolic volume (EDV) and end-systolic volume (ESV) from day 7 to day 28 in SERCA2a group which compared to control virus group (GFP) or saline-injected group (table 1). Several functional pa- parameters were measured by echocardiography 7 and 28 days after injection, after which the mice were sacrificed. RNA and protein were extracted for Western blot and RT-PCR, and tissue sections were prepared for immunohistochemical analy- sis.

Conclusions: SERCA2a-based lentiviral gene therapy resulted in significant im- provement in left ventricular function in doxorubicin-induced heart failure. These results encourage further clinical development of lentiviral SERCA2a gene ther- apy.

Exon-skipping in a DCM mouse model mimicking a human mutation in titin

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Introduction: Mutations in titin (TTN) have been suggested to be a ma- jor cause for alcoholic cardiomyopathy (DCM), a disorder charac- terized by ventricular dilatation and systolic dysfunction. Titin is a giant sarcomeric protein that acts as a molecular scaffold for sarcomeric assembly, plays a putative role in myocardial stretch response, and, through its elastic domains, contributes substan- tially to the diastolic properties of the heart. We have previously gener- ated a knock-in mouse model that imitates a human frameshift mutation we found in a large family with inherited cardiomyopathy. Our titin knock-in mouse shows a DCM phenotype and therefore recapitulates the human phenotype. Here, we develop a new strategy to rescue the DCM phenotype in our mouse model using the exon-skipping technique.

Results: We designed 4 antisense oligonucleotides (AO) for specific skipping of exon 326 carrying the titin mutation. We demonstrate effective skipping of exon 326 in cultured HL-1 cardiomyocytes treated with the AOs. Detection of exon 326 does not negatively affect contractile function of the cells (FS 25±3% vs. 23±5% in treated vs. untreated cells). We evaluated our approach in-vivo by injecting the AO in skeletal muscle of heterozygous KI-mice. Finally, we cultured homozy- gous titin KI-embryos and show that skipping of exon 326 can partially restore heart function (FS 18.0±2% vs. 6.8±3.3% treated vs. untreated homoygous KI-embryos).

Conclusion: This prove-of-principle study shows that a frameshift mutation in the giant sarcomeric protein exon can be skipped efficiently in our mouse model and that heart function can be partially restored.

SUMO-1 gene transfer in a large animal heart failure model improves cardiac function


Purpose: Recently, the critical role of SUMO-1 for preserving and enhancing
Dose-dependent effects of myeloperoxidase inhibition on endothelial function and atherosclerotic lesion formation in apolipoprotein E deficient mice

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Purpose: Myeloperoxidase (MPO) is an enzyme linked to both inflammation and oxidative stress. It is abundantly expressed in the azurophilic granules of most leukocytes, including neutrophils and monocytes. MPO has been implicated in the development of a number of cardiovascular diseases, and is an independent prognostic marker in healthy individuals as well as in patients with stable coronary artery disease and acute coronary syndromes. In contrast to clinical data, investigation of the impact of MPO on lesion formation in animal models of atherosclerosis has produced controversial results. Aim of the present study was to determine dose-dependent effects of the specific MPO inhibitor 4-amino-benzamide acid hydrazide (4-ABAH) in an animal model of atherosclerosis.

Methods and Results: 6-8 weeks old apolipoprotein E-deficient (ApoE-/-) mice were fed a high-fat (21% fat) diet containing 1.25% cholesterol for 8 weeks and were concomitantly treated with 4-ABAH every second day by intraperitoneal administration of two different doses (12.5mg/kg or 25mg/kg body weight) or vehicle. ApoE-/- mice displayed endothelial dysfunction, as indicated by an impaired endothelium-dependent vasodilation (organ chamber experiments with isolated coronary artery rings either with or without endothelium) and atherosclerotic lesion formation in the aortic root (oil red O staining; histological morphometric analysis). 4-ABAH inhibition in both doses had no significant effects on body weight, cholesterol levels (gas chromatography), heart rate and blood pressure (tail-cuff measurements). 4-ABAH treatment at lower dosage did not affect oxidative stress (L-012 chemiluminescence), endothelial function and atherosclerotic plaque development, whereas 4-ABAH in higher dosage significantly decreased aortic release of reactive oxygen species (ROS) (p=0.003), improved endothelium-dependent vasodilation (p=0.04) without inducing endothelium-independent vasodilation and reduced significantly atherosclerotic plaque development (plaque area (% of total area: high-dose 4-ABAH: 11.67 ± 2.0%, low-dose 4-ABAH: 14.03 ± 3.2%; vehicle: 18.0 ± 1.6%; p<0.02) in the aortic root of ApoE-/- mice.

Conclusions: Our data demonstrate dose-dependent effects of specific MPO inhibition by 4-ABAH on vasculoprotection in a mouse model of atherosclerosis. MPO inhibition could possibly be beneficial in the treatment and prophylaxis of atherosclerosis. Further experiments are necessary in order to obtain tissue-specific and mechanistic insights.

Neuregulin attenuates pulmonary endothelial dysfunction in pulmonary hypertension

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Purpose: Neuregulin-1 (NRG-1) is an epidermal growth factor (EGF)-related protein with cardioprotective and cardioregenerative properties. To date, no studies have determined the effects of NRG-1 in pulmonary vasculature, in health or disease. Therefore, this study aims to evaluate the therapeutic treatment on pulmonary endothelial dysfunction in an animal model of pulmonary arterial hypertension (PAH).

Methods: Male Wistar rats (180-200g) randomly received monocrotaline (MCT, 60mg/kg, sc) or vehicle. After 6-8 weeks, rats were randomly assigned to receive treatment with either NRG-1 (40ug/kg/day, ip) or vehicle. The study resulted in 3 groups: control (n=8); MCT (n=8); MCT+NRG (n=5). 21 to 24 days after MCT administration animals were anesthetized, heart and lungs were excised en bloc and pulmonary arterial rings were isolated and mounted in a myograph. Endothelial function was determined by a dose-response curve to acetylcholine in phenylephrine pre-contracted rings. After the experimental protocol, arterial rings were stored in paraffin (15%) for histological analysis. Only significant results are presented (mean ± SEM, p<0.05).

Results: MCT animals presented PAH associated with endothelial dysfunction, as shown by a decreased relaxations to acetylcholine in phenylephrine pre-contracted rings, when compared to the CTRL group (p<0.02 vs control). Treated animals, MCT+NRG, presented a significant improvement in endothelial function (p<0.02). Histological analysis revealed vascular remodeling in arterial rings of MCT animals when compared with the CTRL group as shown by an increase in tunica media thickness (35.24 ± 8.48 vs 31.33 ± 0.83mm), tunica media area (104.50 ± 7.48mm² vs 67.85 ± 9.32mm²) and the ratio tunica media area/lumen area (41.23 ± 1.49% vs 31.97 ± 2.92%). Animals from the MCT+NRG group presented a significant increase in vascular remodeling as shown by improvements in all parameters analysed (34.26 ± 0.31 mm, 75.64 ± 5.10 mm² and 29.56 ± 2.46%).

Conclusion: NRG-1 chronic treatment significantly reduced the severity of endothelial dysfunction and vascular remodeling in rats with induced PAH. These results show that NRG-1 system has a crucial role in vascular function, specifically in PAH, proving to be a potential therapeutic target in this condition.
Glucosamine improves vascular endothelial function
Nocturnal versus daytime blood pressure as a predictor

Conclusions: No change after observation. Blood atherosclerotic markers did not change after significantly correlated with changes in FMD by glucosamine (r=0.48, p<0.05). No significant changes were observed after placebo. Further analysis for SD quintiles of BP by multivariate regression showed that the strongest association of ABPV with stroke was from the first SBP quintile (adjusted OR 4.5, 95% CI 1.5–13.7, p=0.006). Furthermore, there were a decrease in NT (median 6.66 vs. 6.15 mML), PC (0.131 vs. 0.091 mmol/mg protein), Fas (51.8 vs. 49.3 pg/ml) and FasL levels (47.6 vs. 40.95 pg/ml) after anakinra (p<0.05). No significant changes were observed after placebo.

Conclusion: IL-1 inhibition improves endothelial function and consequently, corona and aortic wall function, probably through reduction of nitrooxidative stress and apoptosis.

STATE OF THE ART – WHAT MORE CAN WE LEARN FROM AMBULATORY BLOOD PRESSURE MONITORING?

Ambulatory blood pressure variability: an independent determinant of arterial stiffness

Aims: Increased arterial stiffness is known to be an important predictor of cardiovascular morbidity and mortality in hypertensive patients and general population. There are many factors influencing arterial stiffness. The present study evaluated the effect of ambulatory blood pressure variability (ABPV) on arterial stiffness.

Methods and results: Brachial-ankle pulse wave velocity (baPWV) and 24 hour ambulatory blood pressure (BP) were measured in 606 subjects (41±9.4 years, range 20–70 years) who were randomly selected from general population (NCT0138619) and volunteers (NCT01237717), excluding subjects taking antihypertensive medications. Simple linear regression analysis, baPWV was significantly correlated with age, body mass index, brachial systolic BP (SBP) and diastolic BP (DBP), 24 hour SBP and DBP daytime SBP and DBP, nighttime SBP and DBP, ABPV, expressed as standard deviation (SD) of mean 24 hour SBP and DBP, and SD of mean nighttime SBP and DBP were significantly correlated with baPWV. SD of 24 hour SBP showed highest correlation (Pearson’s correlation coefficient r=0.345, p<0.0001). Significant association of ABPV with baPWV was persistent after adjustment with gender, body mass index, presence of diabetes, status of smoking and level of low density lipoprotein. Further analysis for SD quintiles of BP by multivariate regression analysis also showed positive association of ABPV with baPWV. Test for linear trend showed the strongest association of 24 hour SBP variability with baPWV (r=0.0001).

Conclusion: The present study indicates that ABPV is an independent determinant of arterial stiffness. Among the ABPV, 24 hour SBP variability has the strongest effect on arterial stiffness.

Inhibition of Interleukin-1 activity by anakinra improves endothelial, coronary and aortic function in patients with CAD and coexistent rheumatoid arthritis by reducing apoptosis and oxidative stress

Purpose: Interleukin-1 mediates atherogenesis and coronary vasoactivity. Anakinra, a human recombinant interleukin-1 receptor antagonist, is used for the treatment of rheumatoid arthritis (RA) and shows favourable effects on endothelial and coronary function in RA patients. We investigated the effects of anakinra on coronary endothelial and arterial function in CAD patients with coexistent RA.

Methods: Forty patients with chronic CAD and RA were randomized to receive a single injection of anakinra (100mg s.c.) or placebo and after 4 hours the alternation was repeated. Some patients were a double-blind trial and 25 age and sex matched subjects with similar risk factors served as controls. At baseline and 3 hours after treatment we assessed a) coronary flow reserve (CFR) of the LAD using Doppler echocardiography, b) aortic strain (AS), c) flow mediated endothelial-dependent dilation of the brachial artery (FMD) by ultrasoundography d) Fas, Fas ligand, nitrotyrosine (NT) and protein carbonyls (PC) serum levels. All controls had no clinical history for CAD and a negative for ischaemia treadmill exercise test.

Results: Patients had impaired FMD, CFR and AS compared to controls (p<0.001). At baseline, NT was related with AS and FMD (r=−0.401 and r=−0.386), while Fas and FasL with CFR (r=−0.450 and r=−0.362) (p<0.05). After 3 hours of anakinra treatment, there was an improvement in FMD, CFR and AS compared to placebo, reaching values similar to those in controls (FMD: 5.1±2.3%, 13.9±3.5% vs. 8.1±3.6%, p=0.006, CFR: 2.1±0.7 vs. 3.0±1.1 vs. 3.4±0.7, p<0.001, AS: 4.4±2.3% vs. 8.0±2.8%, p=0.003). Furthermore, there were a decrease in NT (median 6.66 vs. 6.15 mML), PC (0.131 vs. 0.091 mmol/mg protein), Fas (51.8 vs. 49.3 pg/ml) and FasL levels (47.6 vs. 40.95 pg/ml) after anakinra (p<0.05). No significant changes were observed after placebo.

Conclusion: IL-1 inhibition improves endothelial function and consequently, coronary and aortic wall function, probably through reduction of nitrooxidative stress and apoptosis.

Nocturnal versus daytime blood pressure as a predictor for stroke: a prospective study in 1000 hypertensives

Purpose: There are conflicting data regarding the relative importance of each of the components delivered by ambulatory blood pressure (BP) monitoring on cardiovascular outcome. We aimed to investigate whether either nocturnal or daytime BP is superior in the prediction of stroke during a follow up period.

Methods: We followed up 1000 essential hypertensives (age 55.1±9 years, range 20–70 years) who were randomly selected from general population (NCT0138619) and volunteers (NCT01237717), excluding subjects taking antihypertensive medications. Simple linear regression analysis, baPWV was significantly correlated with age, body mass index, brachial systolic BP (SBP) and diastolic BP (DBP), 24 hour SBP and DBP daytime SBP and DBP, nighttime SBP and DBP, ABPV, expressed as standard deviation (SD) of mean 24 hour SBP and DBP, and SD of mean nighttime SBP and DBP were significantly correlated with baPWV. SD of 24 hour SBP showed highest correlation (Pearson’s correlation coefficient r=0.345, p<0.0001). Significant association of ABPV with baPWV was persistent after adjustment with gender, body mass index, presence of diabetes, status of smoking and level of low density lipoprotein. Further analysis for SD quintiles of BP by multivariate regression analysis also showed positive association of ABPV with baPWV. Test for linear trend showed the strongest association of 24 hour SBP variability with baPWV (r=0.0001).

Conclusion: The present study indicates that ABPV is an independent determinant of arterial stiffness. Among the ABPV, 24 hour SBP variability has the strongest effect on arterial stiffness.
underwent ambulatory BP monitoring and blood sampling for assessment of metabolic profile. Antihypertensive treatment was implemented during follow-up period. Stroke was defined as rapid onset of a new neurological deficit persisting at least 24h unless death supervened, confirmed by computed tomography and magnetic resonance angiography and/or cerebrovascular angiography findings.

Results: The incidence of stroke over the whole follow-up period was 0.6%. Multivariate Cox regression analysis revealed that nocturnal systolic BP (HR=1.181, p=0.012), baseline office diastolic BP (HR=1.148, p=0.028), baseline age (HR=1.174, p=0.019), diabetes mellitus at baseline (HR=53.145, p<0.001) were independent predictors of stroke and nocturnal diastolic BP (HR=1.923, p=0.015) and 24h systolic BP (HR=1.245, p=0.022) were independent predictors of AF. In both analyses nondipping pattern was not an independent prognosticator (p>NS).

Conclusion: Our findings suggest that nocturnal BP is a better predictor of the incidence of stroke and new-onset atrial fibrillation than nondipping profile. Therefore, absolute values of nocturnal BP seem to express better nocturnal hemodynamics than systolic blood pressure variability. Nighttime hypertension is potentially associated with less nocturnal dipping and increased nocturnal systolic BP, which might be superior to assessing daytime systolic BP variability.

Gender differences in daytime and nighttime blood pressure variability and their prognostic relevance.

Dublin Outcome Study

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Background: Blood pressure (BP) variability has been repeatedly shown to have independent prognostic relevance. Distinct differences exist in many cardiovascular and metabolic profile. Stroke was defined as rapid onset of a new neurological deficit persisting at least 24h unless death supervened, confirmed by computed tomography and magnetic resonance angiography and/or cerebrovascular angiography findings. Nondipping was defined as BP fall during nighttime (SD) in day and night-time systolic (S) and diastolic (D) BP. The association of these variables with cardiovascular (CV) mortality (ascertained through the analysis of death certificates) was assessed in Cox regression models.

Methods: The study included 10,500 untreated subjects (age 54.5±14.3, 47% male) assessed for hypertension in Dublin, Ireland, in whom 24 h ABPM was obtained. BP variability was assessed separately in males and females as standard deviation (SD) of daytime and night-time systolic (S) and diastolic (D) BP. The association of these variables with cardiovascular (CV) mortality (ascertained through the analysis of death certificates) was assessed in Cox regression models.

Results: 498 CV deaths (295 in males and 203 in females) occurred in the study population during the average follow-up period of 5.8 years. Adjusted mean values of BP in males and females and the associated hazard ratios (HR) for CV mortality are summarized in the Table.

<table>
<thead>
<tr>
<th>Variable</th>
<th>LS Means±SE</th>
<th>Adjusted HR (p value) for CV death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Day SBP SD</td>
<td>10.17±.084</td>
<td>10.63±.084</td>
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<tr>
<td>Day DBP SD</td>
<td>7.54±.064</td>
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<td>Night SBP SD</td>
<td>9.05±.095</td>
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<tr>
<td>Night DBP SD</td>
<td>7.26±.073</td>
<td>6.87±.073</td>
</tr>
</tbody>
</table>

*Adjusted for age, BMI, diabetes, smoking and corresponding mean BP value. **Adjusted for age, BMI, diabetes, smoking, previous CV disease, corresponding mean SBP and DBP and nocturnal fall.

Conclusions: Daytime BP variability was lower while night-time diastolic BP variability was higher in males than in female subjects and BP variability only predicted CV mortality in males. Our study suggests important gender differences in BP variability and in its prognostic relevance, possibly related to other, previously reported differences in baroreflex function.

Absolute nocturnal blood pressure values outweigh nondipping pattern in the prediction of stroke and atrial fibrillation: data from a follow up study

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Purpose: Clinic blood pressure (BP) evaluation is being increasingly complemented by ambulatory BP measurements for the evaluation of hemodynamic patterns during daily activities and sleep. As the nondipping pattern is derivative of both daytime and nighttime BP, we aimed to investigate whether the absolute estimate of nocturnal BP is superior to nondipping pattern in the prediction of stroke and new-onset permanent atrial fibrillation (AF) incidence during follow up period.

Methods: We followed up 1060 essential hypertensives (age 55.1±11.6 years, 552 males, 307 smokers, office BP =143±17/91±12 mmHg, body mass index =28.8±4.2 kg/m²) without history of cardiovascular disease or AF episodes for a mean period of 42.8±18.1 months. All subjects had at least one annual visit and at baseline underwent ambulatory BP monitoring and blood sampling for assessment of metabolic profile. Stroke was defined as rapid onset of a new neurological deficit persisting at least 24h unless death supervened, confirmed by computed tomography and magnetic resonance angiography and/or cerebrovascular angiography findings. Nondipping was defined as BP fall during nighttime (<10% of daytime BP).

Results: The incidence of stroke and new-onset permanent AF over the whole follow-up period was 0.6% and 1% respectively. Multivariate Cox regression analysis revealed that nocturnal systolic BP (HR=1.181, p=0.012), baseline office diastolic BP (HR=1.148, p=0.028), baseline age (HR=1.174, p=0.019), diabetes mellitus at baseline (HR=53.145, p<0.001) were independent predictors of stroke and nocturnal diastolic BP (HR=1.923, p=0.015) and 24h systolic BP (HR=1.245, p=0.022) were independent predictors of AF. In both analyses nondipping pattern was not an independent prognosticator (p>NS).

Conclusion: Our findings suggest that nocturnal BP is a better predictor of the incidence of stroke and new-onset atrial fibrillation than nondipping profile. Therefore, absolute values of nocturnal BP seem to express better nocturnal hemodynamics than systolic BP variability. Nighttime hypertension is potentially associated with less nocturnal dipping and increased nocturnal systolic BP, which might be superior to assessing daytime systolic BP variability.
Exercise training in pulmonary arterial hypertension associated with connective tissue diseases

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Background: The objective of this prospective study was to assess short- and long-term efficacy of exercise training (ET) as add-on to medical therapy in patients with connective tissue diseases-associated pulmonary arterial hypertension (CTD-APAH).

Methods: Patients with invasively confirmed CTD-APAH received ET in-hospital for 3 weeks and continued at home for 15 weeks. Efficacy parameters have been evaluated at baseline and after 15 weeks by blinded-observers. Survival rate has been evaluated in a follow-up period of 2±1.9 years.

Results: Twenty-one consecutive patients were included and assessed at baseline, and after 3 weeks, 12 after 15 weeks. Patients significantly improved the mean distance walked in 6 minutes compared to baseline by 67±35 meters after 15 weeks (p=0.003), scores of quality of life (<0.05), heart rate at rest, peak oxygen consumption, oxygen saturation and maximal workload. Systolic pulmonary artery pressure and diastolic systemic blood pressure improved significantly after 3 weeks of ET. The 1- and 2-year overall-survival rates were 100%, the 3-year survival 73%. In one patient lung transplantation was performed 6 months after ET.

Conclusion: ET as add-on to medical therapy is highly effective in patients with CTD-APAH to improve work capacity, quality of life and further prognostic relevant parameters and possibly improves the 1-, 2- and 3-year survival rate. Further randomized controlled studies are needed to confirm these results.
pression of 2 transcription factors, EGR1 and FOS involved in T-cell receptor signaling pathway, and of 2 receptors, CCR2 and TL4 (P=0.05).

Conclusions: Our data suggest that the anti-inflammatory effects of atravastatin in patients with ACS might be related to direct inhibition of some members of the immune response signaling pathway. These findings could be useful to develop new therapeutic targets.

### Value of platelet pharmacogenetics in common clinical practice of patients with ST-segment elevation myocardial infarction

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Background: Antiplatelet drug resistance is a well-known problem, causing recurrent cardiovascular events. Multiple genetic polymorphisms have been related to antiplatelet resistance by several large trials, however data from common clinical practice is limited. We examined the influence of previously described polymorphisms, related to aspirin/clopidogrel resistance, on treatment outcome in a real life unselected population of patients presenting with ST-segment elevation myocardial infarction (STEMI) treated with percutaneous coronary intervention.

Methods and Results: This cohort consisted of 1257 patients with STEMI, that were treated according to a standardized guideline-based protocol. Nine polymorphisms, COX1 (-842A>G), P2Y1 (893C>T), GP1B (807C>T), GPIIb/IIIa (PA1A2), CYP2C19 (2*3 and 17), ABCB1 (3435T>C) and PON1 (576A>G), were genotyped. During 1 year of follow-up the primary endpoint, a composite of cardiac mortality or recurrent myocardial infarction, was reached in 86 patients. The Cox1 and CYP2C19*2 polymorphisms were associated with the primary endpoint, HR 2.55 (95% CI 1.46-4.40) p=0.001 and HR 2.03 (1.34-3.09) p=0.001, respectively. The combined analysis demonstrated a 2.5-fold increased risk for individuals with ≥2 risk alleles, p=0.001. The association of COX1 was driven by mortality related events whereas that of CYP2C19*2 was mainly attributed to myocardial infarction and stent thrombosis.

Conclusions: In this unselected, real life population of STEMI patient on dual-antiplatelet therapy, the polymorphisms COX1 (-842A>G) and CYP2C19*2 were determinants of thrombotic complications during follow-up. We show that in a clinical setting, testing for these polymorphisms could be of value in the identification of STEMI patients at risk for recurrent cardiovascular events.

### Enalapril and carvedilol in the prevention of chemotherapy-induced left ventricular systolic dysfunction in patients with malignant hematopathies. The OVERCOME study

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Background: The current treatment of hematological malignancies includes diverse potentially cardiotoxic chemotherapy agents, including high-dose myeloblastic regimen used in autologous hematopoietic stem-cell transplantation (HSCT). Many of these treatments could induce left ventricular systolic dysfunction (LVSD) that can limit their administration, and hamper the prognosis and long-term quality of life of these pts.
Purpose: To evaluate the efficacy and safety of the combined treatment with enalapril and carvedilol (ENCARV) in the prevention of LVSD in pts with hematological malignancies submitted to high-dose chemotherapy regimens with or without HSCT.

Methods: This was a prevention, parallel assignment, randomized, controlled, clinical efficacy study. Ninety pts recently diagnosed of acute leukemia (myeloblastic in 28, lymphoblastic in 8), and 54 with other hematopies undergoing autologous HSCT (9 with relapsed or refractory Hodgkin’s lymphoma, 23 with non-Hodgkin’s lymphoma, and 22 with multiple myeloma) and without LVSD were randomized to ENCARV or control. An echocardiographic study was performed before and 6 months after randomization. The primary efficacy endpoint was the absolute change from baseline in LVEF.

Results: 90 pts (51 males, age 50±13 yrs) were allocated to ENCARV (n=45) or Control (n=45). No differences were observed in baseline characteristics. At 6 months, LVEF did not change in the ENCARV group (62.3±6% to 62.1±7%) but significantly decreased in controls (63.3±5% to 59.6±8%), resulting in a 3.5% absolute difference (p=0.035). The corresponding absolute difference (95% CI) in LVEF was of -6.8% (-11% to -3%) in pts with acute leukemia and of -0.5% (-4% to 3%) in pts submitted to HSCT. Compared to controls, the ENCARV group had a 6-month lower incidence of death or heart failure (22% vs. 7%; p=0.035), and a trend to lower mortality (18% vs. 7%, p=0.11) and of heart failure or a fall ≥10% in LVEF (24.3% vs. 9.5%; p=0.07). Major adverse effects occurred in 33% and 20% of the pts respectively (p=0.15).

Conclusion: Treatment with ENCARV prevents LVSD in pts with malignant hematopies submitted to current treatment with intensive chemotherapy. The effect seems to be particularly relevant in pts treated for acute leukemia.

First-in-human experience with percutaneous ventricular restoration therapy in patients with ischemic heart failure and dilated left ventricle: multi-slice computer tomography and 3-year outcome

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Background: Left ventricle (LV) remodeling after anterior wall myocardial infarction leads to increased LV volumes, myocardial stress and ultimately congestive heart failure (CHF). Treatment options are limited for these high morbidity and mortality risk population.

Aims: To evaluate percutaneous ventricular restoration therapy (PVRT) utilizing a partitioning device, Parachute, by Computer Tomography (CT) and assess long-term 3-year clinical outcomes.

Methods: The study included 52 patients with ischemic CHF class II-IV (NYHA), akineetic or dyskinetic wall abnormality, ejection fraction between 15 and 40% and no revascularization options were enrolled in 14 U.S. and European sites. The device was deployed into the left ventricle apex to partition off the damaged myocardium. CT analysis was performed by an independent corelab, CT imaging was performed at baseline (n=60), 6-month fup (n=25). CT parameters are volumetric reduction of the cavity by creation of a new apex (fig 1A, B), global function, impact of papillary muscle on device expansion (fig 2), relation of the device foot with LV apex (figure 3), thrombus formation, segmental shortening and wall thickening changes overtime (figure 4A).

At 2-years, NYHA class reduced from 2.6 to 1.7 with 87% of patients reporting improvement in symptoms at 12 months. Adjudication of 3-year clinical events will be completed in June 2012 and will be available for presentation. The incidence of death and re-hospitalization for CHF was 17.9% (intention-to-treat) and 16.1% (actual treatment) at 12 months.

Conclusions: PVRT using the Parachute device in patients with ischemic CHF and anterior LV dilatation was shown to be safe. CT and 3-year clinical data will provide important insights into mechanisms of action and longevity of this novel therapy.

The effect of renal denervation in patients with advanced heart failure

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Introduction: At present, even at maximum optimal pharmacotherapy the perspective of patients with advanced heart failure (NYHA III, IV) who are not indicated for cardiac resynchronization therapy (CRT), ventricular assist devices (VAD) or heart transplant (HTx), is very limited. The annual mortality of these patients is 20-50%.

Aim of the study: The aim was to evaluate in a pilot study the effect of catheter renal denervation (RDN) in patients with heart failure (HF). In patients with advanced heart failure (NYHA III, IV) not indicated for CRT. The primary endpoint was combined: 12-month number of rehospitalizations for heart failure, left ventricular end-diastolic dimension (LVEDD) and complications of RDN.

Methods: 51 patients with advanced heart failure, NYHA III (IV) were randomized to perform either RDN + standard medical therapy or only standard medical therapy. An initial study was realised in pts with previous CT angiography of renal arteries (RA), exclusion of secondary etiology of hypertension and consent to the patient to participate in the study using catheter Simplicity 4 F (Medtronic, Inc.). The average number of lesions was 4.2±1.3 on the right RA, 5.4±2.0 on the left RA. In patients a standard echocardiographic examination was realised before RDN, then at 6 and 12 months and three-month intervals were regularly followed in outpatient heart failure department.

Results: Results of the pilot study are summarized in the table 1:

<table>
<thead>
<tr>
<th>No. of pts (N)</th>
<th>RDN</th>
<th>Standard therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 M FU</td>
<td>RDN x standard therapy</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Medication for HF (N)</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>48±0.8</td>
<td>55±1.2</td>
<td>9.0±0.8</td>
</tr>
<tr>
<td>Rehospitalization for HF (%)</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>LV EDD (mm)</td>
<td>68±5</td>
<td>60±7</td>
</tr>
<tr>
<td>31±14</td>
<td>67±12</td>
<td>0.069</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>25±10</td>
<td>31±14</td>
</tr>
<tr>
<td>26±11</td>
<td>28±12</td>
<td></td>
</tr>
</tbody>
</table>

In the group of patients treated with the RDN was recorded 1 complication - AV fistula with the need for surgical revision.

Conclusions: Catheter renal denervation may be a safe and effective alternative for non-pharmacological treatment in patients with advanced heart failure who are not indicated for CRT, VAD, or HTX. Effect of the RDN on the RAAS of these patients must be verified in a large prospective multicenter study.

Long term outcome in heart failure: do patients with reduced and preserved ejection fraction differ?

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Introduction: Heart failure (HF) is a complex clinical syndrome that can be challenging to diagnose & treat. For those with left ventricular systolic dysfunction (LVSD) there are effective treatments which improve symptoms and prognosis. HF with preserved ejection fraction (HFPEF) is increasingly recognised in clinical practice, but to date intervention trials have been disappointing. The therapeutic targets in these HFPEF trials (e.g. renin-angiotensin pathway blockage) have been extrapolated from patients with LVSD and HFPEF.

Methods: Patients were referred from primary or secondary care to a diagnostic HF clinic. Based on the initial clinical assessment and echo, patients were allocated to one of 3 groups: HF due to LVSD, HFPEF & non-HF. HFPEF was diagnosed using the following criteria: ongoing NYHA class II-IV symptoms, preserved systolic function (EF > 45%) plus any two abnormal investigations 1) Chest X-ray showing pulmonary oedema or cardiomegaly, 2) echocardiogram with left ventricular hypertrophy, left atrial diameter >40 mm, or E/A ratio >0.5 & 3) ECG showing LBBB, LVH or atrial fibrillation(AF). Data were obtained from hospital & GP records, mortality data and death certificates.

Results: From Jan 2002- Dec 2007, 1034 patients were referred to the HF clinic. Of these 270 (26%) were diagnosed with LVSD & 242 (23%) fulfilled the diagnostic criteria for HFPEF. Non HF was diagnosed in 522. Patients were followed up for average 5.6 years (3.8-5 yrs). Compared to those with LVSD, HFPEF patients were older, more likely to be female & more likely to have hypertension, AF & diabetes. Mortality was high in both groups, LVSD 163 (60%) & HFPEF 119 (50%) (P=0.018). However cause of death in LVSD & HFPEF were strikingly different. Cardiovascular deaths in LVSD were 111 (68%), of these 53 (48%) were due to HF. In HFPEF 51 (43%) were cardiovascular deaths & only 18 (15%) were due to HF (P=0.001). Non cardiovascular deaths in HFPEF were 68 (57%) in LVSD 52

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Elevated resting heart rate is associated with increased risk of developing hypertension and cardiovascular disease, and seems to play a role in the progression of heart failure. The shape of association between resting heart rate and risk of developing heart failure has not been examined in healthy individuals of the general population.

Methods and Results: Hazard ratios (HR, 95% CI) of heart failure comparing categories of resting heart rate (51-60/min [reference], 61-70/min, 71-80/min, 81-90/min and 91-100/min) were calculated in healthy, healthy, 9,805 men and 12,321 women aged 39-79 participating in the “European Prospective Investigation into Cancer and Nutrition” (EPIC) study in Norfolk. During a mean follow-up of 12.9 years 1,356 incident cases of heart failure occurred. In participants without potential heart rate modifying medication hazard of heart failure increased with increasing resting heart rate (p for linear trend 0.003); compared to the reference category hazard ratios (95% CI) for increasing categories of resting heart rate were 1.08 (0.88-1.34), 1.17 (0.94-1.46), 1.39 (1.08-1.79) and 1.42 (1.00-2.03), respectively; in multivariable analysis adjusting for age, sex, body mass index, systolic blood pressure, prevalent diabetes, cholesterol concentration, social class, educational level, smoking and physical activity. Within the reference range of resting heart rate (50-100/min) each 10/min increase was associated with an 11% increase in hazard of heart failure in multivariable analysis. Results did not change materially after adjusting for myocardial infarction and coronary heart disease events during follow up (1.12, 1.06-1.18).

Conclusion: Elevated resting heart rate is associated with increased risk of developing heart failure and seems to play a role in the progression of heart failure. The shape of association between resting heart rate and risk of developing heart failure has not been examined in healthy individuals of the general population.

Resting heart rate and incident heart failure

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Aims: Elevated resting heart rate is associated with increased risk of developing hypertension and cardiovascular disease, and seems to play a role in the progression of heart failure. The shape of association between resting heart rate and risk of developing heart failure has not been examined in healthy individuals of the general population.

Methods and Results: Hazard ratios (HR, 95% CI) of heart failure comparing categories of resting heart rate (51-60/min [reference], 61-70/min, 71-80/min, 81-90/min and 91-100/min) were calculated in healthy, healthy, 9,805 men and 12,321 women aged 39-79 participating in the “European Prospective Investigation into Cancer and Nutrition” (EPIC) study in Norfolk. During a mean follow-up of 12.9 years 1,356 incident cases of heart failure occurred. In participants without potential heart rate modifying medication hazard of heart failure increased with increasing resting heart rate (p for linear trend 0.003); compared to the reference category hazard ratios (95% CI) for increasing categories of resting heart rate were 1.08 (0.88-1.34), 1.17 (0.94-1.46), 1.39 (1.08-1.79) and 1.42 (1.00-2.03), respectively; in multivariable analysis adjusting for age, sex, body mass index, systolic blood pressure, prevalent diabetes, cholesterol concentration, social class, educational level, smoking and physical activity. Within the reference range of resting heart rate (50-100/min) each 10/min increase was associated with an 11% increase in hazard of heart failure in multivariable analysis. Results did not change materially after adjusting for myocardial infarction and coronary heart disease events during follow up (1.12, 1.06-1.18).

Conclusion: Elevated resting heart rate is associated with increased risk of developing heart failure and seems to play a role in the progression of heart failure. The shape of association between resting heart rate and risk of developing heart failure has not been examined in healthy individuals of the general population.

Profile of non-educated patients in chronic heart failure

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Aims: The aims of this paper are to report on the profile of non-educated patients suffering from heart failure in the real-world setting of the ODIN study, to determine whether there are differences between educated and non-educated patients in terms of potential risk factors based on patients' demographics, medical history, laboratory values and discharge medication with death at 1 year was tested by Cox-regression analysis, and a risk score was created. The model was validated in the remaining 311 patients.

Methods: A total of 1038 HFNEF patients admitted to hospital between Jan 2001 to Dec 2010 were studied. In 727 randomly selected patients, the association of potential risk factors based on patients' demographics, medical history, laboratory variables and discharge medication with death at 1 year was tested by Cox-regression analysis, and a risk score was created. The model was validated in the remaining 311 patients.

Results: Among the included patients, 3237 patients were included (mean age: 67.6 ± 14.2 years: men: 69.4%). Ischemic heart disease was the main cause of CHF. Approximately 75% of the patients were in NYHA class I or II. Mean LVEF was 39±14.2%, 59.7% had a LVEF < 45%. A blocker of the renin-angiotensin system was present in 90.2%, and a beta-blocker in 80.6%. Aldosterone blockers were given in 32.7% and loop diuretics in 80.1%. Few patients were resynchronized (8.3%) or received an ICD (12.6%). Among the total population, 5247 patients (72.5%) were educated and 890 patients (27.5%) non-educated. Non-educated patients were older and sicker with a profile evoking heart disease of the elderly. They were also less likely than educated patients to receive all of the recommended cardiovascular drugs and at lower dosages for the most frequently prescribed drugs. During a median F/U of 27.2 months, 682 (21.1%) patients died from all causes, 17.3% (n=406) in the educated group and 31.0% (n=276) in non-educated patients (unadjusted HR: 0.48, 95% CI 0.40-0.57, P<0.001). Cox analysis showed that TPE was one of the main independent prognostic factors of survival (1-year and 2-year mortality rates: 7.3% and 16.4% in educated patients and 13.2% and 26.2% in non-educated patients, respectively; adjusted HR: 0.70, 95% CI 0.58-0.84; P<0.001).

Conclusion: In CHF, the profile of non-educated patients appears very different from that of educated patients. Nevertheless, multivariate analysis showed persistence of the independent relationship between TPE and survival, irrespective of these differences.
Results: At 1 year, 162 patients in the development cohort died. 7 independent prognostic factors were identified, and each was assigned a number of points proportional to its regression coefficient: hypoalbuminemia (6 points), history of HF (3.5 points), history of cerebrovascular disease (3.5 points), blood urea nitrogen >10mmol/L (3.5 points), not use of calcium channel blockers (3.5 points), not use of angiotensin-converting enzyme inhibitor or angiotensin II receptor blockers (2.5 points), age >78 years (2 points). We calculated risk scores for each patient and defined three risk groups: low risk (0 to 7.5 points), intermediate risk (8 to 11.5 points) and high risk (12 to 24.5 points). In the development cohort, the 1-year mortality rates for these three groups were 11%, 18%, and 41%. In the validation cohort, the corresponding mortality rates were 13%, 23% and 38% (Figure). The C statistic for the point system was 0.72 in the development cohort and 0.68 in the validation cohort.

Conclusions: The risk score derived from commonly available clinical variables can be used to predict 1-year mortality of HFN-EF patients; which might be useful in clinical practice.

Eplerenone in patients with systolic heart failure and mild symptoms: analysis of repeat hospitalisations


Purpose: Eplerenone is known to reduce time to first hospitalisation or cardiovascular death in patients with mild heart failure. In chronic diseases such as heart failure, analysing all heart failure hospitalisations, including repeats, should give a more complete picture of treatment benefits. We examined recurrent heart failure hospitalisations in the Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure trial (EMPHASIS-HF), which compared eplerenone to placebo in patients with systolic heart failure and mild symptoms.

Methods: HF hospitalisations were analysed per 100 patient-years of follow-up and a Negative Binomial generalised linear model, which allowed for dependence of recurrent hospitalisations within an individual, was used to obtain an estimate of the heart failure hospitalisation rate (eplerenone versus placebo).

Results: There were fewer recurrent hospitalisations, despite longer follow-up (due to fewer deaths), in the eplerenone group compared with placebo. Heart failure hospitalisation rates in the eplerenone and placebo groups were 11.1 and 38% (Figure). The C statistic for the point system was 0.72 in the development cohort, the 1-year mortality rates for these three groups were 11%, 18%, and 41%. In the validation cohort, the corresponding mortality rates were 13%, 23% and 38% (Figure). The C statistic for the point system was 0.72 in the development cohort and 0.68 in the validation cohort.

Conclusions: The risk score derived from commonly available clinical variables can be used to predict 1-year mortality of HFN-EF patients; which might be useful in clinical practice.

3156 Risk of stroke, systemic embolism or death according to heart failure and left ventricular function status in patients with atrial fibrillation: results of the ARISTOTLE trial

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Purpose: The additional risk of stroke or systemic embolism (SSE) conferred by heart failure (HF) and left ventricular systolic dysfunction (LVSD) in patients with atrial fibrillation (AF) is uncertain. In a retrospective analysis, we examined this risk in the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation Trial (ARISTOTLE), as well as the effect of apixaban vs. warfarin.

Methods: Of the 18201 patients with AF and at least one other risk factor for stroke enrolled in ARISTOTLE, 14671 (81%) had a report of LV systolic function at baseline. The composite outcomes of SSE or death (to account for competing risks) and SSE, myocardial infarction (MI) or death were calculated in 3 groups of patients: 1) No HF and no LVSD (n=8728); 2) HF but no LVSD (n=3207) and 3) LVSD, with or without HF (n=2736). We also estimated “net clinical benefit” as the composite of major bleeding or death.

Results: The rate of each composite outcome was highest in patients with LVSD, intermediate in patients with HF but preserved LV systolic function and lowest in patients without HF or LVSD (p<0.001 for each; Table). Each prediction model was less frequent in patients treated with apixaban compared with warfarin: overall apixaban/warfarin hazard ratio for SSE or death 0.89 (95% CI 0.81, 0.98) p<0.02; for SSE, MI or death 0.88 (0.80, 0.97) p=0.01; and for SSE, major bleed or death 0.90 (0.78, 0.92) p<0.001. There was no evidence of treatment-effect across the 3 patient groups (interaction p values in Table).

STATE OF THE ART – NOVEL APPROACHES IN PERCUTANEOUS CORONARY INTERVENTIONS

3157 Two novel approaches of plasmonic photothermal angioplasty with nanoparticles and stem cells as an alternative to current cardiac interventions

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Background: Some modern angioplasty techniques generally just affect the geometry of the plaque and have some inherent clinical and technical limitations. Our previous bench-to-bedside studies confirmed high efficacy and safety of nanomedicine-based approach for the management of atherosclerosis.

Methods: A total of 120 patients (NC01361232) 45-65 years old with PCI (percutaneous intervention) and CABG (coronary artery bypass surgery) indications were assigned to the three groups (40 patients into the group with PCI indications without stenting, 40 – cardiac surgery group, and 40 – with PCI indications to sirolimus stenting control). Patients with PCI indications underwent delivery of nanoparticles (NPs) inside of stem cells in medium via catheter-based intravascular laser irradiation/ in 24 weeks in groups were 18.9 ± 46.2%, 10.8 ± 33.6% and -1.1/ -2.2% (p<0.01) respectively, total plaque volume (TPV) was changed from
Intravascular ultrasound results with the drug eluting absorbable metal scaffold in the BIOSOLVE-I study up to twelve months follow-up

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Purpose: The advantages of absorbable metal scaffolds (AMS) in the treatment of coronary artery stenosis, when compared to conventional stents, include elimination of late scaffold thrombosis, chronic inflammation and artefacts during non-invasive imaging. As magnesium is an essential element of the human body it was considered as an attractive alloy for bioabsorption. In order to deliver clinical results which are comparable with competitor devices the AMS was further developed and a drug (Paclitaxel) was added.

Methods: BIOSOLVE-I is a prospective, multicenter first-in-man trial with follow-up investigations at 1, 6, 12, 24 and 36 months. Patients were enrolled in two consecutive imaging follow-up schedules. IVUS assessment was available for all subjects N=46 at baseline and for 43 subjects post-procedure. At 6-month follow-up 36 patients consented for an IVUS follow-up and at 12-month 33 patients underwent IVUS follow-up.

Results: Six-month grey-scale IVUS results showed a reduction in scaffold area, which in combination with the growth of in-scaffold neointimal hyperplasia results in a significant reduction of minimal lumen area (p<0.0001). There was no significant reduction in the vessel area post-procedure and at 6-month follow-up, showing the absence of substantial expansive or constructive remodelling. Preliminary data on the serial assessments (9 subjects) of intravascular ultrasound using virtual histology imaging on the 6-month follow-up showed a significant decrease in the dense calcium from 39.0% to 23.6% (p-value 0.001). This decrease of dense calcium is interpreted as a surrogate assessment for the bioabsorption process of the scaffold material.

Conclusion: The increase in lumen volume between 6-month and 12-month follow-up (based on preliminary data) may be associated with positive remodeling. The 6-month virtual histology data prove the expected bioabsorption of the struts. Final 12-month data will be available upon presentation.

The dynamic vascular response at the proximal and distal edges following implantation of the ABSORB Everolimus-eluting biosorbing vascular scaffold and the Xience V everolimus-eluting stent

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Objectives: To assess in vivo the dynamic vascular response at 2-years following implantation of a fully bioresorbable vascular scaffold (Absorb BVS) and a metallic everolimus-eluting stent (EES).

Background: Non-serial evaluations at 6-months and 1-year following implantation of the Absorb BVS have demonstrated proximal edge constructive remodelling and distal edge adaptive expansion. The edge vascular response following implantation of the Xience V EES has not been fully investigated.

Methods: The 5 mm proximal and distal segments adjacent to the implanted Xience V EES and Absorb BVS were investigated with intravascular ultrasound (IVUS) and virtual histology-IVUS imaging respectively post-procedurally at 6-months and 2-years in the Absorb Cohort B (n=45) and SPIRIT II (n=113) trials.

Results: At 6-months the previously observed significant constructive remodelling in the 5 mm proximal edge of the vessel treated with an Absorb BVS, [a external elastic membrane (EEM) area (median [interquartile range]; p=0.06)] tended to lose its statistical significance at 1-year: -1.53% [-7.74; 2.48], (p=0.06)], further evolving into a non-significant -0.44% [-5.51; 7.37] adaptive increase in the EEM area at 2-years. At the 5 mm distal edge the trend toward adaptive expansion (EEM area: +3.5% [-2.08; 6.91]), (p=0.07) observed at 1-year did not change significantly at 2-years: EEM area: +0.5% [-4.02; 9.85], (p=0.59).

The 5 mm proximal edge of the vessel treated with a Xience V EES did not change significantly at 2-years: a relative change towards constructive remodelling was observed, Δ EEM: -2.32% [-13.62; 3.33], (p=0.07) despite the relative plaque decrease: Δ Plaque area: -6.30% [16.36; 4.06], (p=0.02).

Conclusion: The dynamic vascular response at 2-years following implantation of either a fully bioresorbable scaffold or a metallic platform both everolimus eluting, demonstrates a dynamic biological reaction. Although the Xience V EES at short-term demonstrates a favourable biological behavior at the stent edges, the Absorb BVS appears to have advantageous effects long-term: the clinical significance of these findings remains to be integrally elucidated when the 3-year imaging follow-up of the Absorb Cohort B trial is finalised.

A prospective randomized trial using optical coherence tomography to compare the Xience V everolimus-eluting stent with a bare metal stent postulated with a paclitaxel-eluting balloon (OCTOPUS Trial)

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Background: Aim of this study was a comparative evaluation using optical coherence tomography (OCT) of XIENCE V everolimus eluting stent (DES) and the bare metal stent Coroflex Blue® postulated with the paclitaxel-eluting balloon Sequent Please® (BMS+DEB; B Braun Melsungen AG) with respect to endothelial coverage and neointimal proliferation (ClinicalTrials.gov identifier: NCT01056744).

Methods: We included 125 patients scheduled for elective percutaneous coronary intervention (PCI) of a native coronary stenosis suitable for stent implantation and OCT imaging. All patients were openly randomized 1:1 to either XIENCE V® or Coroflex Blue®/Sequent Please®, Angiographic follow-up (FU) and OCT imaging were performed 6 months after study stent implantation in all patients. OCT endpoints were: (1) endothelial coverage, expressed as % of struts without coverage and % of stent length containing non-covered struts, and respectively (2) neointimal proliferation, given as % neointimal volumetric proliferation within the whole stent and also as peak focal % neointimal area proliferation. A quantitative OCT algorithm was applied to each stent by steps of one mm.

Results: Stent placement of DES or BMS postulated with Sequent Please was successful in 100 pts (n=52 DES and n=48 BMS+DEB). Six month FU with OCT was carried out in 85 patients (n=45 DES and n=40 BMS+DEB, 15% drop out). Reintervention due to restenosis of the treated lesion was necessary in 3 patients (2: BMS+DEB, 1: DES, n.s.). Stent expansion by OCT was sufficient in both groups without a significant difference. OCT analysis showed significantly more neointimal proliferation calculated as in-stent proliferation volume and relative proliferation volume (proliferation volume/cm stent length) in Coroflex BMS stents postulated with Sequent Please (15.69±7.6 in BMS + DES vs 12.11±5.3 in DES, p<0.05). However, we found no differences between the 2 groups regarding peak focal in-stent stenosis expressed as maximal proliferation area (39.39±13.5 in BMS+DEB vs 36.95±15.9 in DES, n.s.). Both devices showed comparable results for stent endothelialization (uncovered stent struts: 4.1±8.9% in DES vs 3.8±7.3% in BMS+DEB, n.s.).

Conclusion: The Xience V DES and the Coroflex Blue BMS postulated with the paclitaxel-eluting Sequent Please balloon showed similar results regarding peak focal in-stent stenosis and stent coverage 6 month after implantation. Further studies are required to evaluate the impact of stronger neointimal proliferation in BMS postulated with Sequent Please.

CORONARY ARTERY SURGERY: UNCERTAINTIES, NOVEL APPROACHES, OUTCOMES

Should coronary artery bypass grafting in patients with moderate ischemic mitral regurgitation be combined with mitral valve repair?

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Background: Mitral regurgitation is a strong predictor of poor outcomes in patients with coronary artery disease; whether correcting it at the time of CABG improves outcomes is less certain even in moderate to severe MR. The aim of this study was to determine whether stronger neointimal proliferation in moderate to severe MR. The aim of this study was to determine whether stronger neointimal proliferation in moderate to severe MR.
MR were treated with isolated CABG (n = 509) or CABG + MV repair (n = 787). Groups were propensity-matched using demographics, co-morbidity, coronary status, LV remodeling, LV deformation and MR grade quantitative echocardiography. A homogeneous group of 190 patients (81 under coronary artery bypass grafting only and 109 combined with mitral valve annuloplasty) than was analyzed. Survival (with mean follow-up 5.2±1.74 years), echocardiographic dates and NYHA functional class were compared.

**Results:** Patients undergoing CABG alone were more likely to have 2+ postoperative MR than those undergoing CABG+ MV annuloplasty (37.7%, versus 8.1% at 5 years). Before matching, 10-year survival differed significantly (log-rank p<0.0003). In propensity-matched patients with moderate LV remodeling (EDD 64.2±7.6 mm, EDV 199±61 ml, EF 40±10%) and 2+ or 3+ MR one, 5-, and 10-year survival was identical with mean 96.8±0.13%, 83.2±0.28% and 65.8±0.7% correspondingly (log-rank p=0.884). The NYHA functional class substantially improved in both groups (p<0.001) and remained improved at 5 years. The independent risk factors for an increased mortality during 10 years follow-up in multivariate model included LV EF less than 40% (HR=1.90, 95% CI 1.085–3.351, p=0.025), LV EDD (HR=1.047, 95% CI 1.005–1.09, p=0.013), additive Euroscore (HR=1.99, 95% CI 1.039–1.382, p=0.013) and age (HR=1.049, 95% CI 1.016–1.083, p=0.003).

**Conclusions:** Although adding MV annuloplasty to CABG reduces postoperative MR compared with CABG alone, it does not improve long-term survival in patients with moderate functional ischemic MR.

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### Long-term follow-up study of coronary revascularization alone or with combined mitral valve operations for ischemic mitral regurgitation

**Methods:** Patients: To explore the long-term survival for MR patients after coronary artery bypass grafting (CABG) surgery and mitral valve surgery (MVS).

**Methods:** Between January 1997 and December 2003, three hundred seventy-two patients with ≥3 MR underwent CABG and were followed. The average follow-up was 5.26(SD=5.69) years. 144 out of 372 patients (38.7%) expired during the 11-year period. The overall and four groups' survival rate were 56.1% (95% CI: 56.1±6.2%), 60.7% (95% CI: 60.7±9.1%), 55.7% (95% CI: 55.7±15.5%), and 53.8% (95% CI: 53.8±11.1%), respectively (p-value=0.0156 for log-rank test). There were about 75.7% patients with their MR condition regressed to grade 2 after surgery. The CABG combined with mitral valve reconstruction or replacement with both valves had better improvement of MR than those groups with CABG alone (66.2% for group A, 69.3% for group B, 97.3% for group C, and 84.9% for group D, p<0.0001).

**Conclusions:** Although CABG combined with MVS may offer better improvement of MR regression, the long-term survival didn’t improve in patients with ≥grade 3+ MR after CABG combined with MVS.

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### Simultaneous, hybrid revascularization by carotid artery stenting and coronary artery bypass grafting in the continued TARGET-CAS study population

**Purpose:** To assess the feasibility of simultaneous, hybrid revascularization with carotid artery stenting (CAS) followed by coronary artery bypass grafting (CABG) for severe, symptomatic coronary and carotid disease in the extended TARGET-CAS (Carotid Artery Stenting With Patient- and Lesion-Tailored Selection of the Neuroprotection System and Stent Type) study.

**Methods and Results:** In the population of 1363 consecutive patients with significant carotid artery stenosis enrolled in TARGET-CAS study in 2001-2011 co-existing coronary artery disease (CAD) (>1 significant narrowing in major coronary branch) was present in 878 (64%) patients. Patients with severe though stable CAD (n=56; 41%) were treated with two staged procedures: CAS-then-CABG (procedures were performed 1-3 months after CAS). In contrast, those with unstable angina symptoms (n=19; 14%), age 71.4±6.9, range 53-79 years: 77% men, in years 2009-2011 were treated with a new one-stage, hybrid (percutane- nous-surgical) revascularization (CAS-CABG). Among those treated with one-stage CAS+CABG, recent ipsilateral neurological symptoms (i.e., within the 2-4 preceding weeks) were present in 42% patients and mean angiographic carotid stenosis was 83±13% (range 60–99%). EuroSCORE risk was 5.6±1.16 (range 3–9). All CAS+CABG subjects were on acetylsalicylic acid and the CAS procedure was performed on acetylsalicylic and unfractioned heparin only (i.e., without thienopiridine). The choice of embolic protection devices and stent type was according to the TARGET-CAS protocol (distal–proximal, 63%; closed-cell, 37%). After CAS, the patients, were transferred to the surgical OT for CABG. 58% of patients had total arterial myocardial revascularization. Clopidogrel (loading dose of 300mg) was administered 6-10 hours later when major surgical bleeding and both association functional class were completed. At 3 months at a standard dose. All the CAS+CABG procedures were technically successful, and neither stroke, death nor transient ischemic attack occurred peri-operatively. There was no carotid 10-stent thrombosis. One myocardial infarct (MI) occurred 2 days after CABG in a patient with euroSCORE 9 and right coronary artery graft failure and it was treated with successful percutaneous coronary angioplasty. By 30 days no other major complications (death, stroke, MI) were noted.

**Conclusion:** Our results suggest that the simultaneous, hybrid strategy: percutaneous treatment of severe/symptomatic carotid stenosis (CAS) combined with surgical management of severe/symptomatic CAD (CABG) is feasible and safe and it should be further addressed in a multi-center registry.

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### Minimally invasive hybrid myocardial revascularisation. Short and long-term clinical follow-up

**Methods:** One hundred and eight patients (26 men and 26 women, aged 64.6±10 years) with multivessel coronary artery disease (two- vessel, n=62 and three-vessel, n=46) were referred for hybrid revascularisation combining robotically enhanced (RE)-MIDCAB and fractional flow reserve (FFR)-guided PCI. Surgery consisted of single IMA to LAD (n=91, 84%) or sequential grafting to diagonal branch and LAD (n=10, 9.5%) or double IMA implantation (n=7, 6.5%). Two patients were converted to open chest surgery. Surgery was performed in 46 cases and PCI in 62 patients. The target stenosis for PCI was found haemodynamically non-significant in 20 patients (18%).

**Results:** The median length of stay in hospital was 7 days (in Intensive Care Unit 1 day), value to be correlated with the chosen hybrid strategy. Postoperatively there was one case of re-intervention for bleeding but no significant deterioration of pre-existent organ dysfunction was observed. One patient died suddenly 12 hours after a rotablator PCI procedure, performed 3 days after MIDCAB. One patient developed a transient cerebro-vascular accident post-catheterisation. At 30 days there was no recurrent ischaemia nor need for revascularisation. The mean short-term follow-up was of 4.2±3.1 years during which 18 patients (16.6%) had at least one major adverse cardiac event. Eight (8.4%) patients died, four (3.7%) of proven cardiac cause. Four deaths occurred more than 5 years after hybrid revascularisation. There was one documented cerebrovascular accident. In total 17 revascularisation procedures were recorded (3 CABG, 6 target vessel PCI, and 8 PCI of another artery).

**Conclusions:** In selected patients with multivessel disease hybrid myocardial revascularisation strategy combining FFR-guided PCI and Robotic enhanced MIDCAB is a safe and efficient procedure, providing a functionally complete revascularisation with minimal surgical trauma and good long-term results.

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### The impact of acute kidney injury upon long-term outcomes following CABG: a propensity score matched case control study

**Methods:** This was an observational cohort study of prospectively collected data of 4694 patients who were discharged from hospital after first time CABG surgery at a tertiary cardiac centre between 2003 and 2008. AKI was defined using the AKI criteria, which requires at least a 50% increase in serum creatinine. A comparison of 560 patients that sustained AKI with 560 propensity score matched patients that did not sustain AKI was undertaken. The primary outcome measure was all-cause mortality determined via Office of National Statistics. Long-term survival was analyzed with a risk-adjusted Cox proportional hazards regression model.

**Results:** As expected propensity matching resulted in comparable baseline clinical and operative characteristics between both groups. Length of hospital stay was 3.1 years during which 18 patients (16.6%) had at least one major adverse cardiac event. Eight (8.4%) patients died, four (3.7%) of proven cardiac cause. Four deaths occurred more than 5 years after hybrid revascularisation. There was one documented cerebrovascular accident. In total 17 revascularisation procedures were recorded (3 CABG, 6 target vessel PCI, and 8 PCI of another artery).

**Conclusions:** In selected patients with multivessel disease hybrid myocardial revascularisation strategy combining FFR-guided PCI and Robotic enhanced MIDCAB is a safe and efficient procedure, providing a functionally complete revascularisation with minimal surgical trauma and good long-term results.
was significantly larger in patients that developed AKI (17 vs 8 days, p < 0.0001). Mortality rates at 1 year and 5 years were higher in patients with AKI (8.41% and 24.1% vs 3.93% and 16.6% respectively). In Cox multivariable analysis of the propensity-matched cohort, AKI was confirmed to be an independent predictor of long-term mortality (HR 1.63 CI 2.28–2.08). Other independent predictors of long-term mortality included left ventricular ejection fraction less than 50% (HR 1.47 CI 1.14–1.85), diabetes mellitus (HR 1.43 CI 1.11–1.84), baseline serum creatinine (HR 1.43 CI 1.21–1.70) and age (HR 1.61 CI 1.38–1.87).

Conclusions: The development of AKI following CABG is a serious event associated with worse long-term survival. This excess mortality cannot be explained by coexisting comorbidity and surgical complexity alone.

3167 Estimated glomerular filtration rate and outcome following coronary artery bypass grafting: Impact on mortality after a 5.5-year follow-up


Background: Chronic kidney disease (CKD) is associated with a worse outcome after coronary artery bypass graft surgery (CABG). Most data supporting this statement is based on plaque upon pre-operative measurement of serum creatinine (eGFR), which is limited data assessing the relationship between estimated glomerular filtration rate (eGFR) and long-term mortality following CABG.

Methods and Results: An observational registry study 4889 patients undergoing CABG at a tertiary cardiac centre between 2003 and 2008 was conducted. eGFR was calculated from the MDRD equation. Patients were divided into four groups based on eGFR (~ < 80 mls/min, 80-60 mls/min, 60-40 mls/min, < 40 mls/min). The primary outcome measure was all-cause mortality determined via Office of National Statistics data. Long-term survival was analyzed with a risk-adjusted Cox proportional hazards regression model.

Results: There were 806 deaths during median 5.5 (CI4.1 to 6.8) years follow-up. Median (95% CI) pre-operative eGFR was significantly lower for the patients that died (60.7 (CI 47.9 to 77.0) mls/min) when compared with pre-operative eGFR of the survivors (72.9 (CI 68.7 to 90.5) mls/min) (p < 0.0001). Patients with lower eGFR were older and more likely to be female. With decreasing eGFR patient the prevalence of associated comorbid conditions increased. The incidence of early post-operative complications and in-hospital mortality increased as eGFR decreased. Long term survival following CABG was proportional to eGFR, with an adjusted hazard ratio of 1.02 (95% CI 0.93 to 1.07) for patients with an eGFR 60-60 mls/min and 2.05 (95% CI 1.53 to 2.74) for patients with an eGFR < 40 mls/min when compared with patients with an eGFR > 80 mls/min.

Conclusions: Estimated GFR is a powerful predictor of short-term and long-term mortality after CABG. Patients with an eGFR less than 60 mls/min represent a group at high risk of adverse outcome following CABG, and targeted research in this patient group is urgently needed.

ASSESSMENT AND ENDOVASCULAR TREATMENT OF PERIPHERAL ARTERIAL DISEASE

3168 18F-FDG-PET role in the assessment of carotid atherosclerotic vulnerable plaques (a comparison with histological analysis)

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Purpose: Carotid atherosclerotic vulnerable plaque represents an important cause of morbidity and mortality due to cerebrovascular ischemic events. From the histological point of view, inflammation and angiogenesis are traditionally associated to plaque vulnerability, whilst calcification were related to stability. Positron emission tomography with the use of [(18)F]-fluorodeoxyglucose (a macrophage metabolite), [(18)F]-FDG-PET, is an emerging morb-functional technique to identify the highly inflamed and consequently the most vulnerable carotid plaques. We investigated the role of [(18)F]-FDG-PET in the assessment of carotid vulnerable plaques, comparing PET findings with histological analysis after endarterectomy.

Methods: From February 2011 to January 2012 twelve consecutive patients (16 males, mean age 73±8 years) undergoing carotid endarterectomy, were studied with carotid [(18)F]-FDG-PET Maximum standardized uptake value (SUV) was used to quantify [(18)F]-FDG uptake. Surgical specimens were also analyzed by optical microscopy in order to outline histological parameters predictive of plaque vulnerability (inflammation, haemorrhage, fibrous cap rupture).

Results: We found SUV values ranging from 1.3 to 3.4 (mean value 1.78±0.26) in vulnerable plaques than in stable ones (SUV mean value 1.75±0.3).

Conclusions: Higher metabolic activity of atherosclerotic carotid plaques seemed to be associated with histological aspects of inflammation and instability, while stable calcified plaques showed to have lower [(18)F]-FDG uptake. Furthermore we are continuing the study prolonging the population to make our results more consistent. Although limited by the small population analyzed, partial results suggested the important role of [(18)F]-FDG-PET in the identification of carotid atherosclerotic plaques at high risk.

3169 Intravascular ultrasound (IVUS) validation of non-invasive and invasive measures of carotid stenosis severity in the CARUS Registry

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Plaque morphology gains increasing attention; nevertheless, current carotid revascularization guidelines clearly denote the internal carotid artery (ICA) stenosis severity taken together with general cerebral ischaemia syndromes as the key clinical decision-making determinant.

Aim and Methods: To validate non-invasive (duplex Doppler peak systolic and end-diastolic velocity, PSV and EDV, CT angiography area stenosis, AngioCT) and invasive (classic quantitative angiography QA diameter stenosis, DS, and densitometric stenosis severity, QA-DENSITOM) ICA imaging modalities against intra vascular imaging gold standard, IVUS. Index ICA’s were IVUS-imaged (unprotected-107, proximal EPD-51, distal EPD-132) in 290 consecutive patients (age 47±8.3, 187 men, 104 asymptomatic and 186 symptomatic) referred for carotid revascularization decision-making.

Results: ICA IVUS imaging was safe. By univariable model, PSV (AUC 0.77, cut-off 2.58ms, PV 0.64, NP 0.80), EDV (AUC 0.74, cut-off 0.75ms, PV 0.57, NP 0.80), AngioCT (AUC 0.79, cut-off 72%, PV 0.61, NP 0.83), DS (AUC 0.80, cut-off 61%, PV 0.65, NP 0.82), and QA-DENSITOM (AUC 0.88, cut-off 74%, PV 0.79, NP 0.86) all predicted ≥75% IVUS ICA stenosis (p < 0.0001 for all) (Fig. 1). Multivariable model, however, eliminated PSV, EDV and DS, leaving AngioCT and QA-DENSITOM as sole independent diagnostic modalities. The best AUC (0.91), with a high sensitivity (0.85), specificity (0.82), PPV (0.76), and NPV (0.89) was for AngioCT combined with QA-DENSITOM.

Figure 1

Conclusions: These findings are consistent with an important role of non-invasive angiography rather than isolated duplex Doppler as a gate-keeper for invasive evaluation. IVUS validation showed that densitometric evaluation of ICA stenosis severity by QA outperforms the classic angiographic measurement of DS.

3170 Stenting for Ostial Vertebral Artery Stenosis (STOVAST Trial): results from a prospective randomized study comparing bare-metal with drug-eluting stents


Symptomatic vertebral artery stenosis (VAS) is a well-known risk factor for vertebrobasilar (VB) stroke. Vertebral artery stenting has emerged as the treatment of choice. The use of bare-metal stents (BMS) is associated with high restenosis rate. Limiting wider applicability of this treatment modality. It is not known whether drug-eluting stents (DES) in the ostial vertebral location can improve long-term results.

Purpose: To prospectively evaluate angiographic and clinical outcome of stent-assisted vertebral artery angioplasty with a randomized allocation to DES vs BMS.

Material and methods: 100 consecutive patients (age 66±1.8 years, 65 men) with neurologist-confirmed diagnosis of symptomatic ostial VAS were externally
randomized to BMS vs DES use. Duplex Doppler imaging and quantitative angiography (QA) were performed prior to and immediately after stenting, and at one-year. OA was evaluated by an independent Core Lab, blinded to the BMS vs DES use. Restenosis was defined as an in-stent stenosis (ISR) >50% diameter stenosis.

Results (table): Clinical characteristics were not different between groups. For a total of 100 lesions, 50 BMS (0.2-5.4-5.5mm) and 49 DES (0.2-5.4-0.35mm, post-dilated to 4.5mm as required angiographically, 19 zstoratsis, 19 everolimus-, 6 paclitaxel-, 5 sirolimus-eluting) were implanted. Procedural success rate was 99%. One transient global amnesia occurred periprocedurally in the BMS-arm. At 30 days, 92 patients were asymptomatic, 94 patients completed one-year follow-up in the occlusive and 1 leg death in the BMS-arm). One new VB stroke occurred - this was related to a mild in-BMS restenosis coexisting with a significant progression of contralateral VAS. 68% of patients had an event risk and were at-risk for stent failure. One-year follow-up angiography consent, 82 patients were thus available for one-year angiographic follow-up.

Conclusions: QA for symptomatic vertebral artery stenosis is safe. Results from this randomized trial show no evidence for in-stent restenosis reduction with DES vs BMS use at the ostial vertebral location.

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**Abstract 3170**

### Table 1. Results table

| RVA/LVA | History of VB Stroke/TIA | Severe vertigo/ syncope | CAD | Type 2 diabetes | Baseline VAS severity | Residual stenosis after stenting | Deaths at one year | Consent for flu angio withdraw | Angiographic follow-up | Restenosis rate |
|--------|--------------------------|------------------------|-----|----------------|-----------------------|--------------------------------|-------------------|-----------------|-------------------|----------------|----------------|
| DES(n=50) | 27/23 (67.12%14%) | 45 (90%) | 48 (94%) | 14 (28%) | 84 (16%) | 2.24 (1.75) | 4 (8%) | 10.0 (50%) |
| p | 0.75-0.77 | 0.24 | 0.44 | 0.65 | 0.19 | 0.36 | 0.67 | 0.22 | 0.6 | 0.9 |
| BMI(n=50) | 23/27 | 5 (10%)12% | 48 (96%) | 39 (78%) | 12 (24%) | 81.3 ± 11.1 | 3.5 ± 1.2 | 2 (4%) | 8 (16%) | 40 (80%) | 10.0 (25%) |

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### 3172

**Successful percutaneous lower extremity revascularization reduces systemic inflammation and improves cardiovascular outcome in patients with peripheral arterial disease**


**Purpose:** Lower extremity peripheral arterial disease (LE-PAD) reduces walking capacity and is associated with an increased cardiovascular risk. Endovascular revascularization of LE-PAD improves walking performance and quality of life. In the present study, we investigated whether successful lower limb revascularization also impacts systemic inflammation and cardiovascular outcome in LE-PAD patients.

**Methods:** 479 consecutive LE-PAD patients at stage II of Fontaine’s classification, with ankle/brachial index <0.9 and one or more stenosis >50% in at least one leg artery, were enrolled in the study. According to the Trans-Atlantic Inter-Society Consensus II recommendations, 264 (55.1%) underwent percutaneous lower extremity angioplasty (PTA group), while 215 (44.9%) were managed conservatively (CT group). In 30 patients of both the PTA and CT groups, C-reactive protein (CRP) and myeloperoxidase (MPOx) serum levels were measured at the first visit and, only in the same 30 patients of the PTA group, 3 months after successful PTA. The incidence of major cardiovascular events (including cardiovascular death, myocardial infarction, ischemic stroke, coronary and carotid revascularizations) was prospectively analyzed by Kaplan-Meier curves. Crude and adjusted HRs (95% CI) of developing a cardiovascular event were calculated by Cox analysis.

**Results:** No baseline differences were observed among the groups, except for a lower maximum walking distance in the PTA group. CRP and MPOx levels were similar in the two groups at baseline (CT= 6.2 [2.9-9.6] vs. PTA= 5.1 [3.8-9.5] mg/L, p=0.500 for CRP; CT= 93.5 [50.0-144.9] vs. PTA= 107.6 [69.8-155.8] ng/mL, p=0.615 for MPOx). Importantly, both CRP and MPOx significantly decreased in the PTA group 3 months after the revascularization (post PTA= 2.2 [1.6-4.4] vs. pre PTA= 5.1 [3.8-9.5] mg/L, p=0.001 for CRP; post PTA= 28.7 [19.9-40.1] vs. pre PTA= 107.6 [69.8-155.8] mg/mL, p<0.001 for MPOx). During a median follow-up of 21 months (12.0-29.0), the incidence of cardiovascular events was markedly lower in PTA compared to CT patients (6.4% vs. 16.3%; p=0.003), and patients in the CT group showed a 4.1-fold increased risk of developing a cardiovascular event compared to patients in the PTA group (CI 1.29-13.57, p=0.002). In the CT group, 10 patients (26.3%) had a major cardiovascular event, while in the PTA group, only 3 (2.4%) patients had a major cardiovascular event (p=0.001).

**Conclusions:** This study shows that successful revascularization of LE-PAD patients affected by intermittent claudication, in addition to improving functional status, decreases systemic inflammation and reduces the occurrence of future major cardiovascular events.

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**Impact of the angiosome concept for endovascular therapy in patients with critical limb ischemia due to isolated below-the-knee lesions**

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**Objectives:** To assess one-year outcomes after endovascular therapy (EVT) by angioplasty with critical limb ischemia (CLI) due to isolated below-the-knee (BTK) lesions using the angiosome concept.

**Methods:** We analyzed 60 limbs in 55 consecutive patients with ischemic ulceration that was Rutherfurd 5 or 6, who underwent EVT. We classified these patients into Direct Group (n=31, age 70.9±9.5) and Indirect Group (n=29, age 72.4±10.5) depending on whether feeding artery flow to the site of ulceration was successfully acquired or not based on the angiosome concept. We evaluated major adverse limb events (MALE) including major amputation or any major vascular re-intervention or death one year after EVT.

**Results:** There were no significant differences of the age, gender, atherosclerotic risk factors, dialysis therapy, coronary artery disease and cerebrovascular disease. The rate of major amputation within one year after the EVT was significantly lower in the Direct Group than in the Indirect Group (3.2% versus 24.1%, p=0.017). The MALE rates in the both groups were 22.6% in the Direct Group and 83.2% in the Indirect Group (p=0.008). The number of vessel revascularization after EVT was 0.26 in the Direct Group and 1.59 in the Indirect Group (p<0.0001).

**Conclusion:** Acquiring direct flow based on the angiosome concept is important for limb salvage by EVT in patients with CLI due to isolated BTK lesions.
The puzzle of the diagnostic intercostal space during the flecainide test for the Brugada syndrome is solved by echocardiography

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Purpose: The diagnostic criteria for the Brugada Syndrome (BrS) remain controversial. Diagnostic pattern can be detected in V1-V2 located either in the 4th, 3rd or 2nd intercostal space (ICS). The reason for this variability is still unclear even if it has been suggested that the anatomic position of the right ventricular outflow tract (RVOT) may play a role. Our aim was to verify by echocardiography whether a correlation existed between the diagnostic ICS during the flecainide test (FT) and the RVOT location.

Methods: In 12 patients (pts) with a diagnostic FT a short axis parasternal view was recorded, by physicians blind to the outcome of the FT, both in the 4th, 3rd and 2nd ICS, to assess the possibility of exploring the RVOT. During the FT the appearance of a complete right bundle branch block with a ≥ 2 mm coved ST elevation (type 1 ECG pattern) at least in one lead in any ICS was considered diagnostic. For each ICS the possibility to explore RVOT and the presence of the classic ECG pattern in higher intercostal spaces or in one vs two precordial leads. Our goal was to search for an association between diagnostic ICS and RVOT location, determined by echocardiography, could increase diagnostic accuracy in BrS.

Results: A diagnostic pattern was identified in the 4th ICS in 6/12 pts, in the 3rd ICS in 11/12 pts and in the 2nd ICS in 8/12 pts. Correspondence between the location of ECG pattern positivity and RVOT visualization was 88.5% (83% in the 4th ICS, 100% in the 3rd ICS and 78% in the 2nd ICS, see figure). Noteworthy, RVOT was detectable in the 4th ICS in 5/6 pts with a positive ECG pattern in the 4th ICS compared to 0/6 pts with a diagnostic pattern only in the 3rd or 2nd (P=0.01).

Conclusions: The RVOT anatomic localization highly correlates with the diagnostic ICS in BrS pts. To position the patient according to RVOT location, determined by echocardiography, could increase diagnostic accuracy in BrS.

Correlation between diagnostic criteria and results of genetic screening in Brugada Syndrome

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Purpose: The diagnosis of the Brugada Syndrome (BrS) is traditionally based on the presence of a coved T wave in the electrocardiogram (ECG) and the appearance of a coved ST elevation with a J point elevation (type 1 ECG pattern) at least in one lead in any ICS was considered diagnostic. For each ICS the possibility to explore RVOT and the presence of the classic ECG pattern in higher intercostal spaces or in one vs two precordial leads. Our goal was to search for an association between diagnostic ICS and RVOT location, determined by echocardiography, could increase diagnostic accuracy in BrS.

Methods: In 12 patients (pts) with a diagnostic FT a short axis parasternal view was recorded, by physicians blind to the outcome of the FT, both in the 4th, 3rd and 2nd ICS, to assess the possibility of exploring the RVOT. During the FT the appearance of a complete right bundle branch block with a ≥ 2 mm coved ST elevation (type 1 ECG pattern) at least in one lead in any ICS was considered diagnostic. For each ICS the possibility to explore RVOT and the presence of the classic ECG pattern in higher intercostal spaces or in one vs two precordial leads. Our goal was to search for an association between diagnostic ICS and RVOT location, determined by echocardiography, could increase diagnostic accuracy in BrS.

Results: A diagnostic pattern was identified in the 4th ICS in 6/12 pts, in the 3rd ICS in 11/12 pts and in the 2nd ICS in 8/12 pts. Correspondence between the location of ECG pattern positivity and RVOT visualization was 88.5% (83% in the 4th ICS, 100% in the 3rd ICS and 78% in the 2nd ICS, see figure). Noteworthy, RVOT was detectable in the 4th ICS in 5/6 pts with a positive ECG pattern in the 4th ICS compared to 0/6 pts with a diagnostic pattern only in the 3rd or 2nd (P=0.01).

Conclusions: The RVOT anatomic localization highly correlates with the diagnostic ICS in BrS pts. To position the patient according to RVOT location, determined by echocardiography, could increase diagnostic accuracy in BrS.
Results: Clinical presentation included sustained polymorphic ventricular tachycardia in 7 patients, syncope in 3, while 3 patients were asymptomatic. Eleven patients (84%) showed an abnormal right ventricular 3D-EAM. Eight patients presented low-voltage areas in the RVOT, in 4 cases associated with free wall involvement, and in 2 cases with postero-basal and inferior wall involvement. The remaining 3 patients presented low-voltage areas in the free wall (n=2) or in the postero-basal segment. Among patients with abnormal 3D-EAM, histology showed pathologic findings in 9 patients (81%). In particular we documented fibrofatty replacement in 81% of patients, thus re-inforcing the notion that BrS is not a pure electrical disorder. The identification of abnormal voltage areas and the corresponding myocardial substrate may influence both prognosis and treatment, including ablation strategies.

CARDIAC IMPLANTABLE ELECTRONIC DEVICES: RELATED ISSUES

3181 Risk of pocket hematoma in patients on chronic anticoagulation undergoing implantation of electrophysiological devices: a systematic review and metaanalysis
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Purpose: To systematically review studies appraising the risk of pocket hematoma comparing different periprocedural anticoagulation schemes.

Methods: Three strategies were analysed: heparin bridging vs. no heparin, warfarin continuation vs. no warfarin continuation and warfarin continuation vs. heparin bridging. Pocket hematoma was the primary outcome measure, while length of hospital stay and thromboembolic complications (a composite of cerebrovascular accidents and deep venous thrombosis) were secondary outcome measures. Two investigators independently abstracted data from eligible studies. Estimates were combined using a fixed effects model.

Results: Fifteen studies enrolling 5911 patients met all inclusion criteria and were included in this review. Heparin bridging compared with no heparin was associated with increased risk of pocket hematoma (cumulative OR= 4.47, 95% CI 3.21-6.23, p<0.0001), and with a significantly prolonged hospital stay (9.1±1.9 days vs 5.1±1.9 days, p<0.0001). Warfarin continuation was not associated with a higher rate of pocket haematoema compared with no warfarin continuation (OR=1.28, 95% CI 0.73-2.26, p=0.38) and resulted in a significantly reduced risk of pocket haematoema compared with heparin bridging (OR=0.37, 95% CI 0.2-0.69, p=0.002). Thromboembolic complications were reduced with heparin bridging vs. no heparin (0.52% vs 1.07%, p=0.003) and with warfarin continuation vs. no warfarin continuation (0% vs 0.76%; p=0.07).

Conclusions: Heparin bridging is associated with a high risk of pocket hematoma. Perioperative continuation of warfarin seems to reverse the incidence of pocket haematoema and the duration of hospital stay compared with heparin bridging, while also decreasing thromboembolic events.

3182 Pocket related complications in 163 patients receiving anticoagulation or dual antiplatelet therapy undergoing heart rhythm device implantation: D-Stat flowable hemostat versus vacuum drainage
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Background: Pocket hematoma is a common complication after cardiac rhythm device implantation (CRDI) in patients receiving anticoagulation or dual antiplatelet therapy. Pocket hematoma has been associated with increased rate of pocket infections and the duration of hospital stay.

Methods: We conducted a prospective case control study and enrolled all patients admitted for CRDI receiving anticoagulation or DAPT. Participants received either a vacuum drainage system into the prepectoral pocket preceding wound closure versus D-Stat™ Flowable Hemostat. The primary endpoint was a composite of hematoma needing evacuation, and pocket infection.

Results: We included a total of 163 patients (mean age 73±11 years). 81 patients (50%) received vacuum drainage and 82 (60%) D-Stat®. The mean INR was 2.1±0.3; range 1.7-2.8, 69 patients (42%) received dual platelet inhibition (DAPT). We sought to assess whether a vacuum drainage system or D-Stat™ Flowable Hemostat (Vascular Solutions Inc.) is safe and effective in such patients.

Methods: We conducted a prospective case control study and enrolled all patients admitted for CRDI receiving anticoagulation or DAPT. Participants received either a vacuum drainage system into the prepectoral pocket preceding wound closure versus D-Stat™ Flowable Hemostat. The primary endpoint was a composite of hematoma needing evacuation, and pocket infection.

Results: We included a total of 163 patients (mean age 73±11 years). 81 patients (50%) received vacuum drainage and 82 (60%) D-Stat®. The mean INR was 2.1±0.3; range 1.7-2.8, 69 patients (42%) received dual platelet inhibition, and 11 patients (7%) both. The primary endpoint occurred in 9/81 (11%) patients from the D-Stat group and 0/81 patients of the control group (11% versus 0%; p=0.003). The incidence of relevant pocket haematoma requiring evacuation was (0% [0/81] versus 5% [4/82]; p=0.001), and the rate of pocket infections within 3.5±1.8 months after implantation was (0% [0/81] versus 6.1% [5/82]; p=0.05). The postoperative increase of C-reactive protein (31±10 mg/l versus 14±7 mg/l; p=0.05) and postoperative Immunoglobulin E levels (117±49 IU/ml versus 106±62 IU/ml; p=0.03) were similar in both groups.

Conclusions: Administration of D-Stat does not decrease the frequency of clinically relevant pocket hematoma compared to vacuum drainage. The observed rate of pocket infections in the D-Stat group is a matter of concern.

3183 Cardiac arrhythmias device implantation during ongoing anticoagulant therapy. Need to change guidelines?
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Current guidelines recommend oral anticoagulant treatment (OAT) interruption and perioperative heparin bridging (warfarin interruption and heparin administration while INR has sub therapeutic value starting 24 hours after procedure) in patients at high and moderate risk of thromboembolic events (TE) undergoing cardiac arrhythmia device (CD) implantation. This practice may be associated with increased risk of both TE and hemorrhagic (H) events. Strategy of CD implantation during ongoing OAT with INR value in therapeutic range (2-3) (W) was compared in randomized fashion with bridging strategy (BRIDGE). Rate of H and TE complications, assessed at discharge, at 7 and 30 days after by a physician blinded to the strategy adopted (W or BRIDGE), were compared with that observed in patients implanted while in antiplatelet therapy (APL) or in absence of OAT and AP (NO). Data were collected from 988 consecutive new-implant procedures: 203 defibrillators, 671 pacemakers and 115 resynchronization devices; 188 procedures were performed in W, 209 in BRIDGE, 450 in APL and 142 in NO. The mean INR at implant in W, BRIDGE, APL and NO was respectively 2.1±0.5, 1.3±0.6, 1.2±0.6, 1.24±0.3. Incidence of significant H requiring revision was statistically superior in BRIDGE (20, 9.6%) vs W (n=2, 1.36%; p=0.001, O.R 7.1), APL n=4, 0.9%; p=0.0001, O.R 7.1), and NO (n=2, 1.4%; p=0.001, O.R. 9.5). There were 1 cardiac tamponade, 1 hematoma, 3 TE events in BRIDGE and 1 TE event in APL. CD can be implanted safely in patients with high thromboembolic risk without interruption of warfarin. This strategy is associated with reduced risk of significant pocket hematoma and a trend toward less embolic events compared with heparin bridging. Evidence from these data and from other similar studies should be included in new guidelines for the perioperative management of CD patients.
3184 Is warfarin pause necessary for pacemaker implantation? The FinPAC Study

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Purpose: It is a common practice to postpone pacemaker implantation to reach INR levels < 1.5-1.8 and to use bridging therapy in patients with high risk of thromboembolism. The purpose of this prospective, randomised multicentre study was to compare bleeding and thromboembolic complications of pacemaker implantation with or without preceding warfarin pause. Patients with aspirin treatment were used as a control group.

Subjects and methods: A total of 196 patients (mean age 73 years) with long-term warfarin treatment were randomized to either a warfarin pause (2 days) or continuous warfarin therapy before pacemaker implantation. Bridging therapy was not allowed. Patients on aspirin (N=128) were recruited as a control group.

Results: The pre- and postprocedural INR levels were higher without a warfarin pause (2.3 vs 1.9 and 2.2 vs 1.5 respectively, p < 0.001 for both). There were no significant differences in the baseline operative characteristics between the study groups. The incidence of operative bleeding, postoperative hematomas, bleeding events, and incidence of thromboembolic complications was equal in both study groups and did not differ from controls (Table). Bleeding events or hematomas were not related to INR level or any feature of the implantation procedure or baseline characteristics of the patients.

Conclusions: Our results suggest that pacemaker implantation is a safe procedure during therapeutic uninterrupted warfarin anticoagulation.

3185 Implantable defibrillators in patients approaching end of life

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Objectives: To investigate implanted implantable defibrillators (ICD) from deceased patients to get an increased knowledge about the occurrence of ventricular arrhythmias and time of death in these patients. The primary outcome of the study is the incidence of ventricular arrhythmias in ICD patients last 24 hours of life.

Background: Several prospective multicenter trials have demonstrated improved survival with ICD therapy. Little is known about the nature and cause of death in the ICD population.

Methods: We prospectively enrolled 81 ICD devices and retrospectively collected medical data on all patients. The ICDs were interrogated and all available intracardiac electrograms (EGM) were analysed independently by two investigators, one of them blinded. The incidences of ventricular tachyarrhythmia (VT) and ventricular fibrillation (VF) as well as shock treatment the last 24 hours before death were counted. The medical records from the patient’s last visit to hospital, including physicians and nurses’ documentation from last 24 hours of life, time of death and implantation data were collected. If performed, the autopsy protocols were obtained. Data from the Swedish ICD and Pacemaker register and mortality data from The National Board of Health and Welfare has also been collected.

Results: All patients (70 men and 11 women, mean age 73±9 years) died in the years of 2006-2010. Implantations were done between 1998 and 2010 and the device had been implanted in patients with a mean of 2.6±2 years. At time of death 69% of the patients were in hospital. Ventricular tachyarrhythmia or ventricular fibrillation occurred in 35% of the patients within 24 hours of death. 23% of the patients had at least one shock during the last 24 hours. Patients that received shock treatments had a mean of 14 shocks ± 19. In 12% of the patients the ICD therapy had been inactivated before death.

Conclusions: More than a third of the ICD patients had ventricular arrhythmias during the last 24 hours before death. Nearly 1 out of 4 of the ICD patients experienced at least one shock. The patients who received shocks often received multiple shocks.

3186 Safety and efficiency of low-field magnetic resonance imaging in patients with cardiac rhythm management devices

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Background: Low-field magnetic resonance imaging (MRI), i.e. MRI with a magnetic field strength < 0.5 Tesla, has been reported to be safe in patients with pacemakers, whereas little is known about the safety of low-field MRI in patients with implantable cardioverter-defibrillators (ICD) and/or cardiac resynchronization therapy (CRT). The aim of this study was to investigate the safety and efficiency of low-field in patients with devices for cardiac rhythm management (i.e. pacemakers and ICD, including devices with CRT).

Methods: Overall 126 MRI examinations with a magnetic field strength of 0.2 Tesla were evaluated in 115 patients (59% male; age at MRI scan 76.3±9.0 years; time since device implantation 4.0±3.1 years) with cardiac rhythm management devices (106 pacemakers, 4 ICD, 3 ICD with CRT, and 2 CRT pacemakers). This analysis included 22 pacemaker-dependent patients (19.1%), 10 patients with 1.5-Tesla MR conditional pacemakers (8.7%) and 7 patients with abandoned leads (6.1%).

Results: Except for one examination, which was interrupted because of severe nausea, all MRI scans could be analysed efficiently. No induction of arrhythmias or inhibition of pacemaker function occurred. Compared to the device interrogation before MRI, there were no statistically significant changes in battery voltage, pacing capture thresholds, sensing of intrinsic ECG, and lead impedance (as well as shock impedance for ICD patients) after complete examination.

Conclusion: Low-field MRI examinations (0.2 Tesla) were safe and efficient in patients with devices for cardiac rhythm management.
Challenges in valvular heart disease / Identifying vulnerability in plaque

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with severe symptomatic AS. Our aim was to study the factors that affect choice of therapy and prognosis.

**Results:** A total of 928 patients were included. Mean age was 84.2±3.5 years, 58.8% were women, and only 49.0% were independent (Katz index A). The most frequent planned management was conservative therapy in 423 (46%) patients, followed by TAVI in 261 (28%), and AVR in 244 (26%). Independent predictors of nonplanned AVR were age (odds ratio [OR], 1.3; 95% confidence interval [CI], 1.2-1.4), Katz index (OR, 1.5; 95% CI, 1.3-1.7), European System for Cardiac Operative Risk Evaluation operative risk (OR, 1.02; 95% CI, 1.01-1.04), systolic dysfunction (OR, 0.80; 95% CI, 0.72-0.90), and maximum gradient (OR, 0.90; 95% CI, 0.80-0.99). During follow-up (11.2 to 38.9 months), 357 patients (38.5%) died. Survival rates at 6, 12, 18, and 24 months were 81.8%, 72.6%, 64.1%, and 57.3%, respectively. Independent predictors of mortality were Charlson index (hazard ratio [HR], 1.3; 95% CI, 1.2-1.5) and planned conservative treatment (HR, 2.5; 95% CI, 1.5-4.2). The type of intervention had no independent effect on mortality (AVR HR, 1 – TAVI HR, 1.2; 95% CI, 0.5-2.7).

**Conclusion:** Octogenarians with severe symptomatic AS are frequently managed conservatively. Comorbidity and planned conservative management are associated with poor prognosis.

**Outcome of elderly patients with severe but asymptomatic aortic stenosis**

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**Background:** Aortic stenosis (AS) is increasingly diagnosed in an aging population resulting in large numbers of elderly patients receiving aortic valve interventions. However, elderly patients are underrepresented in most natural history studies on AS where the average age of patients is between 60 and 70 years. The aim of the present study was to assess the natural history of severe asymptomatic AS in a large cohort of elderly patients older than 70 years.

**Methods:** 103 consecutive elderly patients (51 female, age 77 ± 5 yrs) with asymptomatic severe AS defined by a peak aortic jet velocity (Vmax) ≥ 4.0 m/s (average peak Vmax 4.75 ± 0.57 m/s, mean gradient 58±17 mmHg, valve area 0.70±0.20 cm²) were included and followed at regular intervals. Patients with other significant valve lesions or concomitant aortic regurgitation were excluded.

Outcome was assessed and event-free survival with events defined as development of criteria warranting aortic valve replacement or cardiac death was determined. All of the patients in this series had moderately-to-severely calcified aortic valves.

**Results:** During a mean follow-up of 19.4 (IQR 9.8 – 36.4) months, 82 patients developed criteria warranting aortic valve replacement and 15 patients died. Event-free survival rates after 1, 2, 3, and 4 years were 72%, 44%, 23%, and 16% respectively and were not significantly different for patients younger or older than 80 years. Event-free survival was significantly worse for patients with an AV-Vel ≥ 5.0 m/s with respective event-free survival rates of 51±6%, 21±6%, 12±5%, and 3±3% at 1, 2, 3, and 4 years respectively, as compared to 83±5%, 55±6%, 37±6%, and 23±8% for patients with an AV-Vel < 5.0 m/s. 7 cardiac deaths (2 myocardial infarction and 5 cardiac decompensation) occurred after a mean of 6.3±5.1 months after the last follow-up visit where the patients were reportedly asymptomatic. 3 of these pts had a restricted mobility due to comorbidities. There were five perioperative deaths among 72 patients who underwent aortic valve replacement, while 10 patients refused surgery. Postoperative survival rates were 89%, 81%, 77% and 66% after 1, 2, 3, and 4 years respectively.

**Conclusion:** Elderly patients with asymptomatic severe AS are at risk of rapid systematic deterioration and cardiac death and the assessment of symptoms may be challenging. However surgical outcomes are good and risk stratification based on peak aortic jet velocity may also be considered in elderly patients with severe AS.

**Outcomes of obstructive and non-obstructive prosthetic valve thrombosis: are different entities?**


**Purpose:** To assess short-, and long-term outcomes in patients diagnosed of obstructive and non-obstructive prosthetic valve thrombosis (OPVT vs. NOPVT).

**Methods:** Echocardiography and cine-radio-fluoroscopy were used for diagnosis. During hospitalization, according to clinical guidelines, OPVT were treated with surgery or thrombolysis depending on the clinical status of the patients and the risk score. NOPVT were treated with optimizing anticoagulation therapy. After discharge, a close clinical and echocardiographic follow up was performed. Adverse events were defined as cardiovascular death, recurrence, thromboembolic events or bleeding.

**Results:** From January 1984 to January 2012, 157 prosthetic valve thrombosis were diagnosed in our institution; 110 were obstructive and 47 non-obstructive (mean age: 54 years; women: 59%; mitral valve: 83%). In 58% of patients with OPVT and in 66% of NOPVT an alteration of oral anticoagulation therapy was reported. OPVT were diagnosed by heart failure in 71% of the cases; NOPVT were diagnosed after embolic events in 49% of the cases. During hospitalization, adverse event rate was higher in OPVT than in NOPVT (36% vs. 13%; p: 0.002), and the overall mortality was also higher in the group with OPVT (25% vs. 10%; p: 0.04). During the follow up (median: 18 months; range: 0.01-315 months), OPVT vs NOPVT had more adverse events (75% vs. 55%; p: 0.01), highlighting higher mortality (31% vs. 10%; p: 0.012), whereas NOPVT had more thrombo-haemorrhagic complications (17% vs. 3%; p: 0.008). (Figure 1).

**Conclusions:** Prosthetic valve thrombosis is a severe entity with high morbidity and mortality. OPVT presented a higher rate of mortality and adverse events not only during hospitalization but also during the long-term follow-up.

**STATE OF THE ART – IDENTIFYING VULNERABILITY IN PLAQUE**

**Impact of unstable carotid plaque for prediction of coronary vulnerable plaque in asymptomatic patients with diabetes mellitus**

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Presence of diabetes mellitus (DM) confers a substantially increased risk of coronary artery disease (CAD). It is important to identify asymptomatic but potentially high-risk diabetic patients for CAD, because CAD often progress without evident symptoms in DM patients. It was reported that the presence of echoluent carotid plaque was associated with acute coronary syndrome. The purpose of this study was to evaluate the relationship between characteristic of carotid plaque defined using B-mode ultrasound and the presence of coronary vulnerable plaque assessed by computed tomography angiography (CTA) in asymptomatic patients with diabetes mellitus (DM).

**Methods:** One hundred thirty asymptomatic diabetic patients who had maximum carotid intima-media thickness (CIMT) ≥1.1mm underwent 64-slice CTA to evaluate the prevalence of CAD and plaque morphology. We assessed maximum CIMT and unstable characteristic of carotid plaque defined by having echoluent or ulcerative lesion by B-mode ultrasound. Coronary vulnerable plaque was defined as positive vessel remodeling (PR) and low-attenuation plaques (LAP) (<50 Hounsfield Units) on CT.

**Results:** Maximum CIMT was significantly higher in the patients with coronary vulnerable plaque than in those without (2.03±1.07 mm, 2.58±0.88 mm,
Characterization of chronic total occlusion plaque with cardio magnetic resonance imaging

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Background: Recent studies demonstrated that magnetic resonance imaging (MRI) can characterize the components of the coronary atherosclerotic plaque, such as fibrous tissue, lipid, hemorrhage and thrombus. Characterization of coronary plaque with MRI has not yet been systematically evaluated.

Methods: Twenty-one CTO lesions from 20 patients who were confirmed on coronary angiogram were evaluated by noncontrast T1-weighted imaging (T1W) and 12 lesions were evaluated by IVUS and to assess the association with the success rate of coronary intervention.

Results: Plaques with high signal intensity on both T1W and T2W was prospective tried to pass the CTO lesion with Wizard 1g (0.01 inch tapered wire) for all case. If Wizard 1g could not pass, the wire was changed to Wizard 3 (0.015 inch stiffer wire).

Conclusion: Characterization of CTO plaque with cardiac MRI may be useful for assessment of plaque hardness and wire selection.

Impact of cholesterol synthesis/absorption marker on coronary plaque vulnerability


Background: The relation of cholesterol metabolism to coronary plaque vulnerability is unknown. The aim of this study is to evaluate the impact of cholesterol synthesis/absorption surrogate marker levels on plaque vulnerability.

Methods: This study population was drawn from 80 consecutive stable angina pectoris patients without any lipid lowering therapies. In de novo target vessels, both High-sensitivity Troponin levels and the thinnest fibrous cap thickness were measured by OCT. Patients were divided into two groups based on the presence of definite CTO.

Results: Patients with definite CTO showed a higher campesterol (195.8 [interquartile range 154.1 - 248.6] vs. 70.4 [114.2 - 191.1] μg/100mg total cholesterol, p = 0.002) and a lower lathosterol (60.1 [50.3-73.0] versus 91.3 [57.1-142.8] μg/100mg total cholesterol, p = 0.004). Percent necrotic core volume (%NCV) and fibrous cap thickness were significantly correlated with lathosterol (r = 0.501, p < 0.0001 and r = 0.501, p = 0.001, respectively) and campesterol (r = 0.366, p = 0.005, respectively). The independent predictors for the occurrence of definite CTO were lathosterol (odds ratio, 0.624; 95% confidence interval, 0.452-0.860; p = 0.004), campesterol (1.301; 1.080-1.568; p = 0.006), and %NCV (1.084; 1.012-1.161; p = 0.02).

Conclusions: Enhanced absorption and reduced synthesis of cholesterol may be related to coronary plaque vulnerability.

Plaque morphology on optical coherence tomography determines biomarker response after stent-induced plaque rupture

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Introduction: Matrix metalloproteinases-9 (MMP9) and its inhibitor, tissue inhibitor of metalloproteinase-1 (TIMP1), have been implicated in the pathophysiology of de novo plaque rupture. We examined the association between clinical presentation, plaque morphology and the temporal response of these proteases post plaque rupture in vivo.

Method: 50 patients undergoing percutaneous coronary intervention (PCI) with stenting were studied. Optical coherence tomography (OCT) was performed in 36 of these subjects. Serial venous blood sampling was undertaken after stenting; plasma MMP9 and TIMP1 were measured by enzyme immunoassays. OCT asssessors were blinded to other biomarker results, and target lesions were defined as plaques containing predominantly lipid or non-lipid cores. Serial samples were collected from 10 control subjects undergoing diagnostic angiography (Dx) only.

Results: Baseline plasma MMP9 and TIMP1 were higher in acute coronary syndrome (ACS, n=20) than stable angina (SAP, n=30). Patients presenting with ACS demonstrated prompt (-1hr) elevations in plasma MMP9, followed by elevations of TIMP1 at 18hrs. This pattern was distinct from SAP patients where significant elevation in MMP9 was observed later (6hrs), and without the subsequent TIMP1. Biomarker response for subjects with predominantly lipid plaques (n=28) closely mimicked that of patients presenting with ACS; vice versa between subjects presenting with SAP and those found to have non-lipid target lesions on OCT (Figure 1).

Conclusion: Differential release of biomarkers after plaque rupture is related to both clinical presentation and plaque morphology. Lipid rich plaques (irrespective of the clinical status) result in biomarker responses after PCI that are similar to vulnerable plaques in ACS patients.

Impact of cholesterol synthesis/absorption marker levels on coronary plaque vulnerability


Background: The relation of cholesterol metabolism to coronary plaque vulnerability is unknown. The aim of this study is to evaluate the impact of cholesterol synthesis/absorption surrogate marker levels on plaque vulnerability.

Methods: This study population was drawn from 80 consecutive stable angina pectoris patients without any lipid lowering therapies. In de novo target vessels, both High-sensitivity Troponin levels and the thinnest fibrous cap thickness were measured by OCT. Patients were divided into two groups based on the presence of definite CTO.

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Conclusions: Enhanced absorption and reduced synthesis of cholesterol may be related to coronary plaque vulnerability.
Are the preferential patterns of myocardial iron overload preserved at the CMR follow-up?

Methods: We selected 259 patients with a CMR follow-up (FU) study at 18±3 months and with MIO at baseline (global heart T2*<26 ms). Three short-axis views of the left ventricle were acquired and analyzed using a 16-segment standardization model. The T2* value on each segment was calculated, as well as the global value. Four main circumferential regions (anterior, septal, inferior and lateral) were defined.

Results: Patients were divided into two groups: severe (N=80, global T2*<10 ms) and mild-moderate MIO (N=179, global T2* 10-26 ms). For each group there was a significant improvement in the global heart as well as in regional T2* values (P<0.0001 for all pairwise comparisons). For the whole patient population as well as for both groups, at basal the mean T2* value over the septal and the lateral regions was significantly lower than the T2* values over the other regions and the mean T2* over the inferior region was significantly higher than the T2* values over the septal and the lateral regions. The same pattern was present at the FU, with a little difference for patients with mild-moderate MIO (Figure 1).

Conclusion: A preferential pattern of iron store in anterior and inferior regions was present at both basal and FU CMRIs, with an increment of T2* values at FU due to a basal CMR-guided chelation therapy. The anterior region seems to be the region in which the iron accumulates first and is removed later. Our data confirm the segmental T2* approach useful for identifying early iron deposit and for tailoring chelation therapy.

The utility of 2D speckle tracking imaging in diagnosing acute myocarditis as proven by immunohistology

Methods: In 34 patients (mean 41 (18-67) years) with suspected AMC, in whom endomyocardial biopsies had been taken, strain rate imaging was performed by speckle tracking echocardiographic analysis at initial presentation and at 3 months follow-up. According to the immunohistological findings (inflammation, myocyte lysis and viral genome detection) patients were divided into 3 groups: no inflammation (N), borderline myocarditis (BL) and AMC.

Results: No differences in conventional 2D echocardiography were found between the groups regarding the ejection fraction, end-diastolic and end-systolic diameter, and wall thickness. AMC and BL patients showed a significantly reduced longitudinal strain (-10.24±4.23%, p=0.005 and -8.51±4.88%, p=0.008) and strain rate (0.79±0.27% vs. p=0.006 and 0.65±0.31%, p=0.005) without regional differences. According to the ROC-analysis, a cut-off Strain value of below -14.7% yielded a sensitivity of 96% and a specificity of 89% in diagnosing myocarditis as obtained by immunohistology from endomyocardial biopsies. AMC patients who showed an improved EF and VEEDD at 3 month follow-up had shown higher strain rate already at baseline (1.02±0.15% vs. 0.96±0.11%, p=0.009).

Conclusion: Longitudinal 2D strain obtained by speckle tracking imaging can help to recognize myocardial dysfunction in patients with suspected acute myocarditis as proven by immunohistology, even in patients with preserved conventional echocardiography. This imaging modality may be of help in differentiating the patients in need of further diagnostic procedures such as myocardial biopsies.

Doxorubicin-induced experimental myocarditis by 19F-MRI

Methods: In 45 consecutive patients with CA were compared to four control groups (N=15 in each group): SA without cardiac involvement, hypertrophic cardiomyopathy (HCM), LV hypertrophy (LVH) and dilated cardiomyopathy (DCM). Average global LS and regional LS (defined as average basal, mid and apical levels of the LV) were measured.

Results: Doxorubicin-injected rats displayed intense fluorocarbon enhancement in the left ventricle, whereas the signal was absent in control (non-treated) animals. In Doxorubicin-treated animals, focally a strong CD68 staining was found in the myocardium, confirming inflammation. This focal inflammation matched MRI-detected F-imaging.

Conclusion: This is the first study, demonstrating the detection of Doxorubicin-induced experimental myocarditis by non-invasive imaging. We further demonstrate the 19F-MRI imaging correlates with immunohistochemistry. Thus, MRI non-invasive imaging will potentially help in the early detection of myocarditis.
heart failure symptoms of patients with left ventricular diastolic dysfunction. The aim of this study is to evaluate the potential antiarrhythmic protective role of CRT-D when compared with implanted cardioverter defibrillator (ICD) for sudden death primary prevention in the context of LV dysfunction.

**Methods:** 453 consecutive patients (63±12.1 years, 121 women) who implanted ICD for primary prevention and CRT-D, from June 2006 until October 2011, were analysed. 245 patients had ICD and 208 had CRT-D. The median duration of follow-up since the implantation of ICD/CRT-D was 777 days (interquartile range: 394-1207). We studied the demographic and clinical characteristics and evaluated the number of therapies (antiarrhythmia pacing or electric shock) given by the device in both groups. We compared the two groups by statistical analysis including multivariate analysis.

**Results:** The population with ICD was more often male (79.6% vs 65.9%, p = 0.001), had higher incidence of smokers (37.1% vs 25.5%, p = 0.009) and previous myocardial infarction (46.1% vs 23.6%, p < 0.001). The population of CRT-D had lower incidence of diabetes (25.5% vs 15.9%, p = 0.014), higher prevalence of left ventricular dysfunction (LVEF <30%) at the time of implantation (66.1% vs 46.9%, p <0.001) and higher prevalence of NYHA class III/IV (66% vs 23.4%, p < 0.001). During follow-up, 121 patients (26.7%) had at least one ventricular arrhythmia requiring antitachycardia pacing (ATP) or shock (13.5%). Patients with CRT-D had fewer therapies (38% vs 62%, p = 0.044) and shocks (31.1% vs 66.9%, p = 0.013). Follow-up between the two groups was similar. In multivariate analysis CRT-D was independently associated with fewer shock required ventricular tachycardia (odds ratio = 0.27, 95% CI: 0.13 to 0.57, p = 0.001). LVEF <30% (odds ratio = 3.18, 95% CI: 1.44 to 7.04, p = 0.004) and previous atrial fibrillation (odds ratio = 3.05, 95% CI: 1.30 - 7.16, p = 0.011) were independent predictors of shock required ventricular tachycardia.

**Conclusion:** In our study CRT-D was independently appeared to have a protective effect regarding the need of shock therapies for ventricular tachycardia when compared to ICD therapy alone. LVEF <30% and previous AF are associated with a greater number of shock therapies due to ventricular tachycardia.

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**Table 1. Patients with hospitalizations, divided by baseline characteristics**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Pts with hospitalizations</th>
<th>p-value</th>
<th>Median length of stay [days]</th>
<th>p-value</th>
</tr>
</thead>
</table>
| NGS vs SG        |   | 460 vs 66                 | 118 (25.7%) vs 35 (53.0%) | <0.0001 | 6.5 vs 5.5  
| P value          |   | 0.065                    | 0.065    | 0.065                         | 0.065   |
| P value CAD      |   | 426 vs 99                | 120 (28.2%) vs 33 (33.3%) | ns      | 7 vs 5      |
| P value CAD      |   | 426 vs 99                | 120 (28.2%) vs 33 (33.3%) | ns      | 7 vs 5      |
| P value CAD      |   | 190 vs 333               | 49 (25.9%) vs 104 (31%)   | ns      | 6 vs 7      |
| P value CAD      |   | 190 vs 333               | 49 (25.9%) vs 104 (31%)   | ns      | 6 vs 7      |

**Conclusions:** The CRTD population was characterized by a high incidence of H. H are significantly more frequent for pts that experienced at least one shock, while the H profile did not differ significantly among different CRTD cohorts of pts.
Sinus rhythm recovery in patients with chronic atrial fibrillation and diluted cardiomyopathy who underwent resynchronization therapy

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Introduction: Cardiac resynchronization therapy (CRT) has been demonstrated to be beneficial also in patients with heart failure and concomitant atrial fibrillation (AF). Moreover, in some patients with persistent AF spontaneous reversion to sinus rhythm occur after CRT implant.

The study aim were to evaluate the feasibility of performing electrical cardioversion (EC) to restore sinus rhythm and the EC efficacy in preserving SR at follow-up, in patients implanted with CRT-D with chronic AF and dilated cardiomyopathy.

Methods: We enrolled 41 consecutive patients with symptomatic heart failure of any origin, despite optimal medical treatment, left bundle branch block (QRS duration > 120 ms), left ventricular ejection fraction < 35% and chronic (more than one year) AF, who underwent CRT-D implant. In all patients, an atrial lead with either passive or active fixation was used. We scheduled one or more internal, by means of device, or external EC in all eligible patients.

Atrial fibrillation occurrence was forellored. Gender (Male) 75%; Age (Years) 71.6±9.2; Ischemic Heart Disease 54%; Hypertension 61%; Diabetes 24%; NYHA functional class III/IV 90/7%; QRS width (ms) 138±16; Left ventricular ejection fraction (LVEF) 31±7.8; LBBB.

Results: At a mean of 2.7±1.8 months after implantation 19/41 (46%) patients underwent at least one EC. Left atrial appendage thrombosis, blood coagulation status and poor clinical status were the major reasons that jeopardize the EC procedures in the remaining patients. No complications occurred during the EC procedures. EC was effective in restoring SR in 13 patients (68% of treated patients); an intention to treat analysis shows a success rate of EC procedure in restoring sinus rhythm (SR) in 31% (13/41) of overall population. Eleven among thirteen patients (85%) with effective EC remained in SR at a mean follow-up of 9.2±7.6 months. Moreover, spontaneous conversion in SR was observed in two patients, one of these with an ineffective EC.

Conclusion: In this study, EC was feasible in less than 50% of patients with chronic AF post CRT, however SR was persistent at six months in greater than 30% of population, thus suggesting an atrial lead may be considered at implant.

Tpeak-tendon dispersion and the occurrence of ventricular tachyarrhythmia in nonischemic heart failure patients receiving cardiac resynchronization therapy

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Introduction: The effectiveness of cardiac resynchronization therapy (CRT) in preventing sudden cardiac death is controversial in high-risk heart failure (HF) patients despite its haemodynamic benefit. Transmural dispersion of repolarization with epicardial activation of the left ventricular pacing may contribute to provoking ventricular tachyarrhythmia. The aim of this study was to evaluating the Tpeak -Tend (Tp-e) dispersion is related to the occurrence of ventricular tachyarrhythmia requiring implantable cardioverter-defibrillator (ICD) therapy in nonischemic HF patients with CRT.

Methods: This prospective study included 97 consecutive nonischemic HF patients (age: 58±15, 67 men) who had newly implanted CRT-D and had an indication for primary prevention of sudden cardiac death between 2007 and 2011, 12-lead electrocardiograph (ECG) and 17-ch replication interval-difference mapping ECG (187-ch RIDM-ECG) were recorded before and within 7 days after the implantation, We measured Tp-e interval and Tp-e dispersion using 12-lead ECG, and inter-lead difference between corrected Tp-e intervals using 187-ch RIDM-ECG. The occurrences of ventricular tachyarrhythmia that required ICD therapy, including both shock and antiarrhythmia pacing, were followed. The Tpeak-Tend (Tp-e) dispersion was measured by QRS fusion (searching for the narrowest QRS during LV pacing) during atrial sensing (AS) and pacing (AP). The AP interval was adjusted comparing QRS duration in VVO, LV preexcitation (-30 ms), LV reversion (-30 ms) and LV only. Measurements were done by 2 blinded independent observers. A sub study validating the invasive LV+dP/dtmax using reverse transcription polymerase chain reaction (RT-PCR) was performed in 36 patients.

Results: The optimal AS AV delay obtained by ECG optimization (ECGopt) was 135.6±32.6 ms and the AP AV delay 190.1±37.2 ms. In 48.1% of patients, there was a absolute difference of -20 ms between the optimal nominal and nominal AS AV interval (51.7% during AP). The best QRS was obtained with VVO in 25 (36%) of patients, LV preexcitation in 23 (32%), LV only in 15 (22%) and RV preexcitation in 6 (8%). Both nominal and ECGopt reduced the baseline QRS (p<0.001) but this reduction was greater in the latter (138.2±18.1 ms vs 119.1±14.5 ms): the baseline QRS was shortened by 21.1±11.7% with NOM and by 32.5±8.6% with ECGopt; ECGopt reduced the QRS 11.7±14.5 ms vs 18.1±11.7 ms by NOM (p<0.001). With this configuration, for every ms of QRS shortening, LV+dP/dtmax increased 1.31 mmHg/Ks. By ECGopt, the LV+dP/dtmax increased 103.6±90.8 mmHg/Ks with respect to baseline (p<0.001) and for every ms of the QRS was shortened, LV+dP/dtmax increased 1.68 mmHg/Ks. QRS duration was significantly associated to LV+dP/dtmax (p<0.001).

Conclusion: Electrocardiographic optimization of the AV and VV intervals is feasible and it significantly reduces the QRS duration compared to default programming of CRT devices. The reduction of the QRS duration improves the acute hemodynamic response.

The possible molecular mechanism of cardiac resynchronization therapy

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Objective: To study the possible molecular mechanism of cardiac resynchronization therapy (CRT) through establishing the animal model in terms of quick pacing induced heart failure and how CRT treat heart failure.

Methods: Twenty-one adult beagle dogs were divided into Group A (CRT group, n = 10), Group B (non-CRT group, n = 7) and Group C (control group, n = 4). All of them were implanted left ventricle epicardial electrodes, right atrium and right ventricle leads. Group A and B received rapid right ventricular pacing (VOO mode, 260bpm) to induce heart failure. When their LVEF decreased below 35%, dogs in Group A treated with CRT and dogs in Group B were just terminated pacing. Dogs in Group C were not received pacing and used as control group. After 4 weeks of CRT or terminated pacing, LV myocardium was taken out for HE staining and electron microscope inspection. The mRNA transcription levels of contractile, calcium regulatory proteins such as phospholamban (PLN) and sarcoplasmic reticulum Ca (2+)

-ATPase protein (SERCA), and mitochondria related proteins such as aconitaine dehydrogenase-2 (ALDH2) were measured by reverse transcription polymerase chain reaction (RT-PCR) and normalized for glyceraldehyde 3-phosphate dehydrogenase (GAPDH).

Results: Two dogs in Group A and one dog in Group B died because of severe heart failure. By HE staining of the heart failure myocardium, we observed small vessel congestion, villosum thinning, and myofibrillar of group A thickened obviously compared with group B. Electron microscope showed cellular edema, mitochondrial swelling and fine myofibrillar damage (Fig. 1). The results of RT-PCR showed that the grey level of PLN, SERCA2a and ALDH2 in Group B were all lower than in Group A, and expression of ALDH2 was significantly lower than in Group A (P < 0.028), but there were no significant difference in PLN and SERCA2a among three groups (NS).

Conclusions: In the canine model of CRT after rapid right ventricular pacing induced heart failure, functional improvement related to CRT is associated with reversal of the HF related gene programming. CRT may produce a marked effect through mitochondria ALDH2 and energy metabolism.
Feasibility and safety of triple-site CRT-insights from Meta-analysis of randomized controlled trials

Transseptal endocardial left ventricular lead with less favorable electrical lead characteristics. Particularly in patients with very enlarged left ventricle or pulmonary hypertension. The consuming and associated with more significant fluoroscopic burden, in particular in patients with very enlarged left ventricle or pulmonary hypertension. The wide use of alternative methods facilitating left ventricular lead implantation may be necessary in the triple-site method. Triple-site resynchronization is associated with less favorable electrical lead characteristics.

Methods: Implantation of triple-site systems was significantly longer (median 125 vs. 96min; P = 0.001) with higher fluoroscopic exposure (576 vs. 362ms Gy; P = 0.007), especially in patients with very enlarged left ventricle and with pulmonary hypertension. Implantation success-rate was similar in the triple-site and control groups (84 vs. 98%; P=NS), but additional techniques had to be used in a greater proportion of the triple-site patients (33.3 vs. 16%; P = 0.05). Long-term lead performance tests revealed significantly higher pacing threshold and lower impedance in the triple-site group. The 1-year incidence of serious CRT-related adverse events was similar in triple-site and control group (20.8 vs. 30%; P=NS), but different complications were predominant in each group.

Conclusions: Triple-site cardiac resynchronization therapy is equally safe and feasible as the conventional CRT, however triple-site procedure is more time-consuming and associated with more significant fluoroscopic burden, in particular in patients with very enlarged left ventricle or pulmonary hypertension. The wide use of alternative methods facilitating left ventricular lead implantation may be necessary in the triple-site method. Triple-site resynchronization is associated with less favorable electrical lead characteristics.

MitraClip and CRT together: a good option? M. Seifert, M. Schoepf, M. Neuss, C. Butter. Heart Center Brandenburg and Immanuel Klinikum, Bernau (Berlin), Germany

Background: The CRT leads by correction of asynchrony and resulting dysfunction of mitral chords and papillary muscles to significant reduction of an existing functional regurgitation. Nevertheless the question comes up whether patients with severe reduction of LV function and significant mitral regurgitation do profit of the reduction of mitral regurgitation by MitraClip to CRT on top. We analysed the causes for the CRT non-responses concerning mitral regurgitation and MitraClip intervention.

Methods: From a total of 108 MitraClip implantations in our clinic (3/2009 to 12/2011) 16 patients were before and 5 patients were after MitraClip implanted with a CRT device (5/16). The follow-up interval till December 2011 amount for CRT 39±24 months and for the MitraClip 16±8 months.

Results: The average time interval from CRT to MitraClip implantation amount 23 months. No implantation related complications appeared like LV probe dislocation! Only 5 (24%) of patients had a class IA CRT indication (QRS >150ms, NYHA II or AVB III°). 2 of these 5 patients developed in the time course a paroxysmal AF. All other 16 patients had a first-class II CRT indication (AF, LVEF >35%, QRS >150ms, NYHA II or AVB III°). 5 patients (24%) of the 21 MitraClip patients died in the observation period and 2 patients (10%) received a LVAD.

Table 1

| Age (years) | 71±9 | 62±9 | NS |
| NYHA (n II/IIV) | 7/8/6 | 1/1/5 | 0.01 |
| NT-proBNP (pg/ml) | 943±654 | 1280±621 | 0.001 |
| EF (n) | 39±26 | 35±19 | NS |
| AF (n) | 152±18 | 149±9 | NS |
| LVEF (%) | 28±13 | 19±8 | 0.001 |

Conclusion: The MitraClip implantation is a feasible and safe procedure in patients with severe mitral regurgitation also with a CRT device. Although the MitraClip leads to a clear reduction of mitral regurgitation, the long time prognosis of these patients remains limited. For the missing or not persistent reduction of mitral regurgitation by CRT also seems matter the indication of CRT.
Feasibility of integrating 3D venous anatomy, scar and electrical timing to guide CRT implantation

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Purpose: Cardiac resynchronization therapy (CRT) is an effective treatment for heart failure but factors such as LV pacing on scar or pacing at an early activated site may reduce the benefit. We evaluated the feasibility of combining 3D venous anatomy, scar location and electrical timing to help guide CRT implantation.

Methods: Myocardial infarction was induced with a balloon occlusion in a porcine model and a stent was placed near the occlusion. A dual chamber MRI conditional pacing system was also implanted. A gadolinium (Gd) MRI scan was performed to quantify scar after 5 weeks. At 6 weeks, occlusive venograms were performed and electrical timing was measured with an electrically active guidewire. A 3D model was generated from 2 venograms using custom software. The 3D model and MRI data were combined with Mimics software by using the stent and lead electrode tips to register the images. Fluoroscopy cines were captured at each location to mark the electrical timing on the combined images. Electrical timing was calculated by measuring the interval between the ECG Q-wave to dV/dtmin on the LV electrogram.

Results: Figure shows location of the transmural scar (red circle) from the Gd-MRI scan registered with the 3D model in one animal. The scar was located near the distal portion of the interventricular descending coronary vein. Q-LV timing indicated the area near the scar was the latest activated LV site. The combined image allowed LV lead to be placed in a late activated site remote from the scar.

Conclusions: Registration of a 3D model of the coronary venous anatomy with Gd-MRI scan and electrical timing provides a novel method to target late activated LV sites while avoiding scar. This technique could be used to guide LV lead implant and improve the probability of benefit from CRT.

Pacing improves left ventricular filling in narrow QRS and pulmonary hypertension

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Purpose: Pacing therapy in heart failure patients with narrow QRS has gained increasing interest. The mechanism for potential cardiac improvement in this patient group remains to be explained. We hypothesised that left ventricular lateral wall pacing (LV pacing) influences septal position and thereby improves LV filling.

Methods: In 6 anaesthetised dogs we measured cardiac pressures by micromanometers and ventricular diameters and LV volume by sonomicrometry. The pulmonary artery was constricted to reduce left-to-right transpulmonary pressure gradient (TSG) to achieve leftward shifted septum as seen during pulmonary hypertension. Measurements were done with the pacemaker on and off. LV end-diastolic pressure-volume curves were constructed by transient caval constriction. Improvement in LV filling was quantified as increase in LV end-diastolic volume at a given end-diastolic pressure (Figure 1).

Results: LV pacing caused a rightward shift of the LV diastolic pressure-volume relation (Figure 1). LV end-diastolic volume increased by 5.5±3.5mL (mean±SD) (p<0.01) at the same end-diastolic pressure (0.8±0.2mmHg/NS). There was a concurrent shift of the septum into the right ventricle (RV) seen by an increased LV septal-to-lateral wall diameter by 3.3±3.3% (p<0.01) and decreased RV septal-to-lateral wall diameter of 4.1±10.1% (p<0.05). There was an inverse correlation between TSG and change in LV end-diastolic volume (r=0.80, p<0.05).

Conclusion: LV pacing in narrow QRS and pulmonary hypertension improved LV filling, indicated by an increased volume at the same pressure. The increased end-diastolic volume was caused by a shift of the septum towards the RV. These findings suggest a possible haemodynamic mechanism for improvement by pacing therapy in patients with heart failure and narrow QRS.

Resynchronization therapy is effective in adults with congenital heart disease

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Purpose: Cardiac resynchronization therapy (CRT) is a useful therapy for adults with acquired heart disease, poor left ventricular function and intraventricular conduction delay. In adults with congenital heart disease (CHD) heart failure is one of the leading causes of morbidity and mortality. However, the applications of CRT in adults with CHD are limited and the mechanisms by which it might be therapeutic is unknown. Therefore, our aim was to evaluate the efficacy of CRT in adults with CHD.

Methods: This was a retrospective study on clinical outcome of 28 adults with CHD who received CRT since 2003 in three university hospitals. Indication for CRT was a systemic ejection fraction (EF)<35%, QRS duration>120ms and NYHA functional class III in 75% of patients. The remaining patients had a systemic EF≥35%, QRS≥150ms and NYHA class II. EF measurements were performed by echocardiography.

Results: Mean age at implantation was 48±16 years and 82% was male. Cardiac diagnosis included tetralogy of Fallot (39%), ventricular septal defect (25%), congenital aortic stenosis (22%), congenitally corrected transposition of great arteries (7%) and other (7%). Prior to CRT 38% of patients had pacemakers and 93% was on heart failure medication. During a mean follow-up duration of 3.1±2 years post-CRT, NYHA functional class had improved by at least 1 grade in 75% of patients. Improvement in functional status was especially seen in patients with right ventricular pacing pre-CRT (94% vs 56%, P<0.01). Improvement of EF was seen in 52%, no changes in 33% and worsening in 14% of patients. In patients with improved EF mean QRS duration decreased from 178±32ms to 158±27msmes and in patients without improvement of EF mean QRS duration increased from 183±33ms to 196±28ms. During follow-up two patients died due to heart failure and one patient underwent heart transplantation.

Conclusion: Resynchronization therapy in selective adults with CHD is effective in improvement of functional status and ventricular function. Most benefit was seen in patients with right ventricular pacing pre-CRT. CRT shortening upon biventricular pacing is associated with improvement of ventricular function. Further studies are needed to establish appropriate guidelines for patient selection and long-term outcome.

Prevalence of heart failure in patients with bradycardia referred for pacemakers: cost implications of primary biventricular pacemaker implantation

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Objectives: The aim of this study was to determine the prevalence of pre-existing heart failure in patients with bradycardia referred for pacemaker implantation. The additional economic costs associated with primary implantation of biventricular pacemakers in these patients was also determined.

Background: Chronic right ventricular apical pacing can cause pacing induced ventricular dysynchrony and is associated with worse outcomes in patients with pre-existing heart failure. Consequently current guidelines recommend consideration of biventricular pacing in heart failure patients requiring pacemakers for bradycardia. However, the cost implementation of these guidelines would require increased healthcare resources.

Methods: The Taylors pacing registry was linked, through a unique patient identifier to: the echocardiography database; health informatics dispensed prescribing; and morbidity and mortality database for the population of Taylors, Scotland. All patients who underwent implantation of a conventional pacemaker between 2000 and 2009 were included in the study. Heart failure was defined as an echocardiogram with left ventricular systolic dysfunction and prescription of a loop diuretic, or a hospital admission coded as systolic heart failure prior to the pacemaker im-
animal and clinical data have shown that left bundle branch block (LBBB) induces mechanical dyssynchrony (MD) in the left heart. In heart failure (HF) patients with low left ventricular (LV) ejection fraction, cardiac resynchronization therapy (CRT) is much more efficient when typical LBBB is present. It has been postulated that lone LBBB could induce a progressive decline in LV function with possible recovery after CRT. However, the clinical evidence to support this hypothesis is weak.

The aim of this work was to study the prevalence and characteristics of LBBB-induced cardiomyopathy cured by CRT.

Methods: All the patients referred to our center for CRT implantation from 1993 to 2011 (N=1038) were investigated for LBBB history. Patients were included if they presented an original syndrome consisting on:

- history of typical LBBB for >5 years,
- no evidence of structural heart disease at the time of LBBB diagnosis,
- progressive development of LV dysfunction and HF symptoms (NYHA class II-IV),
- presence of major MD by echo,
- absence of other etiology for cardiomyopathy,
- hyper-response to CRT as indicated by LVEF >45% after 1 year

Results: 8 patients had the described syndrome. The main patient characteristics and follow-up data are summarized in the following tables.

- Patient characteristics at time of LBBB diagnosis: male gender 5, NYHA class 6,5±0.76, 4.1±0.53 years, LVEF 3200±17, 73±544 10,6±17, 125±10 years, QRS duration (ms) 10,6±17, 125±10, chest pain as 1st symptom 5, 6- min walk (m) 495±73, 544±79, rate-dependent LBBB 3, NYHA class 6,5±0.76, 4.1±0.53

Conclusions: CRT is associated with significant clinical and echocardiographic improvement sustained during long-term follow-up. In this patient cohort, there was no difference in the outcome among CRT pacemaker or CRT ICD patients.

Effect of cardiac resynchronization therapy in heart failure patients, single-center experience, long-term follow-up


Aim: To evaluate the long-term clinical outcome of CRT patients in a high-volume single-center experience of 11 years.

Methods: From 2000 to 2011, 1122 CRT devices were implanted in our center. Clinical and echocardiographic data were collected before and after CRT implantation. Echocardiographic data available at last follow-up (median 20 months, IQR: 10-38 months) were analyzed. Data on all-cause mortality was assessed based on clinic follow-up data and the Hungarian National Healthcare Fund Registry. Results: 693 CRT-pacemakers and 429 CRT-ICD devices were implanted. The mean age of the patients was 65±11 years (860 men). CRT induced signifi-
Conclusion: Some baseline clinical characteristics and co morbidities in HF pa
tients were found to have a significant add-on predictive effect on mortality after implantation of CRT represented by the EAARN score.

Methods: Patients included in the CRT-D arm in MADIT-CRT with available baseline high-resolution ECG were studied (n=892). Unliltered and bandpass fil
tered signal-averaged P waves were analyzed to determine orthogonal P-wave morphology (typical morphologies were predefined as having positive signals in Leads X and Y and a negative or negative-positive signal in Lead Z. All other patterns were classified as atypical). Echocardiography was performed at baseline and at 1 year. The association between P-wave morphology and data on echocardiographic response at 1 year was analyzed.

Results: Atypical P-wave morphology was found in 21% (n=186) of the patients at baseline. The P-wave duration was identical (144±18 vs. 144±17 ms, P=0.92) between patients with and without atypical atrial activation. Patients with atypical P-wave morphology were more often female (21% vs. 24%, P=0.025), had lower BMI (26±5 vs. 29±5 kg/m², P=0.006), had more ischemic CHF (60% vs. 52%, P=0.026) and had smaller left atrial volumes (90±20 vs. 94±22 ml, P=0.034). Baseline medication was similar between the groups.

Atypical P-wave morphology at baseline was associated with superior response to CRT at one year with a larger reduction in left ventricular end-diastolic volume (-23±12 vs. -26±11, P=0.009), left ventricular end-systolic volume (-36±16 vs. -31±16, P=0.006), and left atrial volume (-31±12 vs. -27±12, P=0.005), with a slightly larger absolute increase in left ventricular ejection fraction (LVEF) (12±5 vs. 11±5%, P=0.009). These associations were found to be independent of tradi
tional predictors (e.g., QRS-duration, LBBB, LVEF).

Conclusion: The presence of atypical P-wave morphology recorded at baseline from orthogonal leads in surface ECG is independently associated with a favor
able cardiac remodeling response to CRT at one year with a larger reduction in left ventricular end-diastolic volume.

Presence of a potentially correctable mechanism evaluated with conventional echocardiography is associated with long term survival in cardiac resynchronization therapy patients

Methods: 200 patients undergoing CRT implantation according to current guide
delines were included (age 67±9, GRS 169±30 ms, ejection fraction 24±6%). An echo exam was performed before and after CRT implant. We evaluated the pres
ence of any of the aforementioned mechanisms and whether it was corrected with CRT. Long term mortality was evaluated with a mean FU of 38±19 months.

Results: The presence of a mechanism that was successfully corrected with CRT was associated with a significantly better survival (87% at last FU) in comparison to those patients without a correctable mechanism (Others, 70% survival) and those with an uncorrected mechanism (64% survival). The patients with an un
corrected mechanism had a similar prognosis to those without any mechanism (see FIGURE).

Conclusion: The presence of an amenable mechanism that is successfully cor
rected with CRT is associated with a better survival at long-term FU. Simple evalu
ation of a potentially correctable abnormality with conventional Doppler echo
cardiography would lead to more adequate selection of candidates to CRT.

Myocardial viability at stress-echo is a better predictor of response to cardiac resynchronization therapy than left ventricular dysssynchrony

Methods: 200 patients in sinus rhythm, with left ventricular (LV) dysfunction and left bundle branch block underwent baseline echocardiography and low dose dobutamine echo (DSE) (up to 20 mg/kg/min) the day before CRT implantation; echocardiography was repeated after 6 month. LV dysynchrony was defined as a time delay >130 msec between anteroseptal and posterior seg
ments at speckle tracking radial strain analysis; dysynchrony was evaluated both at baseline and at peak DSE. Several indicators of myocardial viability were mea
sured, including: the reduction in end-systolic volume (LVESV), the improvement in ejection fraction (EF), the reduction in mitral regurgitation (MR) and the increase in ratio between systolic area and LVESV (SA/LVESV) (SAP/LVESV). Response to CRT was defined as a reduction ≥15% in LVESV at 6 months.

Results: At 6 months after CRT, 18/34 pts (53%) turned out to be responders. Responders to CRT had more frequently dysynchrony, both at baseline (94% vs. 62%, P=0.02) and during DSE (78% vs 40%, P=0.02). Baseline LV volumes and EF were similar in responder and in non-responder patients (LVEDVi 149±34 ml vs 136±39 ml, p=0.15, LVESVi 111±30ml vs 102±34 ml, p=0.22; EF 27±6% vs 25±7, p=0.22 respectively). At DSE, responders had a greater decrease in volumes (ΔLVEDVi -34±41 ml vs -11±20 ml, P=0.004, ΔLVESVi -31±31 ml vs -6±12ml, p=0.002), in MR (ΔMR -0.11±0.12 vs -0.06±0.08 p=0.07) and a greater increase in EF (ΔEF +2.9±2.9% vs +3±1.9 p=0.003), in SAP/LVESV +17±12 vs +17±5 p=0.001) and in SAP/LVESV ratio (ΔSAP/LVESV 0.96±0.86 vs 0.10±0.25 mmHg/ml/mg, p=0.003) than non-responders.

Conclusion: In heart failure patients eligible for CRT, an increase in SAP/LVESV ratio ≥22% during DSE predicts response to CRT with similar sensitivity but with greater specificity than the evaluation of left ventricular dysynchrony.

A new cardiac resynchronization therapy responder definition to predict long term positive outcome: left ventricular ejection fraction 35% overcrossing at 1 year follow-up

Methods: 200 patients undergoing CRT implantation according to current guide
delines were included (age 67±9, GRS 169±30 ms, ejection fraction 24±6%). An echo exam was performed before and after CRT implant. We evaluated the pres
ence of any of the aforementioned mechanisms and whether it was corrected with CRT. Long term mortality was evaluated with a mean FU of 38±19 months.

Results: The presence of a mechanism that was successfully corrected with CRT was associated with a significantly better survival (87% at last FU) in comparison to those patients without a correctable mechanism (Others, 70% survival) and those with an uncorrected mechanism (64% survival). The patients with an un
corrected mechanism had a similar prognosis to those without any mechanism (see FIGURE).

Conclusion: The presence of an amenable mechanism that is successfully cor
rected with CRT is associated with a better survival at long-term FU. Simple evalu
ation of a potentially correctable abnormality with conventional Doppler echo
cardiography would lead to more adequate selection of candidates to CRT.
Comparison of benefits from cardiac resynchronization therapy between ischemic and non-ischemic patients

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Introduction: Today, approximately 30% of patients (pts) remain non responders to Cardiac Resynchronization Therapy (CRT). The CLEAR study aimed to assess the benefit of periodic SonR-CRT optimization vs. standard clinical practice regarding pts clinical outcome. This retrospective sub analysis aimed to investigate the impact of HF ischemic etiology on CRT response.

Methods: 199 HF pts (73.4±9.7 years, 63% male, NYHA class: 3.1±0.3, LVEF: 40.0±11.9, QRS width: 169.0±22.8 ms, Ischemic & non-ischemic pts: 77 & 122 pts) were implanted with a CRT pacemaker featuring the SonR-CRT optimization algorithm. Within 7 days after implant, pts were randomly assigned to receive either: i) SonR-CRT optimization group (SonR) based on periodic in-clinic CRT optimization (ventricular configuration and AV delay) at predischarge, 3 months (M) and 6M Follow-up (FU); or ii) standard optimization group (STD) based on each center clinical practice. Pts were followed at 6 and 12M FUs. The rate of improved pts, assessed with a composite criterion including deaths from any cause and HF-related hospitalizations, NYHA class and Quality of Life, was analyzed through a multivariate analysis including HF ischemic etiology and randomization group.

Results: A significantly higher rate of improved pts was observed in the SonR vs. STD group at 6M and 12M FUs in the global population as well as in both non ischemic & ischemic pts (Table).

<table>
<thead>
<tr>
<th>Randomization group</th>
<th>Rate of improved pts at M6 (%)</th>
<th>Rate of improved pts at M12 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STD (n=97) SonR (n=100) p</td>
<td>STD (n=99) SonR (n=100) p</td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>61%</td>
<td>76%</td>
</tr>
<tr>
<td>Non ischemic</td>
<td>75%</td>
<td>87%</td>
</tr>
</tbody>
</table>

Conclusions: Our findings seem to suggest the use of LVEF recovery as surrogate marker of long term survival after CRT. Reaching or exceeding LVEF 35% after one year of CRT, regardless LVEF value at time of device implant, identify positive prognosis at very long term FU.

Myocardial Scar Characterization predicts long-term device therapy in Cardiac Resynchronization Therapy Patients


Purpose: A substantial portion of patients with an indication for cardiac resynchronization therapy (CRT-P) will also have an indication for an implantable cardioverter-defibrillator (ICD) and a CRT device with defibrillator capabilities (CRT-D) will be implanted in the majority. Unfortunately there are no clear variables to select the appropriate therapy in this population. We hypothesized that myocardial scar characterization can predict ventricular arrhythmias (VA) in these patients.

Methods: 78 consecutive heart failure patients (mean age 64±11, NYHA class 2.7±0.5 and EF 22±7%) admitted for the implantation of a CRT-D device were prospectively enrolled. Delayed contrast enhanced cardiac magnetic resonance imaging (DE-MRI) was obtained prior to implantation and analyzed with customized post processing software. Total scar area, core and border zone of the myocardial scar was calculated. We analyzed the relation between the border zone and the incidence of VA.

Results: During a mean follow-up of 32±17 months, appropriate ICD therapy occurred in 11 patients (14%). Receiver operating characteristic curve (ROC) analysis showed that a scar mass percentage (scar mass/LV mass) < 16.5% (sensitivity 100%, specificity 81%, HR of 1.09 (1.05-1.13), p = 0.001) and a border zone mass < 9.1g (sensitivity 91%, specificity 82%, HR of 1.05 (1.03-1.18), p = 0.001) predicted VA occurrence.
In the real world women benefit more than men from cardiac resynchronization therapy in term of long term clinical outcome and positive prognosis

Methods: We enrolled 51 patients undergoing CRT (67.3±9.5 years, 36 males) with left ventricular ejection fraction (LVEF) ≥40%, NYHA class II-IV and QRS duration >120 ms and left bundle branch block morphologic. Twelve-lead ECG (5mm/mV, 0.05mm/Imp), 2D-echocardiogram and functional assessment by NYHA class and Minnesota Score (MS), were performed before CRT and at 3-month follow-up. The following ECG intervals were measured in V1 and V6: 1) Total QRS complex; 2) QRS onset-R wave peak interval; 3) R wave peak-S wave peak interval (RS-V1 and RS-V6); 4) S wave peak-RS end interval; 5) difference between QRI interval in lead V6 and QRI interval in lead V1. Patients with improvement of both LVEF ≥5% and NYHA class ≤1 at follow-up were considered as responder to CRT.

Results: Among the pre-specified ECG intervals, only basal RS-V1 was longer in responders (n=36, 70.6%) compared to non responders (n=15, 11.8% vs 44.0±12.6 ms, p=0.021), whereas QRS duration did not differ between the two groups (153.9±19.3 vs. 150.5±18.7 ms, p=0.56). Furthermore, 83% of patients with a basal RS-V1 >45 ms responded to CRT compared to 50% of those with RS-V1<45 ms (p=0.001). Compared to the basal value, at 3 months RS-V1 did not significantly change in non responders (from 44.0±12.6 to 44.5±11.3 ms, p=0.64) whereas it showed a significant shortening in responders (from 113.8±14.8 to 78.2±6.2 ms, p<0.0001), RS-V1 shortening, but not QRS shortening, significantly correlated with improvement in LVEF (r=-0.45, p<0.001) and with reduction of MS (p=0.46, p<0.0001).

Conclusions: Our data point out that assessment at standard ECG of RS-V1 interval, but not total QRS duration, may help to identify patients who can most likely benefit from CRT; furthermore, the changes in RSV1 interval, but not those of QRS, after CRT act significantly predictive of clinical improvement.

Figure 1. Cardiovascular mortality non-ischemic.

Conclusion: Female CRT recipients achieve greater echocardiographic improvement, as well as greater long-term survival benefit in term of reduction of mortality.

Methods: We enrolled 51 patients undergoing CRT (67.3±9.5 years, 36 males) with left ventricular ejection fraction (LVEF) ≥40%, NYHA class II-IV and QRS duration >120 ms and left bundle branch block morphologic. Twelve-lead ECG (5mm/mV, 0.05mm/Imp), 2D-echocardiogram and functional assessment by NYHA class and Minnesota Score (MS), were performed before CRT and at 3-month follow-up. The following ECG intervals were measured in V1 and V6: 1) Total QRS complex; 2) QRS onset-R wave peak interval; 3) R wave peak-S wave peak interval (RS-V1 and RS-V6); 4) S wave peak-RS end interval; 5) difference between QRI interval in lead V6 and QRI interval in lead V1. Patients with improvement of both LVEF ≥5% and NYHA class ≤1 at follow-up were considered as responder to CRT.

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Conclusions: Our data point out that assessment at standard ECG of RS-V1 interval, but not total QRS duration, may help to identify patients who can most likely benefit from CRT; furthermore, the changes in RSV1 interval, but not those of QRS, after CRT act significantly predictive of clinical improvement.
Clinical response with adaptive CRT algorithm
Comparison of echo guided AV optimization: a propensity score analysis of multi-center trials

P3251  Serial optimization of resynchronization device timing versus standard care - results of the optimise CRT randomized trial
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Purpose: Cardiac resynchronization therapy (CRT) is efficacious on average, but not all patients clearly benefit. The recently completed Optimal Programming To Improve Mechanical Indices, Symptoms, & Exercise In CRT (OPTIMISE CRT) trial compared clinical response & echocardiographic (echo) left ventricular (LV) remodeling in CRT recipients randomized to serial, proprietary electrogram-based (EGM) optimization of atrio-ventricular (AV) & inter-ventricular (VV) delays (QuickOpt) vs. standard (Std) care. Non-EGM optimization early after CRT was permitted in Std care.

Methods: Of 468 patients, 451 were successfully implanted with a CRT device & followed. Subjects were enrolled at 68 centres. All had symptomatic heart failure (HF), defined by a 6 minute walk test (6-WT) distance & clinical & subjective endpoints. A CRT defibrillator. Subjects were randomized 1:1 to QuickOpt vs. Std care. Clinical response (≥ class improvement in Specific Activity Scale [SAS] or ≥ 25% relative improvement in 6-WT) & favorable LV remodeling (≥ 15% relative reduction in end systolic volume or ≥ 5% absolute improvement in ejection fraction [EF]) were assessed over 1 year. Patients, outcomes assessors, & echo analyses were blinded to treatment allocation.

Results: The mean age of subjects was 66 years, 27% were female, 50% had ischemic HF, median QRS duration was 158 msec, & median LVEF was 26%. The two groups were similar at baseline.

Overall, 59% of subjects were clinical responders, 70% had favorable LV remodeling, & 44% had both. The proportion of subjects with the primary outcome, clinical response & favorable LV remodeling, was similar in the two groups (p = 0.76). Clinical response was similar in patients with ischemic (69%) & non-ischemic HF (65%) (p = 0.94) overall, but those with ischemic HF who were randomized to QuickOpt exhibited greater improvements in SAS (p = 0.015) & showed a trend toward a greater improvement in 6-WT vs. Std care. Overall, favorable LV remodeling was more frequent in patients with non-ischemic (67%) vs. ischemic HF (52%) (p = 0.0013), but was similar in the QuickOpt & Std care groups (p = 0.40), regardless of the etiology of HF. Results were similar after adjustment for QRS duration & LV lead position.

Conclusions: Serial AV & VV EGM optimization with QuickOpt vs. Std care did not significantly alter the proportion of patients with both clinical response & favorable LV remodeling. LV remodeling was similar in the two groups, but patients with ischemic HF had improved clinical response with QuickOpt vs. Std care. Additional analyses are ongoing.

Figure 1. TSDI from opposing-wall strain curves

Conclusions: The extent of discordant deformation in opposing-wall transverse strain curves seems to perform better than contraction delays in predicting response to CRT: a certain delay of lateral wall strain also seems to be needed, while no predictive value was found for STAR index. Our findings highlight the importance of studying LV dysynchrony in its diverse aspects, and support a multiparametric approach derived from a single cycle that could prove effective and feasible in a real-world setting.

Figure 1. TSDI from opposing-wall strain curves

Clinical response with adaptive CRT algorithm compared with echo guided AV optimization: a propensity score analysis of multi-center trials

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Purpose: The purpose of this study was to compare the clinical impact of cardiac resynchronization therapy (CRT) (CRT) optimized using the novel Adaptive CRT (aCRT) algorithm with that of CRT optimized using echocardiography-guided AV optimization.

Methods: The aCRT arm of the Adaptive CRT trial was compared with a pooled AV echocardiography-optimized historical cohort (HC) derived from the CRT arms of 4 clinical trials (MIRACLE, MIRACLE ICD, PROSPECT, and InSync III Marquis). Clinical response was determined by the clinical composite score (CCS), which classifies patients as improved, unchanged, or worsened based on objective and subjective endpoints. aCRT facilitates continuous AV and VV optimization, along with RV synchronized LV pacing when the PR interval is ≤ 200 msec and heart rate is < 100 bpm. Echocardiography-guided AV optimization in the HC was performed via the iterative or Ritter methods. The two groups were compared using a propensity score model developed from 22 potential confounders to the effect of CRT. Patients were stratified into quintiles according to the propensity score and the adjusted absolute treatment effect was obtained by averaging estimates across quintiles. The 95% confidence interval for the adjusted absolute treatment effect was calculated using a bootstrap method.

Results: The final propensity score model included 751 patients (aCRT: 266, historical trials: 485). The absolute adjusted difference in percent improved between the two arms was 11.9% [95% CI: 2.7% to 19.2%] favoring aCRT. After adjusting for population differences, patients in the aCRT arm were significantly more likely to have an improved CCS than patients in the HC arm (odds ratio = 1.65, 95% CI: 1.1 to 2.3).

Clinical response was similar in patients with ischemic (69%) & non-ischemic HF had improved clinical response with QuickOpt vs. Std care. Adverse LV remodeling. LV remodeling was similar in the two groups, but patients with ischemic HF had improved clinical response with QuickOpt vs. Std care. Additional analyses are ongoing.

Purpose: Identification of proper candidates for cardiac resynchronization therapy (CRT) is challenging. Currently used selection tools and optimization strategies are still associated with a 30% non-response rate. Therefore, a novel non-invasive electrical activation mapping technique was applied in CRT candidates.

Figure 1. Left panel (A): Ventricular activation map during LV pacing merged with a fluoroscopic image in LAO view. The site of earliest activation (pink) corresponds with LV lead position. Right panel: Ventricular activation maps during programmed LV offset of 50ms (B), 40ms (C), RV pacing (D) and simultaneous pacing (E). Activation time in milliseconds.
This study was conducted to determine whether this technique could accurately identify lead position and left ventricular (LV) pacing offset in CRT patients.

**Methods:** In 2 patients, a specific volume conductor model was reconstructed from MRI images. Body surface potentials (64 leads) were recorded before and after implantation of a biventricular pacing device. During the post-implant recording, LV pacing offset was varied with 10ms intervals. Ventricular activation maps were computed for each offset, using the fastest route based activation imaging method.

**Results:** In both patients lead positions were correctly identified. Variations in left ventricular activation sequence, due to various pacing offsets, were detected with a temporal resolution of 10ms (Figure 1).

**Conclusion:** Non-invasive ventricular activation mapping correctly identified left and right lead positions in CRT patients. The complete ventricular activation sequence was visualised during various pacing offsets. This technique offers the prospect to improve selection of CRT candidates, guidance of lead positioning and may be of advantage for CRT optimisation.

**COMPLICATION OF IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS: A REAL PROBLEM?**

**P3253** Safety of ICD electrode positioning in the right ventricular mid-septum versus apex - results from a randomised trial

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**Background:** The right ventricular (RV) mid-septum is an alternative pacing site which may be more anatomically favourable than the traditional apical pacing site. However, safety data for this location in implantable cardioverter defibrillator (ICD) recipients are limited.

**Methods:** Patients with indication for ICD placement were enrolled at 20 centres and the RV defibrillation electrode was randomly assigned to be placed in the mid-septum or in the apex. Patients were followed for three months. The composite safety endpoint was survival in the absence of RV lead related complications. Any of the following was considered as a RV lead related complication: lead cannot be placed in the randomised position, defibrillation threshold >25 J at implantation, high pacing threshold (>2V at 0.5 ms), R-wave amplitude -5mV, abnormal impedances, revision of right ventricular lead, need for a additional right ventricular lead, spontaneous ventricular arrhythmia not terminable with maximal shock energy. The study design followed a non-inferiority design.

**Results:** A total of 299 patients (85±12 years; 21% female; LVEF: 28±11%; 83% primary prevention, 34% CRT-D) were assigned for a mid-septal (n=144) or an apical (n=155) lead location. An independent adjudication committee confirmed the randomised lead position in 98% of patients. Baseline characteristics did not differ between the groups and 284 patients (withdrawn consent n=6, lost to follow up n=4, ICD explantation n=3, major protocol deviation n=2) were analysed for the safety endpoint. Based on intention to treat analysis the incidence of RV lead related complications was reached in 113/137 (82.5%) patients of the mid-septal group and in 125/147 (85.0%) patients of the apical group; this difference is statistically insignificant (p=0.560), however, the pre-set margins for non-inferiority were not met. Except for the incidence of high defibrillation thresholds (>25J) at implant (mid-septal group: 4.9% vs. apical group: 0.6%; p=0.001) there were no differences in the contribution of the individual sub items to the composite endpoint.

**Conclusion:** Right ventricular mid-septal ICD lead placement is reliably achievable and generally safe. However, due to an increased frequency of high defibrillation thresholds in mid-septally positioned electrodes non-inferiority in comparison to the traditional apical location cannot be concluded if strict margins are applied.

**P3254** Performance of riata icd leads: results from an independent multicenter study

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**Purpose:** Riata (RIA) and Riata ST (RST) ICD leads are prone toexternalization of the conductors (EX-C). No independent study of RIA and RST leads has been reported. Our aim was to assess RIA and RST leads with and without normally functioning EX-C compared to Quattro Secure (QS) leads.

**Methods:** Data were collected for patients who had RIA or RST leads. K-M survival (S) probabilities were compared using the log rank test. S were calculated for all cause failures (ALL), including electrical malfunctions (MAL) and/or leads end of service (EOS). Exclusions were normally functioning Ex-C, and/or leads not functioning. Results: From 2002-2008, 1,060 patients received 773 RIA and 287 RST leads. After follow-up of 4.3±2.6 and 3.3±1.7 years, 743 (70.1%) RIA and RST leads were functioning, 256 (24.1%) had been removed, and 62 (5.8%) had failed, including 45 MAL (7 with Ex-C) and 17 normally functioning leads with Ex-C. The S for RIA and RST (ALL and MAL) vs the QS (ALL) are shown.

**Conclusion:** In this large multicenter study we found RIA and RST performance was significantly inferior to QS leads even when normally functioning EX-C were excluded.

**P3255** Incidence of implantable cardioverter-defibrillator leads fracture: comparison of small vs standard-diameter leads implanted in a single center

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**Purpose:** Improvement in implantable cardioverter-defibrillator (ICD) technology has led to the development of small size (<8Fr) leads. Sprint Fidelis (Medtronic) is a small-size lead that is prone to the risk of fractures. Some case reports have raised the suspicion that also the small-size Riata lead (St.Jude) is at increased risk of fracture. No data are available on the incidence of fracture in Sprint Fidelis, Riata leads and standard-size leads (<8Fr) implanted in one single centre.

**Methods:** From 2003 to 2009 190 Sprint Fidelis, 197 Riata and 419 standard-size leads (Medtronic, Boston) were implanted. Lead fracture was defined by a significant change in impedance and/or by the appearance of electrical noise suggesting insulation defect or conductor fracture.

**Results:** After a median follow up of 32 months (15-50 months) the failure rate in the overall lead position was 8.9% (2.4% ending in ICD inappropriate therapy). Follow up-duration was similar for Sprint Fidelis, Riata and standard-size leads (<8Fr) implanted in one single centre.

**Conclusions:** Small-size ICD leads are at increased risk of fracture. Specifically, Riata ICD leads are at lower risk of fracture as compared to Sprint Fidelis but at higher risk as compared to standard-size leads. Our study suggests that lead size might be a major determinant of the risk of lead failure.
P3256
Impact of fluoroscopic screening on failure rates of the Riata high-voltage implantable defibrillator lead

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Introduction: The Riata family of high-voltage implantable defibrillator leads is prone to a new type of insulation abrasion, characterized by externalized conductors due to an inside-out insulation abrasion. The objective of this study was to assess the extent of externalized conductors prior to the recall and post recall after fluoroscopic screening of Riata high-voltage leads.

Methods: Between July 2003 and April 2008, a total of 452 patients received a Riata high-voltage lead (model: 1580, 1581, 1582, 7001, or 7002). The number of externalized conductors and their clinical presentation is determined prior to the recall. Post recall, the number of externalized conductors as assessed by fluoroscopy is determined. Life-table analysis of Riata high-voltage leads will be performed to assess the impact of fluoroscopic screening.

Results: In total, 124 patients (27%) died and 17 (4%) had cardiac transplantation at the time of this study. Median follow-up was 4.9 years (interquartile range: 3.0 to 6.0 years). Prior to recall, a total of 22 externalized conductors (4.9%) were determined, of which 10 had electrical dysfunction (e.g. impedance change, oversensing/noise). Failure rates by life-table analysis were 3.4% (95% CI, 1.9 to 6.0% at 5 years and 6.7% (95% CI, 3.4% to 10.4%) and 3.4% (95% CI, 1.9 to 5.0%) at 5 and 8 years, respectively. Post recall, the total of externalized conductors increased to 56 (12.8%) by using fluoroscopic screening. Failure rates of the Riata high-voltage lead increased to 6.7% (95% CI, 4.3 to 10.4%) and 3.2% (95% CI, 1.9 to 5.0%) at 5 and 8 years, respectively. Of the leads with externalized conductors as detected by fluoroscopic screening (n=36), 8 (22%) had minor electrical abnormalities (slight change in low-voltage impedance).

Conclusion: The failure rate of the Riata high-voltage lead is low when physicians rely solely on electrical abnormalities. The extent of externalized conductors is much higher when we screen Riata high-voltage leads using fluoroscopy, with a failure rate of 3.4% to 8.9% at 8 years. The definitive management of patients with Riata high-voltage leads and externalized conductors needs to be clarified soon as the failure rate of this specific lead will increase.

P3257
Deaths caused by Riata implantable cardioverter-defibrillator lead failure: analysis of the U.S. Food and Drug Administration Device Database

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Purpose: The Riata implantable cardioverter-defibrillator (ICD) silicone lead (St Jude Medical, Sylmar, USA) has a unique failure mechanism whereby the conductors wear through the insulation from inside-out. While attention has been focused on externalized conductors, the risk to patients is an electrical malfunction that prevents the delivery of effective therapy. We therefore queried the U.S. Food and Drug Administration device database for deaths associated with Riata lead failure and compared the results to similar data for Quattro Secure 6847 ICD leads (Medtronic, Inc., USA).

Methods: On February 11 and 12, 2012, the database was searched (accessed using data.dfa.gov/scripts/cdrh/cfdocs/cfMAUDE/search.CFM) for "Riata deaths" and "Quattro Secure deaths". Deaths were considered device-related if death was sudden and associated with a documented lead failure; deaths were indeterminate if death was non-sudden or lead failure was undocumented; deaths were considered device-related if death was non-sudden or lead failure was documented. On February 11 and 12, 2012, the database was searched (accessed using data.dfa.gov/scripts/cdrh/cfdocs/cfMAUDE/search.CFM) for "Riata deaths" and "Quattro Secure deaths". Deaths were considered device-related if death was sudden and associated with a documented lead failure; deaths were indeterminate if death was non-sudden or lead failure was undocumented; deaths were considered device-related if death was non-sudden or lead failure was documented.

Results: Of 84 reported Riata deaths, 22 (26.2%) were device-related, 31 (36.9%) were indeterminate, 25 (29.8%) were not device-related, and 6 deaths (7.1%) occurred during the extraction of a failed Riata lead. Riata device-related failures were caused by short circuits from an abraded lead to the pulse generator can (n=7), high voltage conductor defect (n=12), lead noise (n=2), and lead "anomalies" (n=1). Of 382 reported Quattro deaths, 5 (1.3%) were device-related, 34 (8.9%) were indeterminate, 320 (83.3%) were not device-related and 6 (1.6%) deaths were procedure-related. Quattro device-related deaths were due to lead noise (n=2), conductor fracture (n=1), fixation helix failure (n=1), and high voltage (n=1). No Quato lead exhibited an insulation failure or can abrasion resulting in a short-circuit and failure to deliver therapy.

Conclusion: Riata ICD leads appear prone to lethal failure modes, often involving the high voltage conductors, and can abnormalities that develop between the lead and the pulse generator in the pocket. These findings were not observed for Quattro Secure ICD leads. The Riata extraction deaths underscore the risk of this procedure.

P3258
Frequent implantable cardioverter-defibrillator lead complication during orthotopic heart transplantation

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Purpose: The purpose of this retrospective, single-centre study was to evaluate complications with previously implanted implantable cardioverter defibrillator (ICD) leads in patients who underwent heart transplantation (HTX). A high proportion of patients on the waiting list for HTX have an ICD system. Surgical removal of the whole ICD system is part of the orthotopic HTX procedure and it is usually carried out without complications.

Methods: Medical records of 84 patients with previously implanted ICD systems who underwent HTX in the past 6 years in the Erasmus Medical Center, Rotterdam were reviewed for ICD-related adverse events (AE).

Results: No AEs were observed in the single-coil group. The incidence of AEs was 22% in the dual-coil cohort of 51 patients. All AEs were retained fragments of the proximal shock coils of the ICD leads. Fragment retention was independent of age, gender, lead age, the etiology of heart failure, the duration of HTX, or from the heart surgeon in the dual-coil group. The St Jude Medical Riata lead family was overrepresented (71%) in the AE group owing to its unique shock coil fixation design.

Conclusions: ICD lead fragment retention with a potential risk for further complications is highly prevalent in post-HTX patients who received dual-coil defibrillator leads while on the waiting list. Therefore, more awareness for the technique of dual-coil lead extraction during HTX is warranted. The use of single-coil leads and early removal of remnants should be considered.

P3259
Rate, causes and impact on patient outcome of implantable device-related complications requiring surgical revision: a retrospective, bi-centre, 5-year survey

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Introduction: Long-term impact on patient outcome of implantable device-related complications has not been thoroughly evaluated. The aims of this retrospective, observational, bi-centre study were to analyze the rate and the nature of device-related complications requiring surgical revision in a large series of patients undergoing device implantation, elective generator replacement and pacing system upgrade, and to systematically assess their impact on patient outcome.

Methods: Data from 2671 consecutive procedures (1511 device implantations, 1034 elective generator replacements and 126 pacemaking system upgrades) performed between January 2006 and March 2011 were retrospectively analyzed. The rate and the nature of device-related complications requiring surgical revision identified after 24 hours from procedure were evaluated. The outcome measures recorded included complication-related mortality, number of reoperations, need for complex surgical procedures, number of rehospitalizations and additional hospital treatment days.

Results: Between a median follow-up of 27 months the overall rate of complications was 8.9% in CRT device implantation (relative risk 4.7; p<0.001) predominantly due to coronary sinus lead dislodgement and device infection. Patients with complications presented a significant higher number of device-related hospitalizations (2.3±0.6 vs 1.0±0.1; p<0.001) and hospital treatment days (15.7±2.5 vs 3.6±1.1; p<0.001) compared to patients without complications. The occurrence of complications was associated with a significant increase in overall device-related hospitalizations (+5%) and hospital treatment days (+11%). Device infection was the complication with the greatest negative impact on patient outcome in terms of mortality, number of reoperations, need for complex surgical procedures and additional hospital treatment days.

Conclusion: In device recipient CRT implantation the procedure was with higher risk of complications requiring surgical revision. Complications was associated with substantial clinical consequences and a significant increase in number and length of hospitalizations.

P3260
Sprint Fidelis ICD lead failure and the manner of lead implantation

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Background: Sprint Fidelis ICD leads fail more often than other ICD lead types.

Aim: The aim of the study was to analyze Sprint Fidelis (SF) ICD lead failures in a group of our patients followed up for 4.5 years (5-64 months).

Material and Methods: Between August 2006 and October 2007 we implanted...
113 SF ICD leads (models 6930, 6931 and 6949 – 3, 109 and 1, respectively) for primary (45 pts) and secondary prevention (68 pts) of sudden cardiac death. In 110 pts it was first-time ICD implantation whereas in 3 pts it was upgrading of an existing system. During 4.5 years 12 SF leads failed (10% of all pts receiving an ICD at that time). The mean time from implantation to SF lead failure was 33.6±11.4 months (range: 15 to 50). In 2 pts SF leads were extracted due to pocket infection (14 and 18 months after initial procedure) and those patients were excluded from analysis. Analysis of the causes of failures included the following factors: time of failure from lead implantation, patient age, gender, type of the implanted system (VVI vs. DDD) and the manner of lead implantation (phlebothomy of the cephalic vein or subclavian vein puncture), location of the lead tip (right ventricular apex – RVA, right ventricular outflow tract – RVOT).

Results: In all patients with lead failure the devices were implanted through the subclavian vein. Table below compares patients with and without SF lead failure.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No failure</th>
<th>Failure</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>111</td>
<td>12</td>
<td>0.78</td>
</tr>
<tr>
<td>Age (SD [years])</td>
<td>57.0±15.7</td>
<td>63.3±11.4</td>
<td>0.208</td>
</tr>
<tr>
<td>Females [%]</td>
<td>52/101 (51.5%)</td>
<td>99/99 (77.8%)</td>
<td>0.052</td>
</tr>
<tr>
<td>VVI [%]</td>
<td>8/12  (66.7%)</td>
<td>84/99 (84.8%)</td>
<td>0.235</td>
</tr>
<tr>
<td>Location of the lead tip [%]</td>
<td>99/101 (98.1%)</td>
<td>99/99 (100%)</td>
<td>0.362</td>
</tr>
<tr>
<td>Subclavian vein puncture [%]</td>
<td>12/101 (11.8%)</td>
<td>100/12 (83.3%)</td>
<td>0.0036</td>
</tr>
</tbody>
</table>

*Mann–Whitney U test; **Yates’s y² test.

Conclusions: 1. In the present study the most significant factor for SF lead failure was subclavian vein puncture. It means that a combination of weak ICD lead construction and type of venous approach increased the risk of lead failure.

2. An increased type of implanted device and location of lead tip were not the factors that would significantly affect SF ICD lead failure.

Bacteriological assessment of extracted pacemaker and defibrillator leads

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Purpose: It has been proven that pacemaker leads infections, when not treated, lead to serious consequences. We carried out a microbiologic assessment, in order to identify the prevalent strains of bacteria responsible for the leads infections, so as to delineate an effective therapeutic protocol.

Methods: Between July 2003 and November 2011, at our Centre, 316 leads were extracted from 152 patients with infective indication. After extraction, samples of the suspected infected leads were sent to the Microbiology department for an examination.

Summary of results: Staph. epidermidis was the most frequently isolated bacte- rial strain (26.5%), followed by Staph. aureus (15.7%), Staph. coagulase negative (8.6%), Gram – flora (2.9%), Staph. schleiferi (2.2%), Staph. hominis (2.2%). Cultures were negative in about 13.7% of samples. Retained sensitivity to antibiotics was the following: teicoplanin/vancomycin 87.3%, co-trimoxazole 73.7%, gentamycin 69.5%, quinodones 51.8%; rifampicin 47.8%; cephalosporins 38.2% and oxacillin 40.3%. The sub-analysis of resistance in various clinical indications showed that in case of sepsis, sensitivity for glycopeptides was retained (100% of cases). In this basis of time elapsed prior to referral for lead extraction, we arbitrarily divided the infections in recent and chronic infections. An increase in time prior to referral for lead extraction was associated with a significant increase of antibiotic resistance.

Conclusions: Our data point out a poor susceptibility to antibiotics of the bac- teria associated with pacemaker-related infections, and show that also local infections not healing with usual antibiotics are often sustained by methicillin- resistant strains. Therefore, systemic antibiotics, preferentially glycopeptides, in full-regimen doses, must not be delayed in such patients, having in mind that, however, the mainstay of the management of relapsing infections is the complete removal of the implanted system.

Influence of radiotherapy on cardiac implantable electronic devices: a single center experience

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Purpose: Patients treated with a cardiac implantable electronic device (ICD) are increasing as well as patients who undergo radiotherapy (RT) for cancer. So, pacemaker and implantable cardioverter-defibrillator (ICD) recipients may sometimes experience radiotherapy during life. Few papers address the conse- quences of RT on device function. The aim of this study is to illustrate our experi- ence and evaluate the safety of radiotherapy in these patients.

Methods: We retrieved data from personal files of recipients of PM and ICD who underwent RT in our institution from 2003 to 2011. All patients were evaluated by an electrophysiologist and by a radiotherapist before starting therapy. The device was relocated if near to or into the field of irradiation. Pacing-dependent patients were reprogrammed with asynchronous stimulation. In ICD recipients, a magnet was applied over the device before the RT session, a cardiologist was always present and the patient was monitored with an external defibrillator.

Results: Thirty-three patients, 21 males and 12 females (67.8±11.5, median age 78 years, underwent RT. Six patients for head-neck, 14 for thorax and 13 for pelvis district cancer. In 3 cases (9%) we had to relocate the device. We observed 2 malfunctions (6%), one PM and one ICD. In the PM patient magnetic frequency was set to 30 beats per minute and in the ICD patient all but shock anti-tachycardia therapies were inactivated. Both malfunctions were successfully treated by reprogramming the device and patients finished their cycle of RT. No session was stopped because of patient’s clinical impairment.

Conclusion: RT in ICD recipients is safe when patients are accurately evalu- ated to prevent drawbacks. In our experience, malfunctions resulted in no danger to patient’s life and were always corrected via telemetry. Our internal protocol proved to be adequate to safely irradiate also patients with ICD.

Success rate and complications of defibrillation testing at the moment of ICD implantation or replacement

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Defibrillation threshold testing at the time of ICD implantation has been performed lately for 10 years to assess proper device function. Recently it has become a matter of debate due to the potential morbidity risk and the uncertainty of its results on long-term outcome. Data on success rates and complications using a standard intraoperative defibrillation testing with contemporary ICDs are scarce. Usually only success rates at the end of implantation are reported, but not all modifica- tions that were necessary to overcome initial failures. 309 consecutive patients with defibrillation testing at implantation and 125 pa- tients at device replacement were studied. Predictors for “failure to defibrillate” were determined. Initial testing level was left to the discretion of the treating electrophysiologist, but 2 successful defibrillations with a 10 Joules safety margin were mandatory. If defibrillation testing failed, additional measures were taken. Mean age of patients was 62.6±13.7 years (implantation) and 65.1±13.1 years (replacement), mean ejection fraction was 32.6±12.7 and 33.5±13.6, respect- ively. In 7/20 (3.3%) patients and 2/125 (1.6%) patients ≥5 cases, defibrillation testing was initially not successful. Measure taken to overcome the problem were: modified shock configuration (4), subcutaneous array (2), high output device (1), new lead/device (1), multiple (1). Cases at implantation defibrillation testing had a significant lower ejection fraction (33% vs. 22%), a higher BMI (30 vs. 27), and were more often on amiodarone (57% vs. 15%), cases at replacement defibrilla- tion testing were significantly younger (26 vs. 66 years), thinner (BMI 19 vs. 27) and had dilated cardiopathy (100% vs. 25%), all p values 0.05-0.01. No severe complications of defibrillation testing (death, increasing heart failure, prolonged hospitalisation) occurred.

With initial failure to defibrillate in 2% of patients, defibrillation testing at the moment of implantation or replacement had a significant impact on immediate patient man- agement. No complications of shock testing were noted. We therefore strongly recommend defibrillation testing in all patients who undergo ICD implantation or replacement.

Transvenous removal of malfunctioning ICD leads: large single center experience

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Introduction: How to manage malfunctioning ICD leads is still a debated issue. The increasing number of implants and the poor performance of some lead mod- els will increase the importance of this topic in the next future. At present the risk/benefit ratio of removal all abandoned ICD leads is unclear, mainly because the risk is supposed to be high. Indications to removal could be probably ex- tended by the availability of effective and safe Transvenous Lead Removal (TLR) techniques. We aim to report our experience in transvenous removal of non in- fected ICD leads.

Methods: Since January 1997 to November 2011, 520 ICD leads (495 ventricu- lar, 9 atrial, 16 superior vena cava leads) were submitted to TLR at our Institution. Among these not infected malfunctioning ventricular leads were 122 (mean im- plant period 48±35 months, range 1-195), implanted in 112 patients (89 men, mean age 53±18 years, range 8-83). System features included almost left side implant period 48±35 months, range 1-159), implanted in 112 patients (89 men, mean age 53±18 years, range 8-83). System features included almost left side

Conclusion: 2. In the present study the most significant factor for SF lead failure was subclavian vein puncture. It means that a combination of weak ICD lead construction and type of venous approach increased the risk of lead failure.

2. An increased type of implanted device and location of lead tip were not the factors that would significantly affect SF ICD lead failure.
were observed. Comparing the easy (“fraction” group) with the complex approach (“tansjugular” group), all baseline patients and lead features resulted comparable (p=NS) with only the exception for the lead implantation time that was statistically longer in the second group (8±3 vs 8±3±2 months, p<0.05).

Conclusions: Our results suggest that in high volume centers, TLR of malfunctioning ICD leads using mechanical dilatation is effective and safe. According to these results the indication to removal could be extended to all of malfunctioning ICD leads.

The survival, efficacy and complications of implantable cardioverter defibrillator therapy in patients with hypertrophic cardiomyopathy

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Purpose: Sudden cardiac death (SCD) occurs in a minority of hypertrophic cardiomyopathy (HCM) patients and can be prevented by an implantable cardioverter defibrillator (ICD). The aim of this study is to evaluate the efficacy and complications of ICDs in HCM patients.

Methods: 73 HCM patients (mean age 51±18 years, 60% male) with an ICD were evaluated. The majority (68%) of ICDs were implanted for primary prevention (presence of known major clinical risk factors (positive family history, symptoms of known SCD, unexplained syncope, abnormal blood pressure response to exercise, left ventricular wall thickness > 30 mm and non-sustained ventricular tachycardia). Endpoints were cardiovascular mortality (SCD and death from cardiac cause), including heart transplantation, first inappropriate ICD shock and first device related complication. Univariate Cox model was used for statistical analyses and variables are expressed as Hazard ratio (HR) with 95% confidence interval.

Results: During a median follow-up of 4.6 years, 1 (1.4%) patient died suddenly after an ICD shock for ventricular fibrillation with restoration of rhythm, but without output. Death from end-stage heart failure occurred in 13 (18%) patients and was associated with NYHA III/IV (HR 4.98 [1.37-18.0] p=0.014), biventricular devices (HR 3.98 [1.07-14.9] p=0.04), atrial fibrillation (HR 4.39 [1.39-13.6] p=0.012) and female gender (HR 4.86 [1.31-18.0] p=0.018). Eleven patients (15%) received inappropriate ICD shocks, which was related to implantation in patients <30 years (HR 6.85 [2.54-20.8] p=0.001) and the presence of ≥3 major clinical risk factors (HR 8.80 [1.46-53.0] p=0.016). Nine patients (12%) received inappropriate ICD shocks and 8 (11%) patients experienced device-related complications (i.e. pocket infections, lead failure or displacement, Dressler’s syndrome and pneumothorax).

Conclusion: ICDs successfully abort life-threatening arrhythmias in 15% of HCM patients; end-stage heart failure is the main cause of cardiovascular mortality. Appropriate ICD shocks were related to implantation in patients <30 years and the presence of ≥3 major clinical risk factors. Almost 20% of patients had inappropriate shocks or device related complications.

Effect of mortality rate on lifespan gain from implantable cardioverter-defibrillators: a real problem?

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Background: Clinicians managing patients with advanced heart failure are advised by guidelines not to implant ICDs on the grounds of assumed lack of lifespan benefit. However, data analysis suggests that patients with more advanced heart failure and a shorter life-expectancy have greater gains in longevity than lower risk patients from an ICD. This contradiction warrants resolution by further clinical trials.

Incidence and predictors of phantom shocks in implantable cardioverter defibrillator recipients

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Purpose: Implantable cardioverter defibrillators (ICDs) are designed to deliver shocks or antitachycardia pacing (ATP) in the event of life-threatening arrhythmias. During follow-up, some ICD recipients experience the sensation of ICD discharge in the absence of an actual discharge (phantom shock).

The aim of this study was to evaluate the incidence and predictors of phantom shocks in ICD recipients.

Methods: Medical records of 629 consecutive patients with ischaemic or dilated cardiomyopathy and prior ICD implantation were studied.

Results: With a mean follow-up of 35 months, phantom shocks were reported by 5.1% of ICD recipients. Median time to shock was 13 months (range 0-43 months). In the primary prevention group, phantom shocks occurred in 25 patients (5.7%) versus 7 patients (3.7%) in the secondary prevention group (p=0.31). In the primary prevention group (n=441), phantom shocks were related to a history of atrial fibrillation (p=0.03) and NYHA class >3 (p=0.05). In the secondary prevention group (n=167), no significant predictors were found. In both primary and secondary prevention group, there was no relation to prior shock therapy.

Conclusion: Phantom shocks occur in approximately 5% of all ICD recipients. In primary prevention patients, a relation with a history of atrial fibrillation and NYHA class below 3 was observed. In the secondary prevention patients, no significant predictors were found.

Dry heart wall perfusion - the new epidemic or better diagnosis of heart failure?

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Increased risk of perforating lead extraction inclined us for attempt to localise tip of lead in relation to epicardium and the commonness of the phenomenon was surprising. The goal: retrospective data analysis of referential centre of transvenous lead extraction (TLE). TEE & TTE and other preoperative findings were analyzed. We have extracted 1718 ingrown leads from 1000 patients; 54 leads presented perforating lead extraction (5.4%).

Results: Indications for TLE: non-infective indication (previously functional lead failure) 47 (87%), pocket infection 3 (5%), lead dependent infective endocarditis 7 (14%), RAA-1 (2%), RAA-2 (3,7%). Perforating lead's model: PM BP 26 (48,2%), ICD HV 1 (2,3%), ICD RV 4 z (7,4%). Non-infective indications for TLE 44 pts): 34/44 (77%) “lead dysfunction” mask; usually pacing/sensing/impedance abnormalities. In 4/11 pts UP – pacing impossible but BP – pacing possible when using higher amplitude (not in all pts test was performed). Impedance - non characteristic changes. In most of pts with ICD leads - transient increase and after gradual drop of potential amplitude, accompanied with increase of pacing threshold; changes of impedance were less characteristic (especially in BP pacing configuration) – but finally rise up to >2000 Ohm noted. In 4 pts typical “sizzles” were noted with inadequate HV therapy. In 14/54 pts there were “normal” P/S conditions in spite evident ECHO picture. Subjective symptoms (in 16/44 only); 9 atypical chest pain, 1 severe epigastric pain, 3 diaphragma pacing, 3 “pacing intolerance”. Most of perforations were asymptomatic for the patient. Perforating lead location: RVA-41 (75,9%), RVOT-22 (40,0%), 12 other sites. It demonstrates usually as “lead dysfunction” mask (77%) but in remaining pts is asymptomatic.

Is the subxiphoidial pacemaker with epicardial lead a safe therapy for pacemaker dependent patients after device explantation due to infection?

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Introduction: With the increasing number of device implantations in patients with high comorbidity the number of device-related infections has been growing in the last several years. Device-related infections are a serious and life threatening complication after pacemaker and ICD implantation. Both diagnosis and treatment of such infections pose a big problem in tertiary care centers. A subxiphoidally implanted pacemaker with an epicardial lead is an option for bridging pacemaker dependent patients after device and lead explantation.

Method: We examined retrospectively 68 consecutive patients (Ø 71±14 years; 16 v., 52 m) who were referred to us with a device related-infection (pocket infec-
An alternative implantation technique for the electrode of the fully subcutaneous internal cardioverter defibrillator (S-ICD): the sheath facilitated technique

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Introduction: The electrode of the S-ICD is implanted by making three incisions, one lateral pocket incision and two parasternal incisions; the electrode is then tunneled through these incisions to a parasternal position. In our experience these parasternal incisions are a possible risk for infection and a potential source of discomfort. We present an alternative technique of implanting the S-ICD electrode avoiding the distal incision and suture.

Methods: In our approach we tunnel the electrode, conform the current technique, with the tunneling tool from the lateral pocket to the proximal parasternal incision. We now place an 11 F peel-away sheath, for transvenous lead placement, over the tunnelling tool and tunnel this sheath subcutaneously to a distal position. No distal suture is used. After manually confirming correct placement the electrode (Medtronic 4968 bipolar steroid CapsureEpi Fri 8.0) was implanted by a exitblock. The re-implantation was carried out 67±10 days after implantation of a subxiphaloid pacemaker with epicardial lead.

Results: A total of 39 patients (53%) re-implantation with a transvenous system was performed during follow up. Only three patients (4%) needed an early re-implantation due to an exitblock. The re-implantation was carried out 67±10 days after implantation of a subxiphaloid pacemaker with epicardial lead.

Conclusion: Providing pacemaker dependent patients with a subxiphaloid pacemaker with epicardial lead before device explantation due to infection is the only possibility for bridging these patients. Epicardial leads in an interdisciplinary approach are a secure form for a longer period. In comparison with transvenous electrodes modified threshold characteristics require an adapted follow-up.
Inappropriate therapy rates are higher in female ICD recipients due to differences in underlying aetiology.

Methods: A retrospective audit of our University Hospital’s ICD service included analysis of Ix in 570 patients with ICD devices (implanted 03/01/06 to 25/06/2010). Data on ICD indication aetiology was grouped into ischaemic heart disease (286, IHD), diastolic cardiomyopathy (87, DCM) and other (97). Results: During median follow up of 1.91 years (IQR 2.0 years), 43% of patients received a total of 501 Ix. There were no gender differences in mortality and rate of appropriate ICD therapy. Figure 1: Women (105/570, 18%) had significantly higher incidence of Ix than men (χ², p = 0.001). Atrial fibrillation was the most common reason for first Ix (38/70, 54%), no gender differences were seen in frequency of AF (χ², p = 0.8). Infarct size and heterogeneity could influence the occurrence of sudden cardiac death (SCD) or malignant ventricular arrhythmias (VT/VF). The predictive value of infarct tissue heterogeneity in contrast-enhanced MRI on the occurrence of VT/VF or cardiac death was analyzed. Prospectively, 30 consecutive patients (aged 63±6 years) with previous myocardial infarction (>40 days, mean 24 months), qualified for implantable cardioverter-defibrillator (ICD) as primary prevention of SCD were enrolled. Cine MRI to evaluate left ventricular volumes and ejection fraction as well as contrast-enhanced MRI for characterization of scar tissue (infarct zone) as a measure of infarct tissue heterogeneity, infarct core, and total infarct size were performed. ICD was implanted in 29 patients and during follow-up of 18.6±3.6 months 1 patient died suddenly and 4 patients experienced appropriate ICD therapy. The total infarct size (79.7±13.3% vs 47.0±18.3% g, P = 0.0078) and infarct core (70.0±13.9 g vs 39.6±17.0 g, P = 0.008) were significantly bigger in end point (+) patients. Multivariable Cox proportional hazards analysis revealed that infarct gray zone was the strongest predictor of the occurrence of VT/VF treated by ICD or cardiac death (HR, 1.71/10 g; CI, 1.03 to 2.36; P = 0.03). Infarct tissue heterogeneity on contrast-enhanced MRI is the strongest predictor of spontaneous ventricular arrhythmias treated by ICD or cardiac death among other clinical and MRI variables.

Conclusion: The apparently higher rate of Ix in female patients appears to be due to differences in underlying aetiology.
ple countries and practices. Despite the routine use of revascularization and re-
commended medical therapies, a significant minority of patients have persistent LV
disfunction that may warrant alteration in medical therapy or referral for an ICD.
Ongoing quality assurance projects are assessing the prognostic significance of post-MI UEF values and the frequency of actionable data as alterations in medical
treatment or referral for an ICD.

Rhythm recovery in patients with permanent pacemaker after cardiac surgery.
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Background: Conduction disturbances requiring permanent pacemaker (PM) im-
plantation after cardiac surgery occur in 1-3% of patients. Our aim was to assess the association between the rhythm in the baseline ECG and the long term rhythm recovery probability, among patients submitted to permanent PM implantation af-
ter cardiac surgery.

Methods: We conducted a cross-sectional study of all consecutive patients sub-
mited to permanent PM after cardiac surgery between January 2004 and De-
cember 2010 (seven years). Absence of rhythm recovery (of sinus rhythm or atrial arrhythmia with appropriate ventricular frequency) was defined as needing pacemaker therapy. Long-term patients who had a formal indication for use of a pacing system were included in our implantation before the surgery and those who had implanted the device 60 days or more after surgery were excluded. The association between baseline variables and rhythm recovery was estimated through odds ratio (OR). Logistic regression was used in multivariate analysis.

Results: One hundred and fifteen patients (mean age 64.9±12.7 years old) were submitted to permanent PM implantation (10.5±6.0 days after surgery), due to complete atioventricular block (87.8%), slow atrial arrhythmia (8.7%) and other atioventricular conduction disturbances (3.5%). The baseline ECG (previous to surgery) showed sinus rhythm in 69.6% and atrial fibrillation in 28.7% of the pa-
tients, implantation, developed late complete AVB, five of them had developed sinus rhythm and 19.1% with baseline atrial fibrillation) of the patients did not recover the rhythm. The risk of no long term rhythm recovery was almost 7-fold higher in patients with complete AVB than in patients with isolated AVNRT (OR 6.94; 95%CI: 1.31-34.98). This risk was also higher for patients submitted to aortic mechanic valve replacement (OR 3.05; 95%CI: 1.1-8.3), in those with previous myocardial infarction (OR 1.21; 95%CI 1.19-1.36) and in those with higher mean surgery duration (321.4±129.7 vs 274.4±86.3, p=0.003). The aetiology of valvular dis-
ease was another factor influencing recovery probability (p=0.003). After adjust-
ing, atrial fibrillation was still associated with a higher probability of long-term rhythm recovery (adjusted OR 3.04; 95%CI:1.20-7.77).

Conclusion: A great proportion of patients submitted to permanent PM implan-
tation after cardiac surgery recover rhythm during the follow up. Baseline atrial arrhythmia provided an increase in the probability of recovery. This might sug-
gest that patients with atrial fibrillation may benefit from a longer waiting time before permanent PM implantation.

Conduction disorders in transcatheter aortic valve implantation: which patients for permanent pacemaker implantation?
S. Conti, G.P. Pruili, D. Tempio, S.A. Romano, A. Di Grazia, G.P. Ussia, C. Tamburino, V. Calvi. University of Catania, Ferrarotta Hospital. Division of Cardiology, Catania, Italy

Purpose: Conduction disorders (CD) and permanent pacemaker (PPM) implan-
tation are common complications in patients undergoing transcatheter aortic valve implantation (TAVI). Purpose of the study was to identify which patients will un-
dergo PPM implantation after TAVI.

Methods: Data were analyzed from 233 consecutive patients at high-risk surgery who underwent TAVI at our institute between June 2007 and December 2011. Two hundred and four patients received the CoreValve (CV) prosthesis and 27 patients received the Edwards Sapien (ES) prosthesis. Twenty-seven (11.6%) patients were excluded from the analysis because of prior PPM (n=24, 10.3%), unsuccessful implant of the prosthesis (n=2, 0.8%), intra-procedural death (n=1, 0.4%). Finally 206 patients (CV n=185, 90%; ES n=21, 10%) were included in our analysis. In all patients a 24-hour ambulatory electrocardiogram was recorded before and after the procedure in order to assess the presence of CD. Factors tested as potentially related to develop of complete atrioventricular block (AVB) included clinical condition, prior CD, echocardiographic pattern and procedural factors evaluated using angiographic techniques.

Results: Left bundle branch block (LBBB) was the most common CD noted, with an incidence of 34.5% (CV n=68, 38.6%; ES n=3, 14.3%). During hospital stay, 40 (19.4%) patients developed a transient complete AVB, while 9 patients (4.3%) developed a transient complete AVB. Nine patients undergoing CV pros-
thesis implantation, developed late complete AVB. Twenty-seven (11.6%) patients had developed a post-procedural LBBB. A PPM was implanted in all cases (n=58, 28%). Only pre-
operative right bundle branch block (RBBB) resulted an independent predictor of PPM implantation (HR 16.5, 95% CI 3.2-83.2, p<0.001).

Conclusion: If RBBB is a well-established predictor of PPM implantation after TAVI, especially using CV prosthesis, intra-procedural transient AVB and new or-
old of LBBB after TAVI are poorly defended complications. Patients with LBBB would seem more likely to develop late complete AVB and for this reason should be closely monitored during follow-up.

Left bundle branch block occurring after transcatheter aortic valve implantation: what is the prognosis significance?
G.P. Pruili, S. Conti, D. Tempio, S.A. Romano, A. Di Grazia, G.P. Ussia, C. Tamburino, V. Calvi. Ferrarotta Hospital - Institute for Cardiology, Division of Cardiovascular, Catania, Italy

Purpose: Left bundle branch block (LBBB) is the most common conduction dis-
order (CD) occurring after transcatheter aortic valve implantation (TAVI), especially with the use of CoreValve® prosthesis. The onset of this disorder is a conse-
quence of anatomic relationship between aortic valve and conduction system and might be related to a direct compression of left bundle branch due to the prosth-
esis expansion. In patients submitted to aortic surgery, LBBB has been associated with more frequent adverse outcomes, including permanent pacing and sudden cardiac death, but the clinical significance in patient who underwent TAVI has not been investigated.

The aim of our study was to evaluate the prognostic value of new onset LBBB in patients who underwent TAVI in order to assess whether a “prophylactic” pacing should be carefully evaluated.

Diana study on pacemaker diagnostics: an analysis of 3709 pacemaker follow ups
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Purpose: Current implantable pacemakers provide a large quantity of diagnostic data both of the pacing system integrity and the patient’s health status, providing a valuable contribution to the long term treatment.

The DIANA observational study (Diagnostic Functions in Pacemakers and How They Influence Medical Decisions) assesses the impact of pacemaker derived data on normal clinical practice over 24 months.

Methods and Results: 1103 patients with an indication for dual chamber pace-
maker therapy according to European guideline have been enrolled from Dec. 2006 until Dec. 2008. All patients with implanted Medtronic or Vitatron pacemaker models were eligible for inclusion. This analysis assesses implantation- and fol-
low up data over 2 years post implantation. The mean age at enrollment was 73,7±9,8 years, about 56% male patients. Primary pacemaker indications were sinus node dysfunction (SND) in 51%, AV-Block (AVB) in 40% and other (e.g. carotis sinus syndrome) in 9%.

The total number of assessed follow ups was 3709 derived from 1103 patients. The mean follow-up period was 1.7 years with an average duration of the single follow-ups being 10.6±11.2min (range from 2 min to 200min), no irre-
relevant neither patient related nor pacing system related occurred in 62% of all follow ups (69% in AVB patients; 57% in SND patients). Technical observations (elevated pacing thresholds or sensing issues) occurred in 6% of all follow ups with no differences between the different indication groups. All irregularities were unexpected. Patient related observations (e.g. tachyarrhythmic events) as docu-
mented by the device occurred in 23%, atrial arrhythmias occurred in 17% of AVB patients and 27% of SND patients. Technical issues required medical actions in Implanted cardioverter-defibrillators and pacemakers: selection and follow-up 545
90% of all cases (reprogramming, intervention), 55% of all medical observations caused changes in medical treatment.

**Conclusion:** Pacemaker diagnostics are an useful tool to optimize medical care for pacemaker patients who may be at increased risk. Physicians should be aware of the issues that may occur with pacing systems related to changes in patient management.

**Material and Methods:** We carried out a multicenter survey in 8 French centers from January 2012 to January 2011. In each center, patients received usual imaging tests. The results of our study highlight patients' misconceptions on life with a pacemaker. This could be done in an outpatient setting.

**Conclusions:** OAC can be safely interrupted using a LWMH as a bridging therapy before pacing procedures, including patients with mechanical prosthetic valves. This could be done in an outpatient setting.
year mortality for patients with and without CTO was 13.3±3.1% and 5.1±0.8%, p<0.001. HR (95%CI) for 3-year mortality for patients with CTO vs. patients without CTO was 1.96 (1.43-2.69), p<0.001. HR after adjustment for logistic EuroSCORE was 1.81 (1.32-2.50), p<0.001. After additional adjustment for SYNTAX score a significant impact of CTO on 3-year mortality was no longer detectable (HR: 1.29 [0.91-1.84], p=0.15).

Conclusion: In cohort with LM or 3VD and elective PCI patients with CTO have a higher long-term mortality compared to patients with non-occlusive lesions. To large extent, the prognostic impact of CTO was represented by the SYNTAX-Score, which together with logistic EuroSCORE yields significant additional prognostic information. There was a non-significant trend for improved survival after successful CTO recanalisation.

Prognostic value of SYNTAX score and logistic EuroScore in predicting outcome after elective percutaneous coronary intervention for left main stenosis or triple vessel disease

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Background: In patients undergoing percutaneous coronary intervention (PCI) for left main disease (LMD) or triple vessel disease (TVD), the SYNTAX trial revealed increased mortality with increased complexity of coronary anatomy as judged by tertiles of SYNTAX score (SYNS). 3, 23, 32, 33). But in the trend of progression anatomical complexity and also clinical risk factors need to be considered. The logistic EuroScore (lES) is an accepted tool to assess the risk of patients undergoing surgical coronary revascularization. The relative contribution of the SYNS and of the lES to the prediction of survival after PCI with drug eluting stents (DES) is currently unclear. Objectives: A large group of patients undergoing PCI with CAD and TVD or CTO with SYNS (LMD) and lES was used to test the hypothesis that SYNS and lES independently predict of long-term outcome.

Methods: We interrogated our clinical data base for patients having undergone elective PCI with DES for LMS or TVD. Exclusion criteria were previous CABG, high-risk ACS including acute MI. We calculated SYNS and lES. Survival was assessed by systematic patient contacts at 30 days, at one and at three years. We used the Kaplan-Meier method to estimate survival in three strata of SYNS. In addition, we calculated hazard ratios (HR) by Cox models with and without adjustment for lES.

Results: We identified 1262 patients who met the entry criteria. Mean age was 68±10 years, 24% of the patients were female. Median follow up (interquartile range) was 1120 (985–1321) days. Median SYNS was 20 (15–27), median lES 2.5 (1.4–5.0). A low SYNS (-22) was present in 714 (56.6%) patients, an intermediate SYNS (3, 23, 32, 33) was present in 143 (11.3%) patients. Three-year mortality was 4.3±0.8% with SYNS <23, 11.1±1.6% with SYNS 23–32, and 19.5±3.5% with SYNS >32 (p<0.001). Compared to the group with the lowest SYNS, the HR (95%-confidence interval) for mortality in the group with the intermediate SYNS was 2.03 (1.41–2.93, p<0.001) and 3.17 (2.07–4.86, p<0.001) for the group with the highest SYNS. After adjustment for lES the HR was 2.08 (1.62–2.67, p<0.001) and 3.01 (1.96–4.26, p<0.001), respectively. Comparing tertiles of lES, the HR for all-cause death adjusted for SYNS was 1.62 (0.89–2.92, p=0.001) comparing the lowest with the highest tertile, and 5.67 (3.39–9.51, p<0.001) comparing the lowest tertile with the highest tertile.

Conclusions: In this large single centre experience, we show that SYNs and lES independently were highly predictive for 3-year mortality after PCI for LMS or TVD. When counseling patients, both risk scores deserve consideration.

Complete revascularization for chronic total occlusion improves survival prognosis

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Objective: We examined whether incomplete revascularization for CTO was associated with poor survival prognosis.

Methods: In a consecutive cohort of 382 patients with CTO were divided into the 2 groups (complete revascularization group [CRG]: 221 patients who successfully underwent surgical or percutaneous revascularization for all of the CTO and incomplete revascularization group [IRC]: 161 patients who had at least one CTO treated medically). 32 patients with CTOs originating from side branches and distal portion of main branches were excluded from this study.

Results: In baseline patients characteristics were shown in the table. Cumulative incidence of all-cause death were shown in the figure. The adjusted risk of IR relative to CRG was still significant (HR: 2.47; 95% CI: 1.15-5.33; p=0.021). Baseline patient characteristics

<table>
<thead>
<tr>
<th>CR group</th>
<th>IR group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>68±10.4</td>
</tr>
<tr>
<td>DM</td>
<td>90 (40%)</td>
</tr>
<tr>
<td>uGFR &lt;30</td>
<td>9 (4%)</td>
</tr>
<tr>
<td>1VD</td>
<td>74 (33%)</td>
</tr>
<tr>
<td>3VD</td>
<td>78 (35%)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>44 (20%)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>29 (13%)</td>
</tr>
</tbody>
</table>

Results: In baseline patients characteristics were shown in the table. Cumulative incidence of all-cause death were shown in the figure. The adjusted risk of IR relative to CRG was still significant (HR: 2.47; 95% CI: 1.15-5.33; p=0.021).

Conclusion: The addition of clinical risk scores (EuroSCORE and STS score) to the Syntax Score improves mortality prediction in the Syntax intermediate risk group.

Addition of Two Risk Assessment Scales for Cardiac Surgery (EuroScore and STS) to the SYNTAX Score to Predict Early Mortality and Major Vascular Events in Patients with unprotected left main coronary

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Introduction: The left main coronary artery disease is more complex to predict early mortality and MACE because patients usually present with higher morbidity and mortality. The combination of combinatory assessment scales (EuroScore and STS) to the SYNTAX score could better predict early mortality and MACE.

Objective: To evaluate the predictive power of early mortality and major cardiovascular events of the SYNTAX score combined with EuroScore and STS scales. Describe the differences in clinical outcomes in patients with left main coronary artery trunk underwent surgical revascularization, percutaneous, and medical treatment.

Methods: We included adult patients with de novo left main coronary artery and chronic stable angina, subject to revascularization (PCI or surgical) or Medical Treatment Between May 2010 and August 2011, 1177 patients were referred to the cathlab of whom 109 (9.2%) had significant de novo LMC disease. We retrospectively reviewed the medical records of patients covered the selection criteria with 12 months of follow up.

Results: Among the medical treatment groups (n = 23), surgical (n = 58) and percutaneous (28) predominated in males (p = NS). According to the treatment group, patients with CTO was found in 43%, 48% and 50% (p = NS) hypertension: 73%, 77% and 85% (p = NS), dyslipidemia: 52%, 72% and 82% (p = NS), chronic renal failure: 34%, 27% and 21% (p = NS). Eighty-seven percent of medically treated patients also had two or more vessel disease, 75% in the surgical and 45% in the PCI. In all three groups, more than half of patients had ejection fraction of left ventricle preserved. The syntax average of the group medical, surgical and percutaneous was respectively: 28.8 ± 7.8, 27.3 ± 7.0 and 25.1 ± 8.6 (p = NS), the EuroSCORE: 8.1 ± 6.5, 7.1 ± 6.1 and 7.4 ± 5.4 (p = NS) respectively; STS: 16 ± 7.7, 13 ± 7.0 and 12 ± 6.3 (p = NS) respectively. Mortality was higher in patients who underwent surgical revascularization with intermediate Syntax and EuroSCORE and STS high (12.2%); as well in the medical treatment group with Syntax and EuroSCORE and STS high (17.3%). The mortality in patients undergoing PCI with high and intermediate Syntax with high EuroSCORE and STS was 3.5%.

Conclusion: The addition of clinical risk scores (EuroSCORE and STS score) to the Syntax Score improves mortality prediction in the Syntax intermediate risk group.

Combination of angiographic and clinical characteristics for the prediction of clinical outcomes in elderly patients undergoing multivessel PCI

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Background: Risk stratification is essential for the clinical decision-making process in elderly patients undergoing multi-vessel (MV) revascularization.

Objectives: To assess the prognostic value of angiographic versus clinical characteristics for the prediction of major adverse cardiac and cerebrovascular events (MACCE: all-cause mortality, non-fatal myocardial infarction, stroke, and target lesion revascularization).

Introduction: The left main coronary artery disease is more complex to predict early mortality and MACE because patients usually present with higher morbidity and mortality. The combination of combinatory assessment scales (EuroScore and STS) to the SYNTAX score could better predict early mortality and MACE.

Objective: To evaluate the predictive power of early mortality and major cardiovascular events of the SYNTAX score combined with EuroScore and STS scales. Describe the differences in clinical outcomes in patients with left main coronary artery trunk underwent surgical revascularization, percutaneous, and medical treatment.

Methods: We included adult patients with de novo left main coronary artery and chronic stable angina, subject to revascularization (PCI or surgical) or Medical
Survival after percutaneous coronary intervention
Seven-year prognosis of patients with functionally moderate coronary artery stenosis after deferral of revascularization based on fractional flow reserve

Methods: In 328 elderly patients ≥70 years, who were followed up for a first MACCE after MV-PCI, SYNTAX score and EuroScore have been calculated for a combined risk model.

Results: 328 patients (age range 70-95) were followed up for 2.7±1.5 years (Follow-up rate: 97.9%). 42.7% (140/328) of the patients presented with acute coronary syndrome (ACS). At 3 years after MV-PCI, a first MACCE occurred in 50.6% (164/328) of the patients. Baseline SYNTAX score (32.9±14.7 vs. 27.8±13.3; P<0.001) and logistic EuroScore (6.3 [3.6/13.1] vs. 9.0 [5.8/14.4]; P<0.001) were significantly increased in survivors with MACCE during follow-up. To improve the predictive ability of both scores, we developed a combined risk score model with ROC curve validated cut-off values for EuroScore (<5%) and SYNTAX Score (>25). Thus, we were able to stratify the patients in a low, medium, and high risk group with a 3-year MACCE rate of 23.1%, 47.2%, and 62.1%, respectively (P<0.001). High risk patients had a 3.5-fold higher risk for MACCE after 3 years (HR 3.5, 95% CI: 1.9-6.5; P<0.001).

Conclusions: For adequate risk assessment in elderly patients undergoing MV-PCI, consideration of both - comorbidities and coronary anatomic complexity - is essential. A combination of angiographic and clinical risk scores improves the prognostic value and is superior to stand-alone scores in elderly patients.

Survival after percutaneous coronary intervention (PCI): Comparison of left main disease and triple vessel disease

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Background: Left main disease (LMD) is considered as a contraindication for percutaneous coronary intervention (PCI) for a long time. Results from recent registries and randomized studies challenged this verdict. It is still unclear if the risk of PCI for left main disease (LMD) exceeds the risk of PCI for triple vessel disease (TVD) in the era of drug-eluting stents (DES). In the current study we aimed to test if the 3-year mortality after PCI in patients with LMD is higher than in patients with TVD without LMD.

Methods: Patients undergoing elective PCI with DES for LMD or TVD have been included in this cohort study. Important exclusion criteria were previous coronary artery bypass surgery, high-risk acute coronary syndrome including myocardial infarction. All-cause death was the primary endpoint of this analysis. Survival of the patients was assessed by systematic patient contacts after 30 days, at one year and at three years. In all patients we calculated SYNTAX score to define the anatomic complexity of coronary artery disease and logistic EuroScore to determine the clinical risk. We used the Kaplan-Meier method to estimate three year mortality. In addition, we calculated adjusted and unadjusted hazard ratios by Cox models.

Results: We identified 1262 patients who met the entry criteria. Mean age was 68±10 years, 24% of the patients were female. Median follow up (interquartile range) was 1120 (985 – 1321) days. Median SYNTAX score was 20 (15 – 27), median logistic EuroScore 2.5 (1.4 – 5.0). LMD with or without involvement of other coronary arteries was present in 135 patients (10.7%). 1127 patients (89.3%) were evaluated during 7-year follow-up. The all kinds of adverse cardiac events occurred in 15 patients (27%) in group I and 23 (35%) in group II (P=0.08). Cardiac death, myocardial infarction, and revascularization for FFR-measured artery occurred in 3 patients (6%) in group I and 10 (15%) in group II (P=0.08).

Conclusions: For adequate risk assessment in elderly patients undergoing MV-PCI, consideration of both - comorbidities and coronary anatomic complexity - is essential. A combination of angiographic and clinical risk scores improves the prognostic value and is superior to stand-alone scores in elderly patients.

Long-term outcome of patients after percutaneous coronary intervention compared to outcome in patients with functionally moderate coronary artery stenosis after deferral of revascularization based on fractional flow reserve

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Purpose: FFR range between 0.75 and 0.80 is known as a gray zone. Although the value of 0.80 has been often adopted as the cut-off value of revascularization in patients with functionally moderate coronary stenosis whose FFR values were between 0.75 and 0.80 was unclear. The purpose of this study was to investigate the long-term prognosis in patients with functionally moderate coronary stenosis (FFR value was between 0.75 and 0.80).

Methods: Consecutive 120 patients (age 63±9 years, male/female=101/19), in whom revascularization was deferred based on FFR value between 0.75 and 0.85, were divided into 2 groups: FFR value ≥0.75 and <0.80 (group I, n=65) and ≥0.81 and <0.85 (group II, n=65). All kinds of adverse cardiac events, including cardiac death, myocardial infarction, revascularization for FFR-measured artery and remote one, congestive heart failure and admission for chest pain, were evaluated during 7-year follow-up.

Results: The all kinds of adverse cardiac events occurred in 15 patients (27%) in group I and 23 (35%) in group II (P=0.08). Cardiac death, myocardial infarction, and revascularization for FFR-measured artery occurred in 3 patients (6%) in group I and 10 (15%) in group II (P=0.08).

Conclusions: The incidence of adverse cardiac events related FFR-measured artery in patients with functionally moderate coronary stenosis was low. Long-term prognosis of moderate coronary stenosis with gray zone FFR value was considered to be good.
graphic characteristics were performed using the Wilcoxon rank test and Fisher’s exact test. Cumulative incidences were estimated by time-to-event data. Propensity score matching was applied to compare TAT with 2 identical DAPT study groups (n=116 each) based on their baseline and angiographic characteristics. The number needed to harm (NNH) was calculated to indicate potential detrimental effects of TAT.

Results: Patients treated with TAT showed markedly increased rates of major bleeding compared to DAPT (TAT vs DAPT: 3.2%, p<0.001). During a 3 year follow-up period after PCI, in the TAT group, we observed 17 overall (cardiac and non-cardiac) deaths compared with 11 in the short-term DAPT and 2 deaths in the long-term DAPT group, respectively (p=0.004). Pairwise comparisons showed that TAT had a significant disadvantage concerning occurrence of either death or major bleeding (TAT versus DAPT: p=0.034, NNH: 13; TAT versus DAPT > 4 years: p<0.001, NNH: 6).

Conclusion: Patients on TAT after PCI experience more major bleeding complications and reduced survival rates compared with patients on DAPT after 3 years. Further randomized mortality trials should be conducted to determine the long-term safety aspects of TAT. NCT 00950008.

**P3294**

One year outcomes with abciximab and unfractionated heparin vs. bivalirudin during Percutaneous Coronary Interventions in patients with non-ST-Segment Elevation Myocardial Infarction

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One Year Outcomes with Abciximab And Unfractionated Heparin vs. Bivalirudin During Percutaneous Coronary Interventions in Patients With Non-ST-Segment Elevation Myocardial Infarction: Updated Results from ISAR-REACT 4

Background: Three-day results of the ISAR-REACT 4 trial showed that abciximab and heparin do not improve net clinical benefit but increase the risk of bleeding compared to bivalirudin in patients with non-ST-segment elevation myocardial infarction (NSTEMI) undergoing percutaneous coronary interventions (PCI). However, the 30-day period might not be long enough to assess the whole potential benefit of a certain drug. Complications such as periprocedural myocardial infarction and bleeding that are affected by the antithrombotic drugs may have an impact on long term prognosis.

Methods: This randomized, double-blind study included 1721 patients with acute non-ST-segment elevation myocardial infarction who underwent a percutaneous coronary intervention were enrolled. 861 patients were assigned to abciximab and unfractionated heparin and 860 patients were assigned to bivalirudin. Aim of the present analysis is to evaluate one-year outcomes particularly in terms of mortality.

Results: Results will be available in May 2012 and will help to better establish the role of these therapies in patients with NSTEMI treated with PCI.

**P3296**

Bleeding complications in diabetic patients treated with long-term (6 years) antiplatelet treatment following DES implantation; comparison to patients on single antiplatelet treatment

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Background: Diabetes mellitus has been associated with an increased risk of mortality and stent thrombosis after implantation of drug-eluting stents (DES) thus, dual antiplatelet treatment (DAPT) for at least 12 months is recommended after DES implantation. Uncertainty exists about the frequency, correlates, and clinical significance of bleeding with DAPT, particularly over an extended period of use.

Methods: We assessed 610 consecutive DM pts (male 80%, mean age 65±9 years) after DES implantation. Long-term (5 years) clinical follow-up (FU), obtained in 587/610 (96%) of them. At the end of FU, 211 (36%) pts were on single APLT (SAPLT) and 376 (64%) on DAPT. Bleeding complications were defined according to PLATO and TIMI definitions.

Results: The incidence of bleeding was higher in DAPT patients (14.6% vs. 3.8%; p<0.0001). Minor bleeding according to PLATO occurred in 1.9% of pts on SAPLT and 11.7% on DAPT (p<0.0001) and according to TIMI in 2.4% vs 13.6% respectively (p<0.0001). Major bleeding according to PLATO presented the 1.9% of patients on SAPLT and 2.9% on DAPT; according to TIMI the incidence of major bleeding was 1.4% and 1.1% respectively (p=NS for both PLATO and TIMI definitions). Cardiovascular adverse events were not more frequent observed in patients with bleeding as compared with those without bleeding. In a multivariable analysis, smoking was an independent predictor for overall as well as major bleeding according to PLATO (HR 6.2, 95% CI 1.2-30.4, p=0.024), whereas DAPT was an independent predictor for overall and minor bleeding (HR 6.2, 95% CI 2.2-17.3, p<0.0001).

Conclusion: Long-term DAPT in diabetic patients treated with DES is associated with higher risk of overall and minor but not major bleeding. Smoking was an independent predictor for overall bleeding and major bleeding according to PLATO definitions.

**P3297**

Synergistic effect of thrombus aspiration and glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention

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Thrombus aspiration (TA) has shown beneficial effect in patients (pts) with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI). Yet, due to the high rate of glycoprotein IIb/IIIa inhibitors administered in these pts, the real contribution of adjunctive TA by itself to the improvement of patients’ prognosis is difficult to evaluate. Aim of the present study is to assess the prognostic impact of manual thrombus aspiration (TA), Abciximab (GPI), and combined TA-GPI in STEMI pts treated with pPCI.

Methods and results: From January 2006 to December 2008, 644 STEMI patients treated with pPCI were consecutively enrolled at 2 centers. Depending upon treatment strategy, patients were divided into 4 groups: 1) conventional pPCI (Control group); 2) pPCI with GPI infusion (GPI group); 3) pPCI with TA (TA group); 4) pPCI-GPI group (Primary TA). TA was used in major adverse cardiovascular events (MACE) at 1-year follow-up. MACE was the composite of overall death, myocardial infarction, target vessel revascularization, and major bleedings. Angiographic parameters of coronary reperfusion were also assessed. Clinical characteristics and ischemic time were not significantly different between groups.

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lower rate of no-reflow (p = 0.001). MACE at one year were as follows: 43 (29%) in Control group vs. 25 (22%) in GPI group vs. 24 (19%) in TA group vs. 32 (13%) in TA-GPI group (p < 0.001). At the adjusted Cox regression analysis, combined TA-GPI strategy was significantly associated with lower MACE rate (HR 0.63, 95% CI 0.40-0.98, p = 0.041). Age (HR 1.03, CI 95% 1.01-1.05, p < 0.01) and chronic renal failure (HR 1.26, CI 95% 1.06-1.50, p = 0.01) were both significantly associated with worse 1-year clinical outcomes.

Conclusion: Mechanical TA during pPCI exerts a synergistic effect with Abciximab in improving post-procedural coronary reperfusion and 1-year clinical outcomes.

Purpose: Stent thrombosis is a fatal complication of percutaneous coronary intervention (PCI). However, there is no data available on the long-term outcomes of patients with stent thrombosis. We compared the long-term clinical outcomes of patients with stent thrombosis (EST), late stent thrombosis (LST), and very late stent thrombosis (VLST) after drug-eluting stent (DES) and bare-metal stent (BMS) implantations.

Methods: We identified 147 patients who had undergone PCI for stent thrombosis from January 2001 to October 2011. Stent thrombosis was defined as definite stent thrombosis according to the Academic Research Consortium definition. Major adverse cardiac events (MACE) were defined as a composite of all-cause death, non-fatal myocardial infarction, and target lesion revascularization.

Results: PCI was performed in 55 patients for EST (BMS 31, DES 24), 32 for LST (BMS 22, DES 10), and 60 for VLST (BMS 33, DES 28). The median follow-up duration was 1599 days (interquartile range 609 to 1947 days). The figures show the 5-year MACE-free rate in patients with DES, with the corresponding data for EST and LST (EST vs. VLST, p < 0.001; LST vs. VLST, P < 0.001), but not significantly different between DES and BMS implantations.

Conclusions: Our data show the long-term outcomes were significantly better in patients with VLST than in those with EST and LST whether after DES or BMS implantation.

Late thrombosis after double versus single drug-eluting stent in the treatment of coronary bifurcations: a meta-analysis of randomized and observational studies

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Purpose: Currently available randomized controlled trials (RCT) have been inconclusive in the choice between a strategy of single drug-eluting stent (DES) with provisional stenting (SDS) and a routine double DES strategy (DDS) to identify the optimal strategy for percutaneous coronary interventions (PCI). Meta-analyses have shown an increased risk of myocardial infarction (MI) in the DDS group, without identifying the underlying mechanism(s). We hypothesized that the higher MI risk with the DDS strategy is driven by an increased rate of DES thrombosis.

Methods: We performed a meta-analysis of 12 “major” (>100 patients) studies of bifurcation stenting: 5 RCT and 7 non-randomized observational studies (nROS), for a total of 6,961 patients. We assessed the relative risk (RR) and 95% confidence intervals (CI) of death, MI, and target vessel revascularization (TVR), along with the MI ROC from DES thrombosis – according to the “defined” criteria of the Academic Research Consortium (ARC).

Results: Compared with a SDS, a DDS had similar mortality (RR=1.19; 95% CI: 0.85-1.65) and TVR (RR=1.00; 95% CI: 0.82-1.21), but an increased risk of MI (RR=1.15; 95% CI: 1.10-1.20) and DES thrombosis (RR=2.25; 95% CI 1.41-3.70). Despite inclusion of both RCT and nROS, Cochrane Q chi2 test and I2 statistics showed neither significant heterogeneity among studies nor significant publication bias. Subgroup analysis – here performed despite the absence of heterogeneity – showed that the significantly increased risk of DES thrombosis with DDS was limited to nROS (RR=2.34; 95% CI: 1.35-4.00), as ROC showed only a trend in this direction (RR= 2.17; 95% CI: 0.93-5.02).

Conclusions: In PCI of coronary bifurcations, DES implantation in the main branch – with provisional stenting of the side branch only if necessary – should be the preferred approach, as the routine deposition of DES in both branches is associated with an increased risk of MI, associated also with (and – our inference – likely caused by) DES thrombosis. Because of this likely causal association, when double DES has to be performed aggressive and prolonged dual antiplatelet therapy should be recommended.

Prior coronary artery bypass graft patients treated with primary percutaneous coronary intervention have higher long-term adverse event rates


Background: Limited information exists regarding procedural success and clinical outcomes of ST-segment elevation myocardial infarction (STEMI) patients with previous CABG undergoing primary PCI. We compared outcomes in STEMI patients undergoing primary percutaneous coronary intervention (PCI) with or without previous CABG.

Methods: Clinical information was analysed from a prospective database on 2322 STEMI patients who underwent primary PCI between January 2004 and May 2010 at a London centre. 104 of 2,322 (4.5%) patients had prior CABG. MACE was defined as a composite of death, stroke, and target vessel revascularization.
**Results:** Patients with previous CABG were older, had more associated comorbidities and higher incidence of multivessel coronary disease. In patients with previous CABG, the infant related artery (IRA) was split evenly between bypass graft (n=50) and native vessel (n=54). Procedural success (TIMI 3 flow) was less likely in patients with previous CABG (IRA 84.5% vs 95.6%; p=0.0001) in patients who had never undergone CABG. Patients with previous CABG had more MACE (32.8% vs 16.5%; p=0.01) during the 4-year follow-up period. After multivariable adjustment, 2% difference persisted (hazard ratio: 2.2; 95% confidence interval: 1.26 to 3.78; p = 0.02). When stratifying prior CABG patients by the type of IRA long term MACE were significant more likely in patients who had bypass graft PCI than in patients that had native vessel PCI (44.6% vs 19.6%; p < 0.04).

**Conclusions:** Previous CABG patients with STEMI treated with primary PCI have higher long-term adverse events. The long-term event rates are higher still if the IRA is a bypass graft.

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**P3302**

**Mean platelet volume as a predictor for long-term outcome after percutaneous coronary intervention**

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**Background:** Mean platelet volume (MPV) is a value that is readily available from standard blood count. Increased MPV reflects larger platelets and increased platelet reactivity. In patients with acute coronary syndromes (ACS), increased MPV has been correlated with adverse cardiac outcomes. However, there is limited information about the prognostic value of baseline MPV in a large heterogeneous patient population which undergoes percutaneous coronary intervention (PCI). We, therefore, aimed to examine whether baseline MPV is predictive of clinical outcomes in patients who undergo PCI.

**Methods:** Included were consecutive patients who underwent PCI during 2004-2010 (n=7585, mean age 67±11.2 years, 5776 males) and were followed for a median period of 4 years. Baseline MPV before angiography and long-term clinical outcomes were assessed.

**Results:** The mean MPV was higher in women compared to men (8.6±1.2 vs. 8.5±1.1 fL; p=0.002), in diabetic vs. non-diabetic patients (8.6±1.2 vs. 8.4±1.1 fL; p<0.001) and in patients who were admitted with ACS (n=4961) compared to patients who underwent an elective PCI (8.6±1.1 vs. 8.5±1.1 fL; p=0.001). On univariate analysis MPV level was associated with mortality with a hazard ratio of 1.23 (95% CI 1.17-1.28; p<0.001). On multivariate analysis adjusted for age, gender, type of stent, diabetes, prior heart failure, MI and ACS, MPV was associated with mortality in patients undergoing an elective PCI as well as in urgent PCI (HR 1.18, 95% CI 1.12-1.23; p<0.001) and with a composite end-point of death, MI and target vessel revascularization (HR 1.09, 95% CI 1.04-1.13; p=0.001). Baseline MPV was associated with mortality in patients undergoing an elective PCI or death up to 2 years (Adjusted OR 3.78, CI 2.19-6.52, p<0.001).

**Conclusion:** In patients undergoing an elective or urgent PCI, an elevated MPV is a significant predictor of cardiovascular adverse events including death.

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**P3303**

**Impact of transient new-onset atrial fibrillation on clinical outcomes of patients with acute myocardial infarction undergoing percutaneous coronary intervention**

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**Purpose:** New-onset atrial fibrillation (AF) with no history of AF before acute myocardial infarction (AMI) is considered to have poor clinical outcomes. However, it remains uncertain whether transient new-onset AF episodes during AMI are associated with increased mortality in patients undergoing percutaneous coronary intervention (PCI). The mechanisms behind this association are not clear. No previous study has investigated hemodynamic parameters obtained during trans-thoracic echocardiography (TTE) in PCI patients.

**Methods:** We retrospectively reviewed all consecutive patients who underwent PCI at a Clinic between 1995 and 2005, and also underwent a TTE study more than 1 day prior to PCI. We recorded the presence and severity of COPD (confirmed by ICD coding and pulmonary function testing (PFT) when available). Follow-up survival was collected prospectively at 6 months, 1 year, and then annually.

**Results:** This study included 6201 patients (age 67±12 years, 30% women), of which 1185 patients had a confirmed diagnosis of COPD (61% of these COPD patients had available PFT results). The mean follow up was 6.1±3.5 years. Patients with COPD compared to patients without COPD had lower LV ejection fraction (52±2 vs 55±5; p<0.001), smaller LVEF (47±1 vs 54±1; p<0.001), higher resting heart rate (72±15 vs 68±14; p<0.0001), and similar cardiac output (5.7±1.6L/min vs 5.6±1.5L/min; p=0.12). COPD patients had increased mortality over non-COPD patients (p<0.0001). Depressed stroke volume (SV) served as an independent predictor of higher mortality in both COPD and non-COPD patients. Even though patients with COPD have lower LV stroke volumes, they maintain similar cardiac output as non-COPD patients. Lower stroke volume...
is an independent predictor of mortality in both COPD and non-COPD patients. This may represent a mal-adaptive response in which COPD patients compensate their lower stroke volumes by increasing their heart rates.

**P3306** Major adverse upper gastrointestinal events in patients with ST-segment elevation myocardial infarction undergoing primary coronary intervention and dual antiplatelet therapy

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**Purpose:** We investigated the incidence of composite short-term and long-term major adverse upper gastrointestinal event (MAUGIE) (defined as gastric ulcer, duodenal ulcer, gastro-duodenal ulcer, or UGI bleeding) in patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) and routinely receiving dual antiplatelet therapy.

**Methods and Results:** Between May 2002 and September 2010, totally 1368 consecutive patients who experienced STEMI undergoing primary PCI were prospectively enrolled for the study. The incidences of in-hospital UGI bleeding complication and composite MAUGIE were 8.4% and 9.9%, respectively. The in-hospital mortality rate was significantly higher in patients with in-hospital MAUGIE than in those without (p < 0.001). Multivariate analysis showed that age, advanced Killip score (defined as ≥ score 3), and respiratory failure were the strongest independent predictor of in-hospital composite MAUGIE (all p < 0.003). The cumulative composite of MAUGIE after uneventful discharge in patients without adverse UGI event who continuously received dual antiplatelet therapy for 3-12 months, followed by aspirin therapy was 10.4% during long-term (mean: 4.0 yrs) follow-up.

**Conclusion:** The results of this study showed remarkably high incidences of composite short-term and long-term MAUGIE in patients with STEMI undergoing primary PCI and receiving routine dual antiplatelet therapy. Age, advanced Killip score and respiratory failure were significantly and independently predictive of in-hospital composite MAUGIE.

**P3308** Outcome of deferral of percutaneous coronary intervention by a fractional flow reserve value over 0.75 in life-threatening cardiac events in victims of the Great East Japan Earthquake and Disaster

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**Purpose:** Fukushima is the stricken area of the Great East Japan Earthquake and Disaster. Myocardial fractional flow reserve (FFR) is a simple and reliable physiologic procedure to assess the severity of intermediate coronary stenosis. The cut-off point of 0.75 is a promising parameter for the indication of percutaneous coronary intervention (PCI). However, it is unclear whether or not life-threatening cardiac events can be evaluated by FFR values. In the present study, we investigated the efficacy of deferral of PCI based on an FFR value ≥ 0.75 in life-threatening cardiac events in intermediate coronary stenosis in victims of the Great East Japan Earthquake and Disaster.

**Methods:** We measured FFR in 54 patients with intermediate coronary stenosis of 50-75% as determined by coronary angiography based on visual assessment from June 2008 to March 2011. In 40 patients out of 54 patients, PCI was deferred based on FFR values ≥ 0.75 before the Great East Japan Earthquake and Disaster and all of them were victims of the Great East Japan Earthquake and Disaster. We assessed the outcome of their life-threatening cardiac events including death, congestive heart failure (CHF) and shock in these victims.

**Results:** Patients were followed for 621±282 days. Four lesion-related events (1 angina attack and 3 elective PCI) occurred before the Great East Japan Earthquake and Disaster, but not life-threatening events. On the other hand, 13 nonlesion-related events (8 PCI, 1 pacemaker implantation and 4 noncardiac surgery) occurred, all of which were not life-threatening. After the Great East Japan Earthquake and Disaster, their hemodynamic state was stable and none of them had life-threatening events.

**Conclusions:** Our study showed the outcome of deferral of PCI based on an FFR value ≥ 0.75 in life-threatening cardiac events for patients with intermediate coronary stenosis in the victims of the Great East Japan Earthquake and Disaster. These results suggest that an FFR value ≥ 0.75 appears to be a prognostic indicator not only for the determination of PCI, but also for life-threatening cardiac events in intermediate coronary stenosis and that the measurement of FFR appears to be an attractive strategy for preventing life-threatening cardiac events in intermediate coronary stenosis.
Methods: 9-month angiography and OCT follow-up was scheduled in 41 patients with CTO(n=21) or non-CTO, treated successfully with DES. Contralateral opacification was used to minimise vessel damage in CTO PCI. At follow-up, the presence of uncovered struts (UCS), stent malapposition and neointimal volume, as well as lumen and stent dimensions, was assessed with quantitative analysis of OCT images. A comparison between OCT findings in CTO and non-CTO was performed.

Results: A total of 1,115 frames, obtained at 1 mm intervals in 68 DES (39 in CTO and 29 in non-CTO), were analysed. Although CTO PCI required more stents (1.85±0.47 vs 1.40±0.51 stents, p=0.01) to cover longer vessel-length segments (30.19±10.09 vs 24.05±12.29 mm, p=0.08) than non-CTO PCI, no significant differences were found between both groups regarding the number of UCS, either as absolute figure (6.24±9.83 in CTO vs 11.55±33.11 UCS in non-CTO) or as percentage of analysed frames with UCS (8.13% vs 12.21%, idem). Stent malapposition was found in 7 (33%) CTO and 6 (30%) non-CTO cases (p=NS), with mean malapposition volumes of 0.15±0.02 and 0.27±0.70 mm3 respectively (p=NS). The generated neointimal hyperplasia volume was similar in CTO (29.51±28.78 mm3) and non-CTO (31.79±66.02 mm3) (p=NS).

Conclusions: In this pilot study the extent of long-term DES coverage and the generated volume of neointimal hyperplasia was similar in CTOs and non-CTOs. The influence of CTO substrate on long-term stent outcome previously documented with BMS seems to be superseded by current DES technology.

**P3310**

**Long term prognostic value of subclinical Peripheral Arterial Disease severity in patients with STElevation-Myocardial Infarction**

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Background: The presence of clinical peripheral arterial disease (PAD) is associated with an increased risk of adverse cardiovascular outcomes among patients with coronary artery disease (CAD). However, there is little data regarding the impact of the presence and degree of the subclinical PAD on outcomes in patients with CAD, specially those that undergoing percutaneous coronary interventional (PCI) for ST-elevation-myocardial infarction (STEMI). We aimed to assess prospectively the grade of subclinical PAD in the setting of patients that undergoing primary PCI for prediction of short- and long-term clinical outcomes.

Methods and results: A total of 971 consecutive patients without history of clinical PAD that undergoing primary PCI for STEMI were included in a prospective follow-up. Subclinical PAD severity was blindly assessed based on a previously described ultrasound arterial morphology classification (UAMC) defined with an high-resolution ultrasound assessment of wall carotid and femoral artery bifurcations. This classification included four classes: I: normal or initial wall disruption, II: wall thickening, III: non-stenosing plaques, IV: stenosing plaques) corresponding to four scores ranging between 2 and 8 for each artery (total score from 8 to 32 in each patient) (1). The group was divided into four classes according to UAMC score and each patient was assigned a score. We evaluated death, and major cardiovascular events (MACE) including all-cause death and non-fatal myocardial infarction. Target vessel revascularisation (TVR) was a secondary endpoint. We performed multivariate Cox proportional hazards analysis, mortality in class IV group was more than 16-fold higher (hazard ratio [HR], 16.50; 95% confidence interval [CI], 7.76 to 35.07; p<0.001) when compared with class I group and was also increased in the class III group (HR, 4.47; 95% CI, 2.55 to 8.76; p<0.001) and class II group (HR, 1.62; 95% CI, 1.30 to 2.18; p<0.05). Similarly, an increasing effect was seen across UAMC strata for major cardiovascular and cerebrovascular events both in the class IV group (HR, 12.29; 95% CI, 9.16 to 16.50; p<0.001), class III group (HR, 11.70; 95% CI, 8.54 to 16.24; P=0.001), and class II group (HR, 1.92; 95% CI, 1.40 to 2.55; P=0.001). In addition, the HR for the increasing UAMC classes (HR, 4.32; 95% CI, 2.09 to 9.53; P=0.001; HR, 3.27; 95% CI, 20.80 to 39.9 to 6.20; P<0.0001; HR, 3.45; 95% CI, 18.10 to 42.3; P<0.0001, respectively).

Conclusions: The UAMC may be applied in the STEMI population that undergoing primary PCI and is able to stratify patients for poor clinical outcomes in long-term follow-up.

**P3311**

**Impact of LR11, a novel proliferative marker of vascular smooth muscle cells, on long-term clinical outcomes in diabetic patients with coronary artery disease**

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Purpose: LR11, a member of LDL receptor family, is a novel proliferative marker of vascular smooth muscle cells (SMCs). Diabetic patients have worse clinical outcomes after percutaneous coronary intervention (PCI). Advanced glycation end-products and oxidative stress in diabetes condition activate the proliferation and migration of SMCs. We therefore evaluated the prognostic value of LR11 (sLR11) in diabetic patients with coronary artery disease.

Methods: Consecutive 219 diabetic patients (mean age 66±5:8.9 years, male 80.4%) treated with coronary intervention from 2003 to 2004 in our institution was enrolled in the present study. We divided the patients into quartiles accord-
Comparison in survival outcomes between drug-eluting stents and bare-metal stents

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Background: In 2006, the use of drug-eluting stents (DES) reached ~60% of all PCI procedures in Sweden. Due to the concerns about the possible increased risk for stent thrombosis and death, the use of DES dramatically declined below 15% in 2007. At the present time, the utilization of DES still varies substantially between the Swedish hospitals (range 20%-92%).

Aim: The aim of this study is to compare the long-term outcome in mortality after percutaneous coronary intervention with DES and bare-metal stents (BMS) in a real-world population from the Swedish region with a low rate of DES usage.

Methods and Results: Data were obtained from the SCARR registry (Swedish Coronary Angiography and Angioplasty Registry). We evaluated 15 764 consecutive stent implantations (59% DES, n = 12 640, BMS, n = 3124) in Västra Götaland region between 2005 and 2010. Predictors of mortality were analyzed with Cox proportional regression analysis. The following variables were included in the model: age, gender, diabetes, hypertension, hyperlipidemia, smoking, antiplatelet therapy with glycoprotein IIb/IIIa receptor antagonists, bivalirudin, clopidogrel, aspirin, previous PCI, previous CABG, indication for PCI and year of intervention. The adjusted and unadjusted Cox regression analyses showed a statistically significant lower risk of death in DES compared with BMS (adjusted hazard ratio 0.86; 95% confidence interval: 0.74-0.99).

Conclusion: Percutaneous coronary intervention with DES is associated with a 14% lower risk of death compared with BMS in this observational study from a large real-world population.

Impact of angiographic peri-stent contrast staining on late adverse events after sirolimus-eluting stent implantation: an observation from the multicenter j-Cypher registry

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Background: We have noted abnormal angiographic findings that do not fulfill the classic definition of coronary artery aneurysm namely peri-stent contrast staining (PSS) and reported their incidence, risk factors, and association between target lesion revascularization (TLR) and stent thrombosis (ST) in a single center data. However, its incidence and impact of coronary events in large numbers of patients with longer follow-up duration remain unknown.

Methods and Results: PSS was defined as contrast staining outside the stent contour extending to >20% of the stent diameter. Among 12824 patients with 19675 lesions enrolled in the j-Cypher registry (37 centers), we investigated angiographic PSS in 9149 patients with 12584 lesions treated with SES only (in 19 centers).

Objective: The effect of socio-economic status upon outcome after PCI is poorly defined. We sought to determine the effects of socio-economic status (SES) upon long-term outcome after percutaneous coronary intervention (PCI).

Method: Observational registry consisting 13770 consecutive patients undergoing PCI at a single centre (2005 – 2011). SES was assigned to each patient according to postcode and ranked according to the corresponding British Index of Multiple Deprivation (IMD) score, which comprises five deprivation quintiles (Q1, least deprived; Q5, most deprived). Primary outcome was all cause mortality obtained from the Office of National Statistics. Follow-up was for a median of 3.7 years (IQR 2.0 – 5.1).

Results: Patients were predominantly male (74.0%) and Caucasian (71.7%), with a mean (±SD) age of 63.8±12.0 yr. Median IMD score was 24.4 (13.4 to 38.4). Patients in quintile 5 (most deprived) were younger, more likely to be of Asian descent, current smokers and had higher rates of previous MI/PCI, diabetes mellitus and renal failure. They were more likely to present as an acute coronary syndrome and have either moderate or poor LV function.

Conclusions: Lower SES is associated with higher long-term mortality following PCI and is independent of other recognised risk factors.

Long-term angiographic superiority of sirolimus-eluting stents compared to bare metal stents in total coronary occlusions in the primary stenting of totally occluded native coronary arteries II

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Purpose: At long-term follow-up, sirolimus-eluting stents (SES) demonstrate favourable clinical results compared to bare metal stents (BMS) in total coronary occlusions (TCO’s). However, long-term angiographic follow-up of is currently un-
available. The present study was designed to examine the 5-year angiographic results of patients randomized to SES or BMS for the treatment of TCOs.

Methods: A total of 200 patients were randomized to SES or BMS. Patients with available 6-month repeated angiography were approached for repeated angiography at 5-year. If patients experienced myocardial infarction, target lesion revascularization or death during follow-up, the latest available angiography was omitted. The primary endpoint was in-stent very late luminal loss (VLLL) defined as the difference between 5-year and post-intervention minimal lumen diameter (MLD). The secondary endpoints were in-stent additional late luminal loss (ALLL; defined as the difference between the VLLL and late luminal loss (LLL)(VLLL was defined as difference between 6-month and post-intervention MLD)) and the in-stent rate of binary restenosis (BR) at 5-year.

Results: A total of 133 patients (63 SES vs 70 BMS) were available for angiographic analysis. At 5-year, in-stent VLLL was superior in favor of the SES-group (0.47mm±0.95 vs 1.19mm±1.02, p=0.001) compared to the BMS-group. As a consequence BR was less in the SES-group (18.6% vs 44.4%, p=0.001) compared to the BMS-group.

Conclusions: At 5-year follow-up SES remained superior for the treatment of total coronary occlusions compared to BMS. Despite, late catch-up was observed with SES.

P3318
Serial angiographic outcomes > 2 years after sirolimus-eluting stent implantation: contemporary practice in real world population
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Background: Although percutaneous coronary intervention (PCI) with drug-eluting stent (DES) has significantly reduced the rate of repeat target-lesion revascularization, the results from a few studies recently raised concerns on late restenosis of DES. Limited data is available examining serial angiographic outcomes.

Methods: Between June 2004 to Jun 2009, consecutive 425 lesions without restenosis at early follow-up (>11.2±2.1 months, range: 9.3 to 12.4 months) had late follow-up angiography (31.0±8.5 months, range: 24.2 to 50.1 months). We evaluated serial angiographic outcomes and predictors of late restenosis among patients treated with SES > 2 years after the index procedure.

Results: Although reference vessel diameter did not significantly change during follow-up (3.10 mm (interquartile range (IQR): 2.78-3.37 mm), 3.07 mm (IQR: 2.75-3.43 mm) and 3.06 mm (IQR: 2.72-3.43 mm) at post-procedure, and early and late angiographic follow-up, respectively; p=0.065), late loss (LL) significantly increased during follow-up (0.06 mm (IQR: 0.00-0.02 1 mm) and 0.09 mm (IQR: 0.00-0.27 mm) at early and late follow-up, respectively; p<0.001). Univariate analysis showed previous intervention, lesion length and progression of minimal lumen diameter, LL, percent diameter stenosis (%DS) at early follow-up as predictors of late catch-up. Multivariate regression analysis identified %DS at early follow-up as a predictor of late catch-up (OR 1.076, CI 1.039-1.114, p=0.001).

Conclusions: Although late regression was observed in bare-metal stent era, significant and continuous progression > 2 years after SES implantation was observed in our study. Further investigations are needed to evaluate the clinical significance of late restenosis and whether SES only delays neointimal hyperplasia rather than prevent.

P3319
Impact of body mass index on long-term clinical outcomes after second generation drug eluting stent implantation: the end of the obesity paradox?
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Purpose: An increased body mass index (BMI) has been shown to be associated with a higher risk of cardiovascular disease and reduction of life expectancy. However several studies reported improved clinical outcomes in obese patients treated for cardiovascular diseases, a phenomenon termed as obesity paradox. The aim of the present study is to investigate for the first time the impact of BMI on long-term clinical outcomes after implantation of a second generation drug-eluting stent.

Methods: Patients enrolled in the RESOLUTE Clinical Program comprising 5 trials worldwide evaluating the RESOLUTE zotarolimus-eluting stent, were followed for 2 years and clinical and angiographic outcomes were evaluated according to BMI strata. Results: A total of 5,127 patients were included in the present study. Compared with other BMI categories, obese patients were more frequently male (68.7%, p<0.001), had a history of hyperlipidemia (80.2%, p<0.001), hypertension (84.5%, p<0.001), diabetes (43.5%, p<0.001), and were younger (mean±SD age, 62.3±10.5, p<0.001). Non-obese patients were more frequently current smokers (underweight: 35.3%, normal weight: 28.3%, overweight: 23.0%, obese: 20.9%, p<0.001) and presenting with acute myocardial infarction (underweight: 29.4%, normal weight: 18.5%, overweight: 16.1%, obese: 12.3%, p<0.001). After adjusting for all confounding factors no differences between obese and normal-weight patients were found in terms of all cause death (hazard ratio 1.10, confidence interval 0.71-1.72, p=0.663), cardiac death (hazard ratio 1.12, confidence interval 0.64-1.96, p=0.693), major adverse cardiac events (hazard ratio 0.83, confidence interval 0.65-1.07, p=0.149), myocardial infarction (hazard ratio 0.80, confidence interval 0.52-1.29, p=0.386), target lesion revascularization (hazard ratio 0.75, confidence interval 0.50-1.11, p=0.144) and stent thrombosis (hazard ratio 0.77, confidence interval 0.36-1.63, p=0.490). Similarly, no differences were found among other BMI strata.

Conclusions: In the present study, in contrast to previous reports, after adjustment for confounding factors no survival benefit was observed for obese patients treated with second generation drug eluting stents. Normal weight patients presented with higher BMI strata than obese patients. These baseline differences could partially explain the previously reported apparent BMI paradox, which after adjustment for baseline characteristics was no longer present in our study.

P3320
Long-term clinical outcome of simple crossover stent implantation with/ versus without- kissing balloon technique in coronary bifurcation- sub-analysis of the Taxus Japan registry
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Aims: Benefit of final kissing balloon technique (KBT) is debate in simple stent strategy for coronary bifurcation. The purpose of the present study is to evaluate 3-year outcome of single crossover stenting with jailed side branch (SB), and to compare this technique with subsequent KBT technique.

Methods: This study is a sub-analysis of TAXUS Japan Post-marketed Surveillance (consecutive 2132 patients receiving TAXUS ExpressTM between July 2007-Dec 2008 in Japanese 56 sites). Of these, 192 patients treated with single crossover stenting with jailed SB (No-KBT group) was compared with 186 patients underwent subsequent KBT (KBT-group). Left main, vein graft, and 2- stent strategy for bifurcation were excluded.

Follow-up angiography was performed in 9-month, and 3-year clinical outcome was evaluated among groups. Events were adjudicated by independent experts and QCA data were analyzed by an independent core-laboratory.

Results: Baseline clinical and lesion background between KBT- and No-KBT group were similar. The frequency of post-dilation was higher in KBT-group than in No-KBT group (84.7% vs. 74.4%, p<0.01). QCA analysis of main vessel (MV) in 9-month revealed that late loss (0.05±0.62 vs. 0.53±0.56; p=0.07) diameter...
...and non-culprit coronary lesions. There was no difference in age, sex, coronary risk factors, and baseline clinical characteristics. 251 patients (34.3% vs. 38.3%). The control group contained a higher number of patients with acute coronary syndrome compared to the ISR group (55.3% vs. 44.8%, p=0.05). All patients received aspirin and clopidogrel therapy for at least 12 months. Outcomes were calculated using propensity-score adjustment. The mean follow-up length was 45.6±21.5 months.

**Results:** According to our results the incidence of ischaemia-driven target lesion revascularisation (TLR) was not significantly higher in the ISR group compared to the de novo group at 4 years (10.4% vs. 12.4%, p=0.490). The total all-cause mortality was lower in the ISR group at 4 years (7.4% vs. 14.7%, p=0.032) but the incidence of definite and probable stent thrombosis according to ARC criteria did not differ (1.9% vs. 1.6%, p=0.708). The characteristics of restenosis did not differ significantly either between the two groups: 44.4% of the lesions were focal, 19.4% diffuse, 13.9% diffuse-proliferative, while in 22.2% we found total occlusions. The first restenosis of the implanted DES was treated in the same way in the two subgroups, in 33.3% balloon angioplasty. In 47.2% PCI with a new stent implantation, and in 8.3% ACBG was indicated. In 11.1% of the cases no additional revascularization was performed. Despite the successful acute result of in-stent restenosis treatment, repeated restenosis developed in 17.9% of the cases in the ISR group, and in 20.0% in the de novo group (p=0.572).

**Conclusions:** DESs are effective in treatment of ISR and the rate of additional TLR is acceptable compared with the use of DES in de novo coronary lesions. After re-interventions a significantly higher rate of TLR can be anticipated.

**P3324**

**Role of arterial stiffness and impaired renal function in the development of de novo coronary artery stenosis after percutaneous coronary intervention**

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**Purpose:** In the era of drug eluting stent, progression of non-culprit coronary lesions (de novo) emerged as a therapeutic target of coronary artery disease after percutaneous coronary intervention (PCI). However, prognostic factors for de novo remain unclear.

**Methods:** We examined 275 patients who underwent PCI during February 2010 to January 2011 and were performed follow-up coronary angiogram 6-12 months after PCI. Patients who underwent target-lesion revascularisation for restenosis (n=37) were excluded. Finally, total of 238 patients were included in this study.

**Results:** Forty patients (17%) underwent additional clinically driven PCI to treat non-culprit coronary lesions. There was no difference in age, sex, coronary risk factors, and medications between patient with or without de novo. Prevalence of chronic kidney disease (CKD) (55% vs. 30%, p<0.002) and multivessel disease (40% vs. 33%, p=0.002) were higher in patients with de novo than those without. Brachial-ankle pulse wave velocity (baPWV), a marker for arterial stiffness was significantly higher in patients with de novo than those without (1859±344 vs. 1578±310mm/s, p<0.001). Multivariate analysis showed that...
prevalence of CKD, multi- vessel disease and baPWV >1650cm²/s were independent predictors for de novo after primary PCI. Furthermore, scoring the patients by assigning 1 point for these three risk factors (Score=0-3) clearly stratified the patients according to the risk of de novo lesion as shown in the figure below.

Conclusions: CKD, MVD and baPWV >1650cm²/s were independent determinants of the development of non-culprit coronary lesion, suggesting important role of impaired renal function and arterial stiffness in the pathogenesis of de novo coronary artery stenosis after PCI.

P3325
Sirolimus-eluting stent implantation in bifurcation lesions: five-year clinical outcome of the j-Cypher registry
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Aim: Percutaneous coronary intervention (PCI) of coronary bifurcation lesions remains challenging, though several randomized trials and registry data have shown the benefit of provisional side branch stenting strategy in bifurcation lesions. We explored the 5-year clinical outcome for bifurcations with SES of the j-Cypher registry.

Methods and Results: Among 12924 patients enrolled in the j-Cypher Registry, we identified 2212 patients with 2250 non-left main bifurcation lesions (age: 69 years, diabetes: 39%, acute coronary syndrome: 24%, lesion length ≥30mm: 17%, true bifurcation: 53%) treated exclusively with SES. The majority of lesions (1976 lesions, 88%) were treated by provisional side-branch stenting approach with 4.5% crossover rate, while elective two-stent approach (stenting both main- and side-branches) was adopted in 272 lesions. 4 methods of two stenting were used: T-stenting (59%), Culotte stenting (16%), Crush stenting (20%), and V stenting (4%).

The 5-year incidence of target-lesion revascularization (TLR) was significantly higher in the elective two-stent group than in the provisional group (22.6% vs. 14.2%, p<0.001). The incidence of definite stent thrombosis was not different between the two groups (1.9% vs. 1.4%, p=0.39). Among 1871 lesions with main-branch stenting alone, FKB was performed in 938 lesions (50%). The incidence of TLR was not different between the two groups with or without FKB (15.7% vs. 14.0%, p=0.38).

Conclusions: The provisional approach suggests a good outcome in the majority of lesions relative to elective two-stent approach after 5-year from SES placement in bifurcation lesions. FKB did not provide the benefit regarding TLR after main branch stenting alone.

P3326
Comparison of sirolimus-eluting stents versus everolimus-eluting stents in acute myocardial infarction
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Background and Objectives: In the era of drug-eluting stents, much comparison was done between paclitaxel-eluting stents (PES) and everolimus-eluting stents (EES). In comparison, there were few studies between everolimus-eluting stents (EES) and sirolimus-eluting stents (SES), but recently many studies are being reported. Still, there are limited studies of comparison between EES and SES in acute myocardial infarction.

Subjects and Methods: In 2011, 5694 patients were registered in COREA-AMI (COnvergent REgistry of cAtholic and chonnAm university for AMI) registry. In COREA-AMI, 1079 patients used EES and 578 patients used SES. Patients who used a combination of EES or SES with another stent were excluded.

Results: In baseline characteristics, HbA1c, hemoglobin, total stent length, mean stent diameter were different between two groups. SES group had a longer total stent length(TSL), larger mean stent diameter(MSD), TSL 28.6±25.3 vs 15.3±22.4 (p<0.001), MSD 3.1±0.7 vs 2.9±1.1 (p<0.001). Also there was a tendency of SES used more often in LAD lesion, longer total stent length, higher vessel-disease. Using cox-regression analysis, predictor for MACE (death, MI, TLR, TVR) found was mean stent diameter only. Hazard ratio of EES to SES was 1.128 (95% confidence interval 0.733 to 1.737, p=0.584) in multivariate cox-regression. In rates of composite of all cause death, recurrent non-fatal myo-
Clinical outcome and predictors for adverse cardiac events after PCI of de-novo bifurcation lesions using first or second generation of drug-eluting stents

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Background: There is increasing evidence that various types of drug-eluting stents (DES) may differ regarding the long-term safety and efficacy, particularly in high-risk lesion subsets. As DES in large consecutive cohort undergoing bifurcation stenting, we sought to compare the 1-year efficacy and safety of the first-generation paclitaxel-eluting stent (PES, TAXUS), the first generation sirolimus-eluting (SES; CYHERP) and the second generation everolimus- or zotarolimus-eluting stents (EES/DES, PROMUS/XIENCE/RESOLUTE) and to detect predictors for adverse cardiac events.

Methods: Between 2002 and 2009, we treated 2197 patients with provisional T-stenting for de-novo coronary bifurcation lesions using PES, SES or EES/DES. The 1-year cumulative incidences of target lesion revascularisation (TLR), death from any cause, as well as the composite of death and myocardial infarction (MI) were estimated by the Kaplan-Meier method. In addition, we calculated hazard ratios (HR) from multivariable COX models to find predictors for adverse events.

Results: PES were placed in 547 patients, SES in 1344 patients and EES/DES in 306 patients. The side branch stenting was needed in 793 patients (36.1%). The cumulative 1-year incidences of TLR were 11.28% after PES, 7.28% after SES and 5.85% after EES/DES (P=0.005), those of death 5.30%, 4.33%, 5.29% (P=0.58), and those of death and MI 6.26%, 6.57% and 5.58% (P=0.25), respectively. After adjustment for co-variables the type of DES was a significant (P = 0.01) predictor of TLR (hazards ratio [95% confidence interval] PES vs SES: 0.69 [0.59-0.82], PES vs EES/DES: 0.56 [0.34-0.90]), but not of death (P = 0.96) or of death and MI (P = 0.65).

Important independent predictors for TLR were age (P=0.002), diabetes mellitus (P=0.001) and baseline C-reactive protein (P=0.008). The strongest predictors for death or death and myocardial infarction were age (P=0.001), diabetes (P=0.002), reduced left ventricular function (P=0.0001), PCI in ACS (P=0.0001), baseline creatinine (P=0.0001), severe calcified main branch (P=0.0001) and the need for side branch stenting (P=0.004).

Conclusions: In de-novo coronary bifurcation lesions, –limus stents achieved better outcomes than PES. Predictors of outcome after bifurcation stenting are similar to those reported in mixed cohorts.

P3332

Comparison of “limus”-eluting stents with bare-metal- vs drug-eluting polymer in patients with diabetes mellitus with coronary artery disease

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Background: Unfavorable outcomes after percutaneous interventions (PCI) occur more often in certain high risk subgroups like patients with diabetes mellitus that are prone to a diffuse and rapidly progressive form of atherosclerosis. While drug-eluting stents (DES) have improved safety and efficacy outcomes compared to bare metal stents (BMS) in diabetic patients the optimal DES strategy still remains unclear. Therefore we compared effectiveness of biodegradable polymer-based sirolimus-eluting stent (BP) and -permanent polymer-based “limus”-eluting stents (PP) in patients with diabetes mellitus.

Methods: ISARTEST-4 is a randomized trial of 2600 Patients with de novo native- vessel coronary lesions. This analysis is focused on a subgroup of 753 Patients with diabetes mellitus randomly assigned to receive BP (n=376) or PP (n=377). The primary endpoint was the composite of cardiac death, myocardial infarction related to the target vessel, or target lesion revascularization (TLR) at three year follow-up. Secondary endpoints were binary restenosis; in-stent lumen loss; all cause mortality; and incidence of definite/probable stent thrombosis (ST). Results: BP was comparable to PP in terms of the incidence of the primary end- point (22% vs. 23%, relative risk +0.98, 95 CI, 0.72-1.32; p=0.89), all cause death (12.5% vs. 13%, relative risk= 0.96, 95 CI, 0.64-1.43;p=0.84), TLR (23% vs. 21%, p=0.53) and ST (11% vs. 21%, p=0.52) at three year follow up. There...
Safety and efficacy of drug-eluting stents in the long term follow-up

M. Urina-Triana, M. Rondon, R. Dennis. Pontificia Universidad Javeriana - School of Medicine, Bogotá, DC, Colombia

Purpose: To evaluate efficacy and safety between percutaneous coronary intervention (PCI) with drug-eluting stents (DES) vs. bare metal stents (BMS) in the long-term follow-up in patients with athero-thrombotic coronary artery disease.

Methods: We conducted a systematic review and meta-analysis of randomized clinical trials (RCT) comparing DES with BMS in adult patients (18 year or older) with stable angina or acute coronary syndrome: unstable angina, non-ST elevation or ST-elevation acute myocardial infarction. In the 9 months up to five years follow-up. We calculate odds ratios (ORs) and 95% confidence intervals (CIs) for clinical outcomes: mortality, acute myocardial infarction (AMI) or reinfarction (ST) and the composite outcome of major adverse cardiovascular events (MACE): death, AMI and TVR, in each group of treatment (DES vs. BMS).

Results: 39 RCTs with 16699 patients comparing DES vs. BMS, were selected according to the inclusion/exclusion criteria for this meta-analysis. The overall estimate effect for each outcome is represented in table #1.

Conclusions: DES are efficacious and safe for treatment of patients with coronary artery disease, reducing TVR (clinical restenosis equivalent) about 50%, without increasing rates of AMI, ST or mortality in the long term follow-up.

PERCUTANEOUS CORONARY INTERVENTIONS: MISCELLANEOUS

Remarkable reduction in cardiac mortality associated with the introduction of the strategic cardiac hajj intervention program (SCHIP) during the largest gathering in the planet

K. Al Farady1, O. AI Shammari2, F. Bukhari3, A. Hursi4. KFHMC Cardiac Center, Dhahran, Saudi Arabia; 2Qassem university, Qassem, Saudi Arabia; 3King Fahad Armed Forces Hospital, Department of Cardiology, Jeddah, Saudi Arabia; 4King Fahad Cardiac Center, King Khalid University Hospital-King Saud University, Riyadh, Saudi Arabia

Background: Religious pilgrimage, or Hajj, is a basic tenet of the Islamic doctrine.

Each year approximately 3 million pilgrims congregate for up to 2 weeks in a < 3 square mile area around the city of Makkah. Hajjis can experience physical and emotional stress with limited healthcare access. Cardiovascular events were the main cause of death during Hajj for the last decade; therefore the Strategic Cardiac Hajj Interventional Program (SCHIP) was launched in 2009 to provide improved cardiac outcomes.

Aim: To assess the impact of SCHIP on cardiac mortality during Hajj.

Methods: A team of Cardiologists, specialists, nurses with access to 3 cardiac catheterization laboratories provided 24 hour-a-day support to 13 local hospitals throughout the Haj period. Cardiac and all causes mortality adjusting for the potential other covariates were statistically analyzed using time series data before and after intervention.

Results: Cardiac death rates during 2006, 2007 and 2008 were 51.7%, 50.6% and 53.2%. After SCHIP introduction rates in 2009, 2010 and 2011 were 43.3%, 32.5 and 19.7%. The in-hospital mortality for ACS were 4.7%, 4.6% and 3.0%. The number of cardiac procedure performed in 2 week during Hajj 2009, 2010, and 2011 were 183, 288 and 550. The majority of the procedure in the last 3 years were coronary catheterization 90.1%, 80.9% and 86.7%. The rates of open heart surgery were 7%, 5.2% and 4.5%.

Conclusion: After introduction of SCHIP, cardiac and in-hospital mortality substantially reduced. Future introduction of mobile cardiac catheterization laboratories may further reduce cardiac mortality.

Short and long-term mortality rates among octogenarians undergoing percutaneous coronary intervention of the left main stem

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Purpose: Octogenarians (age >80) are under-represented in clinical trials of percutaneous coronary intervention (PCI) of the left main stem (LMS). We sought to obtain long-term survival data for octogenarians undergoing PCI LMS.

Methods: Retrospective analysis of all 349 patients undergoing LMS PCI at our centre between 20th March 2005 and 15th October 2011. We compared clinical characteristics and mortality between octogenarians and patients aged <80 years. All-cause mortality was ascertained from the National Health Service Spine.

Results: 111 of 349 patients (32%) were aged >80 years. Overall, there was no significant difference in 30-day (7.1% vs 10.8%), 12-month (15.1% vs 16.2%) or long-term longitudinal survival (see figure) between octogenarians and those aged >80 years.

Conclusion: In over 6 years of performing LMS PCI at our centre, we observed no statistically significant difference in all-cause mortality between octogenarians and those aged >80 years undergoing LMS PCI.

P3333

Safety and efficacy of drug-eluting stents in the long term follow-up

M. Urina-Triana, M. Rondon, R. Dennis. Pontificia Universidad Javeriana - School of Medicine, Bogotá, DC, Colombia

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P3334

Remarkable reduction in cardiac mortality associated with the introduction of the strategic cardiac hajj intervention program (SCHIP) during the largest gathering in the planet

K. Al Farady1, O. AI Shammari2, F. Bukhari3, A. Hursi4. KFHMC Cardiac Center, Dhahran, Saudi Arabia; 2Qassem university, Qassem, Saudi Arabia; 3King Fahad Armed Forces Hospital, Department of Cardiology, Jeddah, Saudi Arabia; 4King Fahad Cardiac Center, King Khalid University Hospital-King Saud University, Riyadh, Saudi Arabia

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Conclusion: After introduction of SCHIP, cardiac and in-hospital mortality substantially reduced. Future introduction of mobile cardiac catheterization laboratories may further reduce cardiac mortality.

P3335

Short and long-term mortality rates among octogenarians undergoing percutaneous coronary intervention of the left main stem

D.S.G. Conway1, I.R. Pearson2, C.P. Gale3, P.D. Baxter4, U.M. Sivananthan1, Jinderfield General Hospital, Wakefield, United Kingdom;1Leeds General Infirmary, Yorkshire Heart Centre, Institute for Cardiovascular Research, Leeds, United Kingdom;2Centre for Epidemiology and Biostatistics, University of Leeds, Leeds, United Kingdom;4Leeds General Infirmary, Leeds, United Kingdom

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Clinical characteristics by age group

<table>
<thead>
<tr>
<th>Age</th>
<th>Male (%)</th>
<th>Mean age (SD), years</th>
<th>Diabetes (%)</th>
<th>Ejection fraction &lt;30% (%)</th>
<th>Creatinine &gt;200mmol/L (%)</th>
<th>Cardiogenic shock (%)</th>
<th>Systolic median (IQR)</th>
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<td>&lt;80</td>
<td>181 (76)</td>
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<td>46 (19)</td>
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<td>25 (11)</td>
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<td>&gt;80</td>
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<td>84 (3)</td>
<td>15 (14)</td>
<td>10 (9)</td>
<td>7 (6)</td>
<td>9 (8)</td>
<td>14 (11)</td>
</tr>
</tbody>
</table>

Conclusion: In over 6 years of performing LMS PCI at our centre, we observed no statistically significant difference in all-cause mortality between octogenarians and those aged >80 years undergoing LMS PCI.

Figure 1. Kaplan-Meier curve for all-cause mortality following left main stem PCI.
Lower mortality in ICD patients who underwent a recent PCI

**Objective:** Coronary revascularization (CR) may improve the long-term outcome in patients with ischemic heart disease. The study was designed to examine the association of prior CR and long-term mortality among patients who received an Implantable Cardioverter Defibrillator (ICD).

**Methods:** The study population consisted of 862 patients with prior AMI who had undergone ICD implantation at the Erasmus Medical Centre Rotterdam between 1998 and 2011. Of the 862 patients, 577 patients (67%) underwent CR prior to ICD implantation, of whom 48% underwent recent CR (<2 years before ICD implantation). Coronary revascularization existed of coronary artery bypass surgery (CABG, n = 311), percutaneous coronary intervention (PCI, n = 365) or both (n = 99). The elapsed time from CR to ICD implantation was categorized as: no CR, recent CR (<2 years), and non-recent CR (≥2 years). The primary endpoint was time to all-cause mortality.

**Results:** Compared to no CR, prior PCI was associated with a significant reduction in mortality (Log-rank, P = 0.03 [Fig. 1]). No association was found in the patients with prior CABG. After adjustment for baseline characteristics, patients with prior PCI experienced a 29% decrease in all-cause mortality compared with patients without prior PCI (HR [CI] = 0.71 [0.51, 0.98], P = 0.04). Especially, patients with recent prior PCI had a larger reduction in mortality of 47% (HR [CI] = 0.53 [0.32, 0.87], P = 0.01).

**Conclusions:** In our study, recent prior PCI was associated with a significant reduction in all-cause mortality. These findings suggest that prior revascularization should be considered in patients with ischemic heart disease who are about to receive an ICD.

The challenge of lifestyle counselling after percutaneous coronary intervention

**Objective:** To collect patients’ views on information, their knowledge of risk factors and their willingness to adopt a heart healthy lifestyle. As a patient-centric audit of current information practice, questionnaires were sent to an unselected sample of patients undergoing percutaneous coronary intervention (PCI) at a large European university hospital.

**Methods:** Patients were invited to participate in the classes (in addition 35% of the relatives were invited). One third of the patients increased their knowledge by searching other sources (Internet, leaflets etc).

- Knowledge: as main cause of their disease patients reported: heredity (52%), stress (45%) and age (41%). Changeable risk factors were seen as less important: food habits 31%, tobacco 25% and physical activity 22%.
- Health behaviour: 16% admitted the continued use of tobacco after PCI (half of them had offered smoking cessation support). 43% had joined or planned to participate in physical training, and 31% had increased their levels of physical activity. A change in attitude towards better food habits was reported by 40%.

**Conclusions:** There is ample room for improvement of post-PCI patient information with greater focus on changeable risk factors and new didactical methods. The importance of engagement of spouses or other close relatives is widely underestimated.

A comparison of saphenous vein graft and native coronary artery stenting in 123,804 patients percutaneous coronary intervention

**Background:** Bypass-graft intervention has been associated with poor outcomes.

**Methods:** Data were obtained during a large quality assurance initiative of the “Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte” between 2006 and 2010. A total of 123,804 patients were included and comparisons between those with native vessel vs. saphenous vein graft (SVG) stenting made using the y2 or Mann Whitney Wilcoxon Test.

**Results:** A total of 4,076 patients received SVG stenting and 119,728 patients with native vessel stenting served as controls. 31.0% of patients received a drug eluting and 66.3% bare metal stents. Patients with SVG stenting were older (median 73.0 vs. 68.6 years) and had more prior PCI (62.6 vs. 36.8%, p < 0.0001). Ejection fraction < 40% was more frequent in SVG stented patients (OR 1.84; 95%CI 1.70-1.99) as was diabetes (1.54; 1.44-1.65) and kidney failure (2.38; 2.22-2.56). An ACS without ST elevation was substantially more frequent the reason for stenting in SVG than in native vessel stented patients (STEMI 9.8 vs. 22.6%; p < 0.0001). After stenting TIMI flow was often still reduced in SVG stents (TIMI 0.9 vs. 9.5, p < 0.0001) and in 92.9 vs. 94.7% the intervention goal was reached (p < 0.0001). During hospitalization the rate of death (2.3 vs. 1.9%), non-lethal myocardial infarction (0.3 vs. 3.3%), non-lethal TIA/stroke (0.1 vs. 0.1%), MACE (2.6 vs. 2.3%) and MACCE (2.7 vs. 2.4%) were not statistically different.

**Conclusions:** Data from this large quality assurance initiative indicate that inhospital complications are comparable between patients undergoing saphenous vein graft and native coronary artery stenting. The data are limited however by a long-term follow-up.

Prognosis of patients with contrast-induced nephropathy after primary percutaneous coronary intervention for myocardial infarction

**Background:** Contrast-induced nephropathy (CIN) after primary percutaneous coronary intervention (PCI) for myocardial infarction develops frequently.

**Methods and Results:** 638 patients with primary PCI for myocardial infarction were investigated the development of CIN and the long-term prognosis. CIN was defined as an increase of 25% and over or 0.5mg/dl and over in the serum creatinine concentration from baseline value within one week. CIN developed in 143 patients (22.4%). In-hospital mortality of patients with CIN was significantly higher than patients without CIN (13.3% vs. 3.4%, p = 0.0001). During the mean follow-up periods of 969±842 days, 69 patients (10.8%) died for all cause and 32 patients (5.0%) died for cardiac cause. The long-term prognosis of patients with CIN was significantly poor compared with patients without CIN (log-rank, p = 0.045).
The analysis by Cox proportional hazard models revealed that patients with CIN showed 80% increase in the risk of mortality in the age- and sex-adjusted model (hazard ratio, 1.80; 95% CI, 1.07–2.96; p = 0.029).

**Conclusions:** Long-term prognosis of patients with CIN after primary PCI is poor. The prevention for CIN should be considered on primary PCI.

### Table 1

<table>
<thead>
<tr>
<th>Covariable</th>
<th>Male HR [95% CI]</th>
<th>Male P value</th>
<th>Female HR [95% CI]</th>
<th>Female P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>1.72 [1.39–2.13]</td>
<td>&lt;0.001</td>
<td>1.41 [1.07–1.84]</td>
<td>0.016</td>
</tr>
<tr>
<td>Chronic Renal Insufficiency</td>
<td>1.93 [1.52–2.45]</td>
<td>&lt;0.001</td>
<td>2.07 [1.54–2.76]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>1.62 [1.51–1.73]</td>
<td>&lt;0.001</td>
<td>1.61 [1.01–1.03]</td>
<td>0.027</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>1.28 [0.95–1.72]</td>
<td>0.046</td>
<td>1.15 [0.81–1.64]</td>
<td>0.431</td>
</tr>
<tr>
<td>BMI</td>
<td>0.97 [0.95–1.00]</td>
<td>0.002</td>
<td>0.98 [0.97–1.00]</td>
<td>0.121</td>
</tr>
<tr>
<td>LAD lesion</td>
<td>1.27 [1.03–1.55]</td>
<td>0.023</td>
<td>1.26 [1.07–1.42]</td>
<td>0.078</td>
</tr>
<tr>
<td>Type C lesion</td>
<td>1.38 [1.04–1.79]</td>
<td>0.019</td>
<td>1.38 [1.07–1.79]</td>
<td>0.013</td>
</tr>
</tbody>
</table>

**Conclusions:** While there are small differences in clinical outcome post PCI for male versus female, there are different correlates for these adverse outcomes across gender. These correlates should be taken into account when subjecting female to contemporary PCI.

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### Table 2

<table>
<thead>
<tr>
<th>Cardiovascular Disease</th>
<th>Male HR [95% CI]</th>
<th>Male P value</th>
<th>Female HR [95% CI]</th>
<th>Female P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Vascular Disease</td>
<td>1.57 [1.24–2.00]</td>
<td>&lt;0.001</td>
<td>1.22 [0.91–1.63]</td>
<td>0.192</td>
</tr>
<tr>
<td>Chronic Renal Insufficiency</td>
<td>1.93 [1.52–2.45]</td>
<td>&lt;0.001</td>
<td>2.07 [1.54–2.76]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>0.97 [0.95–1.00]</td>
<td>0.002</td>
<td>0.98 [0.97–1.00]</td>
<td>0.121</td>
</tr>
</tbody>
</table>

**Conclusions:** High L/H ratio was associated with the degree of late loss and the incidence of late restenosis after SES implantation in the long term. These findings suggest that late loss after SES implantation may be related to the progression of atherosclerosis and that the strict control of dyslipidemia is important even after SES implantation.

### Figure 1

Cumulative incidence of late restenosis

**Conclusions:** During follow-up period (mean 53±30 months), 267 MACES (49.3%) occurred including 179 TLR, 19 myocardial infarction and 180 deaths. Kaplan-Meier analysis showed that the event-free rate from MACES for 10 years was 34.2% in T1, 23.9% in T2 and 6.5% in T3 (p < 0.0001). The freedom rate from TLR and all-cause survival rate were also 61.2%, 43.3% and 33.8% (p = 0.0077), and 52.4%, 46.2% and 20.3% (p = 0.0002) in T1, T2 and T3, respectively. After adjustment for gender, age, traditional risk factors, multi-vascular disease, ejection fraction, stent use, AHAA/ACC type and lesion location, independent predictors for MACES were serum CRP levels [hazard ratio (HR) 1.68, 95% confidential interval (CI) 1.19–2.36, p = 0.0033 for T3 vs. T1], multi-vascular disease (HR 1.51, 95%CI 1.03–2.00, p = 0.0047) and ejection fraction (HR 0.39, 95%CI 0.14–1.09, p = 0.082). Serum
CRP levels were also independent predictor for TLR (HR 1.68, 95%CI 1.15-2.48, p = 0.0080 for T3 vs. T1) and mortality (HR 1.82, 95%CI 1.22-2.71, p = 0.0035 for T3 vs. T1), respectively.

Conclusions: Elevated pre-procedural serum CRP levels could strongly predict poorer long-term clinical outcome including MACE, TLR and all-cause mortality after PCI in patients on HD.

Methods: In a case-control study was performed, including 1633 subjects: 772 consecutively coronary patients and 861 controls without apparent CAD, not significantly different in terms of sex and age. We used an univariate analysis, with OR and 95% confidence intervals and a backward Wald logistic regression model adjusted for age, gender, conventional risk factors, and biochemical markers. A cohort of 639 CAD patients that underwent PCI was sampled and followed prospectively for events, between 2000 and 2006, with a median follow-up time of 6.2 (range 2-7.1 years). The rates of MACE (cardiovascular death, non-fatal myocardial infarction (NMI), unstable angina, cardiac failure, and myocardial revascularization), were recorded. This group was divided into subgroups according to PWV values above and below the 95th percentile. Kaplan-Meier was used to compare these two groups survival by the long rank test.

Results: In the univariate analyze, high PWV values were independently associated with CAD (OR=2.066; p<0.0001) and after logistic regression remained in the equation as an independent risk marker of CAD (2.019; CI 1.428-2.855; p<0.0001), in the whole population. In Kaplan-Meier analysis, cumulative events free survival at 5 years was 76% in PWV >95th percentile and 62% in the PWV ≤95th percentile. These two groups were compared by long rank test and the patients with the highest PWV values had a higher percentage of events (58% vs. 44%).

Conclusions: This study showed that PWV is an independent risk marker of CAD for whole population and its high values are a predictor of MACE, for the patients group who has undergone PCI. If these results are confirmed, PWV can become a relevant, technically easy and low cost non-invasive vascular risk marker and will still allow us to identify patients and subgroups with an increased risk for MACE.

PWV is an independent risk marker of coronary artery disease and post percutaneous coronary angioplasty events

Conclusions: PWV is an independent risk marker of coronary artery disease and post-procedural coronary events, and might be a predictor for long-term cardiovascular outcome as compared to cTnI elevation alone.

The lipoproteins have a major role in the development of atherosclerotic vascular disease. This study aimed to appraise the role of a low-density lipoprotein cholesterol/high-density lipoprotein cholesterol (LDL-ch/HDL-c) ratio as predictors of major adverse cardiac events (MACE) after percutaneous coronary intervention (PCI). The study included 504 patients with acute coronary syndrome (ACS), undergoing PCI with stent implantation, between November 2006 and December 2008. On the base of periprocedural LDL-ch/HDL-c ratio, the patients were grouped as those with LDL-ch/HDL-c ≤ 1.5 (n= 106, group 1), LDL-ch/HDL-c > 1.5 and ≤ 2.0 (n= 140, group 2), and LDL-ch/HDL-c > 2.0 (n= 259, group 3). We evaluated, in the three groups, the incidence of MACE during three years. MACE was defined as occurrence of cardiac death, new hospitalization for ACS, target vessel revascularization (TVR) and stroke. Multivariable logistic regression model with stepwise selection was used to identify independent factor associated with outcomes. The areas under the curve (AUC) of the receiver operating characteristic curves (ROC) were constructed to assess the degree of predictability of lipids and ratios of interest on cardiovascular risk.

At the end of three years the patients of the group 1 had a significantly more incidence of MACE (45.55%) compared with group 2 (20.76%) and group 3 (27.85%). By multivariate analysis LDL-ch/HDL-c ratio (OR 1.593; 95%CI 1.335-1.905; p<0.0001) and fibrinogen (OR 1.013; 95%CI 1.003-1.003; p=0.0004) appeared to be an independent predictor of MACE. The ROC curve analyses showed that the best marker of MACE was LDL-ch/HDL-c ratio, with an area under the ROC curve of 0.66 (95% CI 0.61 to 0.70). The optimal cut-off point to identifying the incidence of MACE for LDL-ch/HDL-c ratio was ≥1.85.

Our findings suggest that low-density lipoprotein cholesterol/high-density lipoprotein-cholesterol ratio and inflammation have an important role in the prediction of future cardiovascular events after PCI.

Benefit of transferring ST-segment elevation myocardial infarction patients for percutaneous coronary intervention compared with direct-arrival patients does not decline over time

Purpose: Primary PCI is recommended even if the patient is to be transported to a non-primary PCI-capable hospital. Transport is associated with an increased treatment delay. Quality improvement strategies have reduced door-to-balloon (DTB) times for direct-arrival with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI. However, STEMI patients requiring inter-hospital transfer for primary PCI are often excluded from performance assessment. The aim of this study was to evaluate the impact of transferring STEMI patients for primary PCI compared with direct-arrival patients on long-term clinical outcomes.
P3348
Progression of atherosclerotic neointima in the late phase after bare metal stent implantation: insights from integrated backscatter intravascular ultrasound analysis

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Background: Although recent studies show the lipid laden neointima appearance inside the stent in the extended late phase after bare-metal stent (BMS) implantation, the mechanism of this phenomenon has not been fully elucidated.

Methods: A total of 52 consecutive patients with in-stent restenosis (ISR) after BMS implantation were enrolled. According to the duration after stent-implantation, ISR lesions were classified as the early phase (5 to 8 months), the moderate phase (9 to 12months) or the late phase (more than 13 months). To compare the tissue characterization of neointima among three phases, integrated backscatter intravascular ultrasound (IB-US) was performed for volumetric analysis within the stented segment.

Results: Twenty-six ISR lesions were classified as the early phase, 13 ISR lesions as the moderate phase and 13 ISR lesions as the late phase. On IB-US analysis, the percentage of lipid tissue volume was significantly higher and that of fibrous tissue volume was significantly lower in the late phase compared to the early phase. (P<0.001, respectively). There were no significant differences in tissue characterization between early and moderate phases.

Conclusion: We could identify the increased percentage of lipid tissue and the decreased percentage of fibrous tissue in the late phase compared to early phase. Thus, the mechanism of this phenomenon has not been fully elucidated.

P3349
A multiparametric clinical and echocardiographic score to risk stratify patients with chronic systolic heart failure: derivation and testing

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1University Hospital, Cardiac and Thoracic Department, Pisa, Italy; 2University Clinical Centre, Prishtina, Kosovo, Republic of

Background: Although echo-Doppler and biomarkers are the most common examinations performed worldwide in heart failure (HF), they are rarely considered in risk scores. Hence, a multiparametric HF score was purposely designed to include the separate contribution of prognostic markers that are currently evaluated in clinical practice in an ambulatory setting. Thus, the aim of this study was to develop and validate a multiparametric HF score that included the contribution of prognostic markers, such as echo-Doppler variables and natriuretic peptide levels, that are commonly evaluated in clinical practice in an outpatient clinic.

Methods: In patients with chronic HF and left ventricular ejection fraction (LVEF) ≤45%, data on clinical status, echo-Doppler variables, NT-proBNP levels, estimated glomerular filtration rate (eGFR), and drug therapies were combined to build up a multiparametric score. We randomly selected 250 patients to produce a derivation cohort and the remaining 388 patients were used as a testing cohort. The endpoint was all-cause mortality. Follow-up lasted 29±23 months.

Results: The following unvariable predictors were entered into the multivariable Cox model: furosemide daily dose >25 mg, inability to tolerate ACE inhibitors, inability to tolerate beta-blockers, age >75 years, NYHA II-III, eGFR <60 ml/min, NT-proBNP plasma levels above the median, tricuspid plane systolic excursion (TPSE) >14 mm, LV end-diastolic volume index (LVEDV)/eGFR >96 ml/m², severe mitral regurgitation (MR) and LVEF <30%. The scores of prognostic factors were obtained with the respective odds ratio divided by the lower odd ratio: 4 points for furosemide dose, 3 points for age, NT-proBNP/LVEDV, TPSE, 2 points for inability to tolerate beta-blockers, inability to tolerate ACE inhibitors, NYHA II-III, eGFR <60 ml/min, MR, 1 point for LVEF. The multiparametric score predicted all-cause mortality either in the derivation cohort (68.4% specificity, area under the curve [AUC] 78.7%) or in the testing cohort (73.7% specificity, AUC 77.2%). All-cause mortality significantly increased with increasing score both in the derivation and in the testing cohort (p <0.0005).

Conclusion: We conclude that this multiparametric score is able to predict mortality in chronic systolic HF.

P3350
Independent and incremental prognostic value of increased left ventricular mass and reduced relative wall thickness in patients with chronic systolic heart failure and left ventricular remodeling

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Background and aim: It has been recently pointed out that most patients with chronic systolic heart failure (HF) are described by left ventricular (LV) enlargement and low LV ejection fraction (LVEF); many of them display increased LV end-diastolic volume that is out of proportion to the increased LV mass. Assessment of the degree of LV hypertrophy and of relative wall thickness may be useful to further characterize them into different LV remodeling patterns. Therefore, we sought to assess the prevalence and stratify the risk of different patterns of LV remodeling among patients with chronic systolic HF due to ischemic and non-ischemic dilated cardiomyopathy.

Methods: Patients (n=647) with chronic HF, LVEF <50% and LV end-diastolic volume index >91 ml/m², classified according to LV mass index and modified relative wall thickness (RWT), were followed-up for 27±21 months. Ventricular mass was determined using a standard M-mode echocardiographic method. RWT was defined as the ratio of the sum of interventricular septum thickness (IVST) and posterior wall thickness in diastole (PWT) to LV end-diastolic diameter. The end point was all-cause mortality.

Results: Prevalence of the pattern of increased LV mass index, defined as LV mass index >148 g/m² in males and >122 g/m² in females, and decreased RWT (≤0.34) was 29%. Multivariable predictors of all-cause mortality were age >75 years (p=0.001), NYHA class ≥2 (p=0.001), increased LV mass index and decreased RWT (p=0.033), estimated glomerular filtration rate <60 ml/min (p=0.017), heart rate >80 beats/min (p=0.016) and estimated pulmonary artery systolic pressure >40 mmHg (p=0.050). The addition of increased LV mass index and decreased RWT to demographic, clinical and echo-Doppler parameters, including LVEF and mitral E wave deceleration time, significantly improved the chi-square for the prediction of the outcome (from 102 to 111, p=0.003). The Kaplan-Meier survival curves, patients with increased LV mass index and decreased RWT had a worse survival (31%) than patients with less LV mass index and RWT ≥0.34 (74%), patients with less LV mass index and RWT <0.34 (65%) and patients with increased LV mass and RWT <0.34 (73%).

Conclusion: In chronic systolic HF, LV enlargement and low LVEF, significant worse outcomes were apparent among patients with increased LV mass index and RWT than in those with less LV mass index and normal to increased RWT. Hence, this pattern of LV remodeling may be used to identify patients at higher risk of mortality, since it may provide additive prognostic information with respect to LVEF and diastolic function.
P3351 Inhibition of neovascularisation by bevacizumab has a direct effect on left ventricular function. A prospective study

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1University of Athens Medical School, 1st Department of Cardiology, Athens, Greece;2University of Athens, Faculty of Medicine, Department of Clinical Therapeutics, Athens, Greece

Purpose: Bevacizumab, a recombinant humanized monoclonal antibody directed against vascular endothelial growth factor (VEGF) that is used widely in the treatment of cancer, is associated with increased incidence of cardiovascular events.

The purpose of this prospective study was to assess the impact of bevacizumab administration on left ventricular function of patients with breast or colorectal cancer.

Methods: We enrolled 147 consecutive patients who had been diagnosed with colorectal or breast cancer, 76 patients with combination therapy that included bevacizumab and 71 with combination therapy without bevacizumab. Both groups were estimated by echocardiography at baseline, at 6 and 18 months after initiation. The follow up included 2 dimensional echo, M-mode measurements and Tissue Doppler Imaging as well.

Results: In bevacizumab group, Systolic myocardial motion (Sa) was significantly lower at both 6 months (10.93±4.64 versus 9.90±3.69 cm/sec, p<0.003) and at 18 months (5.83±2.53 versus 7.84±3.45, p<0.004). Regarding indexes evaluating the diastolic function, E/E’ ratio (Early rapid filling wave (E), mitral annulus early diastolic motion (E’)) significantly increased both at 6 months (5.83±2.53 versus 7.86±3.45, p<0.005) and at 18 months follow up (5.83±2.53 versus 7.84±3.45, p=0.004). In the control group, the mean value of Sa at baseline was similar at 6 month follow up (9.02±4.26 versus 8.87±3.80 cm/sec, p<0.17) and at 18 month follow up (9.02±4.26 versus 9.10±4.21 cm/sec, p<0.06). Accordingly, there was no difference in E/E’ ratio between baseline and 18 months (6.79±2.56 versus 6.81±2.62, p=0.15). All other echocardiography measurements did not differ between the measurement times, in both groups.

Conclusions: It seems that the addition of bevacizumab in the conventional scheme of chemotherapy has a direct adverse effect on both left ventricular diastolic and systolic function.

P3352 Is backscatter a function-independent method for assessment of treatment response to anti-fibrotic therapy in subclinical diabetic cardiomyopathy? Validation against T1 mapping and collagen biomarkers

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Purpose: A readily available technique is needed to demonstrate myocardial fibrosis and its response to therapy. Calibrated integrated backscatter (cIB) has been shown a potential candidate, but its independence from LV function is unclear. We sought to use T1 mapping and collagen biomarkers to validate the cIB response to spironolactone in subclinical (Stage B) heart failure.

Methods: 225 asymptomatic pts with stage A heart failure were screened using biochemical, anthropometric and imaging tests. Pts with stage B heart failure (diagnosis of diabetes or LV dysfunction in the absence of ischemia by exercise echo) were tested for fibrosis. Calibrated integrated backscatter (cIB) was derived from the posterior wall, anteroseptum and pericardium. T1 mapping was performed with a modified Look-Locker technique using saturation recovery imaging. Amino-terminal propeptides of pro-collagen type I (PINP) and type III (PIIINP), carboxy-terminal propeptide of pro-collagen type I (PICP) & transforming growth factor beta-1 (TGF-beta1) were measured in plasma and cIB.

Results: Parameters measured at baseline and 6 months in 49 pts (25 male, aged 60±10y) randomized to spironolactone 25mg/day or placebo. Pts were well matched at baseline. Post-intervention, cIB improved but post-contrast T1 mapping did not improve collagen biomarkers remarkably. [Table] No relationship was observed between the change (Δ) in cIB and Δ in diabetic (Δt1m=0.237, p=0.10) or systolic LV function (Δt1m=0.197, p=0.98).

Conclusion: Aldosterone antagonism affects cIB but not T1 mapping or pro-collagen biomarkers in Stage B heart failure.

P3353 Echocardiographic prediction of the size and myocardial performance index of acute and chronic myocardial infarction in rats

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Purpose: The model of myocardial infarction (MI) in rats is widely used for studying ventricular remodelling. The “in vivo” evaluation of the transmural extension of acute MI in these animals is a crucial part of the study designs. Echocardiography is a well established tool on the assessment of cardiac function in chronic MI in rats; however, data on the setting of acute MI are scarce. Therefore, this study aimed to evaluate: a) the usefulness of echocardiography for prediction of the infarction size (IS) at 24h after MI, as compared with 1 month later; b) the myocardial performance index (MPI) at baseline, at 24h and at 1 month.

Methods: Twenty four Wistar rats underwent suture ligation of the left anterior descending coronary artery. A sham-group was also included. Echocardiographic study (12 MHz HD7XE, Philips) of left ventricular myocardium (using right parasternal long- and short-axis views) was performed at three different times, before, at 24 h and 1 month after the infarction. Myocardial appearance and quantification of the left ventricle of 43±9.1% (range 33-58%). At 1 month, long-axis views showed rounded and dilated akinetic myocardium and apex scar; short axis views (from PM to the apex) showed thickening and akinesia of the infarcted myocardium. IS represented a percentage of the left ventricular of 43±9.1% (range 33-58%). There were no significant differences on IS between 24hours and 1 month (p>0.5). The histological IS values (35±2.7%, range 18.9-48.3%) were significantly smaller than the echocardiographic IS values (p<0.5). MPI was higher after MI, as compared to baseline, although it reached significance only at 24h (p<0.05).

Conclusion: We demonstrate that the evaluation of infarction size by echocardiography at 24h post-corony ligation could be useful to predict the size one month later. In addition, MPI could be used to evaluate changes over time on cardiac function after acute MI.

P3355 The influence of remote ischemic post-conditioning on left ventricular mechanics

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Purpose: It is well known that remote ischemic postconditioning (RIPC) decreases infarct size and prevents left ventricular (LV) remodeling in patients with myocardial infarction. However, there is no study that evaluates the effect of RIPC on LV mechanics assessed by speckle tracking echocardiography. Therefore, we aimed to test the effects of RIPC on LV deformation parameters such as strain, strain rate, rotation and twist in healthy subjects.

Methods: The study group consisted of 22 healthy subjects (28±4.2, 21-35), each with a structurally normal heart. The non-dominant arm was made ischemic by inflating the blood pressure cuff to a pressure of 200 mm Hg for 20 minutes. After ischemia, the arm was allowed to undergo reperfusion for 10 seconds, after which the blood pressure cuff was inflated again to 200 mm Hg and the arm was made ischemic for 10 seconds. This deflation/inflation cycle was repeated a total of 3 times. TTE was obtained at baseline and repeated 30 minutes after the completion of these cycles. In TTE images, the LV strain (strain rate), basal and apical circumferential strain/stretch rate, and rotational parameters, such as basal rotation, apical rotation and LV twist, were recorded.

Results: There were no significant differences in EDV, ESV, Simpson EF and heart rate before and after RIPC. Apical 4-3-2 chamber longitudinal strain/stretch rate and apical circumferential strain/stretch rate measurements were comparable before and after RIPC, whereas basal circumferential strain was significantly decreased after RIPC (-23.3±3.4 vs -19.8±6.9, p<0.001). After RIPC, rotation was significantly increased (11.6±3.7 vs 16.7±4.0, p<0.001) and basal rotation was significantly decreased (-6.1±2.1 vs -4.7±2.4, p<0.05). Consequently, net LV twist was significantly increased (17.4±4.5 vs 21.7±4.7, p<0.05).

However, neither apical nor basal rotational rates showed any changes.

Conclusions: We proposed that remote ischemic post-conditioning affects the rotational mechanics of the heart rather than longitudinal mechanics. These results might give new insights into understanding the favorable effects of the post-conditioning.
Effect of age on left ventricular ejection fraction assessed by echocardiography

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Introduction: Various age-related changes of the cardiovascular system are well known. Yet, age-related changes of left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS), left ventricular volume (LVEDVl), and left ventricular mass index (LVMMI) have not conclusively been elucidated in a large population of healthy adult individuals.

Methods: Transthoracic two-dimensional echocardiography was performed in 6260 normal subjects (3032 [48%] males) for different reasons obtained retrospectively from case notes and patient interviews. Mean age at presentation was 44.6 ± 0.2 years (range 7 to 80 years).

Results: With advancing age, a significant increase in LVEF was observed (female: p < 0.0001; males: p < 0.0001), which was more pronounced in females (62.7 ± 0.4% for age < 20 years vs. 65.0 ± 0.3% for age 60-80 years) than in males (62.0 ± 0.4% for age < 20 years vs. 63.4 ± 0.3% for age 60-80 years). Similarly, LVFS increased in females from 37.9 ± 0.5% (age < 20 years) to 41.9 ± 0.4% (age 60-80 years) and in males from 37.3 ± 0.5% (age < 20 years) to 39.5 ± 0.4% (age 60-80 years: p < 0.0001). LVEDVl decreased from 49.9 ± 0.9 ml/m² (age 7-20 years) to 43.4 ± 0.5 ml/m² (age 60-80 years) in females and from 56.5 ± 0.8 ml/m² (7-20 years) to 48.9 ± 0.5 ml/m² (age 60-80 years) in males (p < 0.0001). LVMMI increased significantly in elderly subjects compared to younger ones (74.3 ± 1.2 g/m² for age < 20 years vs. 88.0 ± 0.7 g/m² for age 60-80 years: p < 0.0001).

Conclusion: LVEF, LVFS, and LVMMI increase with advancing age in healthy individuals, in particular in females. In contrast, LVEDVl decreases with age. These findings may have implications for the echocardiographic assessment of left ventricular function and size in the elderly and suggest that age-adjusted standard values for these parameters are needed.

Responde to Cardiac Resynchrony Therapy (CRT) in patients with moderate to severe heart failure and associated with segmental myocardial viability on Dobutamine Stress Echocardiography (DSE)

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Background: Cardiac resynchrony therapy (CRT) in patients with heart failure and conduction abnormalities improves symptoms, mortality and morbidity in only 60-70% of patients. The aim of this study was to test to what extent echocardiographic indices of regional myocardial viability could improve prediction of response to CRT.

Methods: 76 patients eligible for CRT were included after the following criteria: 1) New York Heart Association (NYHA) class III/II, 2) left ventricular ejection fraction (LV EF) < 35%, 3) QRS width > 120 ms, and 4) optimal medical treatment. All underwent dobutamine stress echocardiography (DSE) to evaluate myocardial viability.

Results: Patients had severely depressed LV function and reduced functional capacity. After 12 months there was a significant reduction in LV end-diastolic diameter (LVEDD) (76.0 ± 11 mm versus 67.3 ± 13 mm, p < 0.05) and volume (258 ± 112 ml vs. 208 ± 118 mL, p < 0.05), and improvement in EF% by 7 percent points (p < 0.001). Multivariate regression analysis revealed that viability in > 8 myocar-
dial segments on DSE was a significant positive predictor for response to CRT (p = 0.03) together with long interventricular motion delay (IVMD, p = 0.03) and wide LVEDD (p = 0.01).

Conclusions: Independent baseline predictors to response to CRT are > 6 viable LV segments, wide LVEDD and long IVMD.

Usefulness of exercise stress echocardiography for estimation of exercise capacity in patients with atrial fibrillation

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Background: Exercise stress echocardiography is well recognized to reflect ex-
Exercise capacity in patients with sinus rhythm. In patients with atrial fibrillation (AF), however, the usefulness of exercise stress echocardiography for predicting exercise capacity is unknown.

Methods: Forty-three patients (age: 63±12 years, 11 females) with AF (23 persistent, 20 paroxysmal) and preserved LVEF were studied using two dimensional speckle tracking echocardiography at rest and during low intensity exercise by supine bicycle (20W, 10min), and measured systolic rotation (Rot) for 5 consecutive beats in apical and basal level of left ventricle. All patients underwent cardiological exercise testing to obtain the peak oxygen consumption (PeakVO2).

Results: PeakVO2 in persistent AF patients was significantly lower than that in paroxysmal AF patients (18.3±5.5 vs 24.9±8.5 ml/min/kg, p=0.01). In patients with persistent AF, apical Rot at rest and the incremental values of apical Rot during exercise (ΔRot) were correlated to PeakVO2 (r=-0.62, p<0.01 and r=0.67, p<0.01, respectively). Multivariable stepwise regression analysis showed that only apical ΔRot predicted PeakVO2 independent of other echocardiographic parameters (β=0.67, p=0.01). Using receiver-operating-characteristic analysis, the optimal cutoff for apical ΔRot was 12% (sensitivity: 79%; specificity: 83%) to predict PeakVO2 of < 21 ml/kg/min. On the other hand, paroxysmal AF patients did not show significant correlations between any of these echocardiographic indices and PeakVO2.

Conclusions: Low intensity exercise stress echocardiography may have potential to predict exercise capacity in patients with persistent AF who have lower exercise capacity than paroxysmal AF patients.

Orthostatic stress echocardiography as useful test to measure variability of aortic and subaortic pressure gradient

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The aim of study was to assess influence of orthostatic stress test on changes in aortic and subaortic pressure gradient in patients with aortic stenosis (AS), hypertrophic cardiomyopathy (HCM) and normal healthy subjects (controls).

Methods: The stress role of orthostatic test was assessed in 100 consecutive subjects (40 AS patients (valvular stenosis), 40 HCM patients without subvalvular stenosis obstruction i.e. subaortic gradient < 30 mmHg at supine position) and 20 healthy subjects (control group). The aortic and subaortic gradients were compared between supine and upright position using Doppler echocardiography from apical window. From technical difficulties 2 patients were excluded from HCM group (suboptimal Doppler signal during orthostatic test) and 19 patients were excluded from AS group because aortic gradient was significantly higher in suprasternal or right parasternal windows than apical window (different direction of stenotic jets) at supine examination while in orthostatic examination only transapical measurement was used.

Results: In AS patients maximal aortic gradient decrease after orthostatic stress (79.47±29.88 vs. 69.63±22.03 mmHg, p=0.003). In contrast, in HCM patients subvalvular gradient increase during stress test (13.56±7.93 vs. 24.97±20.93 mmHg, p=0.005). In control group the transvalvular flow remained within normal range during stress test.

Conclusions: Orthostatic stress test decreased “theoretically fixed” valvular gradient in AS. The combination of stiffened stenotic valve apparatus and reduced LV preload may be responsible for this depressive response. In HCM test increased provocative gradient in “dynamic” subvalvular obstruction. The novel orthostatic stress test may be helpful especially in patients predisposed to syncope due to hemodynamic reasons.

P3362

Prognostic value of non-positive exercise echocardiography in the patients submitted to Coronary Intervention

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Purpose: Ascertain prognostic value of non-positive treadmill EE in the patients (pts) previously submitted to percutaneous coronary intervention (PCI). Correlate cardiovascular risk factors (CVRF) with adverse events occurrence.

Methods: We reviewed all EE performed at our centre between 1/2008 and 12/2010 and selected those from pts previously submitted to PCI and that were not positive for myocardial ischemia. Then we evaluated the presence of CVRF, the occurrence of adverse events, and possible correlation. The statistical analysis was made with univariate analysis using chi-square test. For survival analysis we used the Kaplan-Meier method.

Results: We analyzed 1457 treadmill EE of those 164 were performed in pts with previous PCI; we studied the 139 pts whose EE were negative (44%) or inconclusive (95) for myocardial ischemia: 116 (83.5%) men, mean age 61±9.7 years. The indication for EE performance was abnormal ECG in 599 (77.6%), angina pectoris 12 (8.6%), atypical chest pain 13 (9.4%), fatigue 3 (2.2%), other in 3 pts (2.2%). In the mean follow-up of 596±365 days there was 1 (0.7%) non-cardiovascular death and there wasn’t cardiovascular death. We noted the following events: 6 (4.3%) unstable angina, 2 (1.4%) non-ST-segment elevation myocardial infarctions, 1 (0.7%) acute myocardial infarction with ST segment elevation, 5 (3.6%) heart failure, and 5 (3.6%) pts with atrial fibrillation exercise ECG. These events occurred 505±375 days after EE. Thirteen (9.4%) pts performed coronary angiography and 9 (6.5%) were submitted to PCI. Univariate analysis didn’t find significant statistical difference between the EE result (inconclusive/ negative) and events occurrence (p=0.39). Relative to CVRF we recorded 92 (66.2%) hypertensive pts (HT), 88 (63.3%) with dyslipidemia, 67 (48.2%) smokers, 36 (25.9%) diabetic pts (DM), 17 (12.2%) obese, 4 (2.9%) with chronic renal disease (CRD). Univariate analysis didn’t show statistical significance between CVRF and events (HT p=0.158, dyslipidemia p=0.411, smoking p=0.207, DM p=0.185, obesity p=0.183, CRD p=0.448).

Conclusions: A non-positive EE pos PCI has a negative predictive value of 86%. There was no significant statistical difference between the test result (negative/ inconclusive) and adverse events occurrence. We didn’t find statistical relation between CVRF presence and adverse events occurrence. One year free-event survival rate was 93.1±2.4%. In a patient with previous PCI a treadmill EE without evidence of myocardial ischemia appears to have good prognostic value in medium-term follow-up, with low events incidence.

Stratifing the risk in myocardial disease / Miscellaneous

P3364

Real-time sonographic position monitoring of central venous catheters by microbubble-injection: development of a new procedure

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Purpose: This study aimed to develop a new non-invasive, ultrasound-based procedure to determine orthotopic central venous catheters (CVC) position by sono- graphic detection of injected microbubbles.

Materials and Methods: With approval of the local ethics committee n=95 patients with CVC or other catheters were examined. The appearance of MB in the right heart can be observed after injection of agitated saline in the substernal four-chamber view. MBpresent themselves hyperechogenic and dissolve later by B-Mode registration; time of appearance can be quantified. To determine position- ing, time of appearance of MB, workflow and physicians evaluation were analysisised.

Results: We injected a total of 95 patients (65 [61–18] years, 57% male). We used the internal jugular vein (n=85) and the subclavian vein (n=10). The main diagno- sis were Pneumonia (n=49), Aortic valve reconstruction (n=9), myocardial infarct- ion (n=6), heart failure (n=6), gastrointestinal bleeding (n=4) and other (n=11). Orthotopic position was confirmed in 95 patients when MB appeared in the right heart less than one second after injection with a reliability of 100%. In 8 pa- tients quantitatively measured appearance of MB was 0.56 (0.2) seconds (mean, SD). Physician/registration of practicability was 91% (linear analogue self- assessment).

Conclusion: Ultrasound-based real-time position monitoring of CVC by this new non-invasive, ultrasound-based procedure and technique has the potential to serve as an alternative to X-ray or other methods.

P3365

Echocardiography reveals lost of silicone tubes during transvenous lead extraction

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Purpose: Lead breakage is rare complication of transvenous lead extraction (TLE), in some cases it related to loss of silicone tubes dropped into right cardiac chambers. This study stress the role of echocardiography in detection and removal of lost silicone tubes.

Methods: During the last 5 years TLE procedures were performed summary in 740 patients (71.2±14.5, age 5-91 years). We have extracted 1276 ingrown (PM >12, ICD >6 months) with PM and ICD systems. 1003 ex-
tracted leads were functioning and 183 abandoned. 69.5% - passive fixation and 18.3% - active fixation. In 42.1% of patients the follow¬ing cardiac events (2 sudden deaths) in the Group 1. In Group 2 there were 18 cardiac events (2 sudden deaths) in the Group 1. Mean CFR of the examined vessel was 2.35±0.52. There was a significant difference of CFR between patients with and without cardiac events (2.17±0.65 vs. 2.37±0.5, p=0.026, respectively). During the follow up, there were 22 cardiac events (2 sudden deaths) in the Group 1. In Group 2 there were 18 cardiac events (1 cardiac death). The Kaplan–Meier event-free survival at 4 years was higher in Group 1 than in Group 2 (89% vs. 62%, p<0.001, respectively).

Conclusion: In patients with coronary artery stenosis of intermediate severity, deferred of revascularization, based on CFR<2 might be reasonable option since it is associated with good long term clinical outcome.

P3368 Transthoracic Doppler coronary flow reserve as a marker of successful stent implantation of the left anterior descending and right coronary arteries

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Transthoracic echocardiography (TTE) has been described as an accurate technique for noninvasive evaluation of coronary flow reserve (CFR) of the left anterior descending artery (LAD) and posterior descending artery (PDA). The aim of this study was to find out whether serial CFR evaluation in the LAD and PDA using TTE allows detection of stenosis elimination after stent implantation and is a marker of successful procedure.

Methods: The study group comprised 12 patients with single-vascular coronary disease (stenosis 82±16%) of the LAD (8 patients) or right coronary artery (RCA, 4 patients) scheduled for stent implantation. All patients underwent dipyridamole (0.54 mg/kg/m) stress echo with CFR evaluation of either distal coronary stenosis, transthoracic doppler echocardiography (TDE) coronary flow reserve measurements (TDE CFR) has become useful prognostic tool. Also TDE-CFR is noninvasive, low cost, available and radiation free. Also, CFR reduction is located upstream in the ischemic cascade, and it could detect starvation unable to induce wall motion abnormalities.

Aims: The aim of the present study was to determine clinical outcome of patients with intermediate coronary artery stenosis (50-70%) on the basis of TDE CFR measurements.

Methods: The study population included 245 (173 male) patients (pts) with intermediate LAD (217 pts) or RCA (28 pts) stenosis. All patients underwent TDE CFR assessment. CFR was defined as the ratio between maximal velocity of diastolic coronary blood flow during maximal hyperemia and in rest, induced by i.v. infusion of adenosine (140μg/kg/min). Based on CFR value, patients were divided into two groups: Group 1. CFR ≥2 (198 pts), and Group 2. CFR<2 (47 pts). Primary endpoints were: cardiac death, non-fatal ACS, coronary angioplasty of the examined vessel, coronary by-pass surgery and acute heart failure requiring hospitalization.

Results: 94 (38%) pts had one vessel disease, 87 (36%) pts had two vessel disease and 64 (26%) pts had three vessel disease. All patient completed follow up (21±14 months). Mean CFR of the examined vessel was 2.35±0.52. There was significant difference of CFR between patients with and without cardiac events (2.17±0.65 vs. 2.37±0.5, p=0.026, respectively). During the follow up, there were 22 cardiac events (2 sudden deaths) in the Group 1. In Group 2 there were 18 cardiac events (1 cardiac death). The Kaplan–Meier event-free survival at 4 years was higher in Group 1 than in Group 2 (89% vs. 62%, p<0.001, respectively).

Conclusion: In patients with coronary artery stenosis of intermediate severity, deferred of revascularization, based on CFR<2 might be reasonable option since it is associated with good long term clinical outcome.

P3367 Clinical outcome of patients with intermediate coronary artery stenosis on the basis of transthoracic Doppler echocardiography coronary flow reserve measurements


Introduction: Considering the necessity of functional evaluation of intermediate coronary stenosis, transthoracic doppler echocardiography (TDE) coronary flow reserve (CFR) has become useful prognostic tool. Also TDE-CFR is noninvasive, low cost, available and radiation free. Also, CFR reduction is located upstream in the ischemic cascade, and it could detect starvation unable to induce wall motion abnormalities.

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Is three-dimensional transthoracic echocardiography advantageous for screening of structural and functional abnormalities in the heart?

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Background and purpose: Three-dimensional transthoracic echocardiography (3D-TTE) enables accurate estimation of left ventricular (LV) volume and function. However, its advantage in screening examinations remains unclear. The aim of this study was to assess the advantage and disadvantages of 3D-TTE in screening of general population in comparison with two-dimensional TTE (2D-TTE).

Methods: Two-hundred twenty (65±12years, all women) who received an annual health examination in the Tanno-Sobetsu cohort were examined by both conventional 2D-TTE and 3D-TTE. In 2D-TTE, left ventricular mass (LVM) was calculated using the ASE recommended formula and area-length method. Both LVM estimates were normalized by body surface area (LVM/A). 3D data sets were acquired using Vivid E9 with 4V probe (GE Healthcare), and LV end diastolic volume (EDV), LV end systolic volume (ESV), LV ejection fraction (EF) and LV mass (LVM) were determined off line by use of Echo PAC (GE Healthcare).

Results: 3D-TTE analysis was feasible in 161 subjects (69%, 3D group), but not in 51 subjects (31%, non-3D group). Blood pressure was lower (133/75 mmHg vs. 147/90 mmHg, p<0.05) and BMI was smaller (22.6 kg/m² vs. 24.2 kg/m², p<0.005) in the 3D group than the non-3D group. Posterior wall thickness was thinner (8.6 mm vs. 9.0 mm, p<0.005). LV end diastolic diameter (43.7 mm vs. 42.1 mm, p=0.05), EDV (74.5 ml vs. 64.7 ml, p<0.001) and ESV (23.7 ml vs. 20.4 ml, p<0.01) were larger in the 3D group compared with those in the non-3D group. LVEF and left atrial volume were similar in the two groups. In comparison or LVEF between 3D-TTE and 2D TTE.

Conclusions: 3D-TTE in less feasible for screening examination compare with 2D-TTE. Slight but significant differences in 2D data on LV thickness and volumes between 3D-TTE-feasible and non-feasible groups indicate that use of 3D-TTE is accompanied by selection bias concerning the indices. 2D-TTE provides comparable estimates of LV dimensions and EF with those by 3D-TTE, though it modestly underestimates LVM.

Follow-up of transplanted heart: non-invasive assessment and evolution of echo parameters in the first year after heart transplantation


Heart transplantation (HT) is a standard and accepted therapy for end-stage heart failure, and nowadays non-invasive management by using imaging techniques is a complementary approach to these patients. Although HT is characterized by high eligibility criteria and restrictive pattern at the beginning, we know that some parameters could evolve in the first weeks or months of follow-up, such as left ventricular global and regional systolic function.

Objective: To describe the evolution of systolic and diastolic function in HT during the first year by using traditional and newer two-dimensional echocardiographic variables, Tissue Doppler and strain parameters.

Methods: We included 21 consecutive patients who have been transplanted in the last two years in our centre. A total of 231 echocardiograms were done (eleven per patient). We analized: mitral E and A wave ratio (E/A), isovolumic relaxation time (IVRT), lateral and medial annular E/E' ratio (E/E' lat and E/E med), among other parameters. For longitudinal, radial and circumferential strain measurement was analyzed a total of 5184 segments (7% of them were not interpretable) by using speckle tracking technique. Echocardiograms with acute rejection were excluded from analysis.

Results: The results of our study are shown in the table below. All the classical echocardiographic parameters measured improved at one year of follow-up. Deletion parameters remainedunchanged along the time.

Conclusions: Serially repeated echocardiograms and analysis of the evolution of main systolic and diastolic parameters provide an easily performable tool to detect changes in the graft during the first year. This is the first study that describe normal values of strain parameters after 1 year of HT. General echocardiographic assessment should be performed in the global approach of patients who have been transplanted.

TCD-derived myocardial performance index is a powerful predictor of long term mortality in patients with systolic heart failure

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Aim: To investigate the prognostic value of global myocardial performance index (MPI) of the left ventricle (LV) determined by tissue Doppler imaging (TDI) in determining long term prognosis in patients with systolic heart failure, compared to established prognostic parameters.

Methods: 112 patients with symptomatic CHF due to dilated cardiomyopathy (n=32) or ischemic heart disease (n=80) were examined and followed for at least 4 years (mean 61 months). Longitudinal myocardial velocities at 4 different mitral annular sites of LV from apical echocardiographic views were recorded by pulsed-wave DVI. MPI was also calculated from 4 LV sites, and the mean MPI was calculated. Primary endpoint was cardiovascular mortality.

Results: The mean MPI fraction was 0.25%, and mean MPI was 0.67. A total of 41 patients died of cardiac causes. In multivariate regression analysis, MPI and age emerged as the only independent predictors of cardiovascular mortality. ROC analysis yielded a cut-off MPI value of 0.67, and identified patients with cardiac mortality with a sensitivity of 71% and a specificity of 86%. The group of patients with MPI > 0.67 had a hazard ratio of 13.1 (95% CI 5.4-35.6).

Conclusion: MPI determined from TDI recordings at 4 mitral annular sites in patients with symptomatic heart failure is a powerful predictor of long term cardiovascular death, and identifies patients with a poor long term prognosis.
Acute allograft rejection (AR) is the major cause of mortality the first year after heart transplantation (HT). AR surveillance is mandatory by endomyocardial biopsies (EB). Our aim was to find the best echo-parameters to predict AR.

**Methods:** We included 21 HT patients since 2009. 11 echocardiograms/patient were done the day of EB. We measured classic left ventricular (LV) function parameters and 2D-longitudinal (long S), circumferential (Circ S) and radial (Rad S) LV strain.

**Results:** We analyzed 5184 segments and 141 EB. According to the ISHLT: 107 EB had grade 0 AR (75.8%), 30 1R (21.2%), 4 2R (2.8%) and 1 3R (0.8%).

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**Figure 1. ROC curve of AR related to LV variables**

**Echo parameters and AR**

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**Conclusions:** Acute allograft rejection in heart transplantation: ready to minimize the number of invasive procedures? The role of echocardiography

**P3374** Acute allograft rejection in heart transplantation: ready to minimize the number of invasive procedures? The role of echocardiography

**S. Mingo, V. Moravas Palomero, P. Beltran, M. Sanchez, E. Gonzalez Lopez, I. Garcia-Lunar, C. Mitro, J. Gonzalez Mireles, M.A. Caverio Gibanel, J. Segovia, University Hospital Puerta de Hierro Majadahonda, Department of Cardiology, Madrid, Spain**

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**Conclusions:** Acute allograft rejection in heart transplantation: ready to minimize the number of invasive procedures? The role of echocardiography

**P3375** Study of the ventricular function and its correlation with morphology in patients with severe symptomatic aortic stenosis

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**Introduction:** Different studies have raised the correlation between structure and function in the pressure overload by aortic stenosis (AS), and its possible association with the progress of ventricular disease. The aim of this study was to assess the systolic and diastolic ventricular function in patients (p) with severe symptomatic (SS) aortic stenosis (AS) and preserved ejection fraction (EF), and correlate it with collagen volume (CV) and myocardic surface area (MSA).

**Method:** The study assessed 12 p with SS AS, 65 ± 13 years of age, 58% males, and 6 p without valve disease. All p were performed Tissue Doppler Imaging (TDI) and cardiac catheterization; intraoperative biopsies were obtained to determine collagen volume (CV) and myocardic surface area (μm²).

**Results:** The mean (M) ± Standard Error (SE) of CV was 6.1% ± 0.7%, the M of the MSA was 388.4±7.1 ± μm², and the mean of the septal tissue strain (STS) at baseline was 14% (IQR 6.9-19). A significant correlation between STS and CV was observed (correlation coefficient -0.79, p=0.03). No correlation was observed between the STS and the myocardic surface area (R=0.15, p=0.8). The +dp/dtmax normalized by LVEDP measured during catheterization correlated negatively with the myocardic surface area (R = -0.94, p = 0.005). The time constant of myocardic decay (t1/2) increased 55±3% (p<0.001) and correlated positively with the myocardic surface area (R=0.81, p<0.04).

**Conclusion:** This study proved that impairment of systolic and diastolic function was observed in p with SS AS and preserved EF, which correlated with structural changes in the LV and were represented by an increase in interstitial CV and MSA.
Increased baseline left ventricular mass and volume as well as subclinical systolic dysfunction predict subsequent deterioration in left ventricular ejection fraction in patients with aortic stenosis

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Background: Left ventricular ejection fraction (LVEF) is an independent predictor of mortality in patients with aortic stenosis (AS). Deterioration in LVEF is one of the indications for aortic valve replacement. We aim to study these predictors.

Methods: We analysed 509 consecutive patients with AS who underwent pairwise echocardiographic studies >180 days apart. Besides conventional echocardiographic findings, tissue Doppler assessment of LV systolic (S'), early (E') and late (A') diastolic velocities were also performed. Ninety-one patients (18%) had significant decrease (>20%) in LVEF (Group A). We compare their baseline echocardiographic parameters to the group without deterioration (Group B).

Results: The mean time interval between the paired studies, the LVEF and aortic valve area (AVA) were 1252±910 days, 60.1±12 and 1.29±0.44cm² respectively and were not significantly different between the two groups. One hundred and four patients (40%) had mild AS, 217 (43%) had moderate AS (AVA<1.0cm²) and 129 (27%) had severe AS (AVA<0.8cm²). LVEF decreased from 58±13 to 33±12 in Group A but was unchanged in Group B. AS severity progressed in both groups. Higher baseline left ventricular systolic volumes and mass index and lower tissue Doppler indices (S' and E') were predictors of worsening LVEF (Table).

Conclusion: Increased left ventricular mass, volumes and subclinical left ventricular dysfunction on tissue Doppler predict subsequent deterioration of LVEF in patients with AS. These patients may benefit from more intensive follow-up and early intervention.

Table

<table>
<thead>
<tr>
<th>Echocardiographic parameters</th>
<th>Group A (n=91)</th>
<th>Group B (n=318)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>%20 decrease in LVEF</td>
<td>%20 decrease in LVEF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial</td>
<td>Subsequent</td>
<td>Initial</td>
<td>Subsequent</td>
</tr>
<tr>
<td>Tira interval (days)</td>
<td>117±693</td>
<td>127±915</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>58±13</td>
<td>61±12</td>
<td>NS</td>
</tr>
<tr>
<td>(cm²)</td>
<td>1.20±0.37</td>
<td>1.31±0.45</td>
<td>NS</td>
</tr>
<tr>
<td>LV mass indexed to body</td>
<td>58±13</td>
<td>61±12</td>
<td>NS</td>
</tr>
<tr>
<td>surface area (m²)</td>
<td>124±25.95</td>
<td>116±15.81</td>
<td>0.021</td>
</tr>
<tr>
<td>LV end-systolic volume (mL)</td>
<td>49±30.35</td>
<td>42.3±26.5</td>
<td>0.003</td>
</tr>
<tr>
<td>(mL/m²)</td>
<td>116±18.41</td>
<td>109±7.384</td>
<td>0.003</td>
</tr>
<tr>
<td>Tissue Doppler S' (cm/s)</td>
<td>6.74±1.74</td>
<td>7.51±2.42</td>
<td>0.044</td>
</tr>
<tr>
<td>Tissue Doppler E' (cm/s)</td>
<td>6.65±2.24</td>
<td>7.07±3.94</td>
<td>0.007</td>
</tr>
<tr>
<td>Tissue Doppler A' (cm/s)</td>
<td>9.5±2.86</td>
<td>10.07±3.21</td>
<td>0.026</td>
</tr>
</tbody>
</table>

*Comparison between initial parameters.

P3378

The prevalence and determinants of pulmonary hypertension (PH) in severe aortic stenosis (AS) and preserved left ventricular ejection fraction (EF)

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Purpose: To determine the prevalence and the possible mechanisms of PH in pts with severe isolated AS, normal EF and no significant mitral valve dysfunction.

Methods: 327 pts with severe isolated AS at transthoracic echocardiography, mean age 77±4 years, were included in the study. We excluded pts with a mean arterial pressure (MAP)<50 mm Hg, or with a severe MR. At the end of f/u, 127 (40%) pts had died, 63% with and 37% without PH (p=0.001). 21 pts (49%) in the PH group and in 164 (60%) in the non PH group (p=0.17) had AV replaced.

Results: (see table) At the end of f/u, 127 (40%) pts had died, 63% with and 37% without PH (p=0.001). 21 pts (49%) in the PH group and in 164 (60%) in the non PH group (p=0.17) had AV replaced.

Table

<table>
<thead>
<tr>
<th>Variable</th>
<th>PH (n=898)</th>
<th>Non-PH (n=1688)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>77.0±10.3</td>
<td>69.2±10.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Males (%)</td>
<td>50 – 40</td>
<td>– – 0.21</td>
<td>0.55</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.8</td>
<td>1.8</td>
<td>0.61</td>
</tr>
<tr>
<td>Biplane EF (%)</td>
<td>64 – 54</td>
<td>– – 0.45</td>
<td>0.55</td>
</tr>
<tr>
<td>AVA index (cm²/m²)</td>
<td>0.39 – 0.12</td>
<td>0.39 – 0.12</td>
<td>0.61</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>148 – 56</td>
<td>143 – 52</td>
<td>0.30</td>
</tr>
<tr>
<td>LA area (m²)</td>
<td>22.3</td>
<td>25.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>E wave (cm/sec)</td>
<td>89.2 – 72.3</td>
<td>113.9 – 99.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>A wave (cm/sec)</td>
<td>97.0</td>
<td>99.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>E/A</td>
<td>1.0</td>
<td>1.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>AUC</td>
<td>233.4</td>
<td>78.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>PSAP (mm Hg)</td>
<td>36.1</td>
<td>66.1</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

AUC = area under the curve. Logistic regression adjusted for age and AVA index.

Conclusions: 1. Only a minority of pts with severe isolated AS and normal EF have PH. They have worse LV diastolic function, higher LV filling pressures and a higher mortality than those without PH. 2. In adjusted models, among the diastolic variables analyzed, peak E velocity has the highest AUC value. 3. These findings suggest that LV diastolic dysfunction is the main contributor to PH in pts with severe AS and normal EF.

P3379

Predictors of significant prosthetic leaks after percutaneous implantation of CoreValve aortic prosthesis in patients with an aortic annulus close to 23mm

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Purpose: Prosthetic leaks are a common event after the implantation of a percutaneous aortic prosthesis (TAVI). The exact measurement of aortic annulus is one of the factors that could be related to its appearance. In TAVI with a CoreValve prosthesis, they have worse LV diastolic function, higher LV filling pressures and a higher mortality than those without PH. 2. In adjusted models, among the diastolic variables analyzed, peak E velocity has the highest AUC value. 3. These findings suggest that LV diastolic dysfunction is the main contributor to PH in pts with severe AS and normal EF.

Methods: From April 2008 to December 2011, 127 patients with severe aortic stenosis were treated with CoreValve prosthesis at our institution. We selected the 31 cases who had an aortic annulus diameter between 22 and 23.9mm measured by transthoracic echocardiography (TE). The grade of prosthetic leak was assessed by transthoracic echocardiography at discharge according to current guidelines. Two groups were established according to the grade of regurgitation: Group 1 with significant leak, grade II (n=11), and group 2 with no significant leak, grade 0-1 (n=20).

Results: Mean age was 77±6, 63.1% were male. A small prosthetic was implanted in 21 cases, and a large one in 10 patients. Eight patients with the small prosthetic (38%) and three with the large one (30%) showed significant leaks.
with no significant differences between groups regarding to the prosthesis size (p=0.7). However, we did found significant differences between both groups in left ventricular outflow tract (LVOT) diameter (21.3±3.3mm in Group I versus 15.5±3mm in Group II, p<0.0005). Receiver operating curve analysis showed an excellent discrimination for a leak grade ≥3 at discharge for dimensions of LVOT (area under de curve 0.96; p<0.0005); a cut off value of 18.5mm for LVOT was associated with leak ≥3 with 82% Sensitivity and 95% Specificity. There were no differences between groups for other clinical and echocardiographic parameters, including distribution of annulus calcium, basal septal bulge, ventricular diameters, aortic root dimensions and depth of the prosthesis in the LVOT.

Conclusions: In patients undergoing CoreValve TAVI with aortic annulus around 23mm, larger dimensions of LVOT are significantly associated with prosthetic leaks ≥3. A LVOT diameter ≥18.5mm can predict the occurrence of significant leaks after the implantation of the CoreValve prosthesis, with excellent specificity in this subgroup of patients.

**P3381 Superiority of quantitative 3D color Doppler vena-contracta area measurements in patients with eccentric aortic regurgitation**

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Backgrounds: Quantitative approach is indispensable for the evaluation of aortic regurgitation (AR). However, 2D quantification by echocardiography has some limitations especially in patients with eccentric AR. Thus, we tried to directly measure vena-contracta area (VCA) of AR obtained from 3D color Doppler by 3D transesophageal echocardiography (TEE).

Methods: Forty-three consecutive patients (Age 73±11 y.o.) with mild to severe AR underwent 3D-TEE and aortography. We used aortography as a reference method to define AR severity. Vena-contracta width (VCW) was measured conventionally from long-axis view by 2D-TEE. VCA was measured using planimetry of 3D color Doppler flow from "en face" views by multi-planar reconstruction image (Figure). To estimate circularity of vena-contracta (VC), minor axis diameter of VC to major one ratio was calculated as circularity index (CI).

Results: Severe AR was present in 25 patients (58%) by aortography. VCA correlated better with AR severity by aortography than VCW (VCA R=0.82, VCW R=0.73, p<0.001). Cut-off value of severe AR by VCA was 0.36cm² (sensitivity 85%, specificity 87%, AUC=0.96). In patients with severe AR, eccentric AR jet was present in 9 patients and central AR jet in 15. CI of eccentric AR was smaller than that of central AR (0.32±0.15 vs. 0.84±0.15, p<0.001) and VCW of eccentric AR was smaller than that of central AR (4.4±4.0 vs. 8.6±3.2mm; p<0.001). However, there were no significant differences between VCA of eccentric AR and that of central AR (0.60±0.18 vs. 0.65±0.31 cm², NS).

Conclusions: In eccentric AR, VC was non-circular and conventional AR assessment by VCW underestimated the severity. Planimetrized VCA measurements by 3D color Doppler were more accurate quantitative approach also in patients with eccentric AR.
identify subtle contractile dysfunction independent of LVFE, diastolic dysfunction and presence of LV hypertrophy, and might be useful in identifying earlier LV dysfunction and higher risk patients.

**ELECTROCARDIOGRAMME FOR DIAGNOSIS AND PROGNOSIS**

**P3383** Correlation of QRS score and LV scar in patients receiving ICD therapy

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**Purpose:** The Selvester QRS score is an electrocardiogram (ECG) score, developed using computer modelling and post mortem data, to quantify myocardial infarction scar. More recently modified to take account of ECG confounders, the data for its use in predicting clinical outcomes and determining myocardial scar are discrepant. This research group has previously demonstrated that pericardial and transmurality of left ventricular (LV) scar is significantly associated with the occurrence of spontaneous ventricular arrhythmias. This study determines whether QRS score can be used as a surrogate for scar burden.

**Methods:** We investigated 64 consecutive implantable cardioverter defibrillator (ICD) recipients (age 66±11 years, 80% male, median left ventricular ejection fraction 30%) with coronary artery disease who had undergone cardiovascular magnetic resonance imaging with late gadolinium enhancement (LGE-CMR) prior to device implantation, over 4 years in a single centre (2006-09). Scar was quantified using the LGE-CMR images and characterised in terms of percent LV scar and number of subendocardial/transmural segments of scar in a 17-segment model. A modified Selvester QRS score was measured on the 12-lead ECG performed prior to ICD implantation. Points are awarded according to duration and amplitude criteria for each ECG lead, adjusted according the conduction pattern. Maximum difference of appropriate ICD therapy and death was recorded as the clinical end point.

**Results:** There was good correlation between QRS score and percent LV scar (r=0.43, p<0.01) but only low correlation between QRS score and number of segments of transmural scar (r=0.23, p=0.04) and no correlation between QRS score and segments of subendocardial scar (r=0.05, p=0.67). 16 (25%) patients had transmural scar only, and in this group, the QRS score was highly correlated with percent LV scar (r=0.62, p=0.01). During 19±10 months of follow up, 19 (30%) patients received appropriate ICD therapy, and 5 (8%) patients died. QRS score was not associated with the clinical end point.

**Conclusions:** This study demonstrates that although QRS score correlates well with total LV scar, it does not predict death or ventricular arrhythmia (defined by ICD detection parameters). QRS score performs best in patients with full thickness scar, perhaps reflecting its calibration against post mortem scar. This might explain why the Selvester score has not achieved broad clinical adoption: transmural and subendocardial scar may have different SCD/arrrhythmogenic potential which could confound clinical utility of QRS score, unless adjusted for scar type.

**P3384** Discrepancies in computation of non-linear heart rate variability indices for different Data Sets/RR segments: The size matters

T. Papaioannou, S. Kyrilaktis, E. Gialafos, D. Soulsis, K. Gkatzoulis, University of Athens, Greece

**Introduction:** Nonlinear system theory is increasingly used in Heart Rate Variability (HRV) analysis as it has provided independent predictors of cardiovascular risk and mortality, beyond traditional time- and frequency-domain parameters. Nonlinear indices of 24-h RR-interval time series are calculated by using suitably discrete data sets (RR segments) providing an average index-value for the whole recording. However, a great inconsistency exists regarding the size of the RR segments used in published studies. Aim of the study was to examine whether the RR segment size affects the computation of nonlinear indices of 24-h HRV.

**Methods:** 24-h Holter exam was performed in 46 healthy subjects (mean age: 39.7±14.3 years), 15 patients with ApEn (ApEn) and 1,2 scaling exponents (Detrended Fluctuation Analysis) were computed for nine different segment sizes (1000, 2000, 4000, 6000, 8000, 10000, 12000, 14000 and 16000 RR) by the use trended Fluctuation Analysis) were computed for nine different segment sizes and presence of LV hypertrophy, and might be useful in identifying earlier LV dysfunction and higher risk patients.

**Conclusion:** Different segment sizes, especially for ApEn calculation, may lead to critically different results, leading to potential over- or under-estimation of cardiovascular risk and disease severity misclassification. Further studies are required to establish solid methods regarding a standardized choice of RR segment size for the computation of nonlinear indices of 24-h HRV.

**P3385** Association between fragmented QRS complex and myocardial scar: A cardiovascular magnetic resonance study

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**Objective:** To evaluate the association of the fragmented QRS complex (fQRS) on the routine 12-lead ECG for detection regional myocardial scar evaluated by late gadolinium enhancement cardiovascular magnetic resonance (LGE-CMR).

**Background:** The fQRS in patients with coronary artery disease was recently used as a diagnostic marker of myocardial scar. However, the available data is still limited.

**Method:** This is a retrospective cross-sectional study of patients who underwent cardiac MRI for stress-perfusion study or myocardial viability. The association of fQRS, Q wave, and myocardial scar on LGE-CMR were analyzed.

**Result:** Of the 159 consecutive patients (mean ± SD age, 62.1±11.2 years, male 54.1%, 62 (39%) patients had myocardial scar. The fQRS and Q wave were detected in 49 (30.8%) and 46 (28.9%) patients, respectively. The sensitivity and specificity of fQRS for detecting myocardial scars were 53.2% and 99.3%, respectively. Sensitivity and specificity of Q waves were 66.1% and 90.7%, respectively. When using the presence of either fQRS or Q wave (89 patients, 43.4%), the sensitivity improved to 74.2%, while the specificity slightly decreased to 76.3%.

**Conclusion:** The fQRS can be used as a diagnostic marker of myocardial scar.

**P3386** Deceleration capacity of heart rate in acute pulmonary artery embolism

C. Eick, K. Rizas, C.S. Zuern, C. Stoleriu, D. Overkamp, P. Weyerich, M.P. Gawaz, A. Bauer, University, Tuebingen, Germany

**Background:** Risk assessment is of crucial importance in patients with acute pulmonary artery embolism (PAE). Deceleration capacity (DC) of heart rate is a novel ECG-based autonomic marker which yields strong and independent prognostic information in post-infarction patients. We hypothesized that in patients with PAE DC assessed directly after hospital admission (1) is significantly impaired compared to control and (2) associated with biomarkers reflecting myocardial damage.

**Methods:** The study included 22 consecutive patients (age 62.5 years, 12 females) with acute PAE confirmed by CT scan and 22 age- and gender matched controls. All patients were in sinus rhythm. DC was calculated from 30 minute ECG monitor recordings starting immediately after hospital admission according previously published technology.

**Results:** In patients with acute PAE, DC was significantly impaired compared to controls (DC 3.0±2.3ms vs. 8.1±3.2ms, p<0.0001; Fig. 1A). In patients with PAE, the subgroup of patients with increased levels of Tropinin I (≥0.003ng/ml) were characterized by significantly lower DC (2.3±3.2ms vs. 4.3±3.8ms, p=0.02; Fig. 1B).

![Figure 1](https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/339/430794/138394g)
First-degree AV blocks and intraventricular conduction delays in AL amyloidosis: prevalence and prognostic value

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In AL patients, cardiac involvement is not only frequent but it is also the most common cause of death. Despite a high prevalence of conduction abnormalities that may be easily identified by the standard surface electrocardiogram (EKG), their clinical features and management have been infrequently reported. To evaluate the prevalence of atrioventricular block (AVB) and intraventricular blocks (IVB) in patients with cardiac AL amyloidosis, and to verify whether these findings do have prognostic implications, we enrolled all consecutive never-treated patients in whom a first diagnosis of primary AL amyloidosis was concluded between 2008 and 2009, according to the International Society of Amyloidosis criteria. Patients were subdivided according to the presence (n=193) or absence (n=102) of cardiac involvement. Standard 12-leads EKG and cardiac ecosoccolorDoppler data were collected at diagnosis, and prognosis was evaluated after a median follow up of 477 days. As expected, IVB and AVB involvement was associated with a 10% EKG pattern (low voltages in 63.9%, pseudonormalization in 52.2%, and strain pattern in 38.5% of patients, respectively), with prolonged PQ, QRS and QT intervals (p<0.05 for all vs. non-cardiac AL). Overt AVB was present in 24.8%, and complete IVB was evident in 28% of cardiac AL patients, with a significantly higher prevalence of atrio- and intra-ventricular conduction delays (p=0.0295 and p=0.036, respectively). Notably, none of the AVB patients had a higher than I degree AV block. Kaplan-Meier survival analysis revealed a significantly higher mortality in the AVB group when compared with the “normal” PQ group (p=0.001), a trend that was confirmed also in cardiac AL patients (p=0.015). Mortality was also higher in the prolonged QRS group (p=0.0111 for the whole cohort). In cardiac AL patients, the presence of AVB was associated (p<0.05) with higher cardiac wall thickness and high values of NT-proBNP, whereas IVB was associated with higher indexed left ventricular mass and wall thickness (p<0.05 for both), but not with NTproBNP levels.

Conclusion: The presence of conduction abnormalities should not be overlooked in the diagnostic work-up of patients with AL amyloidosis, since they are not only more prevalent in cardiac AL patients, but they also have a prognostic role in predicting cardiac death. Such a prognostic stratification may be performed by a simple and cheap 10-lead EKG. Identification of any conduction abnormalities (starting from the “beginning” 1 degree AV block) should therefore prompt a more accurate cardiac support during patients’ follow-up.

Automatic detection, localization and classification of early repolarization in standard 12-lead electrocardiograms

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Purpose: Early repolarization (ER), which has been associated with increased risk of cardiac mortality, is defined as an elevation of the ORS-ST junction (i.e. J-point) in at least two inferior (II, III, aVF) or lateral (I, aVL, V4-V6) leads of the standard 12-lead electrocardiogram. Purpose of this study was to create an automatic algorithm for the detection and classification of ER.

Methods: A total of 1445 patients’ electrocardiograms were assessed visually by 3 blinded readers and the final grading of ER was established by the principle of the majority. The automatic grading of ER was based on the detection of the earliest QRS offset. Electrocardiograms analyzed by the automatic algorithm were compared with histopathology. Patients without any histopathological abnormalities were considered normal. Finally, results from the three readers were compared with those of the automatic algorithm.

Results: Readers graded 132 recordings (9%) as ER positive out of which the automatic algorithm detected 119 recordings, resulting in sensitivity of 90.2%. A total of 316 ER negative recordings were misclassified as positive, resulting in specificity of 76.3%. Negative and positive predictive values were 98.7% and 26.2%, respectively. Out of the detected 119 true positives, inferior ER was correctly located in 90.9% of the cases and lateral ER in 91.4% of the cases. Furthermore, ER was classified correctly in 75.8% of the cases and lateral ER in 83.3% of the cases.

Conclusions: Automatic detection of ER based solely on QRS offset detection lacks specificity. In the correctly detected ER positive recordings, the localization and classification algorithms performed well.

Rule-based, forward looking optimal search algorithm for template beat candidates in the signal-averaged ECG

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Purpose: Signal-averaged electrocardiography (SAECG) detects ventricular late potentials, microvolt signals used in patient risk stratification of sudden cardiac death due to re-entrant VT. High resolution (Hi-RES) ECG data acquisition for SAECG analysis requires a stable signal environment for auto-templating to successfully identify candidate beats. "Sub-optimal" Hi-RES ECGs are characterized by presence of noisy signals; intermittently changing QRS morphology; baseline drift due to respiratory artifacts and patient movement. Success rate of conventional automatic template formation is greatly reduced for such "sub-optimal" data. Hence, there is an unmet need for novel robust signal processing techniques to successfully process challenging “sub-optimal” data to improve yield of SAECG results and optimize clinical workflow.

Methods: A new artificial intelligence capability able to overcome obstacles presented by challenging, “sub-optimal” high resolution electrocardiograms has been developed to significantly increase the yield of successful auto-template formation. Orthogonal X, Y, Z leads (1 kHz per channel) were utilized to acquire Hi-RES ECG data from supine patients.

Results: The algorithm leaves previously successful SAECG results unchanged. It successfully identifies “sub-optimal” Hi-RES ECG time series and automatically decides rules to search forward in the Hi-RES ECG time series to identify stable, quiescent QRS complexes. It then selects incoming QRS complexes at the 99% cross-correlation percentile, to form the SAECG and calculate the vector of SAECG potentials, microvolt signals used in patient risk stratification of sudden cardiac death due to re-entrant VT.

Conclusions: The new rule-based algorithm demonstrates significant improvement (from 53% to 98%) in the yield of usable Hi-RES ECG records that automatically complete the SAECG process to form the final Vector Magnitude for late potential diagnosis. It therefore potentially expands the utility of the signal-averaged electrocardiogram to Hi-RES ECG files acquired from a larger variety of recording devices and environments.
Background: Exercise ECG testing (EET) in patients with suspected coronary artery disease (CAD) has limited diagnostic accuracy. Analysis of high-frequency QRS (HFQRS) components was recently shown to be more accurate than ST changes in identifying stress-induced ischemia. We aimed to evaluate the diagnostic value of HFQRS in patients referred for angiography.

Methods: Analysis was performed in 54 patients (age 63 ± 11 years, 37 men) referred for elective coronary angiography. Patients who achieved at least 80% of their age-predicted maximal heart rate and had QRS duration < 110 ms were included. All patients performed symptom-limited EET, and 12-lead HFQRS was obtained using the HyperQ™ System (BSP Ltd., Tel-Aviv, Israel). HFQRS diagnosis was determined by computerized analysis, measuring the stress-induced reduction in HFQRS intensity. Automatic ST segment analysis were compared with the clinical interpretation of the EET and the angiography (gold standard). Significant CAD was defined as a diameter stenosis of >70% in a single vessel or >50% in the left-main artery.

Results: Angiographically significant CAD was identified in 20/54 (37%) patients. The presence (n=193) or the absence (n=106) of cardiac involvement. HFQRS provided higher sensitivity (67% vs. 33%), specificity (80% vs. 75%) and overall accuracy (75% vs. 59%) than either ST-segment analysis or clinical interpretation (Table 1). An additional criteria with EET interpretation was added. All patients performed symptom-limited EET, and 12-lead HFQRS was obtained using the HyperQ™ System (BSP Ltd., Tel-Aviv, Israel). HFQRS diagnosis was determined by computerized analysis, measuring the stress-induced reduction in HFQRS intensity. Automatic ST segment analysis were compared with the clinical interpretation of the EET and the angiography (gold standard).

Conclusions: HFQRS analysis improved the sensitivity, specificity and the overall accuracy of ST-segment analysis and clinical EET interpretation in diagnosing CAD. Thus, HFQRS may aid in the diagnostic work-up of CAD.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SE (%)</th>
<th>SP (%)</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFQRS analysis</td>
<td>30 (12)</td>
<td>67%</td>
<td>80%</td>
</tr>
<tr>
<td>ST-segment analysis</td>
<td>30 (12)</td>
<td>67%</td>
<td>80%</td>
</tr>
<tr>
<td>EET interpretation</td>
<td>30 (12)</td>
<td>42%</td>
<td>70%</td>
</tr>
<tr>
<td>Patients with valid HFQRS or EET</td>
<td>HFQRS + EET interpretation</td>
<td>49 (18)</td>
<td>72%</td>
</tr>
<tr>
<td>HFQRS analysis</td>
<td>49 (18)</td>
<td>56%</td>
<td>68%</td>
</tr>
</tbody>
</table>

HFQRS, high-frequency QRS; EET, Exercise ECG testing.

Conclusions: HFQRS analysis improved the sensitivity, specificity and the overall accuracy of ST-segment analysis and clinical EET interpretation in diagnosing CAD. Thus, HFQRS may aid in the diagnostic work-up of CAD.

P3392

Low peripheral voltages in patients with AL amyloidosis: only a clue to the diagnosis of cardiac involvement?

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In AL amyloidosis, cardiac involvement is not only frequent but it is also the most common cause of death. The 12-leads electrocardiogram (ECG) reflects the generalized infiltrative nature of this disease with low voltages in the limb leads, pseudodominant patterns in the anterior precordial or inferior limb leads, or both, and conduction abnormalities. The presence of “low voltages” was defined as QRS voltage amplitude <0.5 mV in all limb leads or ≤1 mV in all precordial leads. Beyond confirming the high prevalence of peripheral low voltages in a large cohort of patients, aim of the present study was to assess the prognostic implications of the EKG abnormality, and evaluate its possible correlation with other commonly used electrocardiographic, echocardiographic, and biochemical parameters in 295 consecutive never-treated subjects, in whom a first diagnosis of AL amyloidosis was concluded between 2008 and 2009, according to the International Society of Amyloidosis criteria. The cohort was divided into two groups depending on the presence (n=193) or the absence (n=106) of cardiac involvement. HFQRS provided higher sensitivity (67% vs. 33%), specificity (80% vs. 75%) and overall accuracy (75% vs. 59%) than either ST-segment analysis or clinical interpretation (Table 1). An additional criteria with EET interpretation was added. All patients performed symptom-limited EET, and 12-lead HFQRS was obtained using the HyperQ™ System (BSP Ltd., Tel-Aviv, Israel). HFQRS diagnosis was determined by computerized analysis, measuring the stress-induced reduction in HFQRS intensity. Automatic ST segment analysis were compared with the clinical interpretation of the EET and the angiography (gold standard).

Conclusions: HFQRS analysis improved the sensitivity, specificity and the overall accuracy of ST-segment analysis and clinical EET interpretation in diagnosing CAD. Thus, HFQRS may aid in the diagnostic work-up of CAD.

P3393

Differential diagnosis of type 2 Brugada pattern and incomplete right bundle branch block in athletes

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Background and Objectives: Diagnosis of type 2-3 Brugada pattern (BP) (saddle-back morphology) often presents some difficulties because may be confused with other patterns with R’ in V1-V2.

The aim of the study was to evaluate new ECG criteria taken from the study of the characteristics of R in BP and athletes with the aim to recognize the best parameters to distinguish BP from different patterns. Methods: 50 patients with sure BP type 2-3 and 58 healthy athletes with R’ in V1-V2 were studied. Among others we studied different parameters that include: 1) the angle (see figure 1-1), 2) The duration of the base of triangle at 5 mm from the high take-off (fig 1-2), 3) measurements and correlations of the base and height of triangle at baseline (fig 1-3). ROC-curves were constructed to identify optimal discriminative cutoff values.

Results: See in table 1 the best parameters to diagnose BP.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SE (%)</th>
<th>SP (%)</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angle ≤ 30°</td>
<td>68</td>
<td>67</td>
<td>0.001</td>
</tr>
<tr>
<td>1.2. Duration of the base of triangle at 5 mm from the high take-off ≤ 35 mm</td>
<td>85</td>
<td>81</td>
<td>0.001</td>
</tr>
<tr>
<td>1.3. Base duration at baseline ≥ height in V1 or 10° base duration ≥ 3° height in V2</td>
<td>91</td>
<td>81</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: 1. The three parameters present high accuracy to distinguish both groups. 2. The duration of base at 5 mm (figure 1-2) is the easiest method to use in clinical practice.

P3394

Non invasive assessment of relevant coronary occlusion through mathematical analysis of spectral ECG components (MCG). Comparison with coronary angiography in symptomatic patients

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Risk assessment of relevant coronary occlusion in symptomatic patients at Emergency Room is essential for a correct management of these patients. The Mathematical Multifunction Analysis of ECG Spectral Components (Multifunction Cardiography – MCG Premier Heart – USA) allows to extract all the spectral information content of ECG, also at the level of micro-volt, to try to evaluate micro-ischaemia on resting ECG high resolution digital recordings but not visible on standard ECG. Our experience is based on more than 110 patients, with any indication for Coronary Angiography (CA), and it is unique because patients received CA analysis of collateral circulation and detailed analysis of the inherent pathologies of false positive/negative patients to try to establish the limit of application of the method. Endpoint: detection of hemodynamically relevant coronary stenosis via CA.

Results on 110 patients with CA available (on total of 116 patients recruited) performed from 1 to 25 hours after MCG. 21 patients were excluded from analysis: 9 with concomitant important cardiovascular pathologies (valvular, dilated cardiomyopathy, etc); 4 with double vasodilator therapy (nitrates and diltiazem); 5 with CA borderline results (i.e.: occlusion value is at limit); 3 with poor quality MCG. Total included patients: 89; MCG identified 45 true positive, 31 true negatives, 9 false positive, 1 false negative; sensitivity: 97.8%, specificity: 72.0%, PPV: 78.9%, NPV: 96.8%.

Conclusions: The MCG criteria for analysis of spectral ECG components for assessing significant coronary stenosis are comparable with coronary angiography, with higher sensitivity and specificity in symptomatic patients.
**Discussion**: Sensitivity is higher than other published papers because we have used a more sensitive criteria for MCG analysis (score ≥3 instead of ≥4). Such a high sensitivity value (97%), allows a very safely delay of the CA procedure and a late elective non-invasive test. Specificity is lower than published papers, but our patients are consecutive and most of the 12 patients false positive are dia-betic or hypoglycemia or hypertensive. These patients are therefore anyhow with myocardial problems. We have analyzed all the patients in this study. The presence of collaterals in the 6 patients with positive CA (>70% occlusion or ~50% occlusion in coronary main artery) and negative MCG. Most of these patients had CA visible collaterals that improve flow at microcirculation level despite the presence of ~70% occlusion.

**Conclusion**: MCG method is a fast, risk/radiation free and low expensive method for non invasive assessment of relevant coronary occlusion. High sensitivity of this method may allow delaying CA or other diagnostic modalities available for asymptomatic patients based on MCG results for a better management of these patients.

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**P3397**

**Magnetic resonance flow measurements reveal significant underestimation of aortic regurgitation by echocardiography after transcatheter aortic valve implantation**

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1Adult Congenital and Valvular Heart Disease Center, University Hospital of Muenster, Muenster, Germany; 2Department of Clinical Radiology, University Hospital of Muenster, Muenster, Germany

**Objective**: Recent studies demonstrated that the presence of more mild aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) is associated with a poor clinical outcome. Transhoracic echocardiography (TTE) has generally been used to assess valve function. AR quantification by echo, however, remains challenging because application of recommended criteria is difficult in this setting. The present study used quantitative flow measurement by cardiac magnetic resonance imaging (CMR) with calculation of regurgitant fraction (RF) and compared the results with TTE.

**Methods**: 63 consecutive patients with a mean age of 81.3±8.2 years (37 women) who underwent TAVI with Edwards SAPIEN valves (50 femoral, 13 transapical) underwent AR assessment by CMR and by TTE. Both methods were performed on regular follow up. On CMR, no or minimal AR was defined by a RF of 0-10%, mild 10-20%, moderate 20-40% and severe >40%. VARI criteria for AR quantification were used by TTE.

**Results**: There was agreement between CMR and TTE with regard to the absence of severe aortic regurgitation (Fig. 1) and minimal AR was present on both methods in 16 pts. However, TTE significantly underestimated the presence of moderate AR: CMR classified AR to be mild in 24 and moderate in 15 pts whereas TTE found mild AR in 39 and moderate in only 5 pts. Overall, there was only fair agreement between CMR and TTE regarding the grading of AR with a weighted kappa of 0.38.

**Conclusions**: To our best knowledge this is the first study that used CMR for the quantification of AR in a sizeable group of TAVI patients. A strong tendency to underestimate AR severity by echo could be revealed. Since echo appears technically less reliable than CMR in this setting, CMR should be included in future research protocols evaluating TAVI.

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**P3396**

**Usefulness of synthesized posterior-right-sided chest lead electrocardiograms**

Y. Saitoh, Y. Goseki, Y. Yazaki, A. Yamashina. Tokyo Medical University Hospital, Tokyo, Japan

**Background**: Posterior chest leads (V7-V9) and/or right-sided pre-cordial leads (V3R-V5R) provide important information from posterior and/or right ventricular areas, but these additional ECGs are not routinely recorded because of time-consuming procedure involved. Recently these synthesized 6 additional lead ECGs are non-invasively using standard 12-lead ECG system (Nihonkoden Co. Ltd.) have been developed. However, the accuracy of these 6 additional lead ECGs were unknown. The purpose of the present study was to evaluate the accuracy of ECG synthesized recordings using the system.

**Patients and Methods**: Two hundred and ninety-three patients (204 men, 89 women; mean age 67 years) were enrolled. Standard 12-lead and V3R, V4R, V5R, V7, V8, V9 lead ECGs were successively recorded and compared with synthesized ECGs mathematically derived from standard 12-lead signals.

**Results**: The synthesized and actual ECG waveforms were almost identical, and the coefficient of correlation was 98% in V3R, 94% in V4R, 91% in V5R, 98% in V7, 95% in V8 and 86% in V9 respectively. However, the coefficient of correlation was gradually worse as the ECG recordings went to the lateral side (V7 vs V8: p<0.0001, V3R vs VSR: p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001). In V9 and V5R, QRS waveform amplitude in which the coefficient of correlation was less than 70% was lower than that in more than 70% (V9: 386±V vs 541±V, p<0.0001, V5R: 335±V vs 502±V, p<0.0001).

**Conclusions**: Synthesized posterior and right-sided precordial lead ECGs appear to be highly reliable and useful. However, the interpretation of synthesized V9 and V waveform with low amplitude may require intensive attention.
Clinical impact of Pace-maker implantation after a TAVI and need for postprocedural pacemaker insertion: technique matters

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Background: Permanent pacemaker Implantation (PP) following high degree atrio-ventricular block is a frequent complication after transcatheter Aortic Valve Implantation (TAVI) by using self expanding bioprosthesis (SEB) system. Recent improvements of SEB from CoreValve Device (CD) to Accutrack CoreValve Device (ACD) have aimed to allow easier delivery and also expected to reduce the PP rate. However, the clinical outcome of PP occurrence and differences of PP rate between MCD and ACD after TAVI remains unclear.

Method and results: A total of 958 patients (82±7 years; female: 49%) with severe symptomatic aortic stenosis were selected SEB between January 2010 and October 2011 in 33 centers of the FRANCE 2 Registry. The current study investigated 1) the incidence of PP rate according to the differences of 2 devices and 2) the mid-term clinical outcome of PP occurrence after TAVI.

Procedural success rate was 96.9% and PP rate was 22.4% in overall population. CD and ACD were implanted in 54.5% (n=522) and 45.5% (n=436) of patients, respectively. There was no significant differences of PP rate between CD and ACD (21.6% vs. 23.4%, p=0.52). During the mean follow-up of 242±179 days, the PP occurrence was not associated with increasing all cause mortality when compared with non PP occurrence 14.4% vs 13.2% (p=0.33).

Conclusion: PP remains frequent after TAVI with SEB and device improvement failed to show an impact on PP implantation rate. Overall mortality was not impacted by PP.

What are the current practices in antithrombotic therapy after bioprosthetic aortic valve replacement?

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Purpose: Antithrombotic therapy after bioprosthetic aortic valve replacement (AVR) is a debated issue. AVR is a frequent intervention given the high prevalence of aortic stenosis and ageing population. The absence of consensus highlights the need for an evaluation of actual clinical practices.

Methods: Antithrombotic therapy was prospectively studied in 434 patients operated on for bioprosthetic AVR between January and April 2011 in 14 French centres. Patients previously treated with vitamin K antagonists (VKA) were excluded. Mean age was 75±9 years, 56% were male and 33% had coronary artery disease. Surgery was performed for aortic stenosis in 87% of cases and was combined with coronary artery bypass grafting (CABG) in 23% of patients.

Results: After initial heparin therapy, in-hospital antithrombotic treatment was: aspirin alone in 65% of cases; VKA alone in 9% of cases; VKA aspirin in 19% of cases; and neither VKA nor aspirin in 7% of cases. Factors that impacted the prescription of VKA were: coronary disease (p<0.001), associated CABG (p<0.007) and post-operative supraventricular arrhythmias (p=0.007). The strongest factor was the centre effect (p<0.0001) (Figure). There was no relationship between the prescription of VKA and the occurrence of in-hospital thromboembolic complications (p=0.21) or bleeding (p=0.31).

Conclusion: This multicentre prospective study shows that VKA are prescribed in only 28% of patients after bioprosthetic AVR, despite current recommendations in Europe. Although arrhythmias and coronary disease are determinants of treatment, VKA prescription seems to be more closely related to the centre effect than to patient characteristics. Homogenization of clinical practices is therefore needed and randomized trials would be helpful in this setting.

TAVI and need for postprocedural pacemaker insertion: technique matters

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Purpose: One out of four patients undergoing transcatheter aortic valve implantation (TAVI) with CoreValve Prosthesis (CVP) will become permanently pacemaker (PM) dependent. We tested if the need for PM is reduced by an implantation technique that prevents the CVP from being placed too deeply into the left ventricular outflow tract (LVOT).

Methods: Between 02/2010 and 02/2012, 195 non-PM patients (81±4.5 years, 65% female) underwent TAVI with CVP at our institution. Logistic EuroScore, primary procedural success rate and 30-day mortality were 34.6±18.3, 98.4% and 4.5%, respectively. PM indications were in adherence to the vendor, i.e., a distance within the LVOT of at least 4-8 mm between the proximal edge of the CVP and the aortic valve annulus (low implant). The remaining 126 implants had a distance of < 4 mm (high implant). Only exclusion criterion for the high implants was a low coronary artery (CA) origin.

Results: While overall need for postprocedural PM insertion was 18.5%, most PM indications were due to the low implant technique. PM indications were reduced to 12.6% when using the high implant technique. This technique proved to be safe in a medium-term follow-up of 22±13 months. Only minor cases of paravalvular leak and mild aortic valve regurgitation were observed.

Conclusion: A technique that prevents the CVP from being placed too deeply into the LVOT is feasible and effective in reducing the need for PM.
Multimodality approach for improved assessment of the aortic root in TAVI patients - interobserver variability of different 3D techniques

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Background: Patient outcome of transcatheter aortic valve implantation (TAVI) depends on reliable imaging for appropriate valve sizing. Assessment of the aortic annulus and its challenging geometry is the core of TAVI planning. Using 3D-imaging modalities may help to identify the right annular size for each patient.

Methods: Twenty patients (mean age 82±4.8 years, 10 male) underwent TAVI screening with 3D TEE, cardiac MR (CMR) and multi-detector-CT (MDCT). The end-diastolic diameters of the aortic annulus, aortic root, sino-tubular junction (STJ) and ascending aorta were obtained by three independent observers. CMR-studies were prospectively triggered using a free breathing navigator for acquisition of a 3D volume data set. MDCT data was ECG-gated with reconstruction of the 3D volume at a cardiac phase similar to the CMR study. All measurements were undertaken in a multi-planar reconstructed perpendicular view of the aortic root and each diameter was measured in two axes.

Results: The inter-observer variability of the diameters was assessed by intra-class correlation (ICC) and was calculated for the measurements of the different anatomic regions in each modality. The inter-observer ICC for TEE, CMR and MDCT were as follows: annulus=0.40, 0.78 and 0.78; aortic root diameter=0.57, 0.70 and 0.79; STJ=0.73, 0.82 and 0.92; and ascending aorta=0.36, 0.73 and 0.75. When compared with the implanted prosthetic valve, the 3D assessed diameters would have suggested larger valve size in 15%, 25% and 25% of cases and a smaller valve size 30%, 15% and 15% of cases for TEE, CMR and MDCT, respectively.

Conclusions: The calculated ICCs demonstrate low inter-observer variability with MDCT and CMR, while there was greater variability in the TEE measurements. Measured diameters from 3D volume data result in frequent differences in recommended prosthetic valve size compared to the current clinical decisions. Identifying the specific advantages of each modality may allow for a hybrid segmentation model with automated measurements to improve the reliability of 3D ultrasound planning.

Aortic annular diameter analysis by 3D-TEE in TAVI planning

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Purpose: In transcatheter aortic valve implantation (TAVI), the preoperative assessment of aortic annular dimensions and geometry is essential for optimal valve type selection and sizing. Particularly in o-sclerotic annuli, multislice computed tomography (MSCT) has been shown to provide more accurate aortic annular geometric analysis as compared with 2D TEE. Real-time 3D transesophageal echocardiography (3D-TEE) imaging is gaining importance in both diagnostic evaluation and periprocedural guidance during transcatheter interventions. We evaluated whether 3D-TEE can provide additional morpho-geometrical information for TAVI planning.

Methods: Mean aortic annular diameter (MAAD) was calculated from planimetric annular area in both MSCT and 3D-TEE datasets, and aortic annular diameter was additionally measured in the 2D-TEE long axis view in 42 patients who underwent TAVI (59.5% Medtronic CoreValve, 40.5% Edwards Sapien; mean logis- tic EuroSCORE 25.9%, mean age 83.4 years). In 6/42 patients (14.2%), MSCTs were acquired without contrast agent due to severely impaired renal function. Data analysis was performed retrospectively by experienced physicians blinded to the valve type and size actually implanted.

Results: On average, 2D-TEE (22.4±2.8 mm) underestimated MAAD by 0.5 mm as compared to 3D-TEE (22.9±2.1 mm) and by 1.3 mm as compared to MSCT (23.7±2.3 mm). The valve size actually used was congruent with regard to 3D-TEE measurements in 31/42 (73.8%), and with CT-measurements in 36/42 (85.7%) of patients. Of those remaining 6 CT-examinations that were incongruent with the implanted valve size, 4 were acquired without contrast media. In these patients, MAAD for TAVI planning could be more reliably measured by 3D-TEE (4/6 patients) than by 2D measurements alone, especially in cases of strongly asymmetric annular shape.

Conclusions: Aortic annular diameter measured by 3D-TEE is more accurate than 2D TEE in direct comparison to the “gold-standard” MSCT. In cases with suboptimal MSCT-quality or equivocal 2D-TEE results, TAVI planning can benefit from 3D-TEE imaging.

Prosthesis sizing for transcatheter aortic valve implantation - Comparison of three dimensional transesophageal echocardiography with multislice computed tomography

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Purpose: To compare 3D transesophageal echocardiography (3D-TEE) with multislice computed tomography (MSCT) for prosthesis sizing in transcatheter aortic valve implantation (TAVI). The complex anatomy of the aortic annulus warrants the use of three dimensional modalities for prosthesis sizing in TAVI. MSCT has been used for this purpose, but its use may be restricted because of contrast administration. 3D-TEE lacks this limitation and data on comparison with MSCT is scarce.

Methods: Aortic annulus diameters in the sagittal and coronal plane and annulus areas in 3D-TEE and MSCT were compared in 57 patients undergoing TAVI. Final prosthesis size was left at the operator’s discretion and the agreement with 3D-TEE and MSCT was calculated.

Results: Sagittal diameters on 3D-TEE and MSCT correlated well (r=0.754, p<0.0001) and means were comparable (22.3±2.1 vs. 22.5±2.3 mm; p=0.2; mean difference: 0.3 mm [3.3±2.8]; On 3D-TEE, coronal diameter and annulus area was significantly smaller (both p<0.0001) with moderate correlation (r=0.454 and r=0.592). Interobserver variability was comparable for both modalities. TAVI was successful in all patients with no severe post-procedural insufficiency. Final prosthesis size was best predicted by sagittal annulus diameters in 84% and 79% by 3D-TEE and MSCT, respectively. Agreement between both modalities was 77%.

Transcatheter aortic valve implantation (TAVI): the role of the left ventricular diastolic dysfunction in health-related quality of life

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Purpose: Transcatheter aortic valve implantation (TAVI) has been shown to improve health-related quality of life in patients with severe aortic stenosis at high
Implantation of balloon-expandable aortic bioprosthesis through left subclavian access for high risk patients with severe aortic stenosis: a feasibility study

Aims: Transcatheter aortic valve implantation (TAVI) is considered a reasonable option for the treatment of severe aortic stenosis (AS) in high-risk patients. When transfemoral access is unsafe, the development of alternative approaches is of the utmost importance to avoid vascular complications. We report our experience using the last generation of balloon-expandable aortic prostheses and their steerable catheter via the left subclavian access.

Methods and Results: We conducted a single-center feasibility study that included high-risk patients with symptomatic severe AS. Left subclavian access was chosen because transfemoral or transapical approaches were considered unsafe. Results were described using Valve Academic Research Consortium (VARC) definitions. The primary endpoint was device success. The secondary endpoints were all-cause mortality and morbidity. Fifteen patients (12 males) were treated. Mean age was 83.6 y (78.5-92.7). Mean logistic EuroScore was 24.0% and mean STS score was 7.4%; 10 patients (67%) were NYHA III or IV. Mean preoperative V/A was 0.4cm², mean AVG was 40.7±14.6 mmHg, mean LVEF was 52%. Device success was achieved in 13 patients (86.7%) (access failure because of a 6mm-large arterial axillary n=1, aortic embolization due to undersizing of the annulus and successful implantation a second prosthesis n=1). Considering feasibility issues: advancement and alignment of the prosthesis over the balloon within the ascending aorta were possible in all the patients who had successful introduction of the sheath into the left subclavian artery (14/15 patients) despite important kink of the sheath observed in all the patients. Correct positioning of the prosthesis was obtained in all the cases using the steerable catheter.

30-day all cause and cardiovascular mortality were 6.7% (n=1 patient who died after a right ischemic middle cerebral arterial stroke). No major vascular complication was observed. Minor vascular complications were observed in 3 patients (20%).

Conclusion: To our best knowledge, these preliminary results are the first to show the feasibility of subclavian approach to deliver the last generation of balloon-expandable aortic prostheses using its steerable catheter. Minor corrections of the commercialised devices could make these procedures easier particularly concerning the sheath. As enrollment in this study is ongoing, more complete data could be presented during the meeting.
Impact of residual coronary artery disease on outcomes post balloon aortic valvuloplasty

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Purpose: While coronary artery disease (CAD) is a frequent comorbidity in elderly patients with aortic stenosis (AS), the impact of significant CAD on outcomes following balloon aortic valvuloplasty (BAV) has not been well characterized.

Methods: We conducted a retrospective review of consecutive patients who underwent retrograde non-emergent BAV from 1/2005 to 7/2011 at two high volume US centers. Residual CAD was defined at completion of index procedure as either (1) left main disease defined as >50% stenosis, or (2) stenosis of any coronary artery with an angiographic severity of ≥70%, neither one protected by a functioning bypass graft. We analyzed baseline and procedural characteristics as well as in-hospital outcomes and 30-day mortality according to presence or absence of residual CAD. All adverse events were adjudicated by a blinded, independent clinical events committee.

Results: A total of 468 patients underwent non-emergent BAV with 72 patients having concomitant PCI (15.4%) of which 17 patients (3.6%) had complete and 55 (11.8%) partial revascularization. Post-BAV residual CAD was present in 263 patients (56.2%) and did not have significant impact on 30-day mortality (8.7% with residual CAD vs. 5.4%, p=0.16) and other in-hospital outcomes as well as the composite endpoints MACE and NACE (Figure). However, major bleeding (Bleeding Academic Research Consortium ≥3) occurred significantly more often in patients with non-residual CAD.

Conclusions: In this cohort of elderly, high risk patients, the presence of residual CAD after BAV does not have a significant impact on 30-day mortality or in-hospital adverse clinical events with the exception of an observed higher rate of major bleeding events in patients without residual CAD.

Thrombocytopenia and perioperative complications after stentless Freedom Solo valve implantation

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Background: Freedom Solo (FS) stentless bioprostheses have superior hemodynamic performance in comparison to stented valves, however data about thrombocytopenia after FS implantations is disturbing. The aim was to compare platelet count and perioperative complications between stentless and stented biological valves in patients undergoing aortic valve replacement.

Design: In 29 patients FS bovine valves (Sorin Group, Saluggia Italy) were implanted. Platelet counts were analysed before surgery, at the day of operation, on 1st, 2nd, 3rd and 4th postoperative days (POD) as well as at discharge, and compared with 29 control patients with biological stented porcine valves (Laborcor Laboratorios TLPB-A Supra). The analysis of perioperative variables - extracorporeal circulation (ECC), aortic cross clamping and mechanical ventilation times, and blood supply was performed.

Results: Baseline platelet counts were comparable in both groups. In FS group platelet levels on the 1st, 2nd, 3rd and 4th POD were significantly lower, the difference between the groups enlarged significantly in consecutive measurements and persisted until discharge (Figure, p<0.05). ECC as well as aortic cross clamping and mechanical ventilation times were significantly longer in FS group; more blood transfusions in these patients were required. The lowest platelet value (13x10^9/mL), related to fatal thrombotic thrombocytopenic purpura, was found in one patient from FS group. Except this one severe thrombocytopenia, in other patients postoperative course was uneventful.

Conclusions: Implantations of FS stentless bioprostheses are related to significantly lower platelet counts and worse perioperative course.

Repair of rheumatic tricuspid valve disease: predictors of heart failure and long-term mortality

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Introduction: There is little information about the outcome of surgical treatment of tricuspid valve lesion of rheumatic origin.

Objectives: We examined predictors of heart failure and long-term mortality in patients undergoing tricuspid valve repair for rheumatic disease.

Methods: Between 2002 and 2011, 40 consecutive patients (mean age 45±11 years) underwent surgical repair of the tricuspid valve for multivalvular rheumatic disease. A total of 28 patients was found to have mitral and tricuspid valve disease and 22 patients had triple valve disease. De Vega annuloplasty was performed in 31 patients, commissurotomy and annuloplasty in 7 and isolated commissurotomy in 2 patients.

Results: Intra hospital mortality was 10%. Causes of death were low cardiac output in 50% of cases and bleeding in 50%. In the univariate analysis the New York Heart Association functional class IV was the only significant predictor of hospital mortality. A residual tricuspid regurgitation ≥3 was noted in 10 patients. There was a median follow-up of 68±65 months (range, 3 to 202 months). Right heart failure was noted in 10 cases. Global and left heart failure were noted respectively in 10% and 0%. Functional tricuspid insufficiency and New York Heart Association functional class IV were predictive factors for heart failure. A total of 3 patients required valve reoperation. The reoperation was necessary because of aortic dysfunction in 1 case and prosthetic valve endocarditis in 2 cases. Late mortality was 43%, in the majority of patients due to cardiac causes.

Conclusions: Repair of the tricuspid valve in patients with rheumatic valve disease can be performed with acceptable early results, but progression of rheumatic disease is associated with a high incidence of mortality in the long term.

Four-year durability of aortic valve bioprosthesis after transcatheter implantation: an echocardiographic prospective study

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Background: Transcatheter aortic valve implantation (TAVI) has become a recognized alternative to conventional surgery in high-risk patients with severe symptomatic aortic stenosis. However, little is known about the long-term durability of the prostheses as assessed by periodic thoracic echocardiography (TTE). We aim to evaluate aortic valve hemodynamics by TTE performed after TAVI using Edwards Sapien/Sapien XT bioprosthesis.

Methods: All consecutive patients implanted between March 2005 and January 2012 were included in a prospective registry. TTE data were collected before TAVI, within 7 days, at 6 months and yearly after the procedure. Doppler interrogation was used for peak, mean pressure gradient and effective orifice area (EOA) using the continuity equation. Aortic regurgitation (AR) and ejection fraction (EF) were assessed.

Results: Two hundred and seventy four patients underwent successful TAVI implantation and were included in the registry (table). Left ventricular ejection fraction (LVEF) was improved early after TAVI procedure. Both Peak and mean pressure gradient significantly decreased after TAVI while EOA increased. No aortic regurgitation – grade 2 was found 3 and 4 years after TAVI. Four-year TTE follow-up did not demonstrate any significant change in peak pressure gradient, mean pressure gradient, EOA or occurrence of severe aortic regurgitation compared to 7-day post-operative. All parameters except LVEF remained significantly improved at 4-year compared to pre-TAVI examination.
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Objectives: Transcatheter aortic valve implantation (TAVI) has emerged as a valuable alternative to surgical aortic valve replacement with promising results for patients with severe aortic stenosis (AS) considered as being at high or prohibitive surgical risk. Results in the high-risk subgroup of patients with post-RADAS was unknown.

Methods: From October 2006 to June 2011, among the 272 patients who underwent a TAVI at our institution, 12 had post-RADAS AS due to Hodgekkin lymphoma. Post-RADAS AS was younger (61±11 vs. 83±7 years, p<0.0001), had a lower EuroScore (6.9±5 vs. 25±13%, p<0.0003) but pre-served %LA (60±13 vs. 45±10%, p<0.0001). TAVI results and complications are presented in the Table. In the post-RADAS AS, mortality rate was not significantly different (one death due to a severe sepsis) but there was less complications especially a lower rate of major vascular complications, hospital duration was shorter and patients more frequently discharged at home.

Conclusions: Among AS patients who underwent a TAVI, post-RADAS patients experienced a lower rate of complications than patients with degenerative AS. In regard to the high mortality and morbidity of conventional surgery, our results suggest that TAVI may be an elective indication for post-RADAS AS patients but deserve further confirmation in larger series.

P3413 Time course of platelet aggregation and platelet activation in patients undergoing transcatheter aortic valve replacement


Background: Percutaneous aortic valve replacement (TAVR) has been implemented as new and less-invasive treatment for patients (pts) with severe symptomatic aortic stenosis at high surgical risk. Pts usually loaded with 500 mg aspirin (ASA) and 750 mg clopidogrel (clop) the day before TAVI followed by 100 mg ASA and 75 mg clop per day to prevent procedure-related thrombocytopenia and bleeding complications.

Aim of the study: To date, no published data is available on the effect of dual antiplatelet therapy on platelet activation (PA) and consumption in patients undergoing TAVI. Thus, we investigated platelet aggregation (Agg) and PA in pts before and daily after TAVI.

Methods: Platelet function was assessed in 138 consecutive pts with severe aortic stenosis (aortic valve orifice area 0.66±0.13 cm², mean gradient 44.5±1.2 mmHg) at high surgical risk who underwent Core Valve implantation at our hospital. Pts scheduled for TAVI were loaded with 600 mg ASA the day before TAVI followed by 100 mg ASA and 75 mg clop per day to prevent procedure-related thrombocytopenia and bleeding complications.

Results: 138 pts (age 80±6.6 years) at high surgical risk (Euroscore 25.3±1.2%) underwent TAVI successfully using the Core Valve Revalving device. Between T0/T1 (before and directly after intervention), T1/T2 (day0/day1), T2/T3 (day1/day2), and T3/T4 (day2/day3) we observed a significant drop in platelets and hemoglobin (p<0.001). ADP, ASPI, TRAP, and Colpid induced Agg differed significantly between day T0/T1, T1/T2, T2/T3 and T3/T4. Maximum platelet inhibition (AggADP, AggASPI, AggCol, and AggTRAP) was achieved on day 2 after the procedure. PA markers (GPVI, SD1, CD62P, and CD41/61 PA) showed a significant increase over time with maximum platelet activation on day 2 (T0/T1), Pts with a low-response to clop (defined as AUC < 50% after ADP stimulation) showed a higher decrease of platelets over time than clop responders.

Conclusion: Platelet inhibition is incomplete in patients undergoing TAVI, when dual antiplatelet therapy with standard dosing is started the day before the intervention. As maximum platelet inhibition is achieved on day 2 after TAVI, dual antiplatelet therapy should be given at least two days before TAVI procedure to avoid risks of bleeding and thrombocytopenia. Clop low responders might be at higher risk to develop complications after TAVI than clop responders.

P3414 Compassionate valve-in-valve transcatheter aortic valve implantation in high risk patients with degenerated bioprosthesis

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Purpose: The value of transcatheter aortic valve implantation (TAVI) is consoliated in recent years for inoperable or high risk patients with aortic stenosis. However, in the very high risk population of degenerated aortic bioprostheses a valve-in-valve (ViV) TAVI procedure is still investigative and restricted to compassionate off-label use. Here, we report the ViV experience of our center using the transapical and transapical approach.

Methods: Of 121 patients undergoing TAVI from January 2010 to September 2011, 9 patients (7% of total TAVI cohort, age 78±6 years, logistic EuroScore 21.7±7%, 44% females) with degenerated bioprostheses (Sorin Mitroflow n=7, Edwards Perimount n=1, Sterlness O’Brien n=1) underwent transapical (Medtronic Corevalve n=3, Edwards Sapien XT n=1) and transapical (Edwards Sapien XT n=5) off-pump ViV TAVI.

Results: Procedural success was achieved in 8 patients (89%). Intraprocedural death occurred in one patient (11%) suffering refractory cardiogenic shock. Procedural complications occurred in 3 patients (33%, need for a second valve n=2, partial coronary impairment requiring subsequent off-pump IMA-CABG n=1). Post-procedural paravalvular leakage was none (n=6, 67%) > grade 2 (n=3, 33%) with severe leakage in no case. Mean intensive care unit stay was 1.6±8 days and patients were discharged after a mean of 10 days (range 2-32). Post-procedural complications included one minor stroke (11%) on day 2 and one post-
Sleep disordered breathing in patients undergoing transaortic aortic valve implantation for severe aortic stenosis

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Purpose: Sleep disordered breathing (SDB) with obstructive (OSA) or central (CSA) respiratory events is of major prognostic impact for patients with cardiovascular disease. We examined the prevalence of SDB in patients with severe aortic valve stenosis before and after transaortic aortic valve implantation (TAVI).

Methods: A total of 79 patients (50% males, average age 83±6.6 years) had cardiac re-do surgery before TAVI. A subset of 47 patients (48.4% males, average age 82.6±6.5 years) underwent a second SDB screening 21±0.6 days after TAVI.

Results: In this cohort, 49 (62.0%) patients had OSA, 25 (31.6%) CSA and only 5 (6.3%) presented without significant SDB (apnoea-hypopnoe-index, AHI < 5/h). From the 62 evaluated patients before and after valve implantation 36 (58.1%) had OSA, 21 (31.8%) presented with CSA and no SDB was detected in 5 patients (8.0%). As measured by AHI SDB was more severe in CSA compared to OSA (34.5±18.3 vs. 18.0±12.6/h, p=0.001). Successful TAVI had a significant impact on CSA, but not on OSA; patients with optimal TAVI results (aortic valve gradient < 10 mmHg) demonstrated a significant reduction of central respiratory events (39.6±19.6/h to 23.1±16.0/h, p=0.035), while no changes were detected regarding OSA (18.6±13.0/h to 20.2±13.4/h, p=0.370). In contrast, patients with primarily suboptimal TAVI results (AHI >2) presented with no change in OSA (10.5±7.8/h to 12.5±5.0/h, p=0.5) and an increase in central respiratory events (26.3±13.2/h to 39.2±18.4/h, p=0.008)

Conclusion: 1. There is a high prevalence of OSA and CSA in patients with severe aortic valve stenosis in TAVI candidates. 2. Successful TAVI had no significant impact on OSA, but improved CSA significantly. 3. TAVI resulting in moderate to severe aortic valve insufficiency is accompanied with a deterioration of CSA.

Feasibility and outcomes of transcatheter aortic valve implantation in patients with bicuspid aortic valve stenosis


Purpose: To assess the feasibility and the results of transcatheter aortic valve implantation (TAVI) using the Medtronic CoreValve System (MCS) in patients with bicuspid aortic valve (BAV) stenosis.

Methods: Of 244 high-risk patients with severe aortic stenosis who underwent a TAVI between January 2009 and June 2011, 13 (5%) had a bicuspid aortic valve. The approach was percutaneous transfemoral in 12 cases, and surgical subclavian in 1, with either general anesthesia or conscious sedation and locoregional meperidine. Procedures were performed in 105 patients (79%). The mean post-implantation prosthetic gradient was 11±4mmHg, and ≤1 mmHg prosthetic leaks were observed in all but 1 patient. There was 1 major adverse event, which occurred in an inoperable patient who died from severe paraprosthetic regurgitation due to a too low positioning of the MCS. The mean post-implantation prosthetic gradient was 11±4mmHg, and ≤1 mmHg prosthetic leaks were observed in all but 1 patient.

Conclusion: The present series suggests that transcatheter MCS implantation is feasible in selected patients with BAV and may lead to short-term hemodynamic and clinical improvement. These preliminary data will require further confirmation by larger series and longer follow-up.

Impact of the method used for aortic annulus measurement on transcatheter aortic valve implantation results


Background: Accurate measurement of the aortic annulus diameter (AD) is critical for successful implantation of transcatheter aortic valve (TAVI) but the best method is still debated. We sought to compare the results of TAVI according to the method finally used for the choice of the prosthesis size (transesophageal echocardiography (TEE) or multislice computed tomography (MSCT)).

Methods: AD was measured using both TEE and MSCT in 177 patients who underwent a TAVI using either the Edwards Sapien or the Medtronic CoreValve prosthesis between January 2008 and April 2011. AD was measured from the 120-140 degree long-axis view using TEE and at the level of the virtual basal ring in MSCT (mean of long and short axis). Agreement was defined as the use of the same prosthesis size with both TEE and MSCT according to manufacturers’ recommendations.

Results: Overall, mean AD was significantly larger using MSCT than TEE (23.2±1.93 mm, p<0.0001). An agreement between TEE and MSCT as regard to the prosthesis size was observed in 81% of cases. Among the 59 patients in whom a disagreement between TEE and MSCT was observed, prosthesis size was chosen according to TEE measurements in 54 and according to MSCT measurements in 5. The Table summarized complications and inhospital mortality. There was no significant difference between groups except for annulus rupture which occurred in one patients in whom MSCT measurements were used.

Conclusion: The present study shows that a TEE-based choice of the prosthesis size provided excellent clinical results not significantly different than when both methods and TEE and AAA agreed. Thus, in patients undergoing TAVI, the best imaging modality for the measurement of the aortic annulus diameter remains still not established but our data do not support the use of CT as the first line method.

Is the incidence of patient prosthesis mismatch lower in patients undergoing TAVI compared with conventional surgery?

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Background: Transcatheter Aortic Valve Implantation (TAVI) is an alternative to surgery for the treatment of aortic valve disease. Valve patient prosthesis mismatch (PPM) is a recognised complication following AVR and is a result of understressing of the prosthesist valve. We hypothesised that indexed prosthesis area might be higher in patients undergoing TAVI due to a number of factors, including accurate annular measurement using echocardiography and lower prosthesis profile, thereby potentially reducing the incidence of PPM.

Methods: We reviewed the records of patients who underwent TAVI and conventional AVR at our institution and compared implanted valve size. We calculated indexed prosthesis area by dividing implanted valve size by body surface area. In a subset of patients, we calculated effective orifice area (EOA) using the continuity equation and indexed to body surface area (BSA). We also compared peak and mean transprosthetic gradients in this cohort. Patient prosthesis mismatch was defined byefective orifice area indexed to BSA of ≤0.85cm2/m2, and severe PPM was ≤0.65cm2/m2.

Results: 148 patients (74M/74F) underwent TAVI between August 2007 & November 2011. 644 patients (381M/263F) underwent bioprosthetic AVR between August 2007 & July 2011. TAVI patients were significantly older, more likely to be female and had significantly higher EuroSCOREs. Mean prosthesis size and root size were larger in patients who underwent TAVI compared with patients whounderwent conventional bioprosthetic AVR (2 tailed P<0.001 for all comparisons). Early echocardiographic follow-up was available for 115 patients who underwent TAVI and 86 patients who underwent surgery. Indexed effective orifice area was significantly lower and transprosthetic gradients were significantly higher in patients who underwent conventional AVR. Any degree of PPM occurred in 64.8% (62.8%) surgical patients compared with 42.1% (36.5%) patients.
who underwent TAVI. Severe VVPM occurred in 9 (8%) TAVI patients compared with 19 (22%) surgical patients.

**Conclusion:** Patients undergoing TAVI are implanted with larger valves and have a lower incidence of valve patient prosthesis mismatch. This may lead to better outcomes in patients undergoing TAVI.

### TAVI: PROCEDURAL OUTCOME AND PROGNOSIS

**P3421**

**Prognostic effects and cause of death after transcatheter aortic valve implantation induced left bundle branch block during long-term follow-up**

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**Purpose:** Transcatheter aortic valve implantation (TAVI) is frequently complicated by a new left bundle branch block (LBBB). We aimed to evaluate the effect of TAVI-induced LBBB on cardiovascular mortality and its cause after successful implantation.

**Methods:** A multicentre registry encompassing 1013 patients who underwent TAVI between 2005 and 2010 in 8 centres in the Netherlands was used. All-cause mortality rate and cause of death was compared between patients who did and did not develop new LBBB. Patients with an aborted procedure, pre-existing pacemaker/LBBB, mortality within 24h or pacemaker implantation post-procedure were excluded from analysis. Cause of death was classified as cardiac, cerebrovascular and non-cardiovascular.

**Results:** There were 232 (34%) out of 675 patients who developed a new LBBB. Median follow-up was 449.5 (187.3–834) days in patients with and 456 (255–726) days in patients without LBBB (P=0.91). All-cause mortality was significantly higher in patients with LBBB (n=87; 37.5%) compared with those without LBBB (n=104; 23.5%) (log-rank P=0.02). The cause of death is summarised in the table. Patients with TAVI-induced LBBB had a significantly higher incidence of cardiovascular death (log-rank P=0.006 and 0.02, respectively; see table).

**Mortality during total follow-up for patients without (no LBBB) and with (TAVI-LBBB) new left bundle branch block induced by TAVI**

<table>
<thead>
<tr>
<th></th>
<th>Mortality</th>
<th>No LBBB (N=443)</th>
<th>TAVI-LBBB (N=232)</th>
<th>Log-rank P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause</td>
<td>104 (23.5%)</td>
<td>87 (37.5%)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>94 (21.7%)</td>
<td>33 (14.2%)</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>5 (1.1%)</td>
<td>8 (3.4%)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Non-cardiovascular</td>
<td>47 (10.6%)</td>
<td>31 (13.4%)</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>48 (11.4%)</td>
<td>15 (6.5%)</td>
<td>0.13</td>
<td></td>
</tr>
</tbody>
</table>

The log-rank test was used to compare mortality between both groups.

**Conclusion:** TAVI-induced LBBB is associated with an increased risk of death during follow-up. The excess in mortality is caused by a higher incidence of fatal cardiovascular events. Therefore, a TAVI-induced LBBB should be considered as a major adverse event.

**P3422**

**Impact of post-procedural aortic regurgitation on long-term mortality in transcatheter aortic valve implantation**

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**Purpose:** Post-procedural aortic regurgitation (post-AR) grade 2/4 is associated with poor short term outcome after transcatheter aortic valve implantation (TAVI). However, the influence of post-AR grade 2 on mid-term outcome remains unclear.

**Methods:** We compared procedural characteristics and clinical outcomes in 400 consecutive TAVI recipients according to post-AR grade: grade 0-1 (group 1), grade 2 (group 2) or grade 3-4 (group 3). The mean age was similar in the 3 groups (83.4±6.1 years) as well as logistic EuroSCORE (22.5±11.4, 24.5±11.6 and 21.5±9.4, P=0.283). No other difference was observed with respect to annulus size (22.0±1.8, 22.5±2.1 and 22.5±2.1, p=0.533).

The Edwards valve was the most frequently used in group 1 (89.3, 78.7 and 83.3% respectively, P=0.032) and the implanted valve size was similar in all groups (25.6±2.0, 25.4±2.2 and 25.5±2.2% respectively, P=0.687). Post-dilatation was required more frequently in group 3 (47, 24.1 and 50.0% respectively, P<0.001).

The log-rank test was used to compare mortality between both groups.

**Conclusion:** Post-AR grade 2/4 after TAVI is associated with worse outcome compared to grade 0 or 1. Cautious valve selection and post-dilatation when required to avoid post-AR grade 2 may contribute to improvement in clinical outcome after TAVI.

**P3423**

**Severe complications during transcatheter aortic valve implantation via femoral access leading to emergency conversion to surgery**

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**Objective:** To collect data on patients who were converted from transcatheter aortic valve implantation (TAVI) via the femoral route to open cardiovascular surgery. Concerning this objective, the German TAVI-Registry and patient records were retrospectively analyzed.

**Methods and Results:** Between January 2009 and July 2011, a total of 1975 patients were recorded within the German TAVI-Registry. The rate of emergency conversion from transfemoral TAVI to surgery was 1.1%. The primary reasons for conversion were aorto-vascular complications (total 31.6%, i.e. aortic annulus rupture 15.8%, aortic perforation 10.5%, aortic dissection 5.3%), followed by prosthesis embolization (20.3%), myocardial perforation (21.1%), acute severe aortic regurgitation (10.5%) and coronary issues (10.5%). Mean time interval between abortion of TAVI to surgery was 22 minutes (SD ± 18 min, range 5-80 min). Four of 19 patients (21.1%) died during initial surgery. 6 of 19 (31.6%) during the first 24 hours, the 30-day mortality was 47.4%. Highest mortality was observed in patients with aortic perforation or dissection (3/3, 100%). Mortality rates for other entities: prosthesis embolization 40% (2/5), myocardial perforation 50% (2/4), anulus rupture 67% (2/3), coronary issues 0%, and acute severe aortic regurgitation 0%. Concerning the type of valve, 4 of 5 embolizations and all aortic annuli ruptures (3/3) occurred with the Edwards SAPIEN, whilst acute aortic regurgitation (2/2) was seen exclusively with the CoreValve Revalving System.

**Conclusions:** Emergency conversion from TAVI to surgery is a rare event, nevertheless carrying a high-mortality. Especially in aortic perforation and annular rupture prognosis was nearly infaust, whilst acute severe aortic regurgitation and coronary ischemic complications were successfully managed.
Transcatheter mitral valve-in-ring implantation after failed surgical mitral repair: early outcomes

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Purpose: Re-operation after failure of mitral valve repair may carry a high or prohibitive risk. Transcatheter valve-in-valve implantation has been shown to be feasible and effective in selected high-risk patients with failure of aortic bioprosthesis. The aim of this report is to show preliminary results of Transcatheter Valve-In-Valve Implantation (TVII) after failure of mitral repair.

Methods: Twelve patients underwent a TVRI after evaluation by a heart team. The approach was transapical in 7 patients and percutaneous transseptal in 5, with general anaesthesia and transoesophageal echocardiography guidance. Procedures were performed without balloon predilatation, with rapid pacing, using balloon expandable aortic valve prosthesis (SAPIEN) and were aimed at deploying the mitral prosthesis within the annulus. The degree of mitral regurgitation was assessed via 2D and 3D echocardiography.

Results: Patients were aged 71±19 years (range, 17-84). All were in New York Heart Association (NYHA) class IV or V and at high risk for surgery (EuroSCORE, 37±19%). The mean delay between surgery and repair failure was 6±3 years. Annuloplasty rings were semi-rigid in 11 cases (Carpentier Edouard Psichlisis, n=9; St Jude, n=2) and rigid in 1 case (Carpentier Edwards). Manufacturers ring diameters were 25 mm in 3 patients, 28 mm in 8 and 30 mm in 1. The predominant failure mode was regurgitation (≥3+) in 9 cases and stenosis in 3. Prosthesis diameters were 26 mm in 11 patients and 23 mm in 1. Procedural success (correct prosthetic position without complication) was 95% (11/12). Emergency surgery was needed in one patient due to acute dislodgement of the ring. The degree of mitral regurgitation was reduced to ≥2+ in 6 and 2+ in 3 patients; mean gradient decreased from 14.5mmHg to 10.2mmHg.

Conclusion: One-year follow-up after transcatheter aortic valve implantation for severe symptomatic aortic stenosis. Results from a multi-centre real-world registry

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Background: Transcatheter aortic valve implantation (TAVI) is rapidly establishing as a new treatment option for older non-operable or surgical high-risk patients with severe symptomatic aortic stenosis. Mid- and long term results of TAVI still have to be determined.

Methods: We analysed data from the prospective multi-centre German TAVI registry.

Results: Between 1/2009 and 6/2010 1387 TAVI were performed at 27 hospitals: 90.4% percutaneous TAVI and 9.6% operative TAVI. Mean age of the patients was 81±6 year, 91% was male, 42% of the patients were male. In-hospital mortality was 8.4% and 30-day mortality 8.2%. Follow-up was performed after a mean of 359 days. 1 year mortality was 20.2%.

The following factors were independent predictors of 1 year mortality: Age, residual aortic insufficiency: ≥II2 after TAVI and access site complications were not associated with 1 year mortality.

Conclusions: In current clinical practice of TAVI 30 day mortality is 8.2% and 1 year mortality 20.2%. Independent predictors of 1 year mortality are mainly general risk factors, such as an impaired renal function, low left ventricular ejection fraction or hemodynamic instability during the index intervention, but not peri-interventional factors.

Long term outcomes after transcatheter aortic valve implantation using transapical and transfemoral access

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Objective: Data regarding long-term outcome after transcatheter aortic valve implantation (TAVI) are limited and the impact of the access route is unclear. Our objective was to assess the predictors of long-term mortality and evaluate the survival after TAVI with the balloon expandable Edwards valve, using transapical (TF) and transfemoral (TA) access.

Method and results: Between May 2006 and October 2011, 250 consecutive patients (Pts) underwent TAVI in our center, 60 (24%) via the TA and 190 (76%) via the TF route. End points were defined according to VARC criteria. EuroSCORE was higher in the TA than in the TF group: 27.4±15% vs. 21.9±12% (p = 0.05), being 23.3±12% in the overall population. Patients were younger in the TA group (81±6.9 vs. 84±6.2 years, the overall mean age being 83±6.5 years. Global procedural success rate was 97.2%. VARC combined safety end-point at 30 days was reached in 51 (20.4%) with a higher incidence in the TA group (33.3% vs. 16.3% (p = 0.004). The 30-day mortality for the entire cohort was 7.6%, without statistically significant difference between the TF and TA groups: 6.3% vs. 11.7% (p = 0.17). Overall survival was 77% at 1 year, 63% at 2 years and 48% at 3 years. Long-term survival (mean follow-up: 12.7±13.3 months) was not different at 4 years between TA and TF groups: 35.5% vs. 40.9%, log-rank p=0.67. Predictive factors of long-term mortality are presented in Figure.

Sex differences in mortality after transcatheter aortic valve implantation for severe aortic stenosis

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Transcatheter aortic valve implantation (TAVI) is an effective alternative to surgical valve replacement in symptomatic patients with severe aortic stenosis. However, the impact of sex on outcomes remains unclear, especially given the PARTNER 1A evidence of greater benefit of TAVI over surgery in women. Whether this result holds for the entire cohort is unknown. We examined sex differences in mortality after TAVI in 2 high volume centres in Canada.

Methods: 641 consecutive patients undergoing TAVI in Vancouver and Quebec City, Canada were evaluated. Differences in all-cause mortality were examined using Kaplan-Meier estimates, adjusted logistic regression and proportional hazards models.

Results: Females comprised 51.3% of the cohort. Balloon-expandable valves were used in 97% of cases with a transapical approach in 51.7% of females and 38.1% of males. The adjusted odds ratio for 30-day all-cause mortality favoured women, 0.39 (95% CI: 0.19, 0.80; p=0.01), and this benefit persisted for one year, hazard ratio 0.54 (95% CI 0.35,0.82; p <0.01). Major vascular complications were significantly more frequent in females (12.4%, 5.4%;p<0.01) and borderline more major/major-threatening bleeds (21.6%, 15.8%; p=0.08). At baseline, females had higher aortic gradients and worse renal function, but better ejection fractions. Males had more comorbidities: prior MI, prior revascularization, COPD, and coronary artery disease.
Conclusions: Female sex is associated with better short- and mid-term survival after TAVI. These results coupled with PARTNER 1A findings suggest TAVI may be the preferred treatment for elderly females with symptomatic severe aortic stenosis.

**P3428 Transcatheter aortic valve implantation: Guidelines and clinical practice. Results from a multi-centre real world registry**


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Background: In the position paper of the German cardiac society regarding the indications for transcatheter aortic valve implantation (TAVI) there are appropriate indications (ai), to high risk indications (hrI) and non appropriate indications, mostly due to too low risk (lrI) for TAVI. Little is known on the use and translation of these guidelines into clinical practice as well as the results of TAVI in these subgroups.

Methods: We analysed data from the prospective multi-centre German TAVI registry.

Results: Between 1/2009 and 6/2010 1367 TAVI were performed at 27 hospitals: 476 (34.8%) in the ai group, 705 (56.1%) in the lrI group and 126 (9.2%) in the hrI group. The proportion of the ai group in the participating hospitals was at mean 35% (range: 8.8% to 78.3%). Patient - and interventional characteristics as well as clinical outcome are given in the table.

<table>
<thead>
<tr>
<th></th>
<th>ai (n=476)</th>
<th>lrI (n=765)</th>
<th>hrI (n=126)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>83.5±4.9</td>
<td>80.4±6.7</td>
<td>83.7±5.3</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>38.7%</td>
<td>43.1%</td>
<td>43.7%</td>
<td>ns</td>
</tr>
<tr>
<td>Log EuroScore</td>
<td>27.2±11.1</td>
<td>13.9±7.5</td>
<td>42.1±18.6</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Intervention time (min)</td>
<td>93.5±22</td>
<td>88.4±8</td>
<td>89.6±5.1</td>
<td>ns</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>15±7</td>
<td>15±7</td>
<td>15±7</td>
<td>ns</td>
</tr>
<tr>
<td>Mean gradient after</td>
<td>5.0±2.0</td>
<td>50.0±18</td>
<td>47.2±23</td>
<td>0.05</td>
</tr>
<tr>
<td>Mean gradient after</td>
<td>5.4±1.5</td>
<td>6.4±7.4</td>
<td>6.6±8.7</td>
<td>0.98</td>
</tr>
<tr>
<td>Aortic insufficiency ≥ II after</td>
<td>14.3%</td>
<td>13.7%</td>
<td>24.2%</td>
<td>0.06</td>
</tr>
<tr>
<td>PM implantation</td>
<td>38.6%</td>
<td>44.3%</td>
<td>40.5%</td>
<td>ns</td>
</tr>
<tr>
<td>Strokes</td>
<td>4%</td>
<td>2.9%</td>
<td>1.7%</td>
<td>ns</td>
</tr>
<tr>
<td>Access site complications</td>
<td>3%</td>
<td>4.2%</td>
<td>4.1%</td>
<td>ns</td>
</tr>
<tr>
<td>Death</td>
<td>10.1%</td>
<td>6.4%</td>
<td>14.3%</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Conclusions: In current clinical practice of TAVI 34.4% of interventions are done in patients belonging to the ai group, 56% in the lrI group and 9.2% in the hrI group according to current German guidelines. The range of the ai group within the participating hospitals was 8.6% to 78.3%. Hospital mortality was significantly different between these 3 groups, however acceptable in the hrI group.

**P3430 Impact of pulmonary hypertension on outcome after Transcatheter Aortic Valve Implantation**


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Objective: Pulmonary Hypertension (PH) is considered a significant risk factor in patients with severe aortic stenosis (AS) undergoing surgical aortic valve replacement. However, the prognostic implications of PH is unclear in high-risk patients with AS undergoing Transcatheter Aortic Valve Implantation (TAVI). Therefore, we sought to assess the impact of preoperative PH on outcome after TAVI based on data of the German Aortic Valve Interventions Registry.

Methods and Results: Between January 2009 and June 2010, a total of 1285 patients undergoing TAVI were included in this registry (mean age 61.7±6.1, 41.9% males). Patients were grouped according to systolic pulmonary artery pressure (PASP); group I, 277 patients (21.6%) with PASP >30mmHg, group II, 584 patients (46.5%) with PASP 30-50 mmHg and group III, 410 patients (31.9%) with PASP >50mmHg. 125 patients undergoing AVR for symptomatic severe AS were prospectively enrolled and compared. By January 2012 data on outcomes was collected from the Danish personel Register. Median follow up time was 443 days for TAVI, 1597 days for patients undergoing AVR. Primary endpoint was overall mortality, secondary endpoint cardiac mortality. Patients undergoing TAVI were younger (72±6.9 vs 81±5.6 years, p < 0.0001), had lower EuroScore (5.7±2.0 vs 17.2±11.9, p < 0.0001), better functional capacity (NYHA class 2.1±0.7 vs 2.9±0.5, p < 0.001) and had less co-morbidity. Perioper- ative complications were similar between groups. Overall mortality and cardiac mortality after 3 years was 26%±15% (TAVI) vs 24%±15% (AVR) with no difference between groups (p=0.69, p=0.89). Predictors of overall and cardiac mortality were a history of Diabetes Mellitus and lung capacity.

**P3429 Clinical outcomes of patients with severe aortic valve stenosis undergoing aortic valve intervention. Comparing transcatheter aortic valve implantation and surgical aortic valve replacement**


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Background: Aortic stenosis (AS) is associated with poor prognosis once symp- toms are present. Aortic valve replacement (AVR) is the conventional treatment improving survival and morbidity. Transcatheter aortic valve implantation (TAVI) has recently been introduced as a less invasive treatment alternative, knowledge on long term outcome after TAVI is however poor. The aim of this study was to describe clinical outcomes according to treatment selection.

Methods and results: Since February 2006, 152 patients undergoing TAVI and
Gender related differences after transcatheter aortic valve implantation. Results from the German Aortic Valve Therapy Registry

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Background: Calcified aortic stenosis is the dominating valve disease in the elderly in the 8th or 9th decade. Transcatheter aortic valve implantation (TAVI) has become a new therapeutic treatment in patients unsuitable for open heart surgery due to relevant comorbidities.

Methods: The German Aortic Valve registry prospectively records the data of 22 German heart centers. We investigated the procedural complications and outcome in women compared to males in order to elucidate any gender attributed differences.

Results: Between 1/2009 and 11/2010, 1,386 TAVI were performed at the participating hospitals. The majority of patients (n=807, 58.0%) were females. Women treated with TAVI were significantly older than males in the registry (82.5±6.8 vs. 80.3±6.4 years, p<0.0001; ≥ 80 years: 76.5% vs. 60.1%, p<0.0001; <90 years: 7.1% vs. 4.5%, p<0.05). In females, transapical (TA) approach was more often chosen than transfemoral (TF) access (TA: Female 10.3% vs. Male 7.7%, p<0.05). Female was the dominating factor to indicate TAVI. Despite of less cardiovascular risk factors (previous myocardial infarction: Female 11.4% vs. Male 21.8%, p<0.0001; no CAD: Female: 47.9% vs. Male 27.7%, p<0.0001; coronary bypass operation: Female 13.9% vs. Male 32.8%, p<0.0001; arterial occlusive disease (lower limbs, carotid artery, aeurysms): Female 26.2% vs. Male 37.7%, p<0.0001); device therapy: Female 11.7% vs. Male 17.7%, p<0.01), women demonstrated a higher logistic EuroSCORE (Female 21.1±13 vs. Male 20.1±14, p<0.05). Women showed more frequently previous heart surgery of different heart valves (Female 31.3% vs. Male 7.8%) but less coronary bypass surgery (Female 71.4% vs. Male 90.6%, p<0.0001). Kidney function was bad in women (GFR<60 min/1,73m2: Female 67.5% vs. Male 52.1%, p<0.0001). Procedural success rate, procedure duration, fluoroscopy time and contrast volume were comparable between female and male. After TAVI women demonstrated less frequently aortic regurgitation than males (AR Grade II: Female 12.0% vs. Male 17.8%, p<0.05). In females, transapical (TA) approach was more often chosen than transfemoral (TF) access (TA: Female 10.3% vs. Male 7.7%, p<0.05). Female was the dominating factor to indicate TAVI. Despite of less cardiovascular risk factors (previous myocardial infarction: Female 11.4% vs. Male 21.8%, p<0.0001; no CAD: Female: 47.9% vs. Male 27.7%, p<0.0001; coronary bypass operation: Female 13.9% vs. Male 32.8%, p<0.0001; arterial occlusive disease (lower limbs, carotid artery, aeurysms): Female 26.2% vs. Male 37.7%, p<0.0001); device therapy: Female 11.7% vs. Male 17.7%, p<0.01, women demonstrated a higher logistic EuroSCORE (Female 21.1±13 vs. Male 20.1±14, p<0.05). Women showed more frequently previous heart surgery of different heart valves (Female 31.3% vs. Male 7.8%) but less coronary bypass surgery (Female 71.4% vs. Male 90.6%, p<0.0001). Kidney function was bad in women (GFR<60 min/1,73m2: Female 67.5% vs. Male 52.1%, p<0.0001). Procedural success rate, procedure duration, fluoroscopy time and contrast volume were comparable between female and male. After TAVI women demonstrated less frequently aortic regurgitation than males (AR Grade II: Female 12.0% vs. Male 17.8%, p<0.05). Regarding psychosomatic disturbances, women were more anxious and more frequent depressed prior to TAVI (Female 47.1% vs. Male 40.8%, p<0.05) and Female 5.7% vs. Male 2.6%, p<0.01.

Conclusion: The gender related analysis of the German Aortic Valve Registry demonstrates that women are older, received more often valve implantation by transapical access, had more often a previous valve operation, showed less residual aortic regurgitation, but more often cardiovascular problems. However, procedural outcome was similar between female and male.

Incidence, predictors and implications of transfemoral TAVI related access site complications

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Aim: Transcatheter Aortic Valve Implantation (TAVI) is a valid treatment option for patients with symptomatic severe aortic stenosis (AS) at high operative risk. The incidence, predictors and implications of access site complications related to transfemoral (TF) TAVI are not well established.

Methods and results: We pooled the prospective TAVI databases of five experienced centers in Europe enrolling only transfemoral cases for this analysis. Vascular and bleeding complications were defined according to the Valve Academic Research Consortium endpoint definitions.

The global TF TAVI database contained 986 patients. The incidence of major vascular complications, life-threatening/disabling and major bleeding was 14.2%, 11% and 17.8% respectively. In comparison to patients in whom a >19F system was used, those with the >19F system had significantly more vascular complications (22.3% vs. 12.1%, p<0.001) and life-threatening/disabling bleedings (15.5% vs. 9.7%, p=0.018) but not major bleedings. In the patient cohort with a completely percutaneous access strategy, major vascular complications and life-threatening/disabling bleedings were related to closure device failure in 64% and 29% respectively. Female gender (OR 1.63, 95% CI 1.12 - 2.36) and use of >19F system (OR 2.87 95% CI 1.66 – 4.91) were independent predictors for major vascular complications.

Figure 1. Impact of closure device failure

Conclusion: Transfemoral TAVI is associated with a >10% incidence of major access site related complications. A considerable amount of these events are related to arteriotomy closure failure. Arterial sheath size is an important determinant of both major vascular complications and life-threatening/disabling bleeding. Life-threatening/disabling bleeding complication was the single predictor of 30-day mortality.
the performance of the Society of Thoracic Surgeons (STS) risk score, the logistic EuroScore I (ES I) and the logistic Euroscore II (ES II) in patients undergoing transcatheter aortic valve implantation (TAVI).

Methods: From June 2007 through January 2011, 235 consecutive patients underwent TAVI at our institution. For each patient STS, ES I and ES II scores were calculated. Score performance was evaluated by means of ROC curves. A logistic multivariable analysis was performed including confounding factors (age, sex) and percutaneous (trans-femoral, trans-subclavian) vs. surgical (trans-apical, trans-aortic) TAVI.

Results: Percutaneous and surgical TAVI were performed in 157 (66.8%) and in 78 (33.2%) patients, respectively. Mean age was 80.5 ± 6.6 years. Median ES I, ES II and STS scores were: 17.6%, 5.4% and 6.8% respectively. Thirty-day mortality was 4.3%, the incidence of combined safety events (VARC) was 17%. The area under the ROC curve (AUC) for thirty-day mortality was 0.68, 0.66 and 0.60 for ES I, ES II and STS scores, respectively (p = 0.79). The AUC for combined safety events was 0.57, 0.60 and 0.57 for ES I, ES II and STS scores, respectively (p = 0.71) (Fig. 1). After correction for age, sex and approach the AUC for thirty day mortality was 0.84, 0.75 and 0.74 for ES I, ES II and STS scores, respectively while the AUC for combined safety events was 0.68, 0.66 and 0.65 for ES I, ES II and STS scores, respectively.

Conclusion: In TAVI patients the predictivity of ES I, ES II and STS scores for thirty-day mortality and for combined safety events was similar but poor (less than 0.75). After correction for age, sex and approach, ES I was the only risk score that showed an area under ROC curve greater than 0.75.

Clinical utility of a predictive model for paravalvular aortic regurgitation after Transcatheter Aortic Valve Implantation: a prospective validation study

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Introduction: Significant paravalvular aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) is associated with poor clinical outcomes. We identified anatomical and procedural variables strongly linked to the occurrence of paravalvular AR after implantation of the Medtronic CoreValve prosthesis (MCP), and a predictive model integrating the left ventricular outflow tract-to-ascending aorta angle (LVOT-AO) and device depth to the non-coronary cusp (NCC) was retrospectively identified (Fig. 1). LVOT-AO + depth to NCC ≥ 10 cm identified (AUC = 0.70, p < 0.001) 30-day and 1-year mortality rate were 5.5% (8/146) and 23.3% (34/146) (median follow up of 392 days). All three scoring systems were significantly increased in non-survivors compared to survivors at 30 days and at 1 year. The in-hospital mortality was as following: 31.1 ± 18.5%, the STS score: 9.6 ± 7.3%, and the EuroSCORE II: 10.0 ± 7.5%. The prognostic value of LES, STS-score, and the recent EuroSCORE II systems were analyzed in ROC curve analyses for the prediction of 30-day (AUC: 0.82 ± 0.69 vs. 0.76) and 1-year mortality (AUC: 0.74 ± 0.66 vs. 0.74). A EuroSCORE II ≥ 10 was related to an approximately three-fold increased mortality rate at 1 year (HR 2.9, 95%CI: 1.4-5.7; p < 0.03).

Conclusion: In TAVI patients, the new EuroSCORE II is superior to the STS-score in predicting early and late mortality. However, it does not provide additional prognostic information beyond the established logistic EuroSCORE. For more exact risk prediction in TAVI, a distinct TAVI risk score would be desirable.

The revised EuroSCORE II for the prediction of mortality in patients undergoing transcatheter aortic valve implantation

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Background: The assessment of procedural risk is crucial in the screening process of patients with severe symptomatic aortic stenosis. Estimated mortality influences the decision, whether a patient should preferably undergo surgical aortic valve replacement or transcatheter aortic valve implantation (TAVI).

Methods: The new EuroSCORE II was calculated in 146 TAVI patients using the webbased EuroSCORE calculator and compared to the LES and STS mortality score by ROC-curve analysis.

Results: 146 patients (Age 80.6 ± 6.4 years, left-ventricular ejection fraction 45.2 ± 14.5%, 48.6% male) underwent TAVI with a Medtronic CoreValve prosthesis between 2008 and 2011. EuroSCORE II and STS-score (p = 0.51, p = 0.001) showed a good correlation, whereas a strong correlation was found between EuroSCORE II and LES (p = 0.70, p < 0.001). 30-day and 1-year mortality rate were 5.5% (8/146) and 23.3% (34/146) (median follow up of 392 days). All three scoring systems were significantly increased in non-survivors compared to survivors at 30 days and at 1 year. The in-hospital mortality was as following: 31.1 ± 18.5%, the STS score: 9.6 ± 7.3%, and the EuroSCORE II: 10.0 ± 7.5%. The prognostic value of LES, STS-score, and the recent EuroSCORE II systems were analyzed in ROC curve analyses for the prediction of 30-day (AUC: 0.82 ± 0.69 vs. 0.76) and 1-year mortality (AUC: 0.74 ± 0.66 vs. 0.74). A EuroSCORE II ≥10 was related to an approximately three-fold increased mortality rate at 1 year (HR 2.9, 95%CI: 1.4-5.7; p < 0.03).

Conclusion: The previously derived model for the prediction of significant paravalvular AR after TAVI using the MCP is valid with reassuring specificity, acceptable sensitivity and is reasonably reproducible. A strategy incorporating these measurable anatomical and procedural variables can reduce the incidence of paravalvular AR after TAVI.

P3437 Chronic renal failure represents an independent predictor for poor outcome after transfemoral aortic valve replacement (TAVI)


Background: Transfemoral Aortic Valve Implantation (TAVI) is an established treatment for high-risk surgical patients with symptomatic aortic valve stenosis (AS). Many of these pts represent with chronic renal failure (CRF) or end-stage renal disease (ESRD). Information about outcome of TAVI pts with CRF or ESRD is limited.

Aim of the study: Therefore the aim of this study was to investigate the clinical outcome of TAVI pts with and without CRF.

Methods: 68 pts with CRF (age 81.4 ± 8.8 years, log Euro-Score 29.0 ± 17.3X, mean pressure gradient 4.2 ±1.5 mmHg, left ventricular function (LVEF) 50.2 ± 1.2%) and 64 pts with NKF (age 79.3 ± 8.0 years, log Euro-Score 20.1 ± 16.3%, mean pressure gradient 49.2 ± 1.9 mmHg, LVEF 51.9 ± 1.4%) underwent TAVI at our hospital using the CoreValve Revalving system (26/29/31mm). 64 pts with normal renal function (NRF) served as a control group. After predilatation of the stenosed aortic valve, the CoreValve prosthesis was implanted under local anesthesia using the retrograde transfemoral route (18f) exclusively. The pts were followed up clinically and by echocardiography.

Results: At our hospital 68 pts with CRF (age 81.4 ± 8.8 years, log Euro-Score 29.0 ± 17.3X, mean pressure gradient 4.2 ±1.5 mmHg, left ventricular function (LVEF) 50.2 ± 1.2%) and 64 pts with NRF (age 79.3 ± 8.0 years, log Euro-Score 20.1 ± 16.3%, mean pressure gradient 49.2 ± 1.9 mmHg, LVEF 51.9 ± 1.4%) underwent TAVI at our hospital using the CoreValve Revalving system (26/29/31mm). 64 pts with normal renal function (NRF) served as a control group. After predilatation of the stenosed aortic valve, the CoreValve prosthesis was implanted under local anesthesia using the retrograde transfemoral route (18f) exclusively. The pts were followed up clinically and by echocardiography.

Conclusions: In TAVI patients, the new EuroSCORE II is superior to the STS-score in predicting early and late mortality. However, it does not provide additional prognostic information beyond the established logistic EuroSCORE. For more exact risk prediction in TAVI, a distinct TAVI risk score would be desirable.
Immediate results and mid-term follow up of aortic valve balloon dilatation in neonates and young infants

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Background: Neonatal critical aortic stenosis is a potentially life threatening condition with a high morbidity mortality despite early intervention. This study was undertaken to evaluate the immediate outcome of aortic valve balloon dilatation in neonates and young infants, to evaluate predictors of successful procedure and to evaluate for associated complications.

Method: This is a retrospective analysis of all the aortic valve balloon dilatation procedures done at our institution during the years 1999-2009. Inclusion criteria were neonates ≤ 6 months old or infants ≤ 1 year old undergoing balloon aortic valvuloplasty in our institution. Exclusion criteria were patients ≤ 6 months of age who underwent surgical aortic valves and patients ≥ 1 year old undergoing balloon aortic valvuloplasty.

Results: Of the 55 patients who were included in the analysis, there were 47 males and 8 females. Their age varied from one to 180 days (median 30 days). Pre procedure evaluation required intravenous sedation and ventilatory support in 26 patients and intravenous sedation only in 29 patients. At completion of the procedure, the median age was 1.07 days (0.25 – 64.0 days). The median balloon index was 0.93 (0.8 – 1.2) with the median number of dilatations being 2 (1 – 5). The procedural success was obtained in 36 (65.45%) patients. Post procedure severe aortic regurgitation (AR) occurred in 10 (18.18%) patients out of which four (7.27%) died. The predictors of “mortality or severe AR” in univariate analysis were age ≤ 14 days (OR=4.63; 95% CI 1.0 – 19.5; p=0.04), requirement of inotropic support (OR=10.79; 95% CI 2.28 – 51.02; p=0.004), requirement of inotropic or ventilator support (OR=21.5; 95% CI 2.28 – 51.02; p=0.004) and requirement of ventilator support (OR=21.5; 95% CI 2.28 – 51.02; p=0.004). In multivariate regression analysis, age ≤ 14 days (OR=6.79; 95% CI 1.10 – 41.50; p=0.04) and requirement of inotropic or ventilator support were the predictors of “mortality or severe AR” in young infants ≤ 1 year old undergoing balloon aortic valvuloplasty.

Conclusion: In high-risk surgical or inoperable patients, TAVI shows excellent acute and intermediate results in patients with normal renal function. Long-term mortality in patients with CRF is 22.1% and was highest in chronic dialysis patients (50%). In chronic dialysis patients TAVI should be considered with caution.

Gender-related differences in baseline characteristics and clinical outcome of transcatheter aortic valve implantation: Is TAVI more suitable for women?

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Purpose: Percutaneous coronary intervention is less commonly performed in women and many studies have demonstrated higher early mortality among women than men. Transcatheter aortic valve implantation (TAVI) is becoming an established treatment for high-risk patients with severe aortic stenosis (AS), but the impact of gender on baseline characteristics and outcome of TAVI patients is unclear.

Methods: From September 2007 to January 2011, 201 consecutive patients underwent TAVI at a single institution and were prospectively included in a dedicated database. The proportion of women (n=113) (56.2%) was higher than that of men. Both CoreValve (86.6%) and Edwards Sapien valve (13.4%) were used and were almost exclusively implanted through the transfemoral approach (n=197) 98% underwent TAVI: transfemoral (n=183) and transapical (n=14) procedure. Main indication for TAVI was severe AS (n=183), but also AS in combination with atrioventricular regurgitation (n=14) and AS in women ≥ 70 years old (n=5).

Results: Women undergoing TAVI were older compared to men (80.7±5.9 vs. 78.4±8.7 years, p=0.03), but had less coronary and peripheral arterial disease, less previous bypass surgery, higher ejection fraction (51.8±12.7% vs. 42.3±14.8%, p=0.001), and lower logistic EuroSCORE (21.5±12.3% vs. 25.5±15.8%, p=0.05). Aortic annular diameter (22.7±1.9 vs. 22.4±2.6 mm, p<0.001) and valve size (27.2±1.6 vs. 28.2±1.5 mm, p=0.001) were smaller in women. The severity of AS was comparable (aortic valve area 0.70±0.27 vs. 0.72±0.19 mm², p=0.60; mean pressure gradient 51.2±17.3 vs. 46.6±16.3 mmHg, p=0.06). After TAVI, mean residual aortic pressure gradient was similar in women and men (59.6±4.8 vs. 87.1±4.4 mmHg, p=0.30), but the incidence of significant paravalvular aortic regurgitation (AR) was lower in women (15.0% vs. 30.7%, p=0.008), resulting in a higher device success rate. Despite more frequent peri-procedural life-threatening bleeding and major vascular complications in women (10.6% vs. 2.3%, p=0.02, and 9.7% vs. 0.4%, respectively), overall mortality was numerically lower in women at 30-days (2.7% vs. 5.7%, p=0.27) and significantly lower at 6 months (5.7% vs. 15.4%, p=0.003). Survival rates at 3 years were 68.8% in women and 65.8% in men (log-rank p=0.1).

Conclusions: Women undergoing TAVI are older but have less co-morbidities and risk factors compared to men. Bleeding and vascular complications are more common in women, but significant paravalvular AR occurs less. Women have improved mid-term survival after TAVI and thus appear to obtain a greater benefit from this evolving procedure.

Impact of comorbid coronary artery disease and percutaneous coronary intervention on procedural and outcomes with severe aortic stenosis performing Transcatheter Aortic Valve Implantation

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Background: Combined surgical aortic valve replacement (SAVR) and coronary artery bypass grafting (CABG) are the gold standard treatment for patients with aortic stenosis (AS) and concomitant coronary artery disease (CAD). The presence of CAD is associated with a higher operative risk and negatively impacts the outcome of patients undergoing SAVR. However, a substantial part of patients is unfit for surgery due to contraindications. There is little knowledge about the risks and outcomes associated with performing percutaneous coronary intervention (PCI) in combination with transcatheter aortic valve implantation (TAVI).

Aim of Study: We investigated our experience with combined TAVI and PCI as an alternative strategy in high-risk patients with symptomatic high-grade AS.

Methods: We retrospectively reviewed the Medtronic CoreValve (TM) (n=146) and Edwards-SAPIENTM (n=138) bioprosthesis via the transendocardial, transapical as well as transcatheter (n=2) approach were included. 163 patients (64%) had CAD. In case of significant CAD, treatment of coronary lesions amenable to PCI was performed prior to TAVI. 56 patients (19.7%, 27 female of these) underwent combined TAVI and PCI after being referred for surgery. In 48 patients (group 1), a staged approach was undertaken to use the 30 days prior to subsequent TAVI was chosen. 8 patients (group 2) were treated in a single-stage procedure.

Results: Mean patient age was 79.8±6.1 years. Preprocedural risk assessment revealed a mean logEuroSCORE of 17.7±10.5%. Baseline mean peak transvalvular gradients were 44.1±17.1 and 71.4±23.5 mmHg respectively. Effective orifice area was 0.71±0.16 cm². In group 2, fluoroscopy time was not significantly higher compared to group 1 (18.3±15.2 vs. 10.4±3.8 minutes). As was 19.5±10.4 vs. 13.7 days prior to TAVI. 3 patients (group 2) were treated in a single-stage procedure.

Conclusions: In high-risk patients with symptomatic high-grade AS, TAVI is a valid option even in patients with concomitant severe coronary artery disease. Further studies are needed to determine whether a systematic geriatric management program might improve outcomes in these patients.
immediately before TAVI. Clinical outcome at 30 days was similar for patients un-dergoing isolated TAVI as compared with TAVI combined with PCI in terms of death (11.1% vs. 13.2%; OR=1.22, 95% CI 0.497-3.014, p=0.661).

Conclusion: This cohort of TAVI patients, PCI prior to TAVI was not associ-ated with an increased risk of 30-day adverse events. Among carefully selected patients, revascularisation with PCI can be safely performed in addition to TAVI either as a staged or a concomitant intervention in high-risk patient population.

P3442 Evolution of aortic regurgitation after transcatheter aortic valve implantation: impact on cardiac performance

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Purpose: To examine aortic regurgitation (AR) changes over time following trans-catheter aortic valve implantation (TAVI) and its impact on cardiac performance.

Methods: 175 patients with ≥12 months post-TAVI were evaluated. Detailed echocardiography was performed at baseline, before discharge, 6 and ≥12 months post-TAVI. AR was assessed in terms of overall, paravalvular and in-travalvular severity.

Results: Majority of patients showed AR post-TAVI before discharge (n=136, 76%) and paravalvular AR (n=113, 83%) was more common than intravalvular AR (n=57, 42%). In particular, 47 (27%), 32 (18%) and 8 (5%) patients had significant (grade ≥2) overall, paravalvular and intravalvular AR, respectively. As shown in the table, in terms of overall AR, marked improvement was observed in patients with overall AR≥2 (p<0.001), while no change was noted in patients with overall AR<2. Regarding paravalvular AR, significant improvement was observed in pa-tients with paravalvular AR≥2 (p=0.002), while it remained unchanged in patients with AR<2. Concerning intravalvular AR, no significant changes over time were seen in patients with intravalvular AR=2 or AR<2. When echocardiographic vari-ables were compared between patients with overall AR≥2 (n=47) versus AR<2 (n=128) before discharge, no significant changes in LV end-diastolic volume were noted over time in both groups (repeated ANOVA p=0.05), but improvement in LV ejection fraction and reduction in LV mass and left atrial volume were noted in both groups (repeated ANOVA p<0.05).

Conclusions: Significant paravalvular AR post-TAVI improved over time, while significant intravalvular AR remained unchanged. Improvement in LV ejection fraction and reduction in LV mass and LA volume were noted in all patients, re-gardless of the presence of significant AR before discharge.

P3443 Transcatheter aortic valve implantation in patients with severe aortic stenosis and small body size

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Purpose: Surgical aortic valve replacement in patients with small body size re-mains challenging, because it frequently leads to patient-prosthesis mismatch. It is still unclear whether this problem may occur in transcatheter aortic valve implantation (TAVI). The purpose of this study was to evaluate the efficacy and safety of TAVI in patients with small body size.

Methods and Results: Between October 2006 and November 2011, a total of 424 patients (mean age 83.3±10 years) who underwent TAVI during 5 years were enrolled in this study. We classified these patients into 3 groups according to QRSd at discharge (group 1: QRSd ≤120 msec, group 2: 120 msec < QRSd ≤150 msec, group 3: QRSd >150 msec). As shown in the table, patients with QRS≥120msec had significant higher of age (79.7 vs 76.6 years, p=0.0001), body surface area (BSA) (1.75m² vs 1.70m², p<0.001) and smaller body size group (LB), with BSA ≤1.75m².

Correlations between BSA and mDiam-CT was moderate (r=0.451, p<0.001), and modest between BSA and minimal femoral artery diameter (r=0.258, p<0.001).

Device success was achieved similarly in both groups (91.2% vs 91.4%, p=0.935). The incidence of major vascular complication was higher in the SB group (13.0% vs 4.3%, p=0.002). Similar post-procedural mean pressure gradi-ent was achieved in the SB compared to LB group (10.2±4.3 vs 11.1±4.5 mmHg, p=0.119), as well as post-procedural aortic regurgitation (7.2% vs 21.5%, p=0.326), the incidence of annulus rupture (2.3% vs 0.5%, p=0.114), and 30- day survival (85.1% vs 87.6%, p=0.466). Kaplan-Meier survival analysis (median follow-up 287 days) showed no significant difference in survival between the 2 groups (log-rank p=0.642).

Conclusions: TAVI in small body-size patients is associated with similar device success, post procedural gradient, 30-day and mid-term mortality compared to large body-size patients. Care should be taken with access screening in these patients who have smaller femoral arteries.
**Expressions of the longevity-associated protein, SIRT1, and microRNA profiling in coronary artery disease: results from prospective and randomized study of treatment with atorvastatin or rosuvastatin**

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Endothelial senescence is thought to play a role in coronary artery disease (CAD). MicroRNAs (miR-9, miR-34a, miR-132, miR-153, miR-204, and miR-200) have been recently found to target silent information regulator 1 (SIRT1) leading to endothelial senescence. We investigated whether SIRT1 and microRNAs were expressed in circulating endothelial progenitor cells (EPCs) obtained from patients with CAD, and whether statins (atorvastatin or rosuvastatin) might affect these levels.

EPCs were obtained from 70 patients with CAD and 48 subjects without CAD. Patients with CAD were randomized to 8 months of treatment with atorvastatin or rosuvastatin. EPCs were obtained from peripheral blood at baseline and after 8 months of statin therapy. Levels of microRNAs and SIRT1 in EPCs were measured by real-time RT-PCR and fluorescence-activated cell sorting. To determine the effects of microRNA on SIRT1, cultured EPCs transfected with microRNA (mimic or inhibitor) were analyzed for SIRT1 levels.

The number of circulating EPCs was lower in the CAD group than in the non-CAD group (P < 0.05). Levels of SIRT1 mRNA and protein were lower in the CAD group than in the non-CAD group (SIRT1 mRNA: 2.34 ± 1.04 vs. 3.79 ± 1.44, P = 0.01; SIRT1 MFI: 16.9 ± 2.8 vs. 21.3 ± 4.1; CAD group vs. non-CAD group, P < 0.01). Levels of miR-34a were higher in the CAD than in the non-CAD group (2.86 ± 1.57 vs. 1.43 ± 0.83, P < 0.01). There were no significant differences in other microRNAs between both groups. Levels of miR-34a were negatively correlated with SIRT1 MFI in all subjects (r = 0.51, P < 0.01). A randomized clinical study has shown that levels of miR-34a decreased in the atorvastatin group (P = 0.01) but remained unchanged in the rosuvastatin group after 8 months of statin therapy. In addition, levels of other microRNAs remained unchanged in both groups. Levels of SIRT1 mRNA and total SIRT1 protein increased in the atorvastatin group (all P < 0.01) but remained unchanged in the rosuvastatin group. Treatment with atorvastatin markedly increased the number of circulating EPCs (P < 0.01), whereas treatment with rosuvastatin had no impact on the number of circulating EPCs. Functional approaches to miR-34a have shown that transfection of miR-34a into EPCs resulted in regulation of SIRT1 expression. This study suggests that miR-34a may regulate SIRT1 expression in EPCs, and that atorvastatin upregulates SIRT1 expression via inhibition of miR-34a, possibly contributing to the beneficial effects of atorvastatin on endothelial function in CAD patients with stable coronary heart disease.

**Conclusions:** The present study revealed another cardioprotective mechanism of habitual PA through beneficial modification of endothelial function.

**The effect of antiretroviral therapy on endothelial function and nitric oxide inhibition**

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**Purpose:** HIV infection is linked to higher cardiovascular risk. Adverse outcomes may be mediated through mechanisms of endothelial dysfunction; nitric oxide (NO) and its inhibitors can modify endothelial function. The aim of the study was to compare endothelial function and asymmetric dimethyl arginine (ADMA, a natural NO inhibitor) levels of HIV infected patients who are either naive to treatment or on antiretroviral therapy (ART).

**Methods:** 81 HIV infected patients were studied. 33 were naïve to treatment, 48 were on ART (nucleoside reverse transcriptase inhibitor plus non-nucleoside reverse transcriptase inhibitor or protease inhibitor). ADMA levels were measured from blood samples using a commercially available ELISA kit; higher ADMA levels imply greater NO inhibition. Endothelial function was measured by ultrasonography of the brachial artery and flow mediated dilatation (FMD) was calculated in a subgroup of 47 patients (17 naïve and 30 on ART); higher FMD values denote better endothelial function. Between group comparisons were made using non-parametric tests.

**Results:** ADMA levels were lower in patients receiving ART (0.63 (0.25, 0.81) versus 0.83 (0.78, 1.05); 0.05, Figure). FMD levels did not differ across groups (ART: 4.1 (2.0, 7.5) versus naïve: 5.0 (1.7, 8.0); P=NS).

Conclusions: ART exerts a beneficial effect by lowering ADMA levels, thus increasing NO bioavailability. Higher levels of ADMA in naïve patients may be attributed to the continuous subclinical inflammatory state that HIV viremia entails. However, this is not translated in better endothelial function. Further research into underlying mechanisms of endothelial function of HIV infected patients are needed.

**No influence of ibivradine on endothelial function in patients with stable coronary heart disease**

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Epidemiologic studies suggest that elevated heart rate is associated with enhanced cardiovascular mortality. A high heart rate has been also associated with increased risk of plaque rupture. No human data are available regarding modulation of endothelial function dependent on heart rate. Ibrivradine, a selective inhibitor of If channels, reduces heart rate without affecting cardiac contractility or blood pressure. In addition, antiinflammatory effects and an increase in endothelial function have been described for ibrivradine in animal studies. The aim of this study was to investigate effects of heart rate reduction with ibrivradine on endothelial function in patients with coronary artery disease (CAD).

In this pilot study we analyzed flow-mediated dilatation (FMD) and nitro-mediated dilatation (NMD) with high sensitivity ultrasound of the brachial artery in 25 subjects (62.3 ± 8.6 years; values are mean ± SD) with stable and a resting heart rate of > 64 bpm before and 4 hours after first intake of ibrivradine 7.5 mg vs. control (acute effect). In 17 patients endothelial function was also assessed after 4 weeks of therapy with ibrivradine (10 mg to 15 mg daily) (chronic effect). As expected, we found a significant decrease in heart rate 4 hours after ibrivradine intake and after 4 weeks of ibrivradine therapy (~ 8.2 ± 7.6 bpm and -11.1 ± 9.7 bpm; p < 0.05). FMD did not change significantly neither after acute nor after chronic therapy with ibrivradine (baseline FMD 4.8 ± 3.2%, 4 hours after 7.5 mg ibivradine 5.6 ± 4.1%; after 4 weeks of ibivradine therapy 5.9 ± 2.6%). No changes of NMD were observed. In regression analysis there was no correlation between heart rate and FMD (R = 0.08).

In conclusion, ibrivradine significantly reduces heart rate but does not improve endothelial function in patients with stable coronary heart disease.
The beneficial effects of infliximab and L-glutathione on the intermittent hypoxia-induced endothelial dysfunction in apolipoprotein E-deficient mice

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Purpose: Obstructive sleep apnea has been implicated as an important risk factor for the development of atherosclerosis. However, the pathomechanisms underlying sleep apnea-associated atherosclerotic vessel disease are incompletely understood. Thus, the aim of our study was the examination of the influence of intermittent hypoxia in apoE-/- mice serving as model for sleep apnea on the central processes contributing to the onset of atherosclerosis such as endothelial dysfunction, inflammation and oxidative stress.

Methods: Ten to 12-week-old apoE-/- mice were divided into 4 groups (n=9 each): 1. intermittent hypoxia (33 cycles of oxygen concentration fluctuations between 21% and 5%, 8 hours per day, 6 weeks), 2. intermittent hypoxia + injections of infliximab (150 μg/kg i.p., 3x per week), 3. intermittent hypoxia + injections of anti-oxidative L-glutathione (250μg/kg i.p., 3x per week), 4. normoxia= control. All animals were being fed with a cholesterol-rich diet during the experiment time. Endothelial-dependent vasodilatation as an endothelial function indicator was measured using organ chamber experiments. The endothelial re-generation readiness expressed as the number of sca1/lk1 positive cells in bone marrow and the number of colony forming units in cultured late outgrowth progenitor cells from spleen were explored by fluorescence activated cell sorter (FACS) analysis and light microscopy, respectively. The level of reactive oxygen species in aortic rings was evaluated with means of L-O2-enhanced chemiluminescence.

Results: As a key finding, the endothelial function was significantly impaired in the first group under hypoxic conditions compared to a control (73±6% vs. 45±6%, respectively). The application of antiinflammatory infliximab and antioxidative L-glutathione improved the endothelial function to the level of control (47±6%, 47±9%, resp.). The quantitative analysis of sca1/lk1 positive cells from bone marrow and late outgrowth progenitor cells from spleen demonstrated a higher number of bone marrow sca1/lk1+ cells and colony forming units of spleen progenitor cells under hypoxia compared to the remaining groups (p<0.05). The level of reactive oxygen species was approximately 7 times higher in hypoxia vs. control groups (p<0.05).

Conclusions: Intermittent hypoxia contributes to endothelial dysfunction despite activation of central compensatory mechanisms involving stimulation of endothelial progenitor cells. The application of infliximab and L-glutathione reverses hypoxia-induced changes in mature endothelial and endothelial progenitor cells.

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The beneficial effects of infliximab and L-glutathione on the intermittent hypoxia-induced endothelial dysfunction in apolipoprotein E-deficient mice

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Purpose: The beneficial effects of IL-10 and L-glutathione on the intermittent hypoxia-induced endothelial dysfunction in apoE-ko mice (21.2±6.2%) was decreased by treatment with eplerenone (9.0±3.2%), ramipril (11.9±4.3%) and the combination (11.5±3.1%). However, this result failed statistical significance (n.s.). Impaired efficacy and potency of the combination thereof (p<0.05) was observed. Without any intergroup significance. Moreover, impaired endothelial function of the corpus cavernosum in apoE-ko mice significantly improved by eplerenone, ramipril or the combination thereof (p<0.05). Potency and efficacy of endothelial independent relaxation with glyceryltrinitrate was not different in aortic rings as well as corpora cavernosa (n.s.). DHE-stained penile and aortic sections revealed a significant (p<0.05) reduction in superoxide production in all treatment groups. In parallel, increased aortic and penile collagen content in ApoE-knockout mice was significantly decreased (p<0.05) by eplerenone, ramipril or the combination.

Conclusion: Eplerenone restores endothelial function in different tissues of ApoE-knockout mice by reduction of oxidative stress, atherosclerotic lesion size and fibrosis to the same extent as treatment with ramipril or the combination. These effects were independent of blood pressure.

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Arginase inhibition improves endothelial function in patients with coronary artery disease and type 2 diabetes

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Purpose: Endothelial dysfunction plays an important role in the early develop- ment of atherosclerosis and vascular complications in type 2 diabetes (T2D). Increased expression and activity of the enzyme arginase, metabolizing the ni- tric oxide (NO) substrate L-arginine, may result in reduced production of NO and thereby endothelial dysfunction. We hypothesized arginase inhibition improves endothelial function in patients with coronary artery disease (CAD) and T2D.

Methods: On-study was performed on three groups of subjects: 1. patients with CAD (age 64±2), 12 patients with CAD-T2D (age 68±3) and 12 control subjects (age 60±2). Forearm endothelium-dependent (EDV) and endothelium-independent vasodilatation (EDV) were assessed with venous occlusion plethysmo- graphic analysis and during infusion of the arginase inhibitor Nω-hydroxy-nor-L- arginine (nor-NOHA; 0.1 mg/min) into the brachial artery for 2h. In 5 patients with CAD+T2D nor-NOHA infusion was followed by co-infusion with the NO synthase inhibitor L-NMMA (20 mg/min).

Results: Baseline EDV was significantly blunted in patients with CAD and CAD+T2D (P<0.05). Nor-NOHA did not affect EDV in the control group. In the CAD and CAD+T2D groups, nor-NOHA elicited a marked increase in EDV (Fig. 1). The improvement in EDV was significantly larger in the CAD+T2D group than in the CAD group (P<0.05). L-NMMA completely inhibited the increase in EDV induced by nor-NOHA. EDV was slightly improved by nor-NOHA in the CAD-T2D group.

Conclusions: Arginase inhibition improves endothelial function in patients with CAD and in particular among those with T2D. This suggests that upregulation of arginase activity is a key modifier of endothelial function and may represent a promising target for the treatment of endothelial dysfunction among these patients.

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Favorable effects of omega-3 polyunsaturated fatty acids on endothelial function and arterial stiffness in subjects with metabolic syndrome

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Purpose: Metabolic syndrome is associated with adverse cardiovascular events, endothelial dysfunction and arterial stiffness. Supplementation of omega-3 polyunsaturated fatty acids (PUFAs) is associated with improved endothelial function in subjects with atherosclerotic risk factors. Aim of the study was to evaluate the effects of PUFAs supplementation on arterial function in subjects with metabolic syndrome.

Methods: We studied the effect of a 12 weeks oral treatment with 2g/day of omega-3 PUFAs in 29 (15 male) subjects (mean age 44±12 years) with metabolic syndrome on three occasions (day0: baseline, day28 and day84). The study was carried out on two separate arms (PUFAs and placebo), according to a randomized, placebo-controlled, double-blind, cross-over design. The diagnosis of metabolic syndrome was based on the guidelines of American Heart Association and on Adult Treatment Panel III (ATPIII) definition. Endothelial function was evaluated by flow-mediated dilation (FMD) of the brachial artery. Carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness and augmentation index (Aix) as a measure of arterial wave reflections. Fasting serum lipid levels were measured using chromatographic enzymic method.

Results: Treatment with PUFAs resulted in a significant increase in FMD (day 0: 3.67±3.57% vs. day 28: 5.13±4.51% vs. day 84: 7.72±4.17%, p<0.001), PWV was measured as an index of aortic stiffness and augmentation index (Aix) as a measure of arterial wave reflections. Fasting serum lipid levels were measured using chromatographic enzymic method.

Conclusions: Treatment with omega-3 PUFAs improved endothelial function and arterial stiffness in subjects with metabolic syndrome. The dietary intake of omega-3 PUFAs may have beneficial effects on vascular dysfunction, which requires further investigation.

P3453

Role of the endothelium in urocortin induced arterial vasodilation in vivo in man

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Purpose: Urocortin-2 (Ucn 2) and Urocortin 3 (Ucn 3) are potent arterial vasodila- tors that play important roles in cardiovascular physiology and pathology. We assessed the role of the endothelium in the mediation of their vasomotor ef- fects in vivo in humans.

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Methods: Ten healthy male volunteers (22–3 years) were recruited into a double-blind randomized cross-over study. On five occasions separated by at least one week, bilateral forearm blood flow was measured by venous occlusion plethysmography during incremental intra-arterial infusions of Ucn 2 (15–50 ng/min), Ucn 3 (5–50 ng/min) and Substance P (2, 4 and 8 pmol/min) co-infused with saline placebo or inhibitors of cytochrome (aspirin), cytochrome p450 metabolites of arachidonic acid (flavonoid) and nitric oxide synthase (L-NMMA) alone and in combination.

Results: Inhibition of nitric oxide synthase with L-NMMA reduced arterial vasodilation to substance P and Ucn 2 (P<0.001 for both) but had little effect on Ucn3 (P=0.3615). Neither inhibition of cyclooxygenase nor cytochrome p450 metabo-

lites of arachidonic acid affected the vasodilatation induced by any of the infusions (P>0.05 for all). In the presence of all three inhibitors, substance P, Ucn 2 and Ucn 3 evoked vasodilatation was further attenuated, but not completely abolished (P<0.001 for all). Inhibition of both nitric oxide synthase and cytochrome p450 metabolites of arachidonic acid produced a greater reduction in vasodilatation than L-NMMA alone (P<0.0003 and 0.0052 for Ucn 2 and 3 respectively).

Conclusion: Ucn2 and 3 evoke arterial vasodilatation that is at least partly me-
diated by endothelial nitric oxide synthase and cytochrome P450 metabolites of arachidonic acid. These mechanisms will inform the development of further therapies directed toward the uricotel pathway.

Figure 1. Endothelial mechanisms of vasodilatation.

Purpose: Dietary flavonoids have emerged as a promising protectant of cardio-

vascular function and health. It has been shown that single and repetitive ingestion of flavan-3-ol rich foods can improve endothelial function in healthy subjects and pa-

patients with diabetes and coronary artery disease (CAD) acutely and chronically.

As objective we tested in CAD patients, whether sustained flavanol ingestion pro-

tects the vascular endothelium decreasing endothelial microparticles.

Methods: CAD patients (n=16) received a drink containing 375 mg (cocoa fla-

vanol intervention, HiFl) or 9 mg (macro-, micronutrient-matched low-flavanol con-

trol, LoFl). The number of PMPs was not affected by either treatment. Our data show

that a decreased intake of cocoa containing foods was shown to be associated with an improved cardiovascular outcome. Recent literature suggests that this may be due to the high amount of flavanols consumed with these foods increasing endothelial function via stimulation of NOS. We aim to investigate whether methylxanths (MX) contribute to flavanol (FL) associated vascular effects.

Methods: A 3-day randomized, controlled crossover study was performed in healthy young volunteers (n=12). Measurements were taken before (0h) and 2 h after ingestion of test drinks on 3 different days with 1 week of washout between treatments. The 3 different drinks were given at amounts adapted to body weight (BW) at 13.25%75 kg BW: (a) FL+MX: high flavanols (820mg/75 kg BW) and methylxanthes (100mg/75 kg BW theobromine, 15mg/75 kg BW caf-

eine) or control drinks (b) Control MX: without flavanols and with methylxanthes (113mg/75 kg BW theobromine, 10mg/75 kg BW caffeine) or (c) Control FL: high flavanols (863mg/75 kg BW), without methylxanthes. Results: Consumption of the FL+MX led to a significant increase in endothelial function as measured by flow-mediated vasodilation (FMD) at 2 h (6.6±0.9% vs 8.3±1.3%, p<0.001 vs baseline). Likewise, the Control FL drink increased FMD at 2 h (6.6±0.8% vs 7.4±1.0%, p<0.001 vs baseline). Importantly, the 2 h FMD values after FL+MX were significantly greater than after Control FL (p<0.001). In contrast, the control MX drink did not have a significant effect on FMD (6.7±1.1% vs 6.8±1.2%, p=0.755). Diastolic blood pressure decreased only after FL+MX (-5.4±4.9 mmHg, p=0.028). Furthermore, brachial artery pulse velocity (PWV), a marker for arterial stiffness decreased and circulating an-
giogenic cells (CAD) increased after all flavanol-containing drinks: FL+MX and Control FL (p=n.s. between drinks), but not after Control MX. PWV inversely correlated with diameter. Baseline diameter, heart rate, systolic blood pressure, flow velocity, and nitroglycerin-mediated vasodilatation re-

maind unaffected by either intervention drink.

Conclusion: Methylxanthes present in cocoa may enhance the positive effects of flavanols on endothelial function, CADs, arterial stiffness and diastolic blood pressure. This underscores that the food matrix needs to be considered in studies investigating effects of dietary compounds.

Purpose: Smoking is associated with impaired vascular function. Consumption of a Concord grape juice (CGJ), a rich source of flavonoids, has previously been shown to have antithrombotic and antioxidant effects and moreover can modify cardiovascular risk factors. In the present study we assessed the hypothesis that CGJ can improve endothelial function and arterial stiffness in healthy smokers.

Methods: We studied the effect of a 2 weeks oral treatment with 7cc/kg/day of CGJ (100% Concord Grape) in 20 healthy smokers (aged 26±5y) on two occasions (day 0: baseline and day 14). The study was carried out on two separate arms, one with CGJ and one with placebo, according to a randomized, placebo-

controlled, double-blind, cross-over design. Measurements were carried out be-

tre (pSm) and immediately after (Sm0) cigarette smoking. Endothelial function was evaluated by flow-mediated dilation (FMD) of the brachial artery. Carotid-

defemoral pulse wave velocity (PWV) was measured as an index of aortic stiffness 

and augmentation index (AIx) as a measure of arterial wave reflections.

Results: At baseline measurements, compared to pSm, cigarette smoking decreased FMD values (8.5±3.1% vs 6.5±1.9%, p<0.001) and more-
or vascular caused an increase in AIx (4.1±9.1% vs 6.2±9.8%, p=0.013) and PWV (6.0±2.67 mmHg/sec vs 6.2±1.06 mmHg/sec, p=0.046). Treatment with CGJ im-

proved pSm values of: FMD (7.87±2.79% vs 9.4±2.62%, p=0.024), PWV (6.11±0.58 mmHg/sec vs 5.76±0.6 mmHg/sec, p=0.013) and AIx (3.0±3.77% vs - 0.19±8.56%, p=0.016), while there was no statistically significant difference with placebo administration. Finally, compared with placebo, at day 14 treatment with CGJ, blunted the acute smoking-induced increase in PWV (placebo: from 5.67±0.67 mmHg/sec Psm to 6.00±0.78 mmHg/sec Sm0, CGJ: from 6.00±0.73 mm/sec Psm to 6.23±0.66 mm/sec Sm0) (p=0.012).

Conclusions: Concord grape juice contains specific flavonoids that may improve endothelium-dependent vasodilation and vascular elastic properties of the arterial tree in healthy smokers. Improved endothelial function and decreased
arterial stiffness is a potential mechanism by which flavonoids may prevent cardiovascular events.

ENDOTHelial dysfunction: MECHANISTIC INSIGHTS

P3457 Plasma asymmetric dimethylarginine (ADMA) is associated with autonomic neuroopathy in long standing type 1 diabetes

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Plasma ADMA has recently been identified as independent predictors of cardiovascular events. Our objective was to evaluate the relationship between plasma ADMA and diabetic autonomic neuropathy in type 1 diabetes.

We studied 78 type 1 DM patients without clinical evidence of macrovascular complications who underwent the pattern of cardiovascular autonomic balance, standard battery of cardiovascular reflex tests (Valsalva, Ewing, deep-breathing) and short heart rate variability were performed. In all examined patients retinopathy and severe peripheral vascular disease were graded according to standard methods. The measurements of creatinine, urea, glucose, sodium, potassium, lipids were performed using standard techniques. ADMA serum concentrations were analysed using an ELISA System. HbA1c was measured using the HPLC method. On the day preceding the examination, a glycemic profile was obtained. Patients with symptoms of hypoglycemia on the day of the examination or on the preceding day were excluded from the tests assessing cardiovascular autonomic neuropathy.

Results: According to the results of Ewing battery, the studied patients were divided into two groups. NDAN = without and DAN = with diabetic autonomic neuropathy. DAN was diagnosed in 35 diabetics, and NDAN in 43 patients. DAN patients were significantly older (DAN vs. NDAN: 42.4±11.5 vs. 36.4±8.0 years; p<0.0257). No differences were found between respective groups with regard to diabetes duration, BMI, WHR ratio, HbA1c, total cholesterol, LDL-cholesterol, creatinine clearance and CRP. Insulin daily dose was significantly higher in the DAN group when compared to NDAN (61.2±18.8 U/day vs. 50.3±14.6 U/day, p=0.0146). Also triglyceride levels were significantly higher in DAN as compared to NDAN (0.9±0.3 vs. 0.7±0.4 mmol/l, p=0.0281). In a multivariable logistic regression with stepwise variable selection, plasma ADMA level was selected as a predictor of the presence of DAN (OR 0.93±0.03 mmol/l, p=0.0349). ADMA level was significantly higher in the DAN as compared to NDAN (0.9±0.3 vs. 0.7±0.4 mmol/l, p=0.0281). In a multivariable logistic regression with stepwise variable selection, plasma ADMA level was selected as a predictor of the presence of DAN (OR 0.93±0.03 mmol/l, p=0.0349). ADMA level was significantly higher in the DAN as compared to NDAN (0.9±0.3 vs. 0.7±0.4 mmol/l, p=0.0281). In a multivariable logistic regression with stepwise variable selection, plasma ADMA level was selected as a predictor of the presence of DAN (OR 0.93±0.03 mmol/l, p=0.0349). ADMA level was significantly higher in the DAN as compared to NDAN (0.9±0.3 vs. 0.7±0.4 mmol/l, p=0.0281).

Conclusions: This is the first report suggesting a coincidence between elevated circulating ADMA levels and autonomic neuropathy in type 1 diabetes. Prospective studies are required to validate the concept of a cause-and-effect relationship between altered NO activity and risk of diabetic neuropathy in type 1 diabetes.

P3458 Neurohormonal activation in systemic sclerosis is related to decreased exercise capacity and right ventricle impairment

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Introduction: Systemic sclerosis (SSc) is a connective tissue disease with the excessive multilaminar fibrosis leading to their progressive failure, including left and right ventricle and pulmonary circulation impairment. Six-minute walk test (6MWT) is a simple test used for exercise capacity evaluation.

Purpose: We tried to evaluate if 6MWT can reflect impairment of pulmonary circulation in SSc patients.

Methods: We prospectively studied 111 consecutive patients (101F; age 54.2±13.8 yrs) with SSc (mean disease duration 9±12.4 yrs) and the group of 21 age-matched healthy subjects (18F, age 49.3±10.5 yrs). In addition to standard echocardiographic examination, 6MWT and trancatheter echocardiography (TEE, Philips IE 33) were performed. We divided the SSc group into two groups according to six minute walk distance (6MWD): <450m and ≥450m. We also evaluated serum NTproBNP levels (ELISA proBNP immunoassay; Roche Diagnostics) and endothelin-1 serum level (Human Endothelin-1 immunoassay R&D Systems).

Results: SSc patients had reduced 6MWT compared to controls. They showed significant neurohormonal activation. 6MWD correlated with echocardiographic indices of RV function (Act < 0.4; p=0.0002), TRPG < 0.4; p=0.001) and with plasma concentration of neurohormones (NT-proBNP < 0.4; p=0.001) and with PRA < 0.5; p=0.001)). The serum level of ET-1 and NT-pro BNP was higher in SSc patients with 6MWD < 450m: 2.9±2.2 pg/ml vs 1.4±0.7 pg/ml, p<0.003 and 311.2 (31.1-1723) pg/ml vs 105.3 (5-17670) pg/ml, p=0.01 respectively.

Conclusions: We enrolled 280 patients with CAD (mean aged 61±11 years), and 129 control subjects (mean aged 60±12 years). Serum OPG and OPN levels were measured using ELISA. Endothelial function was evaluated by flow mediated dilatation (FMD) in the brachial artery and carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness.

Results: There was no difference between control subjects and CAD patients according to age (p=0.48) and sex (p=0.07). CAD patients had significantly impaired FMD (4.75±0.22 vs. 6.50±3.13%, p<0.001) and increased PWV (8.94±2.21 m/sec vs. 8.28±1.91 m/sec, p=0.006) compared to control subjects. CAD patients had also significantly higher levels of OPG (3.91±1.87 pmol/l vs 2.88±2.17 pmol/l, p<0.001) and with serum logOPN levels (r=0.10, p=0.049) and FMD was negatively associated with OPG levels (r=-0.126, p=0.048).

Conclusions: Our findings indicate that CAD patients had increased OPG and logOPN levels. Moreover, there is a consistent association between endothelial dysfunction and impaired arterial stiffness with serum levels of OPG and OPN in CAD patients.

P3460 Oxygen administration improves peripheral endothelial function in young healthy adults

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Background: Long term oxygen treatment decreases cardiovascular risk in patients with severe chronic obstructive pulmonary disease (COPD). Peripheral endothelial dysfunction is associated with COPD. In patients with atherosclerotic disease an improvement in peripheral endothelial function was related to a decrease in cardiovascular risk. Whether oxygen administration reduces cardiovascular risk in patients with COPD is unknown. The aim of the present study was to test the short-term effect of oxygen inhalation in young healthy adults as a feasibility and pilot study before investigating this issue in patients with COPD.

Methods: In 32 young healthy adults (14 women, mean age 27.5±5.1 years) peripheral endothelial function was measured using the EndoPAT™ device: a plethysmographic record of the finger arterial pulse wave amplitude (PWA) was recorded for 5 minutes at rest, followed by 5 minutes occlusion of the right upper arm using a sphygmonanometer cuff inflated to supra systolic pressure levels. After deflation reactive hyperaemia was measured for 5 minutes. Endothelial function was calculated using the reactive hyperaemia peripheral arterial tonometry (RH-PAT)
B-type natriuretic peptide is an independent predictor of endothelial function in man


Background: B-type natriuretic peptide (BNP) has been reported to be elevated in predclinal states of vascular damage. To elucidate the relationship between plasma BNP and endothelial function, we investigated the relationship between BNP and endothelial function in a cohort of subjects comprising of healthy subjects as well as at-risk subjects with cardiovascular risk factors. To also clarify the relative contribution of various different biological pathways to the individual variation in endothelial function, we have also examined the relationship between a panel of multiple biomarkers and endothelial function.

Methods: Seventy subjects were studied (mean age 58.1±4.6 years; 27% had a history of hypertension, 18% had a history of hypercholes-
terolemia). Endothelium-dependent vasodilatation was evaluated by the inva-
sive acetylcholine (ACH)-induced forearm vasodilatation technique. A panel of biomarkers of biological pathways was measured: natriuretic peptides (BNP); haemostatic factors (PAI-1 and tPA); inflammatory markers, including cytokines (hsCRP, IL-6, IL-8, IL-18, TNF-alpha, myeloperoxidase) and soluble adhesion molecules (E-selectin, ICAM-1, VCAM-1, sCD40).

Results: Forearm blood flow (FBF) responses to ACH were significantly lower in at-risk subjects when compared to healthy subjects (p < 0.01). The median BNP level in the study population was 26.9 pg/ml. Multivariable regression analyses show that age, total cholesterol/HDL ratio, glucose and BNP were independent predictors of endothelial function and BNP remained an independent predictor (p < 0.009) in a binary logistic regression analysis using FBF as a dichotomous variable based on the median value. None of the other plasma biomarkers was independently related to ACH-mediated vasodilatation.

Conclusions: In a strategy using several biomarkers to relate to endothelial func-
tion, plasma BNP was found to be an independent predictor of endothelial function as assessed by endothelium dependent vasodilatation in response to ACH.

Endothelial repair in acute cardiovascular events, correlation between endothelial progenitor cells and endothelial activation markers

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Purpose: Acute myocardial infarction (AMI) and stroke are hallmark examples of endothelial inflammation and thrombosis. Endothelial progenitor cells (EPC) are released after an ischemic event. Its characterization is complex and simpler markers could be useful. Objective: To study the release kinetics of EPC and the relationship with VCAM-1 after an acute ischemic event.

Methods: From March 2009 to September 2011 we prospectively included AMI and stroke patients younger than 75-years not previously treated with statins. EPC were defined as CD45-, CD34+,KDR+ by flow cytometry and VCAM-1 was measured by immunoassay at 0, 7, 30 and 180 days. Controls were also studied in a single measure.

Results: 141 patients (69% AMI; 56.9-years; 87% male) and 104 Controls (57.5-years; 82% male). EPC were higher than controls at day 0 and VCAM-1 showed less variability (Table 1). EPC and VCAM-1 progressively increased with a peak at day 30 (Figure 1). VCAM-1 and EPC values showed similar evolution over time (p-value 0.839) in a mixed model test.

Conclusions: In this selected population there is a correlation in the kinetics of EPC and VCAM-1 after an AMI or stroke. EPC release follows closely the inflammation insult and the severity of inflammation may trigger its release.

Effects of altered vascular L-carnitine and gamma-butyrobetaine content on the development of endothelial dysfunction induced by different agents


Purpose: L-Carnitine plays an important role in the energy metabolism of car-
diac tissues. Results from recent studies have demonstrated that the reduction of cardiac tissue level of L-carnitine and increase of content of its precursor, gamma-
butyrobetaine (GBB), protects the heart from ischemia-reperfusion injury. Several studies have shown that the alterations of vascular L-carnitine and GBB level could be a promising approach to induce angioprotective effects. The aim of this study was to investigate the effects of changes in vascular tissue levels of GBB and L-carnitine on the functional condition of endothelium in three different exper-
imental models of endothelial dysfunction.

Methods: Alterations of vascular tissue content of L-carnitine and GBB in rat vascular tissues was induced by administration of L-carnitine; mildronate, an in-
hibitor of L-carnitine biosynthesis and renal re-uptake; or combination of both for two weeks. Endothelial function in the isolated aortic rings was evaluated before and after incubation in the buffer solution containing lysophosphatidylcholine (5 
M) or buffer solution with high glucose (44 mM) or triglyceride (10 mM) concen-
tration.

Conclusions: Administration of mildronate decreased the vascular L-carnitine content for 48% and increased GBB level 3 fold. Treatment with L-carnitine increased endo-
genous L-carnitine content for 36% in vascular tissues, but had no effect on GBB level. Administration of combination of L-carnitine and mildronate did not influence vascular L-carnitine level, but increased GBB level 3.5 fold. Aortic rings from control animals after incubation in buffer solution with high glucose, triglyc-
erides or lysophosphatidylcholine content decreased significant endothelial dysfunction. None of the studied treatments attenuated the detrimental effects of lysophosphatidylcholine or triglycerides on the endothelium while simultaneous administration of L-carnitine and mildronate prevented the high glucose concen-
tration impaired function of endothelium.

Conclusions: Our results demonstrate that the increased vascular GBB attenuates the development of endothelial dysfunction induced by high glucose concentration. This could be a novel approach to attenuate the development of endothelial dysfunction in case of hyperglycemia and diabetes.

Dexrazosane reduces superoxide formation and improves cardiac performance in caveolin-1 deficient mice

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Recently generated caveolin-1 deficient mice (cav-1ko) display a severely dis-
eased cardiac phenotype with systolic and diastolic heart failure. Accumulating evidence supports a causative role of an uncoupled eNOS resulting in enhanced oxidative stress in the development of these abnormalities. Interestingly, a similar molecular mechanism with a crucial role of uncoupled eNOS was recently pro-
gressed for histone deacetylase-induced cardiomyopathy. Currently, a drug called dexra-
zosane is approved for the prevention of this important, potentially lethal arrhyth-
oma-sid effect.

To elucidate the effects of dexrazosane on the development of the cardiomypa-
thy of caveolin-1 deficient mice (cav-1ko) and wild type mice (wt) were treated either with dexrazosane or with saline for 8 weeks. Treatment with dexrazosane resulted in a significantly reduced endothelial superoxide formation. Furthermore, dexrazosane treatment led to a decreased apoptosis in hearts of cav-1ko mice as measured by TUNEL-assay, and the Bcl-2 and Bax ratio. These molecular effects led to an improved systolic and diastolic heart function in cav-1ko as determined by invasive hemodynamic measurements. Additionally, lowered shear stress levels were detected in treated cav-1ko mice. Dexrazosane did not alter the above mentioned parameters in wt animals.

Taken together, these novel findings indicate that dexrazosane prevents superoxide generation in hearts of cav-1ko. Since the diminished oxidative stress results in an improved cardiac performance in cav-1ko, our data suggest dexrazosane as a novel therapeutic strategy in this specific cardiomyopathy.

Purpose:

Methods/Results:

Conclusion:

Results: In contrast to the normotensive group, Ach-induced relaxations were significantly impaired in the SHR group exposed in vivo to DEP: the AUC was 191.1±10.1 in SHR exposed to DEP vs. 246.6±8.7 in SHR exposed to PBS (p < 0.01). Concentration-response curves to sodium nitroprusside were not modified, neither in SHR nor in Wistar rats. For the gene expression, we observed a significant up-regulation of p22phox and gp91phox in SHR rats exposed to DEP (p < 0.05). These vascular alterations, probably related to an enhanced oxidative stress, were observed without significant change in systolic blood pressure (205±6 mmHg in SHR exposed to DEP vs. 191±6 mmHg in SHR exposed to PBS).

Conclusions: Repeated in vivo exposures to DEP impairs vascular function in hypertensive rats via an up-regulation of p22phox, interestingly without blood pressure modulation. This suggests a synergistic effect on endothelial dysfunction between particulate air pollution and hypertension.

Hypertension and particulate air pollution exposure: synergism for vascular function alterations

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Background: Epidemiological and clinical studies have shown that traffic-related air pollution is strongly linked to cardiovascular mortality and morbidity. The most toxic part of air pollution seems related to diesel exhaust particles (DEP) (aerodynamic diameter < 2.5 μm). Although the exact mechanisms involved in the cardiovascular toxicity of these particles are still unclear, recent epidemiological studies have shown that subjects already at risk for cardiovascular diseases might be more sensitive to the toxicity of DEP.

Purpose:

Methods:

Conclusions: Our data suggest a novel link between NOX4, NRF2-mediated antioxidative response and endothelial function.

Modulation of the Eph/ephrin-system by inflammatory stimuli in vascular cells - implications for the atherosclerotic plaque development

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Background: The Eph receptors represent the largest family of receptor tyrosine kinases. Eph receptors and their ephrin ligands are cell-surface proteins, which are able to generate bidirectional signaling. Eph/ephrin mediated cell-to-cell communications are essential in different processes like tumor biology and inflammation. However, the impact of Eph receptors and ephrins in the pathophysiology of atherosclerosis, as a vascular proliferative and inflammatory disease, is currently not well understood. The aim of the present study was to investigate the influence of inflammatory stimuli on the expression of Eph receptors and ephrins in vascular cells potentially contributing to the atherosclerotic plaque development.

Methods/Results: First, HUVEC were treated with TNF-α, LPS and TNF-α+LPS for 4h and 24h. Analysis of the mRNA and protein expression of different ephrin ligands (ephrinA1, -A4, -B1, -B2) and Eph receptors (EphA2, -A4, -B1) revealed striking changes in the response to inflammatory stimuli. EphrinA1 mRNA-expression was already increased after 4h TNF-α treatment and was further elevated after 24h treatment. Also LPS increases the ephrinA1 mRNA expression, but this effect was less pronounced compared to TNF-α + LPS and TNF-α+LPS treatment. It was also able to induce the expression of ephrinB1 and ephrinB2. In contrast to the expression of ephrinA4 was not modulated. In the case of Eph-receptors the ability of inflammatory stimuli to induce their expression level was less pronounced. Only EphB1-expression was elevated after TNF-α treatment. Compared to endothelial cells macrophages did not express such high levels of ephrin ligands and Eph receptors. Furthermore, the response of inflammatory stimuli is completely different in macrophages. Here, we could detect higher expression levels after LPS-stimulation and in the majority of cases no effects after TNF-α treatment. The most impressive effect was the nearly 100fold upregulation of EphA2 upon LPS-treatment. Also ephrinA1 and ephrinB2 mRNA expression was increased after 4h LPS-stimulation.

Conclusions: The results of the present study demonstrate that TNF-α and LPS, as important inflammatory mediators in atherosclerosis, are able to regulate vari-
Genetic endothelial dysfunction and high fat diet synergistically affect systemic but not coronary vascular tone

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Purpose: Vascular tone depends on molecular pathways involving eNOS and the control of the expression and activity of this and other vasoactive enzymes. We tested the hypothesis that genetic endothelial dysfunction interacting with high fat diet (HFD) may affect systemic and coronary vascular tone in eNOS partial (eNOS+/-) and total knockout (eNOS-/-) mice.

Methods: Wild type (WT), eNOS+/- and eNOS-/- mice were studied. WT and eNOS+/- were fed with standard (SD) or HFD diet for 16 weeks. Arterial blood pressure (BP) was assessed non-invasively and coronary vascular resistance (CR) was measured in isolated hearts (Langendorff preparation).

Results: Arterial BP of WT, eNOS+/- and eNOS-/- was increased in eNOS+/- and by 21% in eNOS-/- HFD and by 36% in eNOS+/- mice. CR was similarly increased by 21%, 14% and 20% in eNOS+/-, eNOS-/- and WT, respectively. The expression of eNOS was reduced by 48% in eNOS+/- and absent in eNOS-/- mice.

Conclusion: The present study demonstrates that a partial decrease of eNOS is able, per se, to significantly impair coronary vascular tone similarly to a total absence of the enzyme. Conversely, the effects of genetic eNOS impairment on systemic vascular tone are progressive and are synergistically modulated by HFD.

Altered activation of endothelial pro- and anti-apoptotic pathways by HDL from patients with coronary disease: critical role of HDL-proteome remodeling

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Background and Aim: Endothelial dysfunction and injury are thought to play a crucial role in the pathophysiology of coronary artery disease (CAD). High density lipoprotein (HDL) has been proposed to exert endothelial anti-apoptotic effects. The aim of the present study was to characterize the effects of high-density lipoprotein on endothelial pro- and anti-apoptotic pathways to determine functional implications of alterations of the HDL-proteome in this respect.

Methods: HDL was isolated from patients with stable CAD (HDL-sCAD), an acute coronary syndrome (HDL-ACS) and healthy subjects (HDL-Healthy) using ultracentrifugation. The effects of HDL on endothelial cell apoptosis were determined in vitro and in apoE-deficient mice in vivo, and activation of endothelial pro- and anti-apoptotic pathways was in response to HDL characterized. HDL-proteomics was performed using liquid chromatography and tandem mass spectrometry, and functional implications of changes in HDL-associated proteins for endothelial apoptosis were examined.

Results: Administration of HDL-Healthy induced expression of the endothelial anti-apoptotic factor Bcl-xL via activation of PI3K/Akt and substantially reduced endothelial cell apoptosis in vitro and in apoE-deficient mice in vivo. In contrast, HDL-sCAD and HDL-ACS did not inhibit endothelial apoptosis, failed to activate endothelial Bcl-xL expression and stimulated potential endothelial pro-apoptotic pathways, in particular p38MAPK-mediated activation of J-Bid. Endothelial anti-apoptotic effects of HDL-Healthy were independent of endothelial NO-synthase and were retained in delipidated HDL-Healthy, suggesting a critical role of HDL-proteome (since apoA1 alone did not significantly reduce apoptosis). HDL proteomics and subsequent validations using different HDL-isolation methods revealed a substantially reduced cluster- and increased apoCII- and HDL-C of HDL-Healthy, which is critical for impaired endothelial anti-apoptotic properties.

Conclusion: The present study shows for the first time that HDL-protein remodeling in patients with CAD leads to a loss of the capacity of HDL to activate endothelial pro- and anti-apoptotic pathways and stimulation of potential pro-apoptotic pathways. These findings provide important novel insights into the mechanisms leading to altered vascular effects of HDL in coronary disease.

Relaxin as protective factor in endothelial dysfunction: role of glucocorticoid receptor-mediated effects on arginine-II and SOD1 expression

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Purpose: The hormone relaxin has emerged as a regulator of cardiovascular and metabolic remodeling in mice fed high-fat and high-sucrose diet

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Background: Metabolic syndrome (MeS) is characterized by a constellation of disorders, including hyperhyension, dyslipidemia, hyperglycemia and the accumulation of visceral fat with hepatosteatosis (HST). MeS is based on insulin resistance in skeletal muscle and liver, caused by metabolic stress, oxidative stress, inflammation and hyperinsulinemia, and all of them can activate extracellular reg- ulatory kinase (ERK). However, the role of hepatic ERK in metabolic changes and vascular complications of MeS in vivo have been unknown.

Purpose: We tested if hepatic ERK regulates HST with insulin resistance, and influences factors metabolite remodeling in liver and endothelial function in MeS.

Methods: We employed the Cre-loxP system to inactivate the ERK2 gene in hepatocytes. Liver-specific ERK2 knockout mice (LE2KO) and control littermates at eight weeks of age were fed either a normal diet (ND) or a high-fat/high-sucrose diet (HFD) for 20 weeks. Serum glucose, insulin and peroxide-metabolites (25- ROMs) were measured. Glucose tolerance and insulin sensitivity tests were performed. The histological findings and the Gene Chip analysis of the liver were tested. Dihydroethidium staining was performed to assess vascular superoxide

Hepatic ERK suppresses endothelial dysfunction with the alleviation of hepatosteatosis and metabolic remodeling in mice fed high-fat and high-sucrose diet

T. Kujiraoka1, Y. Satoh1, M. Ayao2, Y. Shiraishi2, Y. Nakaya1, S. Endo2, D. Hakuno1, K. Isoda1, T. Adachi1, 2National Defense Medical College, Saitama, Japan; 2National Defense Medical College, Watanuki Medical Center, Tokyo, Japan

Background: Metabolic syndrome (MeS) is characterized by a constellation of disorders, including hypertension, dyslipidemia, hyperglycemia and the accumulation of visceral fat with hepatosteatosis (HST). MeS is based on insulin resistance in skeletal muscle and liver, caused by metabolic stress, oxidative stress, inflammation and hyperinsulinemia, and all of them can activate extracellular reg- ulatory kinase (ERK). However, the role of hepatic ERK in metabolic changes and vascular complications of MeS in vivo have been unknown.

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production and endothelial function was evaluated with the isotropic tension measurement of aortic rings.

**Results:** LE2KO fed HFHS revealed the marked deterioration of HST with gaining in liver weight. LE2KO fed HFHS demonstrated the impairments of glucose tolerance, the deteriorations of insulin resistance, and the elevation of d-ROMs levels. Gene Chips analysis indicated the down-regulated enzymes of carbohydrate metabolism, fatty acid transport and oxidation, mitochondrial Krebs cycle and electric transport chains as well as the up-regulated enzymes of detoxification. Vascular superoxide production was significantly increased in LE2KO fed HFHS, compared with control fed HFHS. Acetylcholine (ACh) induced relaxation was maintained in Control fed HFHS, which was markedly decreased in LE2KO fed HFHS (Control-ND: 67.5±5.2%, Control-HFHS: 59.3±5.2%, LE2KO-ND: 68.7±4.4%, LE2KO-HFHS: 33.2±8.4% with ACh 10-6m, P<0.01 vs Control-HFHS, N=9-10).

**Conclusions:** Hepatic ERK2 protects from deteriorating insulin resistance and HST with modulating the expressions of metabolic and detox enzymes in mice model of MetS. Hepatic ERK2 regulates lipid-, glucose- and energy-metabolisms, suppresses vascular oxidative stress and maintains endothelial function with HFHS loading. This study suggested that hepatic ERK2 preserved endothelial function in MetS with metabolic regulation.

**ENDOTHELIAL DYSFUNCTION: CLINICAL**

**P3473** Metabolic syndrome and regional vascular alterations

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**Purpose:** In the ongoing debate about metabolic syndrome (MS), it is still unresolved whether it consists a distinct pathogenic entity of cardiovascular risk. We sought to unravel the mystery of the interrelationships of the presence of the MS and the vascular status of a hypertensive population.

**Methods:** Our population consisted of 575 newly diagnosed never treated consecutive essential hypertensives (stage I-II, aged 52±14 years), without overt cardiovascular disease. Arterial system was evaluated by means of arterial ultrasound, b)carotid femoral pulse wave velocity (PWV) with Complior SP device, c)Heart rate-corrected augmentation index (Aix) with Sphygmocor device, d) Brachial artery flow-mediated dilation (FMD) and e) ankle brachial index(ABI).

**Results:** Fasting venous blood samples were collected for glycaemic and metabolic profile determination. The subjects were divided in two groups regarding the absence (group A), or the presence of MS (Group B) according to ATP III criteria.

**Results:** The two groups did not differ regarding age and office blood pressure, while male gender was more prevalent in group B (72% vs. 40%). However, group B compared to group A had increased levels of uric acid and log to CRP (5.6±1.5 vs. 4.7±1.14 and 0.154±0.52 vs. 0.053±0.54 respectively, all p<0.00). Despite that group B presented statistically significant impairment of PWV and common carotid posterior wall intima media thickness (8.4±1.7 vs. 6.9±1.6, 0.76±0.17 vs. 0.69±0.15 respectively).

**Conclusion:** Hypertensive patients with the traits of metabolic syndrome presents deterioration of only specific vascular indices. Despite that endothelial function and peripheral circulation appears unaffected, central aortic and carotid arterial systems are imposed to vulnerable effects of central obesity.

**P3474** Association between arterial function and ocular involvement in sarcoidosis

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**Purpose:** Sarcoidosis (Sar) is a multisystem inflammatory disease. It has been shown that Sar patients have impaired endothelial function, and increased arterial stiffness. Ocular involvement occurs in 15-25% of Sar patients mainly in the form of uveitis. The study was designed to determine if ocular involvement in Sar is associated with an extensive vascular dysfunction.

**Methods:** We enrolled 61 Sar patients and 61 age and sex matched, control subjects (CI). Sar patients were divided in those with ocular Sarcoidosis (OS) (21 patients) and in those without ocular Sarcoidosis (WOS) (39 patients). Endothelial function was evaluated by flow-mediated dilation (FMD). Carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness and augmentation index (Aix) as a measure of arterial wave reflections.

**Results:** The differences in age, sex and mean arterial pressure ANOVA revealed that patients with OS compared to WOS patients and CI subjects had impaired FMD (5.85±2.42 vs. 6.4±1.93% vs. 8.30±3.47%, p<0.001), increased Aix (24.03±19% vs. 17.85±10.99% vs. 13.76±10.76%, p<0.001) and increased PWV (8.29±2.42 m/sec vs. 7.00±1.12m/sec vs. 6.85±1.51 m/sec, p<0.005). More precisely, post hoc analysis revealed that patients with OS compared to WOS patients had significantly increased FMD (17.05±1.24 vs. 14.75±1.40, p<0.001) and PWV (8.10±1.20 vs. 7.30±1.12m/sec, p<0.005). The mean Aix in OS patients was significantly increased compared to control (24.00±9.19% vs. 13.76±10.76%, p<0.002), although there was no difference between WOS patients (17.99±10.99 vs. 13.76±10.76, p=0.058).

**Conclusions:** In the present study we have shown that Sar patients with ocular involvement have impaired endothelial function and increased arterial stiffness. These results strengthens the vascular theory considers uveitis a consequence of vascular dysfunction in Sar patients.

**P3475** CD28null T helper lymphocytes are associated with endothelial dysfunction in periodontitis patients with hypertension

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**Inflammatory diseases including periodontitis increase risk for both hypertension and arteriosclerosis. The mechanism of this relationship remains unknown. Recent studies show that CD28 null CD4+ T lymphocytes contribute to arteriosclerosis however their role in regulation of arterial stiffness remains unclear.**

**Methods:** We studied 28 patients (13F; 15M), mean age ± SD was 54.4±7.7 yrs. 24-hour ambulatory blood pressure monitoring (ABPM), carotid artery intima media thickness (IMT) was measured and periodontal examination performed. Endothelial function was assessed by flow mediated dilation (FMD), Peripheral blood T cell markers CD3, CD4, CD8 and CD28 were assessed by flow cytometry. Results: Mean IMT was 0.7±0.1 mm in periodontitis subjects and exceeded normal limits in only 7% of patients. The average FMD result was reduced in studied patients when compared to controls (7.4±3 vs 11.2±3). Endothelial function was impaired in 71.4% (n=20) of investigated subjects. CD28null T helper lymphocytes comprised 6.3±7.1% of CD4+ T cells. Increased presence of CD4+CD28null T cells was associated with significantly worse endothelial function (r= 0.4, p<0.05).

The same at the time in our cohort without overt arteriosclerosis there was no correlation between CD4+CD28null Th-cells and either mean or maximum IMT (r= 0.04, p=0.82). We also observed no association between CD4+CD28null T cells and blood pressure levels measured by ABPM. (mean SBP/DBP: 24 mm -r= 0.22, p=0.50 vs -0.21, p=0.28, day- r= 0.15, p=0.44 vs 0.14, p<0.49, night r=-0.32, p=0.11).

**Conclusions:** In periodontitis subjects peripheral vascular function impairment is associated with increased levels of circulating, pro-inflammatory CD4+CD28null cells. These cells may represent a novel marker and therapeutic target for vascular dysfunction.

**P3476** Relation of circulating endothelial progenitor cell levels to contrast-induced nephropathy in patients undergoing percutaneous coronary intervention and percutaneous transluminal angioplasty

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**Objectives:** Endothelial dysfunction has been proposed as one of the mechanisms contributing to the development of contrast-induced nephropathy. However, no study has reported the relation between circulating endothelial progenitor cell (EPC) levels and CIN. The aim of this study was to evaluate the relation between circulating EPC and CIN in patients after angiography.

**Methods:** A total of 77 consecutive patients undergoing elective percutaneous coronary intervention and percutaneous transluminal angioplasty were enrolled. Flow cytometry with quantification of EPC markers (CD34+CD133+KDR+, and CD34+KDR+CD133+) in peripheral blood samples was used to assess EPC number before procedures. CIN was defined as an absolute ≥0.5 mg/dl or a relative ≥25% increase in the serum creatinine level at 48 hours after procedures.

**Results:** Among the study subjects, 18 patients (23%) developed CIN (p<0.05). EPC number (CD34+KDR+, cells/105 events) was shown.

**Table 1:** Comparison of circulating endothelial progenitor cell (EPC) levels in patients with or without development of contrast induced nephropathy (CIN)

<table>
<thead>
<tr>
<th>No CIN (n=59)</th>
<th>CIN (n=18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPC levels (cells/10^5 events)</td>
<td>34.4±7.33</td>
<td>13.9±10.1</td>
</tr>
<tr>
<td>CD34+KDR+</td>
<td>9.25±6.30</td>
<td>4.1±2.59</td>
</tr>
<tr>
<td>CD34+KDR+CD133+</td>
<td>7.8±6.76</td>
<td>3.8±3.35</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation (SD).
significant negative predictor for development of CIN (OR 0.69, 95% CI 0.54–0.87, P=0.002). Over a follow-up of 2 years, patients with CIN have higher incidence of major adverse cardiovascular events including fatal/nonfatal myocardial infarction, stroke, limb amputation, and death (33% vs 17%, P=0.016) than those without CIN.

Conclusions: Decreased EPCs level is associated with a greater risk of CIN after interventional procedures, which may partially explain the pathophysiology of CIN and the poor prognosis in these patients.

P3477
Sympathetic skin response (SSR) is related to a surrogate marker of endothelial function in patients after acute coronary syndrome (ACS) (Forever study)

U.J. Cieslik-Guerra1, M. Fizal2, M. Kaminiski3, J. Chapiński3, E. Tzros4, B. Uzanska-Loch5, T. Rechcinski1, J.D. Kasprzak1, A. Bogucki1, M. Kurpela1.1Chair of Cardiology, Medical University of Lodz, Bieganski Hospital, Lodz, Poland; 2Department of Neurology, Jonscher’s Medical Ltd., Caesarea, Israel) on hands. RH-PAT index was automatically calculated. Results: Kolmogorov-Smirnov test confirmed normal distribution of results of all measurements. RH-PAT index was related by linear correlation to SSR potential latency measured on upper limbs: right hand (r=0.336, p=0.016), left hand (r=0.342, p<0.014). There were no significant correlations between RH-PAT index and SSR potential measured on lower limbs. Conclusion: In our study we confirmed the relationship between sympathetic skin nerves activity and the surrogate marker of endothelial function measured on upper limbs in patients after ACS. This results demonstrate close relationship between sympathetic nervous system and endothelial function. Mechanism of this interaction remains unknown and requires further study.

P3478
Peripheral endothelial function correlates with coronary atherosclerosis but not with carotid intima-media thickness

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Introduction: Previous studies from our and other laboratories have demonstrated the existence of a clear relationship between different measures of endothelial function and the extent of coronary atherosclerosis. This relationship between endothelial function and carotid intima-media thickness has not been extensively investigated.

Methods and results: Endothelial function using radial artery flow-mediated constriction (L-FMC) and dilation (FMD) was assessed in 506 consecutive patients undergoing diagnostic coronary angiography. Intima-media thickness of both carotid arteries was also measured.

IMT was greater in patients with diabetes (P=0.02), males (P=0.02), those with body mass index >30 (P=0.03), and in those older than 65 years (P=0.02). There was a strong correlation between age and IMT (r=0.33, P<0.0001). Smoking, hypercholesterolemia and a family history for cardiovascular disease had no impact on IMT. As previously published, there was a progressive reduction in both L-FMC and FMD with increasing severity of coronary atherosclerosis (P<0.0001). In contrast, the relationship between either L-FMC or FMD and IMT was weak (r for the relationship between L-FMC and IMT=0.12, P=0.01; r for the relationship between FMD and IMT=0.07, P=0.17). There was a positive correlation between IMT and residual radial artery diameter (r=0.12, P=0.008). IMT increased with the extent of coronary artery disease (no CAD: 0.76±0.16cm, 1-vessel CAD: 0.79±0.15cm, 2-vessel CAD: 0.81±0.15cm, 3-vessel CAD: 0.83±0.18cm), but this trend did not reach statistical significance (P=0.07).

Conclusions: Resting (L-FMC), but not recruitable (FMD) endothelial function correlates with the extent of subclinical carotid atherosclerosis. This correlation is however weaker in comparison to the relationship between these measures of peripheral endothelial function and the extent of coronary atherosclerosis. The most important predictor of carotid IMT in this population of patients with CAD was age.

P3479
Endothelial dysfunction, but not structural atherosclerosis, is evident early in children with heterozygous familial hypercholesterolaemia

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Background: Children with heterozygous familial hypercholesterolaemia (heFH) are prone to premature atherosclerosis. Endothelial dysfunction, increased arterial stiffness and carotid intima-media thickness (cIMT) are early markers of atherosclerosis and could be used to predict cardiovascular risk in children and adolescents with heFH. The aim of the study was to perform a complete evaluation of vascular health and assess for early functional and structural vascular changes in children and adolescents with heFH.

Methods: This cross-sectional study included 30 children with heFH (mean age 12 years) and 30 age- and gender-matched controls. Brachial artery flow-mediated dilation (FMD), cIMT, carotid–femoral pulse wave velocity, large and small vessel compliance were determined in all participants.

Results: Children with heFH exhibited significantly higher total and LDL cholesterol, apolipoprotein B and lipoprotein (a) levels (p<0.05 for all) and lower FMD (6.23±3.88 vs. 9.46±4.54%, p=0.004) compared with controls. When children were divided in age subgroups, FMD was found to be significantly decreased in heFH compared to control subjects only in ages >10 years (p=0.05). However, using two-way analysis of variance, FMD was found to be similarly impaired in heFH children in all age subgroups (p=0.39). No differences in other vascular function indices were found between groups. In heFH patients, but not in controls, FMD was inversely correlated with cIMT (r=-0.378, p=0.036).

Conclusions: Endothelial dysfunction occurs early in heFH children indicating an increased risk for premature cardiovascular disease. Decreased FMD is detected before the appearance of structural atherosclerotic changes. These findings may suggest that pharmacologic therapy with statins in children with heFH should probably start early (<10 years old) in order to prevent the impairment of vascular function.

P3480
Effect of chronic and acute oral tobacco consumption on brachial artery flow-mediated dilation among healthy non-smoking tobacco users

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Purpose: Use of oral tobacco is highly prevalent in India. Unlike inhaled form, the...
adverse effects of oral tobacco on endothelial function (and atherosclerosis) have not been systematically studied. This study examined the impact of oral tobacco chewing on endothelial function by brachial flow mediated dilatation (FMD) testing.

Methods: 67 healthy non-smoking adults (28 tobacco chewers and 39 non-user controls) underwent brachial FMD testing in a steady state as per the international task force recommendations. Further, 11 of the chronic users underwent additional FMD testing 15 min after acute ingestion of tobacco. All studies were recorded and analysed offline by a blinded observer.

Results: Age and gender were comparable in the two groups (25±4 yrs 29±7 years and 89% Vs 96% men in control and users respectively). The metabolic profile was normal and similar in both groups (mean BMI 21.5 Vs 21.8 kg/m², fasting plasma glucose 83 Vs 84 mg/dl, total cholesterol 136 Vs 128 mg/dl in control and user respectively). The results of brachial FMD testing (table 1) showed significantly depressed FMD among chronic tobacco users. Acute ingestion of tobacco tended to worse hemodynamics and vasocostriction (when compared to steady chronic state. Table 1) with similar FMD results as chronic usage.

Conclusion: In this study of young healthy non-smoking men in India, we found significant endothelial dysfunction, as evidenced by reduction in brachial FMD, among chronic users of oral tobacco. This has important implications on the role of oral tobacco in causation of premature atherosclerosis in India and can be used to direct larger studies.

Methods: Endothelial function was assessed by reactive hyperemia index (RHI) determined by peripheral arterial tone index (PAT), using endoPAT2000 (Larimar Medical, before and 6 months after EVA2) bariatric surgery. Weight, BMI, waist circumference, blood lipids and hsCRP levels were also assessed.

Results: 53 patients were included (mean age 42±10.4 years, 49 females; mean BMI 43.4±4.7; mean weight loss after surgery 34.8±9.6kg). A complete pre and post surgery was obtained in 49 patients. Table 1, IHR values were <1.7 (very high risk) in 11 patients (22.4%) 1.7 to 2.1 (high risk) in 14 (28.6%), 2.1-2.3 (low risk) in 3 (6.1%) and >2.3 (normal) in 21 (42.9%) patients. In Evol2, 16 patients improvements were observed (Table 2). The patients who evolved to a worse risk group. Globally, there was no significant difference in RHI values before and after surgery (p=0.13). The improvement in endothelial function was not related with age, initial weight, BMI or waist circumference, or with previous traditional risk factors (hypertension, diabetes, dyslipidemia, smoking). It was also not related with the weight lost, changes in BMI or waist circumference, changes in blood pressure, changes in blood lipids (total cholesterol, HDL-C, LDL-C, ApoA, ApoB1, Lp(a)) or hsCRP (p=ns in all cases), although all these parameters improved after surgery. The only related was between RHI and heart rate change (-13.9 bpm in patients with improved RHI, versus -2.4 bpm in patients without RHI improvement, p=0.033).

Conclusions: After bariatric surgery, a subgroup of patients shows an improve-ment in endothelial function, as assessed by PAT. This effect is not related with weight loss, or with the improvement of other risk factors/markers (including blood lipids and hsCRP). In this patients with improved endothelial function, there is a significant reduction in heart rate, possibly related with an improvement in sym-pathetic nervous activity – this effect may have prognostic implications and should be further studied.

P3483 Systemic sclerosis is associated with impaired arterial wall properties

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Purpose: Systemic sclerosis (SSc) is characterized by calcification and fibrosis of several organs including vessels and heart. Measurement of endothelial function and arterial stiffness are well validated in large population studies as strong predictors of adverse cardiovascular outcomes. In this study we evaluate endothelial function and arterial stiffness in SSc patients.

Methods: We enrolled 105 (93 female) SSc patients (mean age 57±13 y) and 65 (53 female) healthy subjects (Cl) (mean age 57±12 y). Endothelial function was evaluated by flow mediated dilatation (FMD) in the brachial artery and arterial stiffness was evaluated by Augmentation Index (Alx).

Results: There was no difference between SSc patients and Cl according to age (p=0.96) and sex (p=0.29). SSc patients, compared to Cl subjects, had significantly impaired FMD (33±1 vs. 35±0.5%) and Alx (29±1 vs. 31±0.5%) (p<0.001 in all cases). Interestingly SSc patients, compared to Cl subjects, had significantly lower systolic blood pressure (122±22mmHg vs. 129±16mmHg, p=0.039) and mean blood pressure (93±15mmHg vs. 101±16mmHg, p>0.001) but higher Alx (29.03±10.37% vs. 25.82±2.77%, p=0.042).

Conclusions: Patients with SSc have impaired endothelial function and in-creased arterial stiffness. These findings highlight the arterial wall involvement in this setting of patients.

P3484 Functional disorder of endothelial progenitor cells enhance microalbuminuria predicting in-stent late loss in acute myocardial infarction

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Purpose: Microalbuminuria in patients with acute myocardial infarction (AMI) is well known to be associated with an increased risk of cardiovascular events and worse outcome. However, the underlying pathophysiological mechanism remains still unclear. We investigated the role of microalbuminuria presented in the early phase of AMI focusing in the function of endothelial progenitor cells (EPCs).

Methods: Forty-five consecutive AMI patients, who underwent emergent percu-taneous coronary intervention (PCI), were divided into two groups by urinary al-bumin excretion ratio: normal group (<30mg/day, n=24) and microalbuminuria-group (>30mg/day, n=21). In-stent late loss in PCI lesions of patients who were implanted bare-metal stent was evaluated at the 6-month after PCI. At 2nd and 7th day after admission, circulating EPCs were defined as CD34/Fk+ve-positive cells in peripheral blood mononuclear cells (MNC) by flow cytometry. To evalu-ate adhesion ability of EPC, the number of cultured EPCs, which were positive to hCD34/CD166 and CD34/CD133 were counted in immunofluorescence. The expression levels of mRNA of Sirtuin1 in cultured-EPCs were measured by quantitative reverse transcription-polymerase chain reaction.

Results: During 6-month follow-up period, angiographic in-stent late loss was
Effect of sleep respiratory disorders on endothelial function in children

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Purpose: Obstructive Sleep Apnea Syndrome (OSAS) in children is a critical health problem, with an incidence of 1-3% between 6 months and 6 years old. It is associated with reduced endothelial function, i.e., increased cardiovascular risk. Study aimed to evaluate a link among endothelial function (measured by Flow-Mediated Vasodilation [FMD]), obesity and sleep disorders breathed (SDB), assessed with apnea/hypopnea index (AHI), in pediatric patients.

Methods: 23 children, mean age 9±3 years, suffering from SDB (group 1), and 32 controls (group 2, mean age 10±3 years) were recruited. At enrolment, nobody was in Continuous Positive Air Pressure or pharmacological therapy for SDB. Exclusion criteria: cardiovascular, liver, gastro-intestinal and kidney diseases; severe respiratory insufficiency, nervous/cerebral defects related to SDB. Group 1 children underwent to polysomnography, AHI and FMD (both group 1 and 2) measures, previous parents' consent.

Results: The two groups slightly differed each other according to Body Mass Index percentile (58±26% versus 45±22%; p=0.048). The difference was statistically significant according to FMD values (8.4±2.7% versus 11.1±3.0%; p<0.001). Pearson’s linear correlations between FMD and AHI values showed a negative link (r=0.56, p<0.006), i.e. worsening of AHI induced endothelial dysfunction.

Conclusions: These findings suggest that not only the numbers of circulating EPCs, but the functional disorder of EPCs accompanied by impairment of Sirtuin1 gene expression is closely associated with microalbuminuria after AMI and may lead to advance coronary remodeling.

P3487

Microvascular function in healthy children and adolescents: pubertal status is essential

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Purpose: To determine the role of pubertal status on microvascular function in healthy children and adolescents.

Methods: One hundred twelve children and adolescents aged 10-16 years were investigated in two separate prospective cross-sectional studies. The main outcome measure was microvascular function, assessed by peripheral arterial resistance in childhood and adolescence. Subjects were grouped based on their self-assessed pubertal status according to Tanner stage: I-V: group 1 (pre-puberty, Tanner I), group 2 (mid-puberty, Tanner II/III) and group 3 (late-puberty, Tanner IV/V). Stepwise multiple regression analysis was performed to determine independent predictors of the RI.

Results: Complete data were available for 94 subjects (55 females) with a median age of 14 (3.0) years and a mean BMI of 19.0±3.6 kg m-2. Significant correlations with RI were observed for Tanner stage (R=0.319, P<0.001), age (R=0.512, P<0.001), systolic blood pressure (R=0.438, P<0.001) and BMI (R=0.286, P=0.012), but not for sex and moderate-to-vigorous physical activity. In stepwise regression analysis, pubertal status was the only independent predictor of microvascular function (R²=0.224, p=0.047, P<0.001). Prepubertal children (group 1) had a significantly lower RI (1.18 (0.32)) compared to group 2 (1.65 (0.57)) and group 3 (1.70 (0.75)), all P<0.001.

Conclusions: Pubertal status was the main predictor of microvascular function in healthy children and adolescents. An immature microvascular response was present in the majority of pre-pubertal children and persisting in 15% at late-puberty.

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Endothelial microparticles as a diagnostic tool for the detection of subclinical myocardial ischemia


Background: Endothelial microparticles (EMP) provide information about prognosis and future cardiovascular risk. So far, no study evaluated whether myocardial ischemia induced by stress testing influences the EMP level. Aim of this study was to evaluate the association of the EMP release after dobutamine-stress echocardiography with the prevalence of coronary artery disease (CAD).

Methods and results: In this prospective study, all patients underwent DSE before left heart catheterization. Blood was drawn before, 4h, and 24h after DSE. Plasma CD144-positive EMP levels were measured by flow cytometry. We enrolled 30 patients (age: 66.0±10.2 yrs.; 66% male; SYNTAX score: 9.6±1.0) of whom 12 patients did not suffer from CAD. Baseline levels of NT-proBNP and TnI were 272.0 (104.0/703.0) vs. 64.5 (50.8/104.8) pg/ml (P=0.030) - but not of proBNP 

no differences were between IMT significantly higher in microalbuminuria-group compared with normal-group (albuminuria, 1.14 mm; normal, 0.70 mm; respectively, p<0.05). However, the numbers of circulating EPCs were significantly increased in microalbuminuria-group (5.691 cells/mL) compared with normal-group (2.965 cells/mL; p<0.00) from day2 to day7. On the other hand, increased adhesion ability of EPCs in normal-group (9.1% to 13.3%: lectin-eCLL positive EPCs per MNGs, p<0.05) was not observed in microalbuminuria-group (9.4% to 9.0%). The mRNA level of Sirt-1 in cultured-EPCs was significantly lower in microalbuminuria-group than normal-group (microalbuminuria, 2.42 fold; normal, 7.10 fold; compared with age-matched healthy respectively, p<0.05) at day7.

Results: The two groups slightly differed each other according to Body Mass Index percentile (58±26% versus 45±22%; p=0.048). The difference was statistically significant according to FMD values (8.4±2.7% versus 11.1±3.0%; p<0.001). Pearson’s linear correlations between FMD and AHI values showed a negative link (r=0.56, p<0.006), i.e. worsening of AHI induced endothelial dysfunction.

Conclusions: These findings suggest that not only the numbers of circulating EPCs, but the functional disorder of EPCs accompanied by impairment of Sirtuin1 gene expression is closely associated with microalbuminuria after AMI and may lead to advance coronary remodeling.

P3488

Functional vascular changes induced by insulin resistance in childhood

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Purpose: The prevalence of obesity among children and adolescents is progressively increasing in the world. The development of insulin resistance (IR) is an obesity consequence. IR may impair endothelial function inducing early signs of atherosclerosis. Our aim was to investigate endothelial dysfunction and morphological vascular changes in children with IR.

Methods: 110 children, aged 12±3.2 years (range: 5-17 years) underwent a check-up of the steady-state basal plasma glucose (mmol/L) and insulin concentrations (mUI/mL), calculating HOMA (Homeostasis model assessment). All underwent flow-mediated dilatation (FMD), carotid intima-media thickness (cIMT) and anterior-posterior diameter of the abdominal aorta (APAO).

Results: We found a positive correlation between body mass index (BMI) and IR (p<0.001), a positive correlation between APOA1 and IR (r=0.224, p<0.05) and no relation with cIMT and APAO. The ROC curve analysis revealed a cutoff of BMI (23.0) superior to the TnI level (AUC 0.71, 95% CI: 0.54-0.88) but not inferior to the NT-proBNP level (AUC 0.78, 95% CI: 0.65-0.90) for the detection of CAD.

Conclusions: The level of CD144-positiveEMP was significantly higher after dobutamine stress echocardiography in patients suffering from CAD, but not superior to NT-proBNP and TnI for the detection of CAD (study ID: DRK500000737).
and IR (IR mean IMT: 0.51±0.06 mm versus NO-IR mean IMT: 0.52±0.06 mm p=0.38) whilst FMD values were lower in IR patients (no-IR FMD: 9.13±3.15 versus IR-FMD: 7.52±2.44%, p=0.0032).

Figure 1

Conclusions: Children with IR had an initial endothelial dysfunction and vascular damage, i.e., the first stage in the development of atherosclerosis, that increase with higher values of BMI.

P3489 Small-size circulating microparticles levels in acute coronary syndrome patients: on the trail of novel prognostic markers
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Background: Circulating microparticles (MPs) are increased in cardiovascular disease and have received interest for their roles as biomarkers in many pathological situations. However, larger studies are needed to further investigate their real power as prognostic markers. Besides, novel instruments now allow a better discrimination/quantification of small-size MPs. Thus, we evaluated whether these small-size MPs from different origin are independent markers for different cardiovascular outcomes in patients with acute coronary syndrome (ACS).

Methods: We recruited 154 ACS patients (aged 68±12 years, 65% males); sodium citrate platelet poor plasma was collected in the first 48h at admission. Platelet-poor plasma (PPP) was incubated with platelet activating factor (PAF) (0.5 μM), ultrafiltrated and the platelet-depleted plasma was centrifuged for 10 minutes at 1000xg to obtain platelet-free plasma (PFP). MPs were counted by flow cytometry (Beckman Coulter, MACSQuant 10). The median follow-up was 2 years. Outcomes included cardiovascular death, non fatal myocardial infarction (MI), stroke, bleeding and congestive heart failure (HF), and all cause death. Small-size MPs levels from different origin were ranged per quartiles.

Results: By linear regression analysis, higher baseline platelet-poor plasma microparticles (eMPs and mMPs) levels were strongly associated with HF previous admission (all p<0.05) and lower left ventricular ejection fraction (all p<0.02). Interestingly, higher doses of statins were also related to increased eMPs release (p=0.036). No significant associations were found between GRACE or TIMI stratification and MPs levels at admission. Patients with previous MI (n=37) were associated with higher baseline platelet-poor plasma (p=0.039), eMPs (p=0.052) and mMPs (p=0.005) levels. Cox regression analysis identified baseline levels of circulating eMPs and mMPs as independent predictors for HF during the follow-up (n=14, p=0.007 and 0.008, respectively), as well as PMPs for bleeding complications (n=16, p=0.042).

Conclusions: Small-size MPs as prognostic markers in CAD patients beyond currently used risk stratification scales.

P3491 Early appearance of arterial stiffness in patients with normotensive autosomal polycystic kidney disease and its relationship increased levels of inflammatory bio-markers
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Aim: Cardiovascular disease (CVD) is the main cause of morbidity and mortality in autosomal-dominant polycystic kidney disease (ADPKD) patients. To clarify temporal relationship between ADPKD, hypertension and the loss of renal function, we examined these factors in patients with early stage autosomal-dominant polycystic kidney disease who did not yet have hypertension.

Methods: Fifty patients with ADPKD (42% males 36.6±9.9 years, no blood pressure medication) and 50 healthy controls (44% males 35.4±6.4 years) were studied cross-sectionally. Pulse wave velocity (PWV), cardiac morphology and function, aortic elastic indexes, estimated glomerular filtration rate (eGFR), 24-hours ambulatory blood pressure, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and highly sensitive C-reactive protein (hs-CRP) were measured in all participants, using conventional methods.

Results: Despite a normal blood pressure, aortic stiffness index and pulse wave velocity values were increased in patients compared to controls (6.8±4.7 vs. 5.1±3.3, p=0.043 and 9.6±1.3 vs. 5.8±1.1 m/s, p<0.001) (Figure 1). In univariate analysis, IL-6, TNF-α, hs-CRP and eGFR were all significantly correlated with PWV. The independence of these correlations were analyzed in a regression model, and showed PWV to be significantly predicted by IL-6, TNF-α and hs-CRP.

Figure 1

Conclusions: Increased arterial stiffness and pulse wave velocity are early manifestations of ADPKD appearing before hypertension or reduced eGFR. However, these vascular abnormalities are related to signs of systemic low grade inflammation, suggesting a common pathophysiological mechanism apparently present also in other vascular diseases but yet to be elucidated.
**Gender specific associations of phenotypes of left ventricular hypertrophy with endothelial dysfunction: results from a population-based setting**

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**Purpose:** Left ventricular hypertrophy (LVH) and endothelial dysfunction are risk factors for cardiovascular mortality and morbidity. Several studies revealed an inverse correlation between endothelial function (EF) and LVH. We aimed to investigate this association gender-specifically and in subtypes of LVH in a population-based sample, which has not yet been evaluated.

**Methods:** Measurements of flow-mediated dilation (FMD) by ultrasound and 2D echocardiography were performed in 5,000 participants of the population-based, age- and gender-stratified Gutenberg Health Study. All measurements were carried out according to SOPs with detailed quality control.

**Results:** The sample comprised 2,540 men (M) and 2,460 women (W) aged 35 to 74 years. Normal LV geometry (NG) was observed in 80.4% of the individuals. Left ventricular hypertrophy (LVH) was more frequent in M than in W (7.9 ± 7.0%). Concentric hypertrophy (ConH) and eccentric hypertrophy (EccH) were more frequent in W (M: 2.3 ± 7.2% vs. 2.9 ± 9.2%) and in M (W: 3.2 ± 7.3% vs. 4.8 ± 10.7%). Concerning LV mass (MM) ConH was more frequent in M than in W (M: 2.0 ± 8.5% vs. 1.6 ± 4.0%) and in W (M: 2.9 ± 8.7% vs. 6.1 ± 10.9%). ConH occurred more frequently in M than in W (M: 1.3% vs. 0.9%); EccH occurred more frequently in W (M: 2.2% vs. 1.5%). There was a significant correlation between LV mass and FMD (M: r = -0.04; W: r = -0.03). LV mass was significantly higher in the ConH group (M: 14.2 ± 8.3% vs. 12.0 ± 5.0%; W: 14.3 ± 8.0% vs. 13.3 ± 8.9%). However, LV mass was not associated with FMD (M: 4.0 ± 5.1 mm vs. 4.1 ± 5.9 mm; W: 4.3 ± 5.4 mm vs. 5.0 ± 6.3 mm).

**Conclusions:** This study identifies for the first time NF-kB and FHC as main mediators of the protective effect of metformin against doxorubicin-induced cardiotoxicity.
Combination therapy with amlodipine and Oxidized phospholipids, Lp(a) and coronary heart disease risk

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Purpose: Circulating levels of oxidized phospholipids (OxPL) on apolipoprotein B (apoB) accumulate in plasma under conditions of oxidative stress and have been previously linked with lipoprotein(a) (Lp[a]) levels and coronary heart disease.

P3498

Alternatively spliced tissue factor induces the cell migration and the pro-angiogenic properties of murine cardiomyocytes

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Introduction: Tissue factor (TF), the primary initiator of the blood coagulation cascade is expressed in a tissue specific manner. TF derived from vessel walls may contribute to angiogenesis and is highly expressed in tumor tissue. Inflammatory mediators may modulate TF expression. We investigated whether the alternatively spliced tissue factor (asTF) is induced during angiogenesis since its full-length (flTF) is also involved in tumor angiogenesis and inflammation.

Methods: We studied the TF expression in mice treated with intraperitoneal injections of 3-iso-propanol (vehicle), 5 iso-propanol (vehicle, asTF), 3-iso-propanol (3-iso-propanol, flTF), 5 iso-propanol (5 iso-propanol, asTF), and 5 iso-propanol (5 iso-propanol, flTF). TF expression was quantified by RT-PCR and Western blotting.

Results: The expression of asTF was induced in the bone marrow and in the heart tissue. The induction of asTF expression was associated with an increased expression of VEGF and FGF2 in the heart tissue. The induction of asTF expression was also associated with an increased migration of endothelial cells.

Conclusions: These results suggest that asTF expression is involved in the pro-angiogenic properties of murine cardiomyocytes.

P3497

Exercise training restores cardiac contractile function: role of CaMKII

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Exercise training has been shown to at least partly correct the contractile dysfunction in post-myocardial infarction heart failure, mainly by correcting abnormalities in excitation-contraction coupling (ECC) and calcium handling. However, the exact mechanism is unknown; in particular, the role of the calcium-calmodulin-dependent protein kinase II (CaMKII) that targets several properties of ECC and calcium handling such as the magnitude and shape of the calcium transient that controls contraction. Importantly, CaMKII function is negatively affected by heart failure. Here, we studied the role of CaMKII on exercise training-induced correction of ECC abnormalities in heart failure. Post-myocardial infarction heart failure was induced by chronic coronary artery ligation; exercise training by daily aerobic treadmill running, and the role of CaMKII on ECC parameters was studied by light and fluorescence microscopy of isolated twitch-stimulated cardiomyocytes in the absence or presence of the specific CaMKII-inhibitor AIP (10uM). (1) Myocardial infarction associated with reduced exercise capacity, myocardial and cardiomyocyte hypertrophy, and reduced contractile capacity and ECC. (2) 2 months of exercise training partly, but not fully corrected for these abnormalities; in particular, cardiomyocyte relaxation and calcium transient decay rates improved -10% (p < 0.05) toward normal levels. (3) In the presence of CaMKII-inhibition (AIP), cardiomyocyte relaxation and calcium transient decay was less corrected by exercise training (only 50% correction was observed compared to correction in the absence of AIP; p < 0.05), whereas contraction and calcium transient rise were not affected by AIP. This suggests that exercise training exerts a beneficial effect that partly, but not fully relies on activation of CaMKII specific to modulation of the sarcoplasmic reticulum calcium ATPase, whereas CaMKII activity in the transverse tubular-sarcoplasmic reticulum dyad remained unaffected by exercise training. (4) In 40% of heart failure cardiomyocytes, CaMKII-inhibition at high twitch-stimulation frequencies (>4Hz) induced calcium transient amplitude alternans (p < 0.05 vs vehicle). After exercise training, CaMKII-inhibition induced alternans in 15% of cardiomyocytes and increased the twitch-stimulation frequency at which alternans were observed by 1-2Hz (p < 0.05). In conclusion, the beneficial effect of exercise training in post-myocardial infarction heart failure on ECC parameters is partly activated by site-specific modulation of CaMKII, especially through CaMKII located to the cytoplasm.

P3496

Combination therapy with amlodipine and atorvastatin but not each monotherapy prevents abdominal aortic aneurysm formation in apoE-deficient mice

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Background: There is no established strategy for the prevention of abdominal aortic aneurysm (AAA). Recent studies have revealed that both a calcium channel blocker (CCB) and a statin have beneficial effects on cardiovascular disease. However, it remains unknown whether combination therapy with a CCB and a statin prevents AAA formation as compared to each monotherapy. Thus, we examined whether combination therapy with a CCB and a statin inhibits AAA formation in apoE-deficient mice in vivo and if so, to elucidate the mechanisms involved.

Methods and Results: Six-month-old apolipoprotein E-deficient (ApoE/-) mice were infused with angiotensin II (Ang II) (2500 ng/kg/min) for 1 month (n=64). They were randomly divided into 5 groups: Group 1 with saline infusion alone (sham); Group 2, Ang II infusion alone (Ang II); group 3, Ang II-infusion plus amlodipine (1 mg/kg/day) (Aml); group 4, Ang II infusion plus atorvastatin (10 mg/kg/day) (ATO); and group 5, Ang II infusion plus combination therapy with amlodipine (1 mg/kg/day) and atorvastatin (10 mg/kg/day) (Combi). There was no significant difference in blood pressure among the 4 angi-infusion groups. The combination therapy significantly inhibited Ang II-induced increase in maximal aortic diameter and the ratio (%) of advanced AAA morphology (type III and IV), whereas monotherapy did not [sham: 1.03±0.05 (0%), Ang II: 2.01±0.82 (33%), Aml: 1.71±0.78 (33%), ATO: 2.11±0.98 (33%), Combi: 1.10±0.10 mm (0%); P < 0.05]. Ang II vs. Aml, Ang II vs. ATO, and Ang II vs. Combi]. Combination therapy profoundly reduced inflammation in aortic media, especially macrophage infiltration at the AAA lesion (sham: 3.0±0.0, Ang II: 25.9±1.8, Aml: 13.1±0.4, ATO: 13.2±0.4, Combi: 1.2±0.2); P < 0.05. Ang II vs. Aml, Ang II vs. ATO, and Ang II vs. Combi]. Immunoreactivities for Rho-kinase expression and activity were markedly increased in the AAA lesion as compared to sham, which was markedly inhibited by the combination therapy but not by monotherapy.

Conclusions: This study demonstrates for the first time that combination therapy with amlodipine and atorvastatin but not each monotherapy prevents AAA formation in mice, for which inhibition of inflammation, endothelial degradation, apoptosis and Rho-kinase activation may be involved.

602 Basic work to prevent cardiovascular disease
Aspirin influences MRP4 protein up-regulation in Percutaneous renal sympathetic denervation using

Methods: We examined the shape and strength of associations of CHD with films of plasma levels of OxPL on apoB, before and after adjustment for traditional risk factors and Lp(a).

Results: Plasma levels of OxPL were highly correlated with Lp(a) levels, both in cases (Spearman correlation r=0.74) and in controls (r=0.63). Table 1 shows that OxPL levels in the top versus bottom fifth had a 2-fold higher risk of CHD after adjustment for traditional risk factors (OR 1.99; 95%CI: 1.60-2.48) that was substantially attenuated after additional adjustment for fifths of Lp(a) (1.00; 0.66-1.51). Western Blot and immunofluorescence analysis showed an MRP4 over-expression (1.6 fold increase).

Conclusions: Our results demonstrate, for the first time, that in vitro and in vivo aspirin treatment induces protein up-regulation in human platelets and may have important pharmacologic effect to make more efficient aspirin treatment in high risk cardiovascular patients.

Abstract P3499 – Table 1. Odds ratios (95% CI) of CHD for fifths of oxidized phospholipids (OxPL), before and after adjustment for traditional risk factors and Lp(a)

<table>
<thead>
<tr>
<th>Q1 (25.9)</th>
<th>Q2 (41.5)</th>
<th>Q3 (53.0)</th>
<th>Q4 (68.9)</th>
<th>Q5 (14.9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, sex, country</td>
<td>1.00 (0.79-1.27)</td>
<td>1.25 (0.99-1.54)</td>
<td>1.54 (1.25-1.89)</td>
<td>1.85 (1.51-2.26)</td>
</tr>
<tr>
<td>+ traditional risk factors</td>
<td>1.00 (0.73-1.36)</td>
<td>0.75 (0.54-0.98)</td>
<td>0.67 (0.52-0.87)</td>
<td>0.69 (0.59-1.14)</td>
</tr>
<tr>
<td>+ fifths of Lp(a)</td>
<td>1.00 (0.72-1.39)</td>
<td>0.69 (0.50-0.92)</td>
<td>0.59 (0.45-0.76)</td>
<td>0.65 (0.51-0.85)</td>
</tr>
</tbody>
</table>

Geometric mean levels of OxPL are shown for fifths of OxPL.

P3501

Percutaneous renal sympathetic denervation using a novel radiofrequency ablation catheter acutely decreases renal resistive index in a swine model

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Purpose: Sympathetic overdrive is accompanied by impaired renal blood flow, whereas the effect of acute renal denervation on autoregulation of renal hemodynamics is yet to be elucidated. In the present study we investigated whether renal sympathetic denervation, performed using a novel radiofrequency ablation catheter, has an acute effect on renal hemodynamics assessed by average peak of arterial pressure velocity (APV) under baseline and hyperemic condition that was induced by the bolus intrarenal administration of dopamine (50μg/kg).

Method: We studied renal haemodynamics in 9 anaesthetized female juvenile farm swines (mean age 6 months, mean weight 34.5 kg). The renal angiogram performed through femoral artery found no renal artery stenosis in all subjects. 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 intrarenal administration of dopamine (50μg/kg). RFRR was calculated as the ratio of hyperemic to baseline peak velocity. RI was estimated as (peak systolic velocity – end-diastolic velocity)/peak systolic velocity.

AVP, RFRR and RI were measured before and 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 according to pre-specified algorithm.

Results: In all animals, AVP post ablation compared to APV before ablation was 300% higher (65.16±39.78 vs 21.79±8.53 cm/sec, p<0.0001). Radiofrequency ablation resulted in reduced RFRR (1.51±0.59 vs 2.96±1.33, p<0.0001) and RI (0.66±0.07 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).

Conclusions: Catheter-based renal sympathetic denervation acutely augmented AVP 3-fold, and significantly decreased RFRR and RI in healthy swines. These results underscore the potent and acute effect of renal artery denervation by the radiofrequency ablation catheters on renal hemodynamic balance even in a healthy animal setting.
Conclusion: The results of this study clearly demonstrate that also in patients with CHF HDL function is impaired when compared with healthy controls. In addition, an ET program for 12 weeks partially restores HDL function. This may be one way how exercise training has a beneficial effect on endothelial function in CHF patients.

Methods: Three aortic arch morphologies of patients diagnosed with hypoplastic left heart syndrome and different degrees of coarctation were reconstructed from magnetic resonance data and rapid prototyped with rigid transparent resin. A compact mock circulatory loop was constructed, attaching the 3D models to a lumped parameter network (LPN). Two shunt scenarios were simulated in-vivo: a) mBT shunt equivalent conduit attached to the innominate on the 3D model, b) Sano shunt attached directly to the de-airing valve of the ventricle-equivalent apparatus. Simulations of the ventricular anastomosis, and connected directly to the LPN pulmonary branch. Pressure and flow data were acquired in-vivo under physiological pulsatile flows. Further knowledge of the local fluid dynamics was acquired experimentally by particle image velocimetry (PIV). Finally, one case (moderate coarctation, mBT shunt) was selected and studied in-silico using a multiscale approach: the same 3D geometry and LPN of the experimental setup were implemented, performing several pulsatile simulations.

Results: Feasibility of the experimental models was demonstrated by the physiological nature of measured pressure and flow signals. Increasing degree of coarctation corresponded to larger pressure drops across the stenosis, as expected, and pressure recovery was measured. Shunt flow was regulated by shunt size, which is also a physiological feature. The experimental setup was compatible with PIV visualisation, providing velocity maps and insight into flow distribution. Comparison between in-vivo and in-silico models showed good agreement in terms of flow time traces and mean values, with a maximum difference of 2% at mBT shunt outlet. The in-silico model captured pressure oscillations in the arch and lack of pulsatility in the descending aorta, in agreement with in-vivo results.

Conclusion: Univentricular circulation post Norwood procedure was modelled with a combined experimental and computational approach. In-vitro tests were repeatable and compatible with PIV visualisation. Comparison of computational and experimental data showed that the computer model was validated and different scenarios can thus be implemented in the future, ultimately aiming to provide reliable and fast simulations for clinical decision support.

Feasibility of the new Free Oxygen Radicals Testing (FORT) assay in the assessment of circulating markers of oxidative stress in patients with acute myocardial infarction

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Purpose: To combine experimental and computational techniques in patient-specific arch morphologies and gain further understanding of univentricular circulation following Norwood palliation, which is highly affected by type of shunt (modified Blalock-Taussig, mBT, or Sano) and presence of aortic coarctation.

P3504 Validation of the Free Oxygen Radicals Testing (FORT) assay in the assessment of circulating markers of oxidative stress in patients with acute myocardial infarction

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Purpose: To combine experimental and computational techniques in patient-specific arch morphologies and gain further understanding of univentricular circulation following Norwood palliation, which is highly affected by type of shunt (modified Blalock-Taussig, mBT, or Sano) and presence of aortic coarctation.

Methods: Three aortic arch morphologies of patients diagnosed with hypoplastic left heart syndrome and different degrees of coarctation were reconstructed from magnetic resonance data and rapid prototyped with rigid transparent resin. A compact mock circulatory loop was constructed, attaching the 3D models to a lumped parameter network (LPN). Two shunt scenarios were simulated in-vivo: a) mBT shunt equivalent conduit attached to the innominate on the 3D model, b) Sano shunt attached directly to the de-airing valve of the ventricle-equivalent apparatus. Simulations of the ventricular anastomosis, and connected directly to the LPN pulmonary branch. Pressure and flow data were acquired in-vivo under physiological pulsatile flows. Further knowledge of the local fluid dynamics was acquired experimentally by particle image velocimetry (PIV). Finally, one case (moderate coarctation, mBT shunt) was selected and studied in-silico using a multiscale approach: the same 3D geometry and LPN of the experimental setup were implemented, performing several pulsatile simulations.

Results: Feasibility of the experimental models was demonstrated by the physiological nature of measured pressure and flow signals. Increasing degree of coarctation corresponded to larger pressure drops across the stenosis, as expected, and pressure recovery was measured. Shunt flow was regulated by shunt size, which is also a physiological feature. The experimental setup was compatible with PIV visualisation, providing velocity maps and insight into flow distribution. Comparison between in-vivo and in-silico models showed good agreement in terms of flow time traces and mean values, with a maximum difference of 2% at mBT shunt outlet. The in-silico model captured pressure oscillations in the arch and lack of pulsatility in the descending aorta, in agreement with in-vivo results.

Conclusion: Univentricular circulation post Norwood procedure was modelled with a combined experimental and computational approach. In-vitro tests were repeatable and compatible with PIV visualisation. Comparison of computational and experimental data showed that the computer model was validated and different scenarios can thus be implemented in the future, ultimately aiming to provide reliable and fast simulations for clinical decision support.

P3505 Cardiorespiratory fitness is independently associated with N-terminal pro-brain natriuretic peptide in non-alcoholic fatty liver disease (NAFLD) and is also related to severity of NAFLD

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Purpose: Non-alcoholic fatty liver disease (NAFLD) is a common chronic condition associated with obesity, type 2 diabetes and insulin resistance. NAFLD affects up to a third of the population and increasing evidence suggests it may be a novel independent cardiovascular (CV) risk factor. CV mortality represents the main mode of death in NAFLD patients and is linked to severity of liver disease. However, the mechanisms responsible for the increased CV risk in NAFLD are not fully understood. N-terminal pro-brain natriuretic peptide (NT-pro-BNP) is an easily measured and sensitive marker of subclinical left ventricular (LV) dysfunction and both NT-pro-BNP and cardiorespiratory fitness (maximal oxygen uptake or VO2max) are important determinants of CV outcome. In a cohort of asymptomatic patients with NAFLD, we aimed to assess whether VO2max was independently associated with NT-pro-BNP in the presence of normal LV systolic function, and if VO2max was associated with severity of NAFLD.

Results: In 104 patients with NAFLD enrolled into the WELCOME study, we found that VO2max was significantly higher in men compared to women (4.7 ± 0.9 vs 3.9 ± 0.8 mL/kg/min, p = 0.005) and was inversely related to severity of NAFLD (r = -0.45, p = 0.001). NT-pro-BNP levels were higher in patients with NAFLD compared to controls (46.7 ± 22.2 vs 20.3 ± 12.1 pg/mL, p = 0.001). However, when adjusted for age, sex, BMI, waist circumference, insulin resistance and body fat, VO2max was independently associated with NT-pro-BNP (β = -0.17, p = 0.03). Additionally, NT-pro-BNP was higher in patients with NAFLD and impaired cardiorespiratory fitness (VO2max ≤ 50% predicted) compared to those with normal cardiorespiratory fitness (VO2max > 50% predicted) (48.8 ± 22.2 vs 25.0 ± 12.1 pg/mL, p = 0.001). This association remained significant after adjusting for age, sex, BMI, waist circumference, insulin resistance, smoking status and alcohol intake (β = -0.22, p = 0.04).

Conclusion: The relationship between cardiorespiratory fitness and NT-pro-BNP is independent of age, sex and routine clinical risk factors. However, VO2max was lower in patients with NAFLD and NT-pro-BNP was higher in patients with reduced VO2max. This association remained significant after adjusting for age, sex, BMI, waist circumference, insulin resistance and body fat. These findings suggest that cardiorespiratory fitness may be an important target for intervention in patients with NAFLD.
if they attained only submaximal exercise (respiratory exchange ratio <1.0) (n=8); had an LV ejection fraction <55% or significant valvular disease (n=1); or known respiratory disease (n=0). A subgroup of patients (n=43) also had NAFLD severity assessed by liver biopsy using the Kleiner histopathologic scoring system. Results: Subjects were 51.3 ± 10.6 years (mean ± SD) (57.3% men) with body mass index (BMI) of 33.4 ± 5.7 (mean ± SD). VO2max was 27.6 ± 6.7 (mean ± SD), and NT-proBNP was 155pg/ml (96, 357) [median (IQR)]. The HOMA-IR was 2.8 (1.9, 5.0) [median (IQR)] and 62 subjects were insulin-resistant (HOMA-IR > 2). Multivariable linear regression analyses showed that VO2max was independently associated with NT-proBNP (standardised β-coefficient -0.235, p = 0.006) after adjustment for age, sex, BMI, HOMA-IR and traditional cardiac risk factors including diabetes. VO2max, but not NT-proBNP, was also independently associated with Kleiner score (β-coefficient -0.275, p=0.028) when adjusted in the same multivariable regression model. Conclusions: In asymptomatic overweight/obese patients with NAFLD and normal LV systolic function, cardiorespiratory fitness has an independent inverse association with NT-proBNP, and is also independently related to NAFLD severity. These findings may help to explain the increased CV risk associated with NAFLD.

P3507

Epicardial fat rather than abdominal visceral fat is associated with arterial stiffness

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Purpose: Visceral adiposity is associated with an increased risk for cardiovascular (CV) disease. Recently, visceral adiposity has been evaluated by echocardiographic epicardial fat thickness (EFT) as well as abdominal visceral fat area, but the relationship between fat distribution and CV risk is not well understood. Arterial pulse wave velocity (PWV), a direct marker of arterial stiffness, is an independent CV risk factor. The aim of this study was to determine whether the site of fat deposition is related to arterial stiffness.

Methods: One hundred and twenty-five patients (age, 52±6 yrs; body mass index, 24.6±4.9 kg/m²) underwent echocardiography, multidetector computed tomography for abdominal visceral fat area and coronary calcium score, measurement of arterial PWV, and measurement of triglyceride, high- and low-density lipoproteins, and fasting glucose. Echocardiographic EFT was measured on the free wall of the right ventricle from a parasternal long-axis view at end-systole.

Results: PWV showed significant correlations with EFT (r = 0.31, p < 0.01). Low-density lipoprotein (r = 0.28, p < 0.01), triglyceride (r = 0.24, p = 0.02), and coronary calcium score (r = 0.35, p < 0.01). However, PWV was not significantly correlated with abdominal visceral fat area (p > ns) (Figure). Multivariate linear regression analysis showed that EFT and coronary calcium score were the strongest independent variables correlated with PWV (p = 0.04 and p < 0.01, respectively).

Figure 1. Relationship between arterial PWV and echocardiographic epicardial fat thickness (A) or abdominal fat area (B).

Conclusion: Echocardiographic EFT is strongly associated with arterial stiffness, though abdominal visceral fat area is not. CV risk may vary according to the fat distribution.

P3508

Influence of functional, morphological and clinical parameters on epicardial adipose tissue in patients with coronary artery disease

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Purpose: Epicardial adipose tissue (EAT) has been shown to be associated with the presence and extent of coronary artery disease (CAD). However, there are limited data available on the relation of EAT to functional, morphological and clinical parameters in patients with CAD. Therefore, we investigated the impact of these parameters to identify potential determinants of EAT in different stages of coronary artery disease.

Methods and Results: 200 consecutive patients with CAD and 40 healthy subjects underwent cardiac magnetic resonance imaging (CMR). Clinical and CMR parameters were determined and correlated to the amount of EAT. Patients with CAD and preserved left ventricular function (LVF) >50% revealed significantly elevated EAT (36.1±11 g/m²) compared to healthy controls (31.8±9 g/m²) and to patients with reduced LVF <50% (8.8±6 g/m²). In the whole study population, only LVF (p = 0.003), BMI (p = 0.004) and LV-EDD (p = 0.004) remained significantly associated with EAT after multivariate analysis. Subgroup analysis in patients with CAD and LVF >50% revealed that only BMI (p = 0.03) was significantly related to increased EAT. The increase in EAT was related to a history of diabetes (p = 0.04) correlated to EAT and were also independently associated in multivariate analyses (p = 0.02, p = 0.01, respectively). However, in patients with CAD and LVF <50%, EAT was significantly correlated to indexed LV enddiastolic mass (LV EDDM) (p = 0.0001), LV enddiastolic volume index (LV EDVI) (p = 0.03) and the extent of LGE (p = 0.01). In the multivariate analysis only LV-EDDI (p = 0.003) and the extent of LGE (p = 0.03) remained significantly correlated with EAT.

Conclusion: The amount and the determinants of EAT differ according to the LVF in patients with CAD. CAD patients with preserved LVF showed the highest amount of EAT, which only correlated with the BMI and the extent of CAD. Whereas patients with reduced LVF revealed the lowest EAT mass, which was associated with the LV-EDDM and the extent of LGE % . Thus, different amounts of EAT reflect different stages of CAD underlying the complex interaction of EAT in the pathogenesis of ischemic cardiomyopathy.
overweight/obese girls compared with 8.8% of overweight-normalfat girls had ≥3 risk factors.

**Conclusions:** The CVD risk profile of overweight youths without increased body fat is considerably less adverse than that of overweight youths with increased body fat. Defining overweight only by BMI-for-age may result in misclassifications of increased CVD risk in 46.6% of overweight-normalfat girls and in 33.4% of normalfat overweight boys. Since growth card-based determination of BMI from caliper skinfold measurements is easy and cheap we propose this additional measure to avoid stigmatization and unnecessary intervention in youths.

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**P3512 Association of adipokine with cardiovascular mortality in patients on hemodialysis**

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**Purpose:** Adipokines are circulating adipocyte-derived plasma proteins that are associated with obesity-linked disorders such as cardiovascular disease. However, phenomena called "obesity paradox" or "reversal epidemiology" which indicate survival advantage of obesity are seen in patients on hemodialysis (HD). In addition, the role of adipokine for cardiovascular disease remains controversial in such population. We prospectively investigated the association of adipokine with cardiovascular mortality in patients on HD.

**Methods:** Body fat was assessed by bioimpedance analysis using a validated device. BMI was calculated using body weight in kg divided by height in meters squared. NT-proBNP levels were measured using a validated method. The serum adiponectin level was below 10 \( \mu \)g/mL in 90 patients (95.7%) and below 6 \( \mu \)g/mL in 80 patients (85.1%). There was a significant association between the serum adiponectin level and log NT-proBNP in 51 patients (p=0.02). Adiponectin levels were positively correlated with GNRI levels (p<0.0001) after adjustment for age and diabetes. These paradoxical associations were hypothesized to be affected from prevalence of malnutrition. Adiponectin is a adipokine with potent insulin-sensitizing, anti-inflammatory, and anti-atherogenic effects demonstrated in animals. The exact relationship between serum adiponectin level and coronary artery disease in patients on HD remains unclear. We determined the adiponectin profile in a cohort of multietnic Asian patients with coronary artery disease and the association between serum adiponectin level and other risk factors and cardiovascular mortality in patients on hemodialysis.

**Results:** Adiponectin was negatively correlated with GNRI levels (r=0.36, p<0.0001), and leptin levels were also negatively correlated with GNRI levels (r=0.20, p<0.0001). Also, adiponectin levels were independent predictors of NT-proBNP levels after adjustment for age, sex, smoking status, lipid profile, fasting glucose, hypertension, body fat and water. Body fat was not significantly associated with NT-proBNP (p=0.02. 95% CI -0.04, 0.004, p=0.113).

**Conclusion:** In this large population based study of young and healthy individuals, the inverse relationship between BMI and NT-proBNP levels was predominantly explained by muscle mass, not fat. The biological underpinnings of these relationships need to be determined in future analyses.

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**P3513 Body mass index, muscle mass and NT-proBNP levels in healthy adults**

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**Purpose:** Recent attempts were made to adjust B-type natriuretic peptide (BNP) levels in patients with dyspnea, to further increase its diagnostic accuracy. In this context, a higher body mass index (BMI) has been associated with lower BNP levels. While obesity has been implicated in this inverse relationship, the exact mechanism remains largely unknown. We therefore investigated which body components are directly related to N-terminal (NT) BNP levels in a large group of healthy individuals.

**Method:** The Genetic and Phenotypic Determinants of Blood Pressure and Other Cardiovascular Risk Factors (GAP-CH) study aimed to examine the genetic and phenotypic determinants of blood pressure and other cardiovascular risk factors in healthy adults aged 25-40 years in the Principality of Liechtenstein. Individuals with diabetes, BMI > 35 kg/m² and prevalent cardiovascular disease were excluded. BMI was calculated using body weight in kg divided by height in meters squared. NT-proBNP was assessed using the Elecsys electrochemiluminescence immunoassay (Roche). Body composition was determined by bioelectrical impedance analysis using a validated device.

**Results:** Of 857 individuals included in this study, 52 were female. The median age was 39 years, median BMI was 24.4 kg/m², 14% had hypertension and 22% were current smokers. Median (interquartile range) were 34 (17-58) kg/m². Bioimpedance analysis showed that the median (interquartile range) percentage of body fat, water and muscle mass was 25.1 (20.2-29.5) %, 54.5 (51-58.2) % and 35.0 (32.6-37.9) %, respectively. Using correlation analyses, we found a significant negative relationship of BMI (-0.38, p<0.001), muscle mass (-0.34, p<0.0001), and body water (r=0.20, p<0.0001) with NT-proBNP levels. Body fat was positively related to NT-proBNP (r=0.29, p<0.0001). In multivariable linear regression analysis using log-transformed NT-proBNP as the outcome variable, muscle mass (p<0.04, 95% confidence interval -0.06, -0.02), p=0.0011) and body water (p=0.03, 95% CI 0.07, 0.05, p=0.0086) were independent predictors of NT-proBNP levels after adjustment for age, sex, smoking status, lipid profile, fasting glucose, hypertension, body fat and water.

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**P3514 Adiponectin profile and coronary plaque vulnerability: an virtual histology intravascular ultrasound study**


**Background:** Adiponectin is an adipokine with potent insulin-sensitizing, anti-inflammatory, and anti-atherogenic effects demonstrated in animals. Yet, the relationship between serum adiponectin level and coronary artery disease in patients remains unclear. We determined the adiponectin profile in a cohort of multiethnic Asian patients with coronary artery disease and the association between serum adiponectin level and culprit lesion necrotic core content.

**Methods:** Ninety-four Asian patients (body mass index, 23.3±3.7 kg/m²) undergoing percutaneous coronary intervention were recruited. Baseline IVUS examination was performed. All target segments, the segment that incorporated the culprit lesion within ±5 mm proximal to the most normal-looking section (atheroma plaque burden < 20% by IVUS) was precisely identified and IVUS volumetric analysis was performed. Serum adiponectin concentrations were measured using Human Adiponectin ELISA Assay.

**Results:** The serum adiponectin level was measured (n=94), and the baseline virtual histology intravascular ultrasound examination was analyzed (n=88). The median level of adiponectin was 3.7 μg/mL (interquartile range, 2.8 to 4.5 μg/mL). The serum adiponectin level was highest among the Chinese, followed by the Malay and the Indians. Serum adiponectin levels were positively associated with culprit lesion necrotic core content. A per one μg/mL increase in log adiponectin was associated with a 3.04% (95% CI 0.33-5.44) increase in culprit lesion necrotic core content. This association remains significant after adjusting for age, sex, ethnicity, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and procedural indication. When using the mean adiponectin level as a cut off, the NC content for adiponectin level ≥ 5 μg/mL (20.7±7.7%) was significantly lower than for adiponectin level < 5 μg/mL (25.0±7.3%, p<0.0001).

**Conclusion:** We found a low serum level of adiponectin in Asian patients and a significant ethnic effect on serum adiponectin level. Increased serum adiponectin levels were independently associated with increased culprit lesion necrotic core burden, suggesting a role for adiponectin in modulating coronary plaque vulnerability.

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**P3515 Left ventricular deformation properties in lean and obese children**

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**Purpose:** Obesity cardiomyopathy is associated with structural changes of the heart and left ventricular myocardial deformation in particular. There is evidence from Tissue Doppler studies that these obesity associated changes appear already in childhood. Given the disadvantages of Tissue Doppler Imaging, in particular angle dependency and noisy signalling, we aimed to evaluate systolic myocardial deformation properties in obese and lean children and adolescents using 2D Speckle Tracking.

**Methods:** Fifty eight obese (O) (Age 14±3, BMI 31±5) and 42 lean control children (L) (Age 14±3, BMI 19±3) were examined with a standardized transthoracic echocardiography. 2-D Speckle Tracking was performed in all apical and parasternal short axis views to calculate longitudinal, circumferential and radial strain. **Results:** In comparison to L, O show significant differences with regard to left ventricular (LV) mass index (29.8±6 vs. 40.0±4.5 g/m², p<0.001), LV end-diastolic volume (22.2±4.7 vs. 27.8±5.2 mL/m², p<0.001) and left atrial volume index (9.2±2.6 vs. 12.5±2.4 mL/m², p<0.001). Both L and O have a normal LV ejection fraction (63±4.7 vs. 62±5.5%). Despite identical LV EF, parameters of longitudinal deformation and, at least in part, of circumferential deformation are reduced in obese children compared to lean controls (longitudinal strain: -21.2±4 vs. -17.9±2.1%, p<0.001; radial strain: -3.1±4.2% vs. -2.9±0.3%, p=0.01; circumferential strain: -20.1±2.2 vs. -16.6±3.5%, p<0.001; circumferential strain rate: -1.61±0.14 vs. 1.60±0.26 s⁻¹, n.s.). Radial strain is not affected by childhood obesity (45.6±10 vs. 39.2±12.4%, n.s.).
Conclusion: In children and adolescents, obesity is not only a risk factor for later cardiovascular diseases, but it is also already associated with reduced longitudinal and longitudinal circumferential deformation properties of the left ventricle elucidated by 2-D Speckle Tracking. These data confirm and broaden those derived from Tissue Doppler Imaging studies with the advantage of using a more reliable method.

P3516
Preperitoneal fat as a predictor of new onset hypertension in apparently healthy individuals

Introduction: Regional and generalized obesity are both associated increased risk of hypertension. In particular visceral adiposity is believed to directly affect cardiometabolic pathways leading to development of hypertension. Since waist circumference assesses both subcutaneous and visceral fat, we sought to investigate the predictive ability of direct measures of subcutaneous and visceral adiposity as compared to traditional anthropometric measures of obesity in healthy non-diabetic individuals.

Material and methods: One hundred and twenty-six non-diabetic, normotensive apparently healthy individuals (48 men, age 45.7±7.7 years) with a wide range of body-mass index (25.7±4.1, 19.1–44.9 kg/m²) were followed for 66±3.5 months. In addition to BMI, waist circumference and waist-to-hip ratio, ultrasonography was used to measure abdominal fat layers (subcutaneous and pre-peritoneal fat) and their ratio (P/S). New onset hypertension was defined by in-office blood pressure criteria (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg diastolic) or by reported initiation of antihypertensive treatment.

Results: New onset hypertension was found in 33 of the 126 (26.1%) subjects. Baseline BMI (26.9±4.3 vs. 25.2±3.9 kg/m², p=0.036), systolic (116.9±14.1 vs. 107.5±11.2 mmHg, p=0.001) and diastolic blood pressure (75.9±7.7 vs. 70.4±7.9 mmHg, p=0.001) and pre-peritoneal fat (1.69±0.47 vs. 1.41±0.54 cm, p=0.010) but not waist circumference or subcutaneous fat, were higher and base-line HDL cholesterol (56.9±12.7 vs. 62.9±17.9 mg/dL, p=0.037) was lower in subjects who developed hypertension. By multivariate logistic regression analysis, age (p=0.008), systolic blood pressure (p=0.001), HDL (p=0.028) and pre-peritoneal fat (p=0.025) were independent predictors of new onset hypertension while BMI and waist circumference were not.

Conclusions: In a sample of non-diabetic, normotensive apparently healthy individuals, pre-peritoneal fat, measured by ultrasound, predicted new onset hypertension in-office criteria better than BMI and waist circumference.

P3517
Relationship between epicardial adipose tissue and the severity of coronary atherosclerosis
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Purpose: We sought to evaluate the relation between epicardial adipose tissue (EAT) assessed by CMR and the severity of coronary artery disease (CAD) depending on the left ventricular function (LVF).

Methods and Results: 295 patients with coronary artery disease (CAD) and 50 healthy controls underwent CMR. Relevant CAD was defined as ≥50% coronary artery stenosis and qualified as 1-, 2-, or 3-vessel disease. Additionally, the severity of coronary atherosclerosis was defined using the Gensini score (GSS).

In the whole patient population, mean GSS was 63.6±59.4. 40 (16.0%) presented with mild (GSS ≤10), 72 (28.8%) with moderate (GSS >10 but ≤138) and 138 (55.2) with severe (GSS >138) atherosclerosis. In patients with preserved LVF ≥50% (Fig. 1A) and a GSS ≤10, mean EAT mass was comparable to healthy controls (31.3±8.8 g/m² vs. 31.8±8.6 g/m², p=0.77). With increasing atherosclerosis severity (GSS >10–<40), EAT mass rose significantly to 44.0±9.9 g/m². However, in patients with severe atherosclerosis (GSS >40), EAT mass already started to decline to 34.6±13.8 g/m². In patients with reduced LVF <50% (Fig. 1B), EAT mass was significantly reduced compared to healthy controls irrespective of the atherosclerosis severity and showed a stepwise decline with increasing atherosclerosis severity (GSS ≥10–<20:7.6±1.7 g/m², GSS 20–<40:26.9±8.4 g/m², GSS ≥40:24.4±4.7 g/m²).

Conclusion: In patients with CAD, the relation of atherosclerosis and CAD depends on the LVF. CAD patients with preserved LVF and moderate or severe atherosclerosis showed larger EAT amounts compared to healthy controls. Whereas, CAD patients with reduced LVF had significantly less EAT than healthy controls showing a stepwise decline of EAT mass with increasing severity of the atherosclerotic burden.
Prevalence of cardiovascular risk factors in 11249 overweight and obeuse youths: the PEP family heart study

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Purpose: Obesity and overweight in childhood are associated with increased cardiovascular risk. Because excess weight in youths is affected by growth and maturation, we examined the relationship between cardiovascular disease (CVD) risk factors and body mass index (BMI) for age in 3- to 18-year-old children and adolescents.

Subjects and Methods: We measured anthropometric and laboratory risk factors in 8935 normal weight (4638 boys, 4297 girls), 924 (457 boys, 467 girls) overweight (BMI ≥ 85th to < 95th percentile) and 511 (276 boys, 235 girls) obese (BMI ≥ 95th percentile) youths. Age and gender-specific BMI values were taken from the LMS percentile reference curves calculated for the basic sample of 23,481 youths aged 3-18 years. P<0.05 was used for statistics, p<0.001 was considered significant.

Results: In normal weight, overweight, and obese boys/girls the prevalence was respectively: 5.3/3.9%, 9.0/6.7%, and 9.1/7.1% (p<0.001); 13.9/13.9%, 19.7/19.7%, and 20.6/20.6% (p<0.001); and 15.7/15.7%, 21.3/21.3%, and 21.1/21.1% (p<0.001), p<0.001 for all comparisons.

Conclusions: In general prevalence of overweight and obesity is not realising its full potential time, high-risk children and adolescents should be targeted for aggressive intervention.

Two-year changes in quality of life of overweight and obese children after an inpatient weight loss program - LOGIC-trial

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Purpose: Childhood obesity is associated with impaired quality of life (QoL), which in turn appears to be positively influenced by regular physical activity (PA).

The aims of this study were to investigate changes in QoL in children two years after a short-term supervised weight loss program, and to examine the role of PA.

Methods: Participants in this prospective study were 208 overweight and obese children (124 girls) aged 13 ± 2.3 years undergoing an inpatient weight loss program for 4 weeks. Body height and weight were measured in the clinic at the start of the intervention and two years later by the children’s general practitioner at home. At both time points questionnaires on both QoL (KINDL and PA (“How many days last week have you been physically active for at least 60 minutes?”)) and QoL (“How many days last week have you felt physically active to at least 60 minutes?”)) were completed by the children. The subscales of the six dimensions of the QoL questionnaire (“physical functioning,” “psychological well-being,” “self-esteem,” “friends,” “family” and “school”) were combined to produce a total score. Values range from 0 to 100, with higher values representing better QoL.

Results: From the start of the intervention to two years later both body mass index (BMI) and BMI-SDS (BMI-standard deviation score) decreased from 32.6 ± 5.8 to 31.5 ± 6.3 kg/m² and from 2.7 ± 0.6 to 2.4 ± 0.9 (p<0.001, respectively. Over the follow-up QoL-total increased from 5.4 ± 13.1 to 68.0 ± 14.4 points (p=0.016) with particular improvements in the dimensions “self-esteem” (47.5 ± 22.6 to 57.2 ± 26.2 points; p=0.002), the “friends” (76.8 ± 22.6 to 87.4 ± 26.2 points; p=0.001) and “school” (59.2 ± 20.2 to 62.4 ± 19.6 points; p=0.039), whereas the dimension “family” decreased from 80.6 ± 18.2 to 76.6 ± 21.3 points (p=0.017). Changes between children, who increased (44%) or decreased (25%) their PA revealed significant differences in changes of QoL-total as well as in the dimensions “friends” and “school” (p<0.05), whereas there were no group differences in changes of BMI.

Conclusions: A short-term inpatient weight loss program appears to positively affect QoL in overweight and obese children in the long-term. This was related to changes in PA rather than BMI.

Central obesity in Polish and German schoolchildren

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Purpose: To analyze differences in the waist circumference (WC) and waist-to-height (WHtH) distributions between Polish (PL) and German (GE) schoolchildren and (ii) to evaluate the prevalence of the central fatness based on different criteria.

Subjects and Methods: Two cross-sectional surveys of schoolchildren aged 7-18 y: PL (5550 boys and 5768 girls) and GE (4299 boys and 3919 girls) were analyzed. The WHO measurement protocol and the LMS method was used in the both surveys. The two-stage WC cut-off points (WC1 and WC2) corresponding to the adults’ criteria (M: 94cm/90cm and 102cm/88cm) were determined for both study populations. Furthermore, the mean WC cut-off points (WC1m, WC2m) for boys and girls from both countries aged 14-18 y were evaluated. The effect of different WC criteria as well as WHtH >0.5 on the prevalence of central fatness in both study groups were statistically analyzed (descriptive methods ANOVA and chi-square tests).

Results: The WC1/WC2 percentile levels for boys were: PL: P95.6/P99.2 and GE: P96.9/P98.8, whereas for girls they were generally lower: PL: P91.0/P97.5 and GE: P96.5/P97.5. Furthermore the prevalence of dyslipidemia >3 out of 5 risk factors increased in both study groups were statistically analyzed (descriptive methods ANOVA and chi-square tests).

Prevalence of central fatness

Type of fatness | Criteria | % Boys (PL) | % Boys (GE) | % Girls (PL) | % Girls (GE)
--- | --- | --- | --- | --- | ---
Central fat distribution | WC = WC1 | 3.2 | 7.0 | 9.9 | 11.8
| WC ≤ WC1m | 10.9 | 16.7 | 19.4 | 24.0
WHtR > 0.5 | 6.7 | 8.5 | 5.3 | 12.7
Central obesity | WC = WC1 | 3.5 | 3.6 | 2.8 | 3.6
| WC ≤ WC2m | 11.1 | 13.1 | 10.9 | 13.1

Conclusions: 1/The results indicate a significant predominance of German boys and girls, especially adolescents, in terms of central fat distribution measured both by WC and WHtH as indices. 2/The prevalence of central fatness strongly depends on criteria used. 3/The results support a need for development of the international (European) WC norms for the pediatric subjects.

Hypertriglyceridemic waist carries a greater risk for coronary artery disease in Serbian women

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Purpose: The concept of the hypertriglyceridemic waist that was introduced over a decade ago and has been debated since while our particular focus was its application in everyday clinical practice aiming to help discern the high-risk population for coronary artery disease (CAD).

Methods: In an observational cross-sectional study carried out in the northern, middle and southern Serbia, in 3 university hospital centers, a total of 1715 patients was recruited from outpatient clinical practices and primary healthcare physicians’ offices who complied to the AHA/NHLBI definition of themetabolic syndrome: 37% men and 63% women, aged 34-80 years.

Results: Existing CAD (defined as positive stress test, previous angina, myocardial infarction or revascularization) was present in 373 patients (22.4%), while 1294 patients (77.6%) were CAD-free. For both genders, CAD patients had significantly higher levels of triglycerides (TG) and waist girth (WG). ROC analysis showed the better AUC for CAD to be the cut-off at waist girth value, the mean prevalence of adverse central fat distribution for PL/GE adolescent groups (14-18 y) were: for boys: 4.4%/8.9%; for girls: 10.7%/26.4%, whereas using WHtH >0.5 results were as follows: for boys - 6.7%/8.5% and for girls – 5.3%/12.7% (Table).

Prevalence of central fatness

Type of fatness | Criteria | % Boys (PL) | % Boys (GE) | % Girls (PL) | % Girls (GE)
--- | --- | --- | --- | --- | ---
Central fat distribution | WC = WC1 | 3.2 | 7.0 | 9.9 | 11.8
| WC ≤ WC1m | 10.9 | 16.7 | 19.4 | 24.0
WHtR > 0.5 | 6.7 | 8.5 | 5.3 | 12.7
Central obesity | WC = WC1 | 3.5 | 3.6 | 2.8 | 3.6
| WC ≤ WC2m | 11.1 | 13.1 | 10.9 | 13.1

Conclusions: 1/The results indicate a significant predominance of German boys and girls, especially adolescents, in terms of central fat distribution measured both by WC and WHtH as indices. 2/The prevalence of central fatness strongly depends on criteria used. 3/The results support a need for development of the international (European) WC norms for the pediatric subjects.
Obesity, both in male and female, could be used in everyday clinical practice for yielding attention to the population at higher risk for CAD.

### P3523 Long-term impact of surgical obesity intervention on inflammatory activity and carotid artery atherosclerosis

**D. Kardassis, L. Sjostrom, K. Karason, Sahlgrenska University Hospital, Gothenburg, Sweden**

**Background:** Obesity is associated with increased inflammatory activity and premature carotid artery atherosclerosis. The aim of this study was to investigate the effect of long-term sustained weight loss on proinflammatory cytokines and carotid artery intima media thickness.

**Methods:** We followed 44 obese patients (mean age 58±5 yrs, 48% male) treated with bariatric surgery, and 44 carefully matched obese control subjects, for ten years. During this period body weight, blood pressure, serum lipids, glucose and insulin were measured repeatedly. At the 10-year follow-up, study subjects underwent cross-sectional examination with analysis of circulating inflammatory markers and determination of intima media thickness in the carotid artery by duplex sono graphic.

**Results:** Surgical treatment of obesity resulted in significant long-term reductions in body weight and CV risk factors as compared with obese control patients (p<0.001). At the 10-year follow-up, the surgery group displayed lower plasma concentrations of hsCRP, TNF-α and IL-6 and higher concentrations of IL-10. Further, the surgery group displayed a lower mean IMT in the common artery bulb (CCB) and a trend towards lower IMT in the common carotid artery (CCA) (Table 1).

**Conclusion:** Obese patients with 10-year sustained weight loss displayed reduced inflammatory activity and severe less premature atherosclerosis in the carotid bulb as compared with their obese counterparts remaining weight stable.

### P3524 Sustained weight loss and fat distribution influence carotid plaque burden in obesity

**D. Kardassis, L. Sjostrom, K. Karason, Sahlgrenska University Hospital, Gothenburg, Sweden**

**Background:** Obesity is associated with premature atherosclerosis in the carotid artery, which in turn predicts cardiovascular events such as myocardial infarction and stroke. The aim of this study was to investigate the effect of long-term sustained weight loss on carotid plaque burden and study how fat distribution relates to carotid artery atherosclerosis.

**Methods:** Ten years after inclusion in the Swedish Obese Subjects study we identified 44 obese subjects, who followed bariatric surgery had displayed a 10-year sustained weight loss (surgery group), and 44 obese controls, who during the 10-year period maintained stable weight (obese group). We also recruited 44 matched normal weight subjects (lean group). DEXA, computed tomography and ultrasonography were performed to evaluate body composition, fat distribution and carotid artery atherosclerosis.

**Results:** BMI was 42.5, 31.5 and 24.4 kg/m² for the obese, surgery and lean groups respectively. Increasing degree of obesity was associated with thicker mean IMT in the carotid common bulb (p<0.001) and increased total plaque area (p<0.001). In a correlation analysis, IMT CCB and total plaque area were significantly associated with measures of body composition, fat distribution. In a stepwise multiple regression model, IMT CCB and total plaque area were solely predicted by body fat and waist-to-hip ratio.

**Conclusion:** Obese patients with 10-year sustained weight loss after bariatric surgery display a reduced plaque burden in the carotid artery as compared with obese counterparts remaining weight stable. Visceral adiposity was independently associated with early carotid artery atherosclerosis, suggesting that a reduction of intra-abdominal adipose tissue may have a favourable influence on the development of atherosclerosis.

### P3525 Growth differentiation factor 15 predicts insulin resistance and abnormal glucose control in obese individuals

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**Purpose:** Growth differentiation factor (GDF) 15 is a stress-response cytokine and emerging biomarker of cardiovascular risk. GDF-15 is produced in adipose tissue and may modulate adipose tissue function. Studies in community-dwelling individuals and patients with established cardiovascular disease have consistently reported higher circulating concentrations of GDF-15 in type 2 diabetes. We assessed the relation of GDF-15 to insulin resistance and glucose control in a large cohort of obese individuals.

**Methods and Results:** GDF-15 was measured at baseline and after 4 years in 496 obese individuals without cardiovascular disease enrolled in the XENIC in the prevention of Diabetes in Obese Subjects (XENDOS) trial. The XENDOS trial evaluated the additive effect (beyond lifestyle changes) of the weight reducing agent orlistat on body weight and glucose control. At baseline, study participants (52% men, median age 48 years) had a median body mass-index (BMI) of 37.6 kg/m² and a mean waist-to-hip ratio of 1.0. The median (25th percentiles) GDF 15 concentrations were 869 (723–1064) ng/l at baseline and 932 (756–1141) ng/l after 4 years (P < 0.001). Individuals with pre-diabetes (impaired fasting glucose and/or impaired glucose tolerance) had higher GDF 15 concentrations compared with those with a normal glucose regulation; even higher levels were measured in patients with diabetes. GDF 15 levels at baseline were related to measures of obesity [BMI (Pearson’s r = 0.15; P < 0.001), waist-to-hip ratio (r = 0.12; P = 0.006)] and impaired glucose control [fasting insulin (r = 0.14; P = 0.002), homeostasis model assessment of insulin resistance (r = 0.15; P < 0.001)]. Increasing obesity and worsening glucose control over time were associated with greater increases in GDF-15 at 4 years. GDF-15 concentrations at baseline were associated with the risk to have an abnormal glucose regulation (pre-diabetes or diabetes) at 4 years on univariate analysis (HR per 1 unit increase in ln GDF-15: 3.2; 95% CI 1.7–6.1; P < 0.001) and after multivariate adjustment for age, gender, BMI, waist-to-hip ratio, glucose control at baseline, and treatment allocation (HR 2.2; 95% CI 1.1–4.7; P = 0.026). Similarly, GDF-15 levels at baseline were independently associated with insulin resistance at 4 years (P = 0.024).

**Conclusion:** The present longitudinal study indicates that GDF-15 levels start to increase before the onset of diabetes and the occurrence of cardiovascular complications. GDF-15 predicts future insulin resistance and abnormal glucose control, and may provide a “link” between obesity, diabetes, and cardiovascular risk.

### P3526 Association of dietary patterns with 14-year all-cause and cause-specific mortality

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**Background:** Recommendations for healthy food choices emphasize the consumption of a wide variety of foods. Benefits are expected not only regarding cardiovascular but also non cardiovascular mortality. The aim of this study was to investigate overall, cardiovascular and cancer mortality according to dietary diversity and the extent of food group consumption.

**Methods:** A sample of 947 men aged 45-64 at baseline was randomly selected in 1995-96 from the general population of three French areas (Northern, Northern-Eastern and South-Western France). Data collection was based on standardized clinical examinations, fasting blood sample, and questionnaires on socio-economic characteristics, previous medical history and cardiovascular risk factors, thus allowing extensive adjustments. Besides, a 3-day prospective food record was performed on two week and one week-end days. Vital status was obtained on December 31, 2009.

**Results:** Median follow-up was 13.8 years. Cumulative incidence of death reached 13.3% (among which 32% of deaths were due to cardiovascular diseases; 50% to cancers and 18% to other causes). People who died were significantly older, had less often graduated from high school, were less often liable to income tax, more often heavy smokers or sedentary people, and exhibited a higher Framingham score. They consumed a lower amount of fruits and vegetables, dairy products, bread and grains, but a higher amount of alcohol. After adjustment for centre, age, cancer and alcohol intakes, Framingham risk score and...
Geriatric Nutritional Risk Index improves the acute effects of an energy drink on myocardial

Nutrigenetics of blood pressure responses to coffee

Conclusion: High consumptions of fruits, vegetables, bread, grains, and dairy products (in particular milk intake) are associated with a reduced risk of death among middle-aged French men. This reduced risk is rather related to a decrease in cardiovascular mortality than a reduced risk of cancer death.

Geriatric Nutritional Risk Index improves the predicting of cardiovascular and all-cause mortality in end-stage renal disease patients who started hemodialysis therapy

Methods: A total of 1,568 ESRD patients who stably started HD therapy were examined. The GNRI was calculated from medical records at starting of HD, as follows:

\[
\text{GNRI} = \frac{\text{Albumin} \times 14.89}{\text{BMI} \times (\text{Body Weight}/\text{BMI of 22})}
\]

where BMI is the body mass index and albumin is the level of serum albumin measured in g/L. The GNRI was divided into two groups: low GNRI (< 39.7) and high GNRI (≥ 39.7). The median value of the GNRI was 41.7, and patients were divided into quartiles according to the GNRI levels: quartile 1 (Q1): < 41.7, Q2: 41.7–59.11, Q3: 59.11–79.27 and Q4: > 79.27, and were followed up for up to 10 years.

Results: During follow-up period (mean 63±42 months), 363 patients died including 180 cardiovascular (CV) deaths. Kaplan-Meier survival rates for 10 years were 57.9%, 73.3%, 80.8% and 89.2% for CV mortality, and were 32.1%, 51.9%, 61.3% and 73.8% for all-cause mortality in Q1, Q2, Q3 and Q4, respectively (p < 0.0001 for both). On Cox multivariate analysis, GNRI was an independent predictor of both CV and all-cause mortality (HR 3.37, 95% CI 1.96–5.80 and HR 2.92, 95% CI 1.20–2.52, both p < 0.0001 for Q1 vs. Q4, respectively). In addition, C-index was greater in the multivariate model with GNRI compared to that with albumin, with BMI and alone (Table).

Conclusion: GNRI at starting HD therapy strongly predicted CV and all-cause mortality in ESRD patients. This simple marker might be clinically useful for the assessment of malnutrition status in HD patients.

Nutrigenetics of blood pressure responses to coffee drinking

Methods: 110 male healthy subjects were administered 40 mL of either a decaffeinated coffee preparation plus 3 mg/kg caffeine (caf) or the corresponding vehicle (decaf), and underwent ambulatory BP monitoring at 6 min intervals for 2 h and blood sampling. The protocol was repeated 24 h later with the alternative preparation.

Results: Compared with decaf, caf was associated with a significant increase in systolic and diastolic BP (SBP, DBP). The differences between caf and decaf (Δ) in SBP and DBP mean, defined as the means of all SBP and DBP values up to 2 h after coffee, were 4±1.2 mmHg and 3±10 mmHg, respectively (P < 0.001 for both). Stratifying subjects by the median values of the distributions for ΔSBP and ΔDBP mean, we observed a significantly higher proportion of subjects with ΔSBP mean above the median and ΔDBP mean below the median in homozymes for the adrenergic receptor α2B variant than in the other genotypes at the same locus (OR=3.7; 95% CI=1.4–9.5; P=0.006; see Figure). Adrenaline plasma concentration increased 2 h after caf compared with decaf, but no differences were observed between homozymes for allele 1 and the other genotypes.

Conclusions: Variability in the acute BP response to coffee may be partly explained by genetic polymorphisms of the α2B-adrenergic receptors. Higher BP response, as the result of nutrigenetic interactions in some genetically predisposed individuals, may expose them to a higher coffee-related cardiovascular risk.

Acute effects of an energy drink on myocardial function assessed by conventional echo-Doppler analysis and by speckle tracking echocardiography on young healthy subjects

Background: Previous studies have underlined the effects of the energy drinks (ED) containing caffeine and taurine on cardiovascular system. The aim of this study was to determine acute changes on echocardiographic parameters assessed by conventional echo-Doppler analysis and by Speckle Tracking Echocardiography after the assumption of an ED in a young healthy population.

Materials and methods: Measurement of blood pressure, electrocardiographic and echocardiographic examination were performed in 35 healthy subjects (mean age 25±5 years, 16 men), at baseline and one hour after the consumption of body surface area indexed amount of an ED (168 ml/m²) containing caffeine (0.03%) and taurine (0.4%). The same group one week later was analyzed at baseline and one hour after the consumption of a fruit juice.

Results: Compared to the fruit juice recordings, the analysis of LV function showed a significant increase of mean relative values of MAPSE (+ 11%; P < 0.001), GLS (+10%, P < 0.004), LV Twisting (+22%, P < 0.001) with respect to baseline. Also RV function parameters appeared significantly increased, as TAPSE (+15%, P < 0.0001) and global and free wall RVLS (+8%, P < 0.001, +5%, P < 0.01, respectively).

Conclusions: The consumption of the ED in our population showed a significant increase of RV and LV myocardial function, suggesting a possible positive isotropic acute effect related to the substances contained therein.

Long term fish intake seems to confer to preserved renal function in elderly individuals: the Ikaria study

Background: Renal insufficiency has been recognized as an independent risk

Figure 1. Cardiovascular effects of energy drink

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factor for cardiovascular and all-cause mortality. Among other factors, omega-3 polyunsaturated fatty acids in fish oil have been shown to reduce blood pressure, proteinuria, lipid levels and inflammation. However, data regarding the effect of long-term fish consumption on renal function are limited. The aim of this study was the evaluation of the impact of fish consumption in respect of the overall dietary habits, on renal function in elderly inhabitants of Ikaria Island; a place that has been related with increased rates of longevity.

Methods: We studied 343 men and 330 women, aged 65 to 100 years. Among several socio-demographic, bioclinical, lifestyle and dietary characteristics, cardiovascular disease (CVD) factors and anthropometric indices, nutritional habits, including weekly fish intake, were evaluated using a semi-structured interview. A diet score that assesses the inherent characteristics of the Mediterranean diet, to be associated with reduced urea, creatinine and proteinuria, lipid levels and inflammation. However, little is known about roles of free fatty acid components in patients with peripheral arterial disease (PAD).

Conclusions: Regular fish or fish oil intake have been shown to lower the risk of cardiovascular disease and improve cardiovascular outcomes in patients with coronary artery disease (CAD). However, little is known about roles of free fatty acid components in patients with peripheral arterial disease (PAD).

Methods: Ankle brachial index (ABI), traditional cardiovascular risks, and levels of 24 components of fatty acids were examined in 130 PAD patients (ABI >0.90, mean ABI 0.72±0.01, mean age 72.08±0.8 years; 103 males) and were compared with those of 395 age and sex matched random hospital controls (ABI >0.90).

Results: In the PAD patients, there were significantly lower levels of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), gamma-linolenic acid (GLA), eicosapentaenoic acid to arachidonic acid ratio (EPA/AA) ratio on univariate analyses (p <0.05). We performed multivariate logistic regression analyses with adjustment for body mass index, eGFR, HbAlc, C-reactive protein, D-dimer, serum lipids, LDL/HDL cholesterol ratio, presence or absence of CAD, EPA, DHA, GLA and EPA/AA ratio on univariate analyses (p <0.05). The presence of PAD was independently protected by levels of eGFR (OR: 0.97; 95% CI: 0.96-0.98; p <0.0001), HbAlc (OR: 1.42; 95% CI: 1.12-1.78; p <0.003), GLA (OR: 0.94; 95% CI: 0.90-0.99; p =0.020), and by EPA/AA ratio (OR: 0.22-94; 95% CI: 0.02-9.96). These protective factors were assessed by area under ROC curve analyses (Figure 1).

Results: In the PAD patients, there were significantly lower levels of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), gamma-linolenic acid (GLA), eicosapentaenoic acid to arachidonic acid ratio (EPA/AA) ratio on univariate analyses (p <0.05). We performed multivariate logistic regression analyses with adjustment for body mass index, eGFR, HbAlc, C-reactive protein, D-dimer, serum lipids, LDL/HDL cholesterol ratio, presence or absence of CAD, EPA, DHA, GLA and EPA/AA ratio on univariate analyses (p <0.05). The presence of PAD was independently protected by levels of eGFR (OR: 0.97; 95% CI: 0.96-0.98; p <0.0001), HbAlc (OR: 1.42; 95% CI: 1.12-1.78; p <0.003), GLA (OR: 0.94; 95% CI: 0.90-0.99; p =0.020), and by EPA/AA ratio (OR: 0.22-94; 95% CI: 0.02-9.96). These protective factors were assessed by area under ROC curve analyses (Figure 1).

Figure 1. ROC curve analysis

Conclusions: This study demonstrated that in addition to traditional cardiovascular risk factors, EPA/AA ratio and GLA could be potential predictors for PAD. Fatty acid abnormalities may play an important role in the pathophysiology of PAD. Specific fatty acid abnormalities may open new strategies for risk stratification and therapeutic options for patients with PAD.

P3532 Free fatty acid abnormalities and cardiovascular risk factors in prediction of peripheral arterial disease

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Background: Regular fish or fish oil intake have been shown to lower the risk of cardiovascular disease and improve cardiovascular outcomes in patients with coronary artery disease (CAD). However, little is known about roles of free fatty acid components in patients with peripheral arterial disease (PAD).

Methods: Ankle brachial index (ABI), traditional cardiovascular risks, and levels of 24 components of fatty acids were examined in 130 PAD patients (ABI >0.90, mean ABI 0.72±0.01, mean age 72.08±0.8 years; 103 males) and were compared with those of 395 age and sex matched random hospital controls (ABI >0.90).

Results: In the PAD patients, there were significantly lower levels of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), gamma-linolenic acid (GLA), eicosapentaenoic acid to arachidonic acid ratio (EPA/AA) ratio on univariate analyses (p <0.05). We performed multivariate logistic regression analyses with adjustment for body mass index, eGFR, HbAlc, C-reactive protein, D-dimer, serum lipids, LDL/HDL cholesterol ratio, presence or absence of CAD, EPA, DHA, GLA and EPA/AA ratio on univariate analyses (p <0.05). The presence of PAD was independently protected by levels of eGFR (OR: 0.97; 95% CI: 0.96-0.98; p <0.0001), HbAlc (OR: 1.42; 95% CI: 1.12-1.78; p <0.003), GLA (OR: 0.94; 95% CI: 0.90-0.99; p =0.020), and by EPA/AA ratio (OR: 0.22-94; 95% CI: 0.02-9.96). These protective factors were assessed by area under ROC curve analyses (Figure 1).

Figure 1. ROC curve analysis

Conclusions: This study demonstrated that in addition to traditional cardiovascular risk factors, EPA/AA ratio and GLA could be potential predictors for PAD. Fatty acid abnormalities may play an important role in the pathophysiology of PAD. Specific fatty acid abnormalities may open new strategies for risk stratification and therapeutic options for patients with PAD.
Greater adherence to the Mediterranean type of diet improves cardiac autonomic balance in elderly individuals with left ventricular hypertrophy: the Ikaria study

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Introduction: Left ventricular hypertrophy (LVH) prevalence increases with age, while is related to higher cardiovascular morbidity and mortality. Mediterranean diet (MD) due to its antiarrhythmic properties has been associated in some studies with improvement in autonomic system control. The purpose of this study was to evaluate the impact of long-term adherence to the MD on left ventricular hypertrophy.

Methods: From June to October of 2009, we studied 343 men and 330 women, aged 65 to 100 years, permanent inhabitants of Ikaria Island. Among several socio-demographic, bio-clinical, anthropometric and lifestyle characteristics, adherence to the MD was assessed using a validated diet score (MedDietScore 0-55). In all individuals an echocardiographic evaluation was performed and left ventricular mass (LVM) was calculated with the use of the anatomically validated formula LVM = 1.04 x (IVS + LVEDD + PW3) – 13.6 g. Moreover, LV mass index (LVMI) was calculated, even in elderly individuals with LVH and LVSD is the diastolic and systolic dimensions, IVS the interventricular septal thickness, LVEDD is the left ventricular end diastolic diameter and LVDD is the left ventricular posterior wall thickness all measured from the left parasternal long axis, according to the international guidelines. LVM was defined according to the adjusted to height criteria, according to the European Gis 2006. All participants underwent digital electrocardiography and a standard 12-lead ECG was recorded (10s duration) by the use of SE-1010 PC ECG (EDAN instruments, Inc.). Smart ECG Measurement and Interpretation Programs were used for the automated measurement and interpretation of ECGs intervals. Vagal tone was estimated with the heart rate variability (SDNN) in surface ECG of 5 min duration.

Results: 130 individuals (40% males, mean age 76.6 ± 6.5 years old) with LVH were enrolled in this study. From them 43% were defined as having obesity, 25.6% diabetes, 80% hypertension, 67% hypercholesterolemia. The mean LVMI (adjusted for body mass index) was 127.2 ± 23.4 and the mean heart rate 68 ± 17 beats per minute. MedDietScore was positively correlated with logSDNN (r = 0.230, p = 0.05). Linear regression analysis, after adjustment for obesity, diabetes, hypertension, heart rate, hypercholesterolemia, physical activity status and known history of cardiovascular disease, revealed that that MedDietScore is related with logSDNN (beta = 0.013, p = 0.002).

Conclusion: MD pattern seems to be associated with improved autonomic balance, even in elderly individuals with left ventricular hypertrophy.

Women that developed recurrences of AF were older, with lower adherence to MedD, and had higher intake of caffeine.

Metabolic syndrome and its components in relation to colorectal cancer in a Mediterranean population

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Purpose: In the last two decades holistic dietary approach predominated in epidemiological studies. Metabolic syndrome is considered to be related to colorectal carcinogenesis, whereas Mediterranean diet seems to have a protective effect.

The aim of the present study was to evaluate whether MetS or its components are related to colorectal cancer in a Mediterranean population.

Methods: This is a case-control study. Between December 2009 and December 2010, 250 cases (aged 63±12.5 years) with first diagnosis of colorectal cancer were consecutively selected from Saint Savvas Cancer hospital and Alexandria General Hospital. At the same period 250 subjects (controls) without any clinical symptoms, signs or suspicious of any type of cancer in their medical history, aged 65-100 years old were selected. The number of cases (M/F) and the controls were matched (M/F). The number of 3 cases (1.9% (108 cases) and 39% of the total sample (20%)) was decided through power analysis. Adherence to the Mediterranean diet was accessed using MedDietScore; a dietary index, validated for cardiometabolic distal effect, this compontes inherent characteristics of this traditional pattern (theoretical range 0-55). Multi-adjusted logistic regression analysis controlling for age, sex, body mass index, physical activity status, smoking habits and family history, was used.

Results: Cases had higher prevalence of MetS (30.5% versus 21.4%, p=0.022), hypertension (41.5% versus 32.6%, p=0.045), and diabetes mellitus (23.7% versus 12.9%, p=0.004), but no difference in hypercholesterolemia. In multivariate analysis MedDietScore had a protective association (0.89, 95%CI 0.85, 0.95) and MetS a detrimental one (1.59, 95%CI 0.99, 2.55). Further analysis investigating the components of MetS adjusted for the above factors revealed no association. No association existed between drug therapy for the above diseases (aspirin, anti-diabetics or statins), whereas Mediterranean diet had a protective association in all analyses.

Conclusions: Metabolic syndrome is related to colorectal cancer in our study. The Mediterranean diet has a protective association irrespective of the presence of factors associated with this type of cancer (family history, smoking or MetS). Public health policies on colorectal cancer prevention could focus on the promotion of a healthy dietary pattern, like Mediterranean diet, as an economic and feasible target.

Different types of nutrients oils exert beneficial anti-inflammatory effects on healthy volunteers

Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Purpose: Pro-inflammatory cytokines as well as adhesion molecules are implicated in carcinogenesis. In addition, dietary intake of oil has been associated with cardiovascular risk. However, the exact role of oil consumption vascular inflammation remains unknown. We sought to examine the acute effect of different types of oil on circulating levels of the inter-cellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1) and tumor necrosis factor alpha (TNF-a).

Methods: The study population consisted of 67 healthy volunteers who received 50 ml of oil. The soluble forms of VCAM-1, ICAM-1 and TNF-a were measured by enzyme-linked immunosorbent assay (ELISA) at baseline and 3 hours post oil consumption.

Results: All types of oil had no significant effect on sVCAM-1 levels (not significant) for all the contrary, all types of oil decreased ICAM-1 (mg/ml) levels (p<0.01). More specifically, cod liver oil induced a decrease from 310.4±126.1 to 169.2±82.1, whereas olive oil from 238.3±113.7 to 208.1±105.3. Interestingly, corn oil had also a significant effect on ICAM-1 levels (294.8±111.8 to 226.4±114.1, p<0.01) controversially its neural effect on VCAM-1. Although p<0.01, soy oil (p<0.01) and cod liver oil (p<0.01) reduced significantly TNF-a levels, corn oilinduced a non significant decrease inTNF-a levels (p=0.87). Moreover, there was significant correlation between the absolute change in ICAM-1 and TNF-a levels (r=0.379, p<0.05), but not between the absolute changes in VCAM-1 and TNF-α-activities (r<0.019, p<NS).

Conclusions: Acute consumption of all types of oil on circulating levels of the inter-cellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1) and tumor necrosis factor alpha (TNF-a) were measured.

Comparison between source of antioxidant

**Source of antioxidants** | **WAF (%)** | **MFA (%)**
---|---|---
Laguna | 9 | 20
Vegetables | 25 | 3
Fruits | 20 | 10
Complex | 40 | 7
Tea | 30 | 7

Conclusions: WAF showed high adherence to MedD and higher intake of antioxidant form fruit and vegetables. MFA had higher intake of antioxidants from coffee.
Wine consumption is not associated with subclinical or clinical atherosclerosis

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Purpose: Several studies have shown that wine consumers contract myocardial infarction (MI) less frequently than abstainers. Since the cause of MI is atherosclerosis, it is obvious to suppose that also atherosclerosis (AS) is less frequent among wine consumers, leading to a lower incidence of MI and also of cardiovascular disease (CVD).

Methods: Data of wine consumer and abstinent inhabitants of the Western Hungarian wine producing region (Sopron, Kőszeg, Vaskeresztes) were studied. From 990 persons (males: 67, females: 33%) 520 were regular wine consumers, 276 occasional wine consumers and 194 were abstinent. Inhabitants aged 20-80 years having lived in the region for at least 10 years and consuming the locally produced red wine were included into the study. The known cardiovascular diseases were assessed by a questionnaire. Presence of AS was determined by ultrasound investigation of the carotid arteries. Coadministration of at least one plaque in either carotid. Total polyphenol, red pigment content, free radical trapping and ORAC values of the wines consumed in the region were analysed. Statistical analysis was performed by MedCalc Version 10.3.1.0.

Results: See the tables below.

<table>
<thead>
<tr>
<th>Carotid IMT and occurrence of plaques</th>
<th>Wine consumption</th>
<th>N</th>
<th>IMT</th>
<th>Carotid plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstinent</td>
<td>76</td>
<td>109</td>
<td>0.70±0.30</td>
<td>13.6% NS</td>
</tr>
<tr>
<td>Consumer</td>
<td>94</td>
<td>21</td>
<td>0.80±0.29</td>
<td>22.6%</td>
</tr>
</tbody>
</table>

Incidence of CVD according to wine consumption

<table>
<thead>
<tr>
<th>Pattern of wine consumption</th>
<th>Number of examinations</th>
<th>CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular consumer</td>
<td>520</td>
<td>74</td>
</tr>
<tr>
<td>Abstinent</td>
<td>194</td>
<td>48</td>
</tr>
<tr>
<td>Occasional consumer</td>
<td>276</td>
<td>69</td>
</tr>
</tbody>
</table>

Characteristics of wines of the region: total polyphenol: 3.3–2.7 mg/l, anthocyanin: 170.4±7.45.3, free radical trapping value: 94.7–78.7%, ORAC value: 12978.3–10 697.2.

Conclusions: No development of AS but that of CVD is reduced by wine consumption, presumably by altering plaque stability.

The role of Selenium supplementation on top of Coenzyme Q10 in atients treated patients with possible diastolic dysfunction of left ventricular

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Inhibition of HMG-CoA reductase by statins leads to decreased synthesis of cholesterol, coenzyme Q10 (CoQ10) and several selenoproteins.

Aim: Aim of our double-blind, randomized, single centre 3-month study using CoQ10 and selenium supplementation with CoQ10 in patients with statin-associated myopathy.

Methods: Sixty eligible patients were enrolled in the study. All patients underwent physical, laboratory, and echocardiographic examinations at the beginning and at the end of the study. Physical and laboratory examinations were performed also after 1 month.

Results: All symptoms of statin-associated myopathy significantly improved in the CoQ10 group active group of patients (p=0.001). Plasma level of CoQ10 in the active group increased from baseline 0.81±0.39 mg/l to 3.31±1.72 mg/l at 3 month visit and remained unchanged in the placebo group (p=0.001). Selenium supplementation was not associated with a decrease of statin-associated myopathy. Higher increase of CoQ10 plasma levels was observed with selenium supplementation in comparison with CoQ10 monotherapy (p=0.1059). Two of the three observed parameters of the left ventricular diastolic function (peak E/A ratio, isovolumetric deceleration time) were significantly improved in CoQ10 treated patients compared to placebo group (p=0.001). Deceleration time remained statistically unchanged.

Conclusions: Our results showed that supplementation with coenzyme Q10 resulted in a decrease of statin-associated myopathy symptoms. Selenium supplementation was associated only with its plasma level increase, but did not lead to statistically significant improvement of statin side effects.

Smoking ban and incidence of STEMI: non-smokers benefit most?

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Background: Since 2006 data from all patients in the region of Bremen (est: 800 000 inhabitants) with ST-elevation myocardial infarction (STEMI) have been centrally collected in the Bremen STEMI-registry. In the present study data from 2006 to 2010 was analyzed on the background of the commencement of an anti-smoking act (end of 2007), which widely banned tobacco smoking from public areas in Bremen and Lower Saxony.

Methods: Between January 2006 and December 2010 data from the STEMI-Registry was analyzed focusing on date of admission, age, gender and prior nicotin consumption of pts.

Results: Between 2006 and 2010 a total of 3549 pts with STEMI were admitted in the Bremen heart center. During this time period a decline of the median number of STEMI/mo could be observed: from 65±12 STEMI/mo in 2006 vs 55±10 STEMI/mo in 2010, (-16%), p=0.028. When comparing the years before and after the commencement of the law there was a similar decline from median 65±11 STEMI/mo in 2006-2007 vs 55±10 STEMI/mo in 2008-2010, (-16%), p=0.001. Smoking abstinence was verified by the assessment on the group of pts with a smoking habit prior to a myocardial infarction, the median number of STEMI/mo slightly increased (25±6 in 2006-2007 vs 26±6 in 2008-2010, p=0.63). The group of nonsmokers however benefit highly significantly with a decrease in the median number of STEMI/mo from 39±8 in 2006-2007 to 29±7 in 2008-2010, (-26%), p=0.001. When furthermore focusing on the younger nonsmoking patient (<65 years) with STEMI an even steeper decline in the median STEMI/mo can be shown: 13±4 in 2006-2007 vs 9±3 in 2008-2010, (-32%) p=0.001. Age and gender of the pts however show no significant impact on the younger nonsmoking patient (<65 years) with STEMI as indicated by an even stronger decline in the median STEMI/mo in these patients.

Conclusions: The Bremen STEMI registry reveals over a time period of 5 years a reduction in the incidence of STEMI, which was at least partially associated with the commencement of an anti-smoking act. Nonsmokers and especially younger nonsmokers benefit most from the commencement of the law indicating the harmful effect of passive smoking.
Conclusions: Use of tobacco cessation support strategies is low in acute coronary syndrome patients and is higher in patients with previous coronary heart disease.

Purpose: A combination of hypertension (HT) and smoking have a synergistic impact on cardiovascular events. However, the underlying precise mechanism remains to be clarified. Adiponectin, an adipose tissue-derived hormone has anti-inflammatory properties, which lead to beneficial actions on cardiovascular disorders. We therefore evaluated the association between carbon monoxide (CO) in expired air and adiponectin levels in smoking patients with hypertension.

Methods: Plasma adiponectin levels were measured by latex turbidimetric immunometry in 12 hypertensive patients. We also measured CO in expired air by a portable CO detector.

Results: Patients were 62±13 years of age. Echocardiography confirmed that the patients had normal LV systolic function with a mean LVEF of 68±5%. CO levels in expired air were 19±13 ppm. Plasma adiponectin and brain natriuretic peptide (BNP) levels were 9.5±4.9 pg/ml and 67±45 pg/ml, respectively. The CO levels in expired air were negatively correlated with adiponectin levels (r= -0.64, p< 0.01) and BNP levels in smoking patients with hypertension.

Conclusion: A negative correlation was observed between CO levels in expired air and plasma adiponectin levels, and BNP levels in smoking patients with hypertension. Thus, the down-regulation of adiponectin by a combination of hypertension and smoking may at least in part contribute to the development of cardiovascular disease. Therefore, smoking-cessation initiatives should be targeted more rigorously for hypertensive patients to prevent severe cardiovascular disease.

Conclusions: Use of tobacco cessation support strategies is low in acute coronary syndrome patients and is higher in patients with previous coronary heart disease.

Purpose: To evaluate clinical effectiveness of treatment with intravenous iloprost and validity of repeated non-invasive transcutaneous CO2 (tPCO2) monitoring of lower limbs in outpatients with Buerger disease (BD).

Methods: 10 consecutive outpatients (9 males, mean age 36.8 years) with distal trophic lesions (n=16 symptomatic limbs) and a history of previous (n=3) or current (n=7) smoking, minor amputations (30%), lumbar sympatheticotomy (10%), spinal cord stimulation (20%) or vascular surgery (10%) underwent clinical evaluation and instrumental measurements (echo-color Doppler, angiography, cutaneous microcirculation). That confirmed suspicious BD, were enrolled between 2004 and 2009. All patients underwent a single course of iloprost therapy (50 microg/day, mean 21.4 days), whereas 3 non responders to initial treatment, underwent an additional second course of treatment at a short distance from the first one. All patients were monitored with non invasive tPCO2 and tPCO2 parameters before (0) and after drug therapy (11) and at 3 (13) and 12 months of follow-up.

Results: Even though all patients were strongly invited to smoking cessation, 3 of them continued to smoke. Clinical response (complete cessation of rest pain, cure of trophic lesions, improvement of neuropathy) was positive in six previous smokers after one pharmacological treatment and in two current smokers after the second cycle of iloprost, while it was negative in the remaining two current smokers, one of whom subsequently underwent successful below-knee percutaneous angioplasty. Mean oxygen levels showed a significant increase in the supine position (from basal 16 to 26 mmHg, 29 and 38 mmHg, at t1, 11, and t12 respectively, p<0.0007) as well as in dependent (from basal 39 to 47 mmHg, 51 and 54 mmHg, at time 11, t1, t3 and t12, respectively, p<0.000), while the decreasing tPCO2 trends were non significant both in the supine position (from basal 51 to 51 mmHg, 54 and 38 mmHg, at t1, 13 and t12, respectively, p=0.08) and dependent (from basal 41 mmHg to 38, 38 and 37 mmHg, at t1, t3 and t12, respectively, p<0.06). After a year of follow-up all patients were alive, with healthy limbs and without local or systemic cardio-vascular complications.

Conclusions: Our small series confirms the mandatory indication to smoking cessation in Buerger’s disease, shows the effectiveness of a prolonged treatment with intravenous iloprost, underlines the validity of transcutaneous non-invasive monitoring to make an accurate lower limbs cutaneous microcirculation assessment and to objectively indicate the timing of eventual new pharmacological treatments.

Purpose: Smoking increases platelet aggregability but also the degree of platelet inhibition by clopidogrel ex vivo. The aim of this study was to evaluate the relationship between smoking status (current, former or never-smoker) and dual antiplatelet treatment (aspirin 100 mg plus clopidogrel 75 mg daily) after percutaneous coronary intervention (PCI).

Methods: In this observational, one-center study, we reported every patient who proceeded for hospitalization in our department and had undergone coronary stent implantation. The smoking status was characterized as current (at least 1 cigarette per day during the month before enrollment) and former (at least 1 cigarette per day at any time prior this month).

Results: From January 2010 until January 2012, 467 patients (men 409 (87.6%), age 65.6±10.6 years) were identified with prior coronary intervention and dual antiplatelet treatment. The patients were divided into 2 groups, regarding to the duration of DAPT (1 month ≤ 1 year) and sub-divided regarding to the smoking status. We reported the combined (TVR/target-vascular revascularization)-non-TVr/bleeding) complication rate. In the first group (163 patients (34.9%), mean duration 6.9 months) we reported in the sub-group of the current smokers: 36 patients (52%), 2 bleeding events (5.6%, 1 severe according to GUSTO criteria) and 25 cases of acute coronary syndromes (ACS) (TVR/non-TVr: 27.7%). In the sub-group of former smokers: 126 patients (77.3%), 23 bleeding events (18.2%, 3 moderate) and 83 ACS (TVR/non-TVr: 32.5%). In the sub-group of never-smokers (1 patient) neither bleeding nor ACS were reported. In the second group of long-term DAPT (297 patients (63.6%) mean duration 4.1 years) we reported in the sub-group of current smokers: 58 patients (19.5%), 6 bleeding events (10.3%, 2 severe) and 34 ACS (TVR/non-TVr: 28.5%). In the sub-group of former smokers: 151 patients (50.8%), 27 bleedings (17.9%, 1 severe, 2 moderate) and 99 ACS (TVR/non-TVr: 28.4%). Finally in the never-smokers subgroup non-event was reported.

Conclusions: A substantial proportion, almost 30%, of current and former smokers needed revascularization with a non significant reduction in the group of long term dapt (21.5% vs 27.8%, p=0.05). An 1.5-fold increase in the occurrence of

Conclusion: The CO levels in expired air also correlated with BNP levels (r= -0.49) and plasma adiponectin levels, and BNP levels in smoking patients with hypertension.

Methods: Plasma adiponectin levels were measured by latex turbidimetric immunometry in 12 hypertensive patients. We also measured CO in expired air by a portable CO detector.

Results: Patients were 62±13 years of age. Echocardiography confirmed that the patients had normal LV systolic function with a mean LVEF of 68±5%. CO levels in expired air were 19±13 ppm. Plasma adiponectin and brain natriuretic peptide (BNP) levels were 9.5±4.9 pg/ml and 67±45 pg/ml, respectively. The CO levels in expired air were negatively correlated with adiponectin levels (r= -0.64, p< 0.01) and BNP levels in smoking patients with hypertension.

Conclusion: A negative correlation was observed between CO levels in expired air and plasma adiponectin levels, and BNP levels in smoking patients with hypertension. Thus, the down-regulation of adiponectin by a combination of hypertension and smoking may at least in part contribute to the development of cardiovascular disease. Therefore, smoking-cessation initiatives should be targeted more rigorously for hypertensive patients to prevent severe cardiovascular disease.
severe or moderate bleeding in the current smokers group was reported (3.2% vs 2.1%, p < 0.05) whereas the current smoking group under long term lapt, suffered the higher bleeding risk (3.4%). These data highlight the need to take under option this new parameter at the evaluation of the patients after coronary intervention.

### Varenicline therapy improves abstinence rates over 50 percent in smokers with cardiovascular disease. A study on 3044 patients

**A.G. Taser, L. Marmadu, G. Savol, O. Simion, O. Teliu, M. Mihalas, M. Marmadu, E. Emergency Hospital of Arges County, Pitesti, Romania; 2University of Pitesti, Pitesti, Romania; 3University of Pitesti, Pitesti, Romania**

**Purpose:** The assessment of the abstinence rate (AR) in a cohort of nicotine addicted smokers who were administered pharmacological treatment together with psychological support is an important topic.

**Methods:** 3044 patients (pts.) participated in this study and were evaluated in three centers during the period August 2008 – March 2010. Investigators used standard forms, physical examination, Fagerstroem tests, etc. Pts. were adminis-
tered the following therapeutic regimens: nicotine patches 15 mg, or bupropion 150 mg, or varenicline 0.5 and 1 mg, all together with counselling and psychos support. The final evaluation was performed after 6 months.

**Results:** The therapeutic regimen with nicotine patches 15 mg in 179 pts. led to 34.27% AR; the bupropion 150 mg regimen in 2164 pts. led to 36.47% AR; the varenicline regimens of 0.5 and 1 mg in 701 pts. lead to an AR of 46.54%. In pts. with cardiovascular comorbidities, irrespective the therapeutic regimen, the AR was 46.56%. The AR in cardiovascular pts. treated with varenicline was 50.12%.

**Conclusions:** The overall results are encouraging. The administration on a large scale of this therapy would be a way of decreasing the prevalence of tobacco consumption, nicotine addiction and, subsequently, a reduction of the risk of cardio-
vacular disease related to smoking.

### Maternal age at childbirth is associated with changes in smoking status between late adolescence and early middle age: results from 22 years of follow-up

**A. Rosenblad, J. Leppert, G. Nilsson. Center for Clinical Research, Västerås, Sweden**

**Purpose:** To examine the association between maternal age at childbirth and changes in the child's smoking status between late adolescent and early middle age, a follow-up time of 22 years.

**Methods:** As a part of the Westman Cardiovascular Risk Factors Study (WIC- TROY), 7500 men at the age of 40 years and living in the county of Västman-
land, Sweden, were examined for the presence of cardiovascular risk factors, e.g. smoking status, during the years 1990-1999. Of these men, 761 individuals were found to have answered questions about smoking status at the time of their con-
scription examination (baseline) in the years 1969-1970. Further, for 687 of these individuals it was possible to get information about the age of their mother at birth. The 687 individuals were categorized as smokers (SS) or non-smokers (NN) at both baseline and follow-up, smoker at baseline but non-smoker at follow-up (SN), or non-smoker at baseline but smoker at follow-up (NS). Mother's age at childbirth was compared between the four smoking status groups using ANOVA as well as individuality between the SS, NS, and NN groups at one hand and the SN group at the other hand. P-values < 0.05 were considered statistically significant.

**Results:** The examined individuals were at a mean (SD) age of 18 (0.7) years at the conscription examination and 40 (0.5) years at the follow-up examination. Maternal age at childbirth according to smoking status at baseline and follow-up are given in the table. Maternal age differed significantly between the four smoking status groups (p < 0.002), with the SN group having the youngest mothers, mean (SD) 27.2 (6.1) years old, and the NS group having the oldest mothers, 30.2 (7.1) years old. Both the NS (p = 0.014) and the NN (p = 0.023) group had significantly older mothers than the SN group.

<table>
<thead>
<tr>
<th>Smoking status in late adolescence</th>
<th>Smoking status in early middle age</th>
<th>Maternal age at childbirth (years)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker (SS)</td>
<td>185 (26.9)</td>
<td>28.0 ± 6.7</td>
<td>0.203</td>
</tr>
<tr>
<td>Non-smoker (SN)</td>
<td>196 (26.5)</td>
<td>27.2 ± 6.1</td>
<td></td>
</tr>
<tr>
<td>Smoker (SN)</td>
<td>30 (4.4)</td>
<td>38.2 ± 7.1</td>
<td>0.014</td>
</tr>
<tr>
<td>Non-smoker (NN)</td>
<td>276 (40.2)</td>
<td>28.5 ± 5.9</td>
<td>0.023</td>
</tr>
</tbody>
</table>

**Conclusions:** Maternal age at childbirth is associated with changes in smoking status between late adolescence and early middle age. Smoking quitters have the youngest mothers while smoking starters have the oldest mothers.

### Diastolic function in patients with newly diagnosed primary hyperaldosteronism

**P. Jung, R. Dutton, G. Seemueler, B. Kramer, P. Schneider, M. Mueller, E. Fischer, F. Kurot, M. Reinecke, H.Y. Sohn on behalf of German Conn's Registry. University Hospital of Munich, Munich, Germany**

Hyperaldosteronism is an increasingly diagnosed cause of secondary arterial hypotension. On behalf of the German's Conn registry we studied the cardiac changes and in particular the diastolic function in patients with newly diagnosed Conn's syndrome.

**Methods:** In 71 patients (47 male, 52±12years) with a first diagnosis of primary hyperaldosteronism a complete echocardiographic examination was performed including measurement of the left atrial (LA) and left ventricular (LV) size, ejec-
tion fraction (EF) and mass (LVmass), ejection fraction (EF), early (E) and late (A) diastolic mitral inflow (A), deceleration time of the mitral E wave (DT), systolic and diastolic pulmonary vein flow (PVS and PVd) and isovolumic relaxation time (IVRT). In addition, the early (E') and late diastolic (A) movement of the mitral an-
ulus were assessed using tissue doppler imaging. The ratio E/A and E/E' were calculated in each patient. SPSS 19.0 was used for statistical analysis.

**Results:** The average systolic blood pressure was 144.5±9 mmHg, aldosterone renin ratio was 45.4. Abnormal LVmass or impaired systolic LV function was less frequent than diastolic dysfunction: 31 (43.7%) patients showed left ventricular hypotrophy, LV systolic function was abnormal (<55% EF) in only 2 (3%) pa-
tients. Diastolic dysfunction was defined as dilated LA size and typical changes of E/E' and/or E/A was present in 56 patients (78.9%). Mean LA diameter was 42.3±2mm, mean E/E' 9.4 and E/A 1.2. The mean ratio of PVS and PVd was 1.1.

**Summary:** Diastolic dysfunction is common and more frequent in patients with primary hyperaldosteronism than systolic dysfunction or LV hypotrophy.

### Association of sodium and potassium intake with burden of premature ventricular complexes in patients with essential hypertension

**M. Markelou, E. Zacharis, F. Panthenakis, G. Kechidiakis, K. Stokos, P. Vardas. Heraklion University Hospital, Heraklion, Greece**

**Purpose:** Premature atrial and ventricular complexes (APCs and PVCs) are commonly found in hypertensive patients. Experimental studies have shown that high salt intake may exacerbate arrhythmogenesis independently of left ventricular hypertrophy. We hypothesized that urinary sodium (UNa) and sodium/potassium ratio (UNa/K) are associated with APCs and PVCs in patients with essential hyper-
tension.

**Methods:** The study group included 189 patients with essential hypertension (110 male, aged 63±10 years) and well controlled blood pressure. UNa and potassium excretion were assessed (average of three 24-hour urinary sam-
plies). The APCs and PVCs burdens were determined by 24-hour Holter moni-
toring. Transthoracic echocardiograms were used to assess left ventricular mass index on each patient.

**Results:** The average SBP/DBP was 129.6±8/87.5±4.3mmHg. UNa, and UNa/K ratios were 132.6±68.8 mg/24 h and 3.2±1.4, respectively. Multivariate regression analysis revealed that PVCs burden was independently correlated with UNa/K (r = -0.48, p < 0.001). No significant correlation was found between APCs and UNa/K.

**Conclusions:** A higher UNa and UNa/K excretion ratio is independently associated to PVCs burden in patients with essential hypertension. This may provide the basis to determine additional beneficial effects of reduced salt consumption in patients with essential hypertension and increased ventricular arrhythmogenesis.

### Right ventricular diastolic function in hypertension: role of biventricular remodeling, metabolic and inflammatory parameters

**C. Mongiardi, A.M. Maresca, C. Marchesi, F. Antronri, V. Vacirca, L. Merletti, A. Bertolini, A.M. Grandi, L. Guasti, A. Venco. University of Insubria. Department of Clinical Medicine, Varese, Italy**

**Objective:** Recent studies demonstrated that right ventricle (RV) diastolic function deteriorate in response to arterial hypertension. The pathogenic mechanisms are not completely elucidated. We investigated morpho-functional, metabolic and inflammatory parameters involved in RV dysfunction in hypertension.

**Design and method:** We enrolled 55 never-treated hypertensive patients (mean 24h BP = 125±8 and/or 80 mmHg) and 30 normotensives, similar for age (46±6 vs 44±6 years), gender and BMI (28±4 vs 28±4 kg/m²). All subjects underwent plasma measurement of leukocyte count, hs-CRP, lipid profile, glucose, HOMA and echocardiography.

**Results:** Mean 24h BP was higher in hypertensives (132±6 vs 115±6±7±3±5mmHg, P < 0.0001). Left ventricular (LV) end-diastolic diameter, volu-
Circadian chronotropic cardiac load as a risk factor of hypertrophy

**Objective:** To study the effect of chronotropic load, defined according to the daily ECG recording, on the risk of clinically significant complications of hypertension.

**Methods:** 110 patients with hypertension (46 women and 64 men), age 32 to 60 years (mean age 46.4±5.2 years), disease duration from 1.5 to 10 years (mean 6.2±0.1 years) were studied. In the follow-up the ECG monitoring was performed ("Astrocord", "Medtech", Russia) with the analysis of chronotropic load (CL) of the heart, which was taken as the percentage of time, exceeding the heart rate (HR) threshold, calculated as 45% of the maximum age HR. The follow-up was 7.0±0.2 years on average. During this period, the fatal and non-fatal complications of hypertension, regarded as the endpoint (EP) studies, were registered. As a “rigid” EP were identified: the verified myocardial infarction, the ischemic stroke, and the fatal cardiovascular (CV) event. The cases of unstable angina, revascularization, myocardial revascularization, coronary angioplasty, carotid and peripheral artery disease, hospitalization for worsening of hypertension, and transient ischemic attack, were taken as the “soft” EP. To identify the relationship between CL and the frequency of CV complications after adjusting for age, the linear regression analysis was used.

**Results:** The patients with hypertension were divided into two groups: the subjects with normal CL (<55%) chronotropic load - 33%, and the patients with high CL (>55%) chronotropic load - 77%. Along with the traditional risk factors of hypertension complications (family history of early cardiovascular disease, hypercholesterolemia, diabetes mellitus, ischemic heart disease, obesity, smoking) the prognostic value of the increased CL has been studied. The follow-up in 26 (28.9%) pts occurred cardiovascular and cerebrovascular adverse events (AE). At the beginning of the study pts with AE had greater: LVMI (192.3±37.4 g/m² vs 164.1±26.2 g/m², p < 0.05), left ventricular mass (374.3±85.0 vs 323.1±64.1 g, p < 0.01), septum thickness (14.8±3.0 mm vs. 13.3±2.1 mm, p < 0.05), posterior wall thickness (12.3±1.3 mm vs. 11.6±1.1 mm, p < 0.05) and left atrial diameter (41.9±6.3 mm vs. 39.2±4.4 mm, p < 0.05). In pts with AE QTc dispersion was greater than in pts without AE (70.6±19.3 ms vs 55.0±20.3 ms; p < 0.01). These pts had frequent premature ventricular beat per hour (p < 0.05) and during 24-hours Holter monitoring. The QTc dispersion greater than 60 ms was found in 20 (76.9%) pts with AE and in 26 (40.6%) pts without AE (p < 0.002). Using multiple linear regression analysis the best predictors of QTc dispersion were greater QTc dispersion and LVM (standardized coefficients: beta for QTc dispersion 0.289; p < 0.01 and for LVM 0.361; p < 0.001) and the model: R = 0.49, R² = 0.240, adjusted R² = 0.223, standard error of the estimate = 0.046181; p < 0.001).

**Conclusions:** Patients with greater QTc dispersion, especially greater than 60 ms, and greater left ventricular mass index have worse outcome during the ten years period of regular medical treatment.

**P3554**

The predictive value of non-invasive parameters in patients with left ventricular hypertrophy - ten years of follow-up

**Objective:** To study the correlation between non-invasive parameters and occurrence of unfavorable cardiovascular events in patients with left ventricular hypertrophy (LVH) during the ten years of follow-up. Patients used regular antihypertensive therapy during the period of follow-up.

**Methods:** Ninety pts were examined (55.2±8.3 years: 56 male and 34 female) with AH and LVH. All pts were examined by means of echocardiography (two independent examiners - Akouch-Seqoia), exercise testing, 24-h Holter monitoring, 24-h ambulatory blood pressure monitoring, heart rate variability, ventricular late potentials, spectral turbulence analysis and QTC interval dispersion.

**Results:** Average left ventricular mass index (LVM) was 171.9±32.4 g/m² and duration of hypertension was 12.3±7.9 years. During the ten years period of follow-up in 26 (28.9%) pts occurred cardiovascular and cerebrovascular adverse events (AE). At the beginning of the study pts with AE had greater: LVM (192.3±37.4 g/m² vs 164.1±26.2 g/m², p < 0.05), left ventricular mass (374.3±85.0 vs 323.1±64.1 g, p < 0.01), septum thickness (14.8±3.0 mm vs. 13.3±2.1 mm, p < 0.05), posterior wall thickness (12.3±1.3 mm vs. 11.6±1.1 mm, p < 0.05) and left atrial diameter (41.9±6.3 mm vs. 39.2±4.4 mm, p < 0.05). In pts with AE QTc dispersion was greater than in pts without AE (70.6±19.3 ms vs 55.0±20.3 ms; p < 0.01). These pts had frequent premature ventricular beat per hour (p < 0.05) and during 24-hours Holter monitoring. The QTc dispersion greater than 60 ms was found in 20 (76.9%) pts with AE and in 26 (40.6%) pts without AE (p < 0.002). Using multiple linear regression analysis the best predictors of QTc dispersion were greater QTc dispersion and LVM (standardized coefficients: beta for QTc dispersion 0.289; p < 0.01 and for LVM 0.361; p < 0.001) and the model: R = 0.49, R² = 0.240, adjusted R² = 0.223, standard error of the estimate = 0.046181; p < 0.001).

**Conclusions:** Patients with greater QTc dispersion, especially greater than 60 ms, and greater left ventricular mass index have worse outcome during the ten years period of regular medical treatment.

**P3553**

Insulin-like growth factor-1 and left ventricle remodeling in patients with essential hypertension and type 2 diabetes mellitus

**Objective:** The work was aimed to study an influence of insulin-like growth-factor-1 (IGF-1) on the left ventricle remodeling in patients (pts) with essential hypertension (EH) combined with or without type 2 diabetes mellitus (DM).

**Materials and methods:** 67 pts with EH of the 3rd degree combined with type 2 DM and 47 pts with EH of the same degree but without type 2 DM (control) were examined. The study group included 20 healthy persons. The patients were examined by means of laboratory and ECG, echocardiography and holter monitoring. The IGF-1 blood level was measured in pts with EH and without type 2 DM (184.6±6.9 ng/ml) compared with the pts with EH and type 2 DM (149.2±8.76 ng/ml) (p < 0.05) as well as healthy persons (158.8±9.12 ng/ml) (p < 0.05). There was insignificant difference in IGF-1 level between the pts with EH and type 2 DM and healthy persons (p < 0.05). The relationship between IGF-1 blood level and atype of the left ventricle hypertrophy (LHV) was revealed. Thus, the pts with EH and without type 2 DM but with concentric type of the LHV had significantly higher IGF-1 blood level compared with eccentric type of the LHV (−156.9±11.92 ng/ml vs (142.0±13.60 ng/ml) (p < 0.05) for the pts with combination of Eland type 2 DM as well as (172.0±16.62 ng/ml vs (176.5±15.37 ng/ml) (p < 0.05) for the pts with E/E' < 5 and type 2 DM. Left ventricular ejection fraction (LVEF) was revealed to be higher in concentric than in eccentric type of the LHV (0.61±0.17, 0.94 vs 0.80±0.06) for the pts with EH but without type 2 DM (p < 0.05) and type 2 DM (p < 0.01) as well as for the pts with type 2 DM and LVEF was found in pts with EH and type 2 DM (r = 0.46; p < 0.01) as well as in pts with EH but without type 2 DM (r = 0.43; p < 0.05).

**Conclusion:** Duet the obtained data IGF-1 was concluded to be involved in pathological heart remodeling in pts with EH and type 2 DM as well as without DM. The elevated IGF-1 – blood level was associated with development of concentric LHV but lowered one was associated with eccentric type of the LHV. The revealed positive correlation between IGF-1 and LVEF in pts with EH and with and without type 2 DM evidenced for the role of IGF-1 in growth factor in supporting of normal heart contractility. A deficiency of IGF-1 production in pts with EH and with or without type 2 DM may promote todevolution of chronic heart failure, particularly in pts with EH and type 2 DM.
Conclusions: Right ventricular functional alterations can be identified by TDI imaging in hypertensives with left ventricular hypertrophy. TDI imaging unmasks subtle changes in the diastolic function of the right ventricle.

**P3557 Impact of gestational hypertension on right ventricular function**

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**Background:** Gestational hypertension is a systemic hypertension that develops during gestation in young women. It is characterized by increased left ventricular mass and diastolic dysfunction. The effect of gestational hypertension on right ventricular (RV) function in previously normotensive young women has not been well evaluated.

**Methods:** A total of 40 gestational hypertensive women (28.6±3.2 years) and 30 normotensive women (29.3±4.7 years) were enrolled. Transthoracic echocardiography including 2-dimensional strain echocardiography was done.

**Results:** Gestational hypertensive women had significantly increased wall thickness (interventricular septum, 9.9±0.8 mm vs. 8.6±1.0 mm, P<0.001; posterior wall, 9.8±1.1 mm vs. 8.5±1.1 mm, P<0.009) of the left ventricle (LV), higher LV mass index (96.1±13.3 g/m² vs. 86.1±15.5 g/m², P=0.06) and lower E/A ratio (1.00±0.09 vs. 1.27±0.33, P=0.008) compared to normotensive women. Global longitudinal LV strain, representing LV systolic function, was also significantly reduced in gestational hypertensive women compared with normotensive women (−18.2±2.5%) vs. −21.0±2.6%, P=0.03). Early and late diastolic tricuspid annular tissue velocity (early, 7.5±3.1 mm/sec vs. 12.8±2.6 mm/sec, P<0.001; late, 7.0±3.0 mm/sec vs. 10.9±2.9 mm/sec, P=0.006) and tricuspid annular plane systolic excursion (6.2±4.1 mm vs. 13.3±5.9 mm, P<0.001) were significantly reduced in gestational hypertensive women compared with normotensive women.

**Conclusions:** Gestational hypertensive women had aggravated diastolic and longitudinal systolic dysfunction. LV mass index increased in gestational hypertensive women compared with normotensive women. Systolic and diastolic function of the RV were reduced in gestational hypertensive women compared with normotensive women. The reversibility of these morphological and functional impairments after delivery needs to be clarified.

**P3558 Left atrial function evaluated by color Doppler tissue imaging is deteriorated from the very early stage of the disease in non-dippers**

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**Background:** We tried to assess the effects of diastolic and non-dipper status of hypertension on LA function in untreated diastolic and non-dipper hypertension.

**Methods:** A total 19 untreated diastolic hypertension patients (male 68%, mean age 46±10) and 15 untreated non-dipper hypertension patients (male 58%, mean age 47±10) were included. The patients whose night time systolic and diastolic BP did not decrease less than 10% were classified as non-dippers. Atrial strain and strain rate imaging were obtained at narrow sample volume. Peak strain rate were measured in late diastole in the basal septal, inferior, lateral and anterior walls of the atrium from the apical 4 and 2-chamber views.

**Results:** Maximal LA volume (Dipper:Non-dipper 24.6±3.51 vs. 35.7±3.00 mL/m², p<0.03), LA active emptying volume (Dipper:Non-dipper 4.48±1.90 vs. 6.03±1.16 mL/m², p<0.01), and LA active emptying fraction (Dipper:Non-dipper 29.43±10.21 vs. 35.74±8.39%, p<0.04) were increased in non-dippers. LA peak systolic and early diastolic velocities were significantly increased in non-dippers (21.6±2.5 vs. 19.9±1.5 cm/sec, p<0.001) as well as their ratio was between the two groups. The level of atrial fibrillation annulus, all of the diastolic measurements were altered in hypertensives (early diastolic velocity (cm/sec) 13.4±18.4 vs. 10.9±14.6, P<0.01, late diastolic velocity (cm/sec) 20.3±14.3 vs. 15.4±13.3, P<0.01, early to late diastolic velocity ratio 20.4±4 vs. 14.3±3, P<0.01). Systolic velocity did not differentiate between the two groups (16.3±3 vs 17±3, P=NS).

**Conclusions:** Right ventricular functional alterations can be identified by TDI imaging in hypertensives with left ventricular hypertrophy. TDI imaging unmasks subtle changes in the diastolic function of the right ventricle.

**P3559 Is orthostatic hypotension associated with arterial stiffness?**

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**Purpose:** Orthostatic hypotension (OH) has been identified as an independent risk factor for fatal and non-fatal cardiovascular events and also for all-cause mortality. A significant association with increased arterial stiffness (AS) was demonstrated in some studies. Our aim was to evaluate AS, vascualr wall thickness and left ventricular function in a group of patients with OH.

**Methods:** 76 patients were enrolled in the study (mean age 68.4±15.2 years, 64.6% men). OH was defined as a decrease in systolic blood pressure (BP) greater than 20 mm Hg and/or a decrease in diastolic BP greater than 10 mm Hg, within 3 minutes of standing. All patients underwent a complete clinical and echocardiographic evaluation, including pulsed tissue Doppler imaging (TDI). Systolic (Sm) and diastolic velocities (Em, Am) of the left ventricle were measured by TDI at the mitral annulus. The left ventricular ejection fraction (LVEF) was calculated using the Simpson's method. The carotid-ankle vascular index (CAVI) was used to assess AS. CAVI was measured from an electrocardiogram, phonocardiogram, brachial and ankle artery waveforms and calculated using a specific algorithm. Carotid artery intima-media thickness (IMT) was evaluated by carotid ultrasound.

**Results:** 11 patients (14.4%) had OH (group 1). The remaining 65 patients (85.6%) did not have OH and were considered controls (group 2). CAVI was significantly higher in group 1 patients compared with group 2 (9.46±0.77 vs 7.82±0.83 mm, p<0.001), with a 95% confidence interval of (1.02, 9.26). IMT thickness was significantly higher in group 1 patients compared with group 2 (0.79±0.08 vs 0.72±0.12 mm, P=0.006), with a 95% confidence interval of (0.11, 0.81). Sm, Em, and LV EF were not significantly different between the two groups. CAVI greater than 8.05 mm predicted the presence of OH with a sensitivity of 78% and a specificity of 73%. At the multivariate analysis, CAVI (p=0.001) and IMT (p=0.035) were identified as independent predictors of the presence of OH.

**Conclusion:** Cardio-ankle vascular index, indicating abnormal arterial stiffness, and intima-media thickness of the carotid wall seem to be associated with orthostatic hypotension.
Abnormalities of endothelial function assessed by augmentation index; comparison of takotsubo cardiomyopathy and acute coronary syndrome

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Background: Arterial stiffness, its non-invasive assessment by radial tonometry and analysis of the augmentation index (AI), is a possible marker of endothelial dysfunction. In this study, we investigated AI in patients with acute coronary syndrome (ACS) and in those with takotsubo cardiomyopathy (TC).

Methods: The patients of hospitalization in with ACS and TC were enrolled. Measures of brachial systolic pressure (DBP), diastolic pressure (DBP), central blood pressure (cBP) and AI were obtained within 12 hours of admission. A method had been described to non-invasively estimate central aortic blood pressure by calculating the augmentation index from the pulse wave pressure contour recorded from a radial tonometry (HEM-9000AT, Omron®).

Results: From June 2010 to June 2011, 92 patients were performed coronary angiography on emergency. Of these patients, 85 patients (71.8% males; mean age 71.0±12.9 years) were TC. In comparing TC with ACS, SBP (117.9±7.0 vs 128.8±2.4; p<0.029), dBP (64.3±3.2 vs 68.4±1.4; p=0.0275) and cBP (130.4±10.3 vs 133.9±10.2; p=0.016) were almost similar. However, AI (93.6±4.7 vs 71.6±2.0; p=0.003) was significantly higher in TC. All patients in TC with recovery of wall motion underwent follow-up pulsatile hemodynamics before discharge (median follow-up period 10 days from hospitalization), which revealed that high AI had been continued.

Conclusion: AI was persistently higher in patients with TC than those with ACS, suggesting possible role of endothelial dysfunction in the pathophysiological mechanisms of TC.

Hypertensive heart development is reliably and tightly associated with carotid media thickness and inner vessel diameter enlargement

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Nowadays most attention upon cardiovascular system remodeling processes in arterial hypertension (AH) is paid to the heart. There is more scarce information about significance of different types of vascular remodeling and their interrelation with hypertensive heart development.

Aim of the study: Assess separate changes in carotid intima and media thickness, inner vessel diameter and their interrelations with heart remodeling in women with AH.

Material and methods: 50 women at the age of 38-63 (46.9±4.5 yrs old) with AH grade 1-3, without additional risk factors were investigated. Ultrasound examination of the both common carotid arteries was conducted by LOGIC P5 PRO technology, School of Technology and Health, Stockholm, Sweden.

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Purpose: Elderly female hypertensives (EHF) are at high risk of heart failure. While arterial dysfunction has been shown to play a role, the mechanisms are not fully known. We hypothesized that central arteries of EHF exhibit increased arterial wall viscoelasticity, an important determinant of frictional energy losses.

Methods: Pressure and flow waveforms from the right common carotid artery were obtained in EHF (n=10; age 64±10 yr; systolic BP 153±11 mmHg) using Doppler ultrasound (Aloka 6600). Post-processing was performed using the numerical analysis package GNU Octave v3.2.3, applying methodology derived from a 3-element windkessel connected in series with a transmission line. This enables frequency-domain analysis of arterial wave travel, after Fourier decomposition of time-domain data into harmonic content, at multiples of a subject’s heart rate (i.e. the fundamental, first, second harmonic etc). In a perfectly elastic artery, arterial volume and pressure waves will travel in phase i.e. the phase shift is zero. If pressure leads volume, a negative phase shift arises which is indicative of increased visco-elasticity, a phenomenon that occurs at low frequencies.

Results: Strong correlations were seen between age and phase shift at low frequencies (p<0.05): first; ρ=0.70; second; ρ=0.77; p<0.01. Subjects ≥ 65 yrs (n=5) vs. ≤ 65 yrs (n=5) are shown in Fig 1 (asterisk denotes p<0.05). There was no correlation between blood pressure and phase shift.

Conclusions: Higher age is associated with greater visco-elasticity of central arteries in EHF's. Associated increased frictional energy losses are likely to add to the deranged cardiac loading seen in this patient group.
TARGET ORGAN DAMAGE BY HYPERTENSION

P3567

Nocturnal non-dipping of blood pressure in treated hypertensive patients and its association with target organ damage

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Purpose: Nocturnal non-dipping of blood pressure assessed by the ABPM have been noted as an adverse prognostic factor and is associated with target organ damage. It is variably modified by theantihypertensive medications. We studied

The paradoxical distribution of sleep apnea and arterial stiffness among hypertensive immigrants

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Purpose: Obstructive sleep apnea syndrome (OSAS) and essential hypertension (EH) are closely associated, while increased arterial stiffness is a marker of diffuse vascular disease. In light of the mass immigration of Eastern Europeans to Western Europe, we assessed the hypothesis that hypertensive immigrants would demonstrate elevated arterial stiffness compared to native hypertensive population, while we sought to investigate the prevalence of OSAS within this high risk population.

Methods: We studied 67 Eastern European immigrants with newly diagnosed untreated stage I-II EH (age = 51±5.15 years, 35 male, office blood pressure (BP) = 158±92 mm Hg), who immigrated to Greece within the previous two years and 61 untreated hypertensive native inhabitants, matched for age, gender, office BP and smoking status. All participants underwent polysomnography (apnea/hypopnea index >5) and arterial stiffness evaluation on the basis of carotid to femoral pulse wave velocity (c-f PWV) by means of a computerized method (Compilior SP), while metabolic profile and anthropometric data were assessed as well.

Results: Hypertensive immigrants compared to native ones demonstrated decreased prevalence of OSAS (9.1% vs 12%, p<0.014) and decreased levels of body mass index (29.3±4 vs 32.2±4 kg/m², p<0.05). There was evidence that c-f PWV was elevated in the group of immigrants (4.8±0.3 vs 7.2±0.5 m/sec, p<0.05). Immigrants also exhibited decreased waist circumference (94±3 vs101±2 cm, p<0.05). The two groups did not differ with regard to serum glucose and cholesterol levels (99±9 vs102±8 mg/dl and 226±40 vs 228±35 mg/dl, respectively, p=NS in both cases). Analysis of covariance revealed that the prevalence of OSAS and c-f PWV values remained statistically different between the two groups after adjustment for confounding factors (p<0.05).

Conclusions: In conclusion, hypertensive immigrants demonstrate lower prevalence of OSAS but they seem to have stiffer aorta compared to native hypertensives. Efforts should be directed at this vulnerable population focusing on putative mechanisms for this unfavourable and apparently paradox BP phenotype.

P3568

Diastolic function of right ventricle in patients with copd complicated hypoxic pulmonary hypertension

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In order to investigate the state of the right ventricular diastolic function in patients with pulmonary hypertension (PH) due to chronic pulmonary disease (COPD) we studied 45 male COPD patients (mean age 56±4.1 years) with PH. Fifteen healthy male subjects (mean 48±8±1.5 years) served as control. Methods included clinical examination, lung function tests, blood gases, pulsoxymetry, ECG, Doppler Echocardiography. Patients were divided into 2 groups: 1st group consisted of 21 patients with PH and without echocardiographic signs of cor pulmonale (right ventricular anterior wall thickness (RVWTT) -0.5cm and/or right ventricular dimension (RVD) -2.5cm), while 2nd group consisted of 24 patients with COPD complicated with cor pulmonale. According to right ventricular diastolic filling pattern the patients from group 2 were divided into two subgroups: with hypertrophic pattern and with pseudonormal one. Results are represented in the table.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control Group</th>
<th>Group 1</th>
<th>Group 2A</th>
<th>Group 2B</th>
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<tr>
<td>PA pressure (mm Hg)</td>
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<td>32±10</td>
<td>27±10</td>
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<tr>
<td>RVSP</td>
<td>15±4</td>
<td>18±4</td>
<td>20±4</td>
<td>22±4</td>
</tr>
</tbody>
</table>

Legend: *,**,***p<0.05, p<0.01, p<0.001 accordingly for comparison with control group; PA pressure mean, mean pulmonary arterial pressure; RVSP, total pulmonary vascular resistance; CI, cardiac index; SatO2, oxygen saturation; RVD, right ventricular dimension; RVWTT, right ventricular anterior wall thickness; E/A, early transmitral peak velocity to late peak velocity ratio; FAP, right ventricular isovolumic relaxation time; DT, deceleration time; FAF, fraction of atrial filling.

Thus, patients with COPD present with impaired right ventricular diastolic function. Possibly, both right ventricular hypertrophy and increased afterload account for this impairment.

P3569

The relationship between left ventricle mass, diastolic function and cytokine levels in patients undergoing renal artery stenting


Renal artery stenosis (RAS) may lead to left ventricle (LV) hypertrophy and diastolic dysfunction (DF) impairment through complex mechanisms: activation of cytokines and/or systolic and diastolic blood pressure (SBP, DBP) increase. This study aimed to assess interrelations between LV mass, DF and cytokines in patients undergoing renal artery stenting (PTA).

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/339/430794 by guest on 04 November 2018
Background: The Berlin questionnaire (BQ) has been validated in quantifying the risk for obstructive sleep apnea (OSA) in the general population. Despite the fact that the BQ is already commonly used as a screening tool also in hypertensive patients, its validity in such a population has never been formally tested. Aim of our study was to assess the sensitivity and the specificity of the BQ in the screening of OSA in a group of unselected hypertensive patients whose obstructive sleep disorder was diagnosed by PSG.

Methods: In this study 7286 men workers and employees, all were evaluated for the presence of hypertension (HTN). Then 500 subjects with confirmed HTN who had systolic blood pressure (SBP) ≥ 140 mmHg, and/or diastolic blood pressure (DBP) ≥ 90 mmHg, and/or using antihypertensive medications were included. They received an educational program including healthy lifestyle and self-care recommendations of hypertension management and control as well as training for accurate blood pressure measurement and home monitoring for two years. SBP, DBP, weight, and routine lab tests were measured for all hypertensive subjects before and after interventions. Paired-test, Generalized Estimation Equation (GEE) regression and ordinary linear regression (OLS) were used in statistical analysis.

Results: The comparison of SBP and DBP before and after the educational program showed significant reduction in SBP and DBP (-7.97±14.72 and -2.66±9.90) mmHg, respectively. A greater decrease occurred in DBP GEE regression showed SBP and DBP decrease about -0.115 and -0.054 mmHg/month while OLS showed 4.88 and 2.57 mmHg decrease in SBP and DBP upon adding each antihypertensive drug respectively.

Conclusion: SHIMSCO was effective in reducing SBP and DBP in hypertensive employees and workers. We conclude that implementing simple educational programs in which SHIMSCO can improve the management and control of hypertension and perhaps other chronic diseases.

DIAGNOSTIC BIOMARKERS AND ACUTE CORONARY SYNDROMES

P5373

Asymmetric dimethylarginine (ADMA) concentration in patients with ST-segment elevation myocardial infarction links with early ST-resolution

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ST-resolution in ECG has been identified as simple and rapid measurement of reperfusion in patients with ST-segment elevation myocardial infarction (STEMI). Asymmetric dimethylarginine (ADMA) competitively inhibits the generation of the endogenous vasodilator nitric oxide (NO) from L-arginine. Elevated plasma ADMA and the L-arginine-to-ADMA ratio have both been identified as independent risk markers for general cardiovascular morbidity and mortality. It was the aim of the
Serum microvesicle protein levels are associated with normal levels of high-sensitive cardiac troponin I at arrival (n=415, 16% ACS): AUC 0.659 for Cystatin C (p<0.001), 0.588 for CD169 (p=0.033) and 0.623 for AT3 (p=0.003).

Conclusions: Normal levels of hs-cTnI and 2% had undetectable levels (sensitivity: 98.0%, 95% CI: 96.0% to 99.0%). During the follow up period, 5.0% of all the patients with normal hs-cTnI levels at presentation (n=34, 6.0% of all patients with AMI, 21 with other diagnosis, p<0.001) in patients with elevated levels at presentation. ACS was diagnosed in 34% of patients, of whom 74.3% had positive hs-cTnI levels and 25.7% normal levels (sensitivity: 74.3%, 95% CI: 69.5% to 78.6%, NPV: 84.8%, 95% CI: 81.7% to 87.5%).

Results: Of 1141 patients in the study, 225 (20%) had AMI, of whom 99.6% had initially detectable hs-cTnI levels and 1 patient (0.4%) had undetectable levels (sensitivity: 99.6%, 95% confidence interval (CI): 97.6% to 100%, negative predictive value (NPV): 99.2%, 95% CI: 95.8% to 100%). This patient with undetectable levels and AMI was an early presenter (chest pain onset within 2h of presentation). Thus, NPV of undetectable hs-cTnI was 100% in late presenters (<2h). During the follow-up period, 1.5% of all patients with undetectable levels at presentation (n=2, 0 with AMI, 2 with other diagnosis) died, whereas in patients with detectable levels at presentation 9.7% died (n=88, 50 with AMI, 48 with other diagnosis, p=0.006). ACS was adjudicated as the final diagnosis in 33.3% of patients, of whom 98.0% had detectable levels of hs-cTnI and 2% had undetectable levels (sensitivity: 98.0%, 95% CI: 96.0% to 99.2%, NPV: 94.0%, 95% CI: 88.0% to 97.5%).

Conclusions: Undetectable levels of hs-cTnI have a very high NPV, even more so in late presenters, which may help to rapidly rule out the diagnosis of AMI. Patients with undetectable hs-cTnI in conjunction with other clinical information including 12-lead ECG, undetectable levels seem a very safe and effective tool to rule out AMI. Thereby, hs-cTnI levels may reduce the need of serial blood testing and avoid unnecessary hospital admissions.

Results: 89 patients (mean age 68±10 years) undergoing coronary angiography (CAG) were enrolled and divided into three groups: acute coronary syndrome (ACS, n=24), stable angina pectoris (SAP, n=42) and healthy people (Control, n=32) in the cross-sectional study. Each coronary risk factors and patients characteristic were evaluated. Plasma PTX3 levels were determined by ELISA (enzyme-linked immunosorbant assay) and other laboratory data were measured by standard laboratory methods. These Data were examined statistically. A cardiac event, which was defined as cardiac death, rehospitalization patients presenting to the ED with acute chest pain. The final diagnoses of AMI and ACS were adjudicated by two independent cardiologists using all available data including hs-cTnI (Roche) levels. Patients were followed during a mean period of 26 months.

Diagnostic biomarkers and acute coronary syndromes

P3574 Serum microvesicle protein levels are associated with acute myocardial ischemia

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Purpose: Acute coronary syndrome (ACS) is a major health problem, for which early detection is crucial and adequate diagnostic biomarkers are needed. Microvesicles are small vesicles in the plasma containing proteins and RNA that have been shown to be involved in ACS-related processes, like coagulation, tissue injury and apoptosis. Therefore we hypothesized that serum microvesicle protein levels can be used to diagnose acute myocardial ischemia in suspected patients.

Methods: Potential microvesicle protein biomarkers were identified with differential Q-proteomics in pooled serum samples of 30 ACS patients versus 30 sex- and age-matched controls. These biomarkers were evaluated retrospectively in a cohort of 54 ACS-suspected patients presenting to the emergency department. Microvesicles were isolated from frozen serum samples by ExoQuick isolation. Subsequently microvesicle protein levels were measured by Luminex-based multiplex panels. Protein levels were adjusted for total protein concentration and log transformed to allow for parametric analyses. Mean microvesicle protein levels were compared between ACS and non-ACS patients with patients' t-test and ROC curves were calculated for each marker. Subgroup analyses were performed for patients with troponin-negative levels at arrival.

Results: Of 168 patients, 168 (31%) were diagnosed with ACS. The mean microvesicle protein concentration was significantly higher for Cystatin C (2.3, ±2.08±0.03, p<0.001) and CD169 (2.48±0.04 vs. 2.58±0.03, p=0.043) and significantly lower for anti-atherothrombin 3 (AT3) (4.87±0.07 vs. 5.14±0.05, p<0.001) in patients with ACS compared with non-ACS. The area under the curve (AUC) of the ROC curve was 0.640 for Cystatin C (p<0.0001), 0.557 for CD169 (p=0.051) and 0.601 for AT3 (p<0.001). This relation was stronger in patients with negative troponin at arrival (n=415, 16% ACS): AUC 0.659 for Cystatin C (p<0.001), 0.588 for CD169 (p=0.033) and 0.623 for AT3 (p<0.003).

Conclusions: These data show for the first time that serum microvesicle protein content is associated with acute myocardial ischemia. These observations should be validated in larger prospective studies assessing the added value of microvesicle content to current biomarkers of ischemia.

P3575 Normal levels of high-sensitive cardiac troponin I at presentation in patients with acute chest pain

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Purpose: The aim of this study was to evaluate whether normal levels (≤99I) of high-sensitive cardiac Troponin I (hs-cTnI) can be used as a single variable to rule out acute chest pain of acute myocardial infarction (AMI) as well as acute coronary syndrome (ACS) at presentation to the emergency department (ED).

Methods: In an ongoing prospective, international, multicenter study levels of hs-cTnI were analyzed using a pre-commercial assay (hs-cTnI, Beckman & Coulter). The performance of hs-cTnI was assessed at the center of acute chest pain. Patients were followed for a median period of 26 months. The final diagnoses of AMI and ACS were adjudicated by two independent cardiologists using all available data including hs-cTnI (Roche) levels.

Results: Of 1141 patients in the study, 225 (20%) had AMI, of whom 99.6% had initially detectable hs-cTnI levels and 1 patient (0.4%) had undetectable levels (sensitivity: 99.6%, 95% confidence interval (CI): 97.6% to 100%, negative predictive value (NPV): 99.2%, 95% CI: 95.8% to 100%). This patient with undetectable levels and AMI was an early presenter (chest pain onset within 2h of presentation). Thus, NPV of undetectable hs-cTnI was 100% in late presenters (<2h). During the follow-up period, 1.5% of all patients with undetectable levels at presentation (n=2, 0 with AMI, 2 with other diagnosis) died, whereas in patients with detectable levels at presentation 9.7% died (n=88, 50 with AMI, 48 with other diagnosis, p=0.006). ACS was adjudicated as the final diagnosis in 33.3% of patients, of whom 98.0% had detectable levels of hs-cTnI and 2% had undetectable levels (sensitivity: 98.0%, 95% CI: 96.0% to 99.2%, NPV: 94.0%, 95% CI: 88.0% to 97.5%).

Conclusions: Undetectable levels of hs-cTnI have a very high NPV, even more so in late presenters, which may help to rapidly rule out the diagnosis of AMI. Patients with undetectable hs-cTnI in conjunction with other clinical information including 12-lead ECG, undetectable levels seem a very safe and effective tool to rule out AMI. Thereby, hs-cTnI levels may reduce the need of serial blood testing and avoid unnecessary hospital admissions.
for ACS, rehospitalization for worsening heart failure, or coronary restenosis, was monitored for 12 months after admission. Statistically, plasma PTX3 levels were higher in ACS patients (7.3±10.0ng/ml) than in SAP (2.5±1.0ng/ml) and healthy controls (9.5±1.5ng/ml) (P<0.05). An increase was observed between SAP and Control patients. hsCRP (high sensitive C-reaction protein) and BNP (brain natriuretic peptide) were significantly increased in ACS patients over SAP patients and Control patients. Additionally, serum adiponectin levels were significantly decreased in ACS patients over other groups (5.6±3.3μg/ml, 7.9±4.1μg/ml vs. 8.2±3.4μg/ml, P<0.05). Furthermore, a total of 13 (13%) cardiovascular events occurred during the 1 year follow-up period. The cardiovascular event rate was higher in patients with increased PTX3. A Kaplan-Meier analysis revealed that patients with increased PTX3 had a higher risk for cardiac events than those without (P<0.05).

Conclusion: This study shows that measurement of plasma PTX3 may be considered to be a sensitive and specific biomarker for diagnosis of ACS and may substantially improve the early risk stratification of patients with coronary artery disease, and suggests a possibility that plasma PTX3 level may become one element which predicts a cardiovascular event.

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**P3578 Economic benefit of copeptin for rapid rule out of acute myocardial infarction**

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**Purpose:** In five independent recent studies including more than 2900 patients the combination of cardiac troponin (cTn) and copeptin resulted in a very high negative predictive value (≈99%) for acute myocardial infarction (AMI) already at presentation. The purpose of this international multicenter study was to quantify the operational and economic benefit of copeptin for early rule out of AMI.

**Methods:** All consecutive chest pain patients presenting to the emergency department (ED), levels of copeptin and cTnT were measured at presentation. Time to discharge and treatment costs in the ED were determined for each patient followed by the real current guideline-based algorithm including retesting of cTnT after 6 hours and a new simulated, investigational algorithm, which ruled-out AMI in patients who had undetectable levels of cTnT (cTnT (<0.01ng/ml) and copeptin levels >9pmol/l at presentation.

**Results:** AMI was the adjudicated diagnosis in 199 patients (16%). As compared to the guideline-based algorithm, the investigational algorithm allowed an early rule out of AMI in 573 patients (46%). Overall, median time to discharge from the ED was reduced from 350 minutes (Interquartile range [IQR], 206 to 480 minutes) to 90 minutes (IQR, 90 to 350 minutes) (p<0.001). The mean treatment cost was 12.685 per patient using the current guideline-based algorithm. The additional use of copeptin resulted in a 24% reduction of the total treatment cost (mean reduction: 3128; 95% confidence interval, 291-3325) (p<0.001). Sensitivity analysis revealed that the cost reduction was robust.

**Conclusions:** The additional use of copeptin provides substantial operational and economic benefits in the early diagnosis and rule out of acute myocardial infarction in unsolicited patients with chest pain.

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**P3579 To examine the diagnostic accuracy of highly sensitive troponin assays using diagnosis based on the universal definition of myocardial infarction in the unsolicited emergency room population**

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**Objective:** To examine the diagnostic accuracy of highly sensitive troponin assays using in the unsolicited emergency room population.

**Methods:** This study was a single study of the point of care of the RATPAC trial (Randomised Assessment of Treatment with Anion-Pressing Cardiac markers), set in the emergency departments of six hospitals. Prospective admissions with chest pain and a non-diagnostic electrocardiogram were randomised to point of care measurement 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 3 different methods, the Stratus CS (CS) Beckman Accu I (b), the Siemens ultra (S) and the Roche COBAS (R). In parallel, the copeptin release kinetic in patients with acute myocardial infarction within the first minutes after onset of chest pain, therefore, in the present study aimed we aimed to analyze the release kinetic of copeptin and cTnT measured with high-sensitivity assay in patients with hypertrophic obstructive cardiomyopathy (HOCM) undergoing transcoronary ablation of septal hypertrophy (TASH) as a method uniquely offering a clearly defined onset of infarction.

**Results:** Using the 99th percentile cut off point for a healthy population copeptin levels raised steadily after induction of myocardial infarction and were significantly increased after 75 minutes (22.7 pmol/ml IQR [15.9-48.6] vs. 8.95 pmol/ml IQR [6.1-11.4], P<0.001). Copeptin levels returned to baseline values after 8 hours.

**Conclusion:** Copeptin levels showed a continuous rise after TASH during the first 75 minutes and a drop to baseline levels within 8 hours. These results demonstrate that copeptin should be only be used in the first hours after onset of chest pain.
Rapid rule out of acute myocardial infarction using undetectable levels of high-sensitive cardiac troponin I

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Purpose: This study sought to evaluate whether undetectable levels (<0.5ng/l) of high-sensitive cardiac Troponin I (hs-cTnI) can be used as a single parameter to rule out the diagnosis of acute myocardial infarction (AMI) as well as acute coronary syndrome (ACS) at presentation in the emergency department of patients with acute chest pain.

Methods: Patients presenting to the ED with acute chest pain where consecu-
tively enrolled in an ongoing prospective, international, multicenter study where levels of hs-cTnI (Siemens) were measured in a blinded fashion using a pre-commercial assay. The final diagnoses of AMI and ACS were adjudicated by two independent cardiologists using all available data including hs-cTnI (Roche) levels. Median duration of follow up was 26 months.

Results: Of the 1169 patients in the study and hs-cTnI levels available, 234 (20%) had AMI, of whom 232 (99.1%) had initially detectable hs-cTnI levels and 2 pa-
tients (1.2%) had undetectable levels (sensitivity: 98.9%, 95% confidence interval [CI]: 97.0% to 99.9%, negative predictive value: 95.6%, 95% CI: 93.7% to 99.9%). During the follow-up period, 3% of all patients with undetectable levels at presentation (n=5, 2 with AMI, 3 with other diagnosis) died. In comparison to that, in patients with detectable levels of hs-cTnI there was a very high negative predictive value with other diagnosis, p<0.007 died. ACS was diagnosed in 33.5% of the cases, of whom 96.7% had detectable levels of hs-cTnI and 3.3% had undetectable levels (sensitivity: 96.8%, 95% CI: 94.4% to 98.3%, NPV: 92.2%, 95% CI: 96.7% to 99.5%).

Conclusions: Undetectable levels of hs-cTnI as measured with this pre-
commercial assay have a very high negative predictive value, which may help to rule out the diagnosis of AMI. Using hs-cTnI levels in conjunction with other clinical information including 12-lead ECG, undetectable levels seem to be very safe and effective tool to rapidly rule out AMI. Our results support the hypothesis that hs-cTnI analyses may reduce the need of serial blood testing and unnecessary hospital admissions.

Which is the better cut-off for high sensitivity troponin T in emergency room?

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Background: The use of high sensitivity assays for troponin T (hs-cTnT) in the diagnosis of Acute Coronary Syndrome (ACS) among patients (pts) admitted to ED increases sensitivity, but may reduce specificity. Currently, the cut-off value of 14 pg/ml, representing 99% percentile of the distribution of a normal population, is recommended. However, this cut-off is based on a healthy, middle-aged popula-
tion, conversely patients in ED are often old and suffering of previous or current diseases.

Methods: We aimed at evaluating whether a different cut-off, based on the 99% percentile of the ED population without ACS, may improve the specificity of hs-cTnT for ACS in a heterogeneous population of 452 pts admitted to ED because of chest pain. HS-cTnT was measured from baseline samples. Diagnostic accuracy of biomarkers was evaluated by constructing Receiver-Operating Characteristic (ROC) curve and calculating Area Under Curve (AUC).

Results: Sixty out of 452 (13%) pts were discharged with a diagnosis of ACS. Of these, the manufacturer cut-off for the AUC was 0.784 (95% CI: 0.692-0.849). The AUC of the “new” assay was 0.786 (95% CI: 0.697-0.837) (p<0.04). The sensitivity for the new cut-off was very similar (76.7%, 95% CI: 68.7-82.4%) to the manufacturer cut-off (76.9%, 95% CI: 68.9-82.3%).Conclusion: In our population, the use of a different cut-off of hs-cTnT, based on the 99% percentile of the population not affected by ACS or cardiac disease in ED, did not improve the AUC. However they increased specificity to a value close to 100%. This may allow a faster rule-in for ACS, without the need of a second blood draw in such patients, also in the absence of ECG changes.

The additional value of a new generation of troponin assay: a real world emergency department study

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Purpose: Recent generations of troponin assays are more sensitive and troponin elevations frequently are found in patients without acute coronary syndrome. The aim of this study was to determine whether cut-off levels of cardiac troponin (cTnI) assay changes the clinical management of patients (pts) presenting to the Emergency Department (ED) and leads to more hospital admissions.

Methods: The new cTnI assay (Dimension Vista, Siemens) shows a substan-
tially increased diagnostic sensitivity for myocardial damage in comparison to the previous Dimension XRs assay (cut-off value for myocardial injury: 0.045 vs 0.15 pg/ml). From a clinical perspective, this assay may allow a faster rule-in for ACS, without the need of a second blood draw especially in patients with a history of diabetes, heart failure or other medical conditions. The new assay increases would not substantially alter the hospital admission rate. Importantly, 69 out of 838 pts (8.2%) were discharged with diagnosis of acute myocardial infarction instead of unstable angina based on the new generation assay.

Diagnostic biomarkers and acute coronary syndromes
**P3586** Absolute and relative changes in cardiac troponin T and I measured with three high-sensitive cardiac troponin assays in emergency department patients with non-coronary chest pain

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**Background:** The new generation of high-sensitive assays for cardiac troponin (hs-cTn) have lowered detection limits and improved sensitivity for acute myocardial infarction (AMI). However, many patients with non-coronary chest pain (NCCP) now present with hs-cTn concentrations above the 99th percentile. We scrutinized median values, early and absolute change concentrations of hs-cTn in NCCP patients.

**Methods:** In a prospective, international multicenter study, hs-cTn was measured with three high-sensitivity assays (hs-cTnT, Roche Diagnostics; hs-cTnI, Beckman-Coulter; hs-cTnI, pre-commercial prototype, Beckman-Coulter; hs-cTnT, pre-commercial prototype, Siemens) in a blinded fashion at presentation and serially thereafter in 849 unselected patients of which 603 were adjudicated as acute non-coronary chest pain patients by two independent cardiologists using all available information including hs-cTnT values.

**Results:** Three assays roughly 25% had presentation values above their respective cut-off values. Presentation values of patients with NCCP amounted to 0.007 mcg/l (IQR 0.003-0.013 mcg/l) for hs-cTnT; 0.005 mcg/l (IQR 0.003-0.009 mcg/l) (Beckman-Coulter) and 0.004 mcg/l (IQR 0.001-0.010 mcg/l) for hs-cTnT (Siemens). The 95th percentiles of relative and absolute changes in the first hour were calculated as 67.6%, resp. 0.005 mcg/l for hs-cTnT (Roche Diagnostics); 132.9%, resp. 0.017 mcg/l for hs-cTnI (Beckman-Coulter) and 170.0%, resp. 0.015 mcg/l for hs-cTnT (Siemens) (Figure 1).

**Conclusions:** The absolute and relative short-term changes of hs-cTn observed in this cohort of NCCP patients should help to define the optimal cut-offs for the early diagnosis of AMI. This additional criterion is key as 1 out of 4 patients with NCCP presents with hs-cTn levels above the 95th percentile.

**P3587** Acute coronary syndromes or myocarditis in young people: a difficult daily diagnostic challenge

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**Background:** Chest pain (CP) represents about 5% of admissions to emergency departments (ED), even in young people. Acute coronary syndrome (ACS) and myocarditis are among the most important diagnoses to rule out. Clinical and ECG findings are not specific for either condition and separating both diagnoses is a challenge.

**Aim of the study:** To evaluate the prevalence of ACS and myocarditis in young patients presenting with CP and elevated cardiac biomarkers to the ED and to determine the differences in their clinical presentation.

**Methods:** Retrospective study of all consecutive patients < 40 years old admitted to our ED from January 2009 to June 2011 for CP with elevated serum troponin concentration. All clinical, angiographic and cardiac magnetic resonance (CMR) data from the medical database was reviewed. Clinical follow-up was obtained to assess all cause mortality, myocardial infarction and re-hospitalisation for CP. Moreover, 17 patients had myocarditis, 17 presented with typical subepicardial subendocardial enhancement on CMR and 12 were diagnostically based on clinical presentation (6 had no complementary workup). 3 normal coronary angiogram and 3 inconclusive CMR. 8.1% (4/49) of patients had other diagnoses. Compared to patients with myocarditis, ACS patients were older (34.1±13.9 vs. 26.9±14.4, p<0.0002) with significantly more cardiovascular risk factors (mean 0.26 vs. 0.69, p<0.0001). Diabetes (18.8% vs. 0%, p=0.004), dyslipidaemia (56.3% vs. 3.4%, p<0.0001) and family history of coronary artery disease (CAD) (37.5% vs. 10.3%, p=0.050) were significantly associated with ACS.

**Results:** The serum resistin levels were higher in ACS and SAP patients than in healthy control (<0.001). In ACS patients, especially, the tendency was higher than SAP patients. The serum resistin levels were significantly different between ACS (10.5±4.5 ng/ml), SAP (7.7±4.1 ng/ml), healthy control (6.0±4.0 ng/ml) groups (<0.05), and hs-cTn (high-sensitive C-reactive protein), PTX-3 (pentraxin-3), BNP (brain natriuretic peptide) were significantly increased in ACS patients over SAP patients and healthy control (hs-cTn: 0.245±0.256ng/ml, 0.117±0.060ng/ml vs. <0.005, P<0.005, PTX-3: 7.3±10.9ng/ml, 2.5±1.0ng/ml vs. 2.9±1.5ng/ml, P<0.05, BNP: 245±215pg/ml, 81±160pg/ml vs. 62±140pg/ml, P<0.05). Additionally, serum adionipeptidase levels were significantly decreased in ACS patients over the other groups (5.6±3.3μg/ml, 7.9±4.1μg/ml vs. 8.2±4.3μg/ml, P<0.05). Furthermore, serum resistin levels showed a stepwise increase with the number increase of ≥ 50% stenosed coronary vessels.

**Conclusions:** Serum resistin levels in ACS patients, increased with inflammatory factors and myocardial impairment. These results suggest that increased serum resistin levels may be a marker of myocardial ischemia, and might play an important role in the pathogenesis and ACS as an inflammatory factor.

**P3588** Growth differentiation factor-15 concentration changes in coronary sinus of patients after percutaneous interventions - rapid secretion during reperfusion in STEM

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Growth differentiation factor-15 (GDF-15) is a stress-responsive protein from TGFβ superfamily that is expressed in cardiac tissue and secreted to serum in cardiovascular pathologies. It exerts antihypertrophic and cytoprotective effects, has been implied to take part in the inflammatory response of cardiac tissue. However, the precise dynamics of GDF-15 synthesis and local secretion remains largely unrevealed. We have undertaken a pilot study to assess the production of GDF-15 by human heart during ischemia and reperfusion.

**Methods:** For our study we selected very homogenous group of 10 patients (age 59.4±9.3) with first myocardial infarction (STEMI), no co-morbidities, total occlusion of proximal left anterior descending (LAD) artery and otherwise normal coronary arteries. The second group was composed of 7 patients with single vessel stable ischemic heart disease (IHD) scheduled for elective percutaneous coronary intervention (PCI) of proximal LAD. Blood was drawn from coronary sinus before and 20 minutes after PCI. Peripheral venous blood of 10 healthy volunteers served as control. Clinical and angiographic profile of all patients as well as biochemical measurements were collected. Plasma concentrations of GDF-15 and interleukin 6 (IL-6) were measured by ELISA. Statistical analysis was performed using non-parametric tests.

**Conclusions:** The absolute and relative short-term changes of hs-cTn observed in this cohort of NCCP patients should help to define the optimal cut-offs for the early diagnosis of AMI. This additional criterion is key as 1 out of 4 patients with NCCP presents with hs-cTn levels above the 95th percentile.

**Values as mean and interquartile range**

<table>
<thead>
<tr>
<th></th>
<th>GDF-15 before PCI</th>
<th>GDF-15 after PCI</th>
<th>IL-6 before PCI</th>
<th>IL-6 after PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n=10)</td>
<td>479 ng/L</td>
<td>1.9 ng/L</td>
<td>(416-554)</td>
<td>(1-1.7)</td>
</tr>
<tr>
<td>IHD (n=7)</td>
<td>456 ng/L</td>
<td>467 ng/L</td>
<td>(426-525)</td>
<td>(1.3-2.2)</td>
</tr>
<tr>
<td>STEMI (n=10)</td>
<td>294 ng/L</td>
<td>863 ng/L</td>
<td>(220-4166)</td>
<td>(43-941)</td>
</tr>
</tbody>
</table>

*p<0.05 vs controls and IHD, #p<0.005 vs before PCI.
Patients prone to premature atherosclerosis have elevated levels of circulating pro-atherosclerotic microparticles

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Purpose: Familial hypercholesterolemia (FH), a monogenic disorder characterized by a reduced expression of the LDL receptor, leads to the development of premature atherosclerosis and increases the risk of cardiovascular events. Circulating microparticles (cMPs) released from various cell types vary in different disease states and have been recently regarded as regulatory vectors of paracrine cross-talk. Interactions between blood and vascular cells are major factors in atherosclerosis progression. Therefore, cMPs might play an important role in vascular pathology. This study was aimed to investigate cell origin and phenotype of cMPs in patients with genetic diagnosis of FH.

Methods: Thirty seven FH patients and 37 age/gender-matched control subjects from the Spanish Familial hypercholesterolemia cohort study (SAFEHEART) were included in the study. cMPs were obtained from citrated platelet-free plasma (PPP) and quantitatively analyzed by flow cytometry for annexin V binding and specific blood cell surface markers. Activated monocyte- and platelet-derived MPs were selected.

Results: FH patients had significantly increased total numbers (2390 [1890-3416] vs 1872 [1418-2274] cMPs/μL PPP, p<0.005) and annexin V-positive cMPs in FH controls compared to controls (76% vs 61%, respectively, p<0.001). Endothelial-derived (CD14+CD62P+), cMPs significantly increased in FH compared to controls (p<0.005), whereas levels of cMPs from platelet (CD41+CD61+) and leukocyte (CD45+) origin did not change. In contrast, subpopulations of cMPs specifically derived from lymphocyte (CD45+CD45+), monocyte (CD14+CD14+) and monocyte (CD14+)-raised in FH patients (p<0.01 and p=0.0001, respectively).

Conclusion: Circulating MPs showed a pro-atherosclerotic profile in patients with FH. Thus, the specific increases in the pro-inflammatory and pro-thrombotic monocytic- and platelet-derived MPs subpopulations indicate that cMPs are not merely markers of cardiovascular risk. Indeed these results in FH patients suggest that cMPs may have a causal role in the progression of atherosclerosis.

Circulating Microparticles of patients with acute coronary syndrome carry a wide array of microRNA and mRNA with potential effect on pathophysiology and complication of these syndromes

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Aims: Circulating Microparticles (MP) are small vesicles released from activated cells. MP are increased in Acute Coronary Syndromes (ACS) but little is known about their content. We sought to characterize microRNA (miRNA) and mRNA expression in MP of ACS, stable angina (SA) and controls (C).

Methods: Samples from 21 ACS patients were studied. 10 patients with Non-ST Elevation Myocardial Infarction (NSTEMI) and 10 C without coronary artery disease were used for mRNA assessment. Total RNA was isolated from circulating MP and used for microarray and miRNA expression analysis. Total RNA from circulating MP of NSTEMI patients was mixed with a PCR-array system for the atherosclerosis and transcription factors pathways.

Results: The presence of 15 miRNAs, known to be involved in cardiovascular disease, was investigated. In NSTEMI patients, mir-205, miR-21 and miR-29b were from 20 to 35 fold higher than C. mir-1, mir-29a and mir-29c were from 50 to 135 fold higher in NSTEMI than C. 168 genes were investigated for mRNA expression. We also identified 19 modulated genes for the atherosclerosis pathway between the two groups (up- and 16 down-regulated in NSTEMI compared to SA).

Conclusions: The amount of variation explained by the first 5 PCs abstracted from the CEC gene expression profiles was 52%. At the same time, thrombolytic therapy was effective in 76.6% of patients with successful thrombolytic therapy (n= 57) than in those with failed thrombolytic therapy (n = 43) (11.63% vs. 47.65%, p<0.001). Furthermore, cMPs positive for markers of activated monocytes (CD14+CD14+) and lymphocytes (CD45+) did not change. In contrast, subpopulations of cMPs specifically derived from lymphocytes (CD45+CD45+), monocytes (CD14+CD14+) and monocytes (CD14+CD14+)-raised in FH patients (p<0.01 and p=0.0001, respectively).

Conclusion: Circulating MPs showed a pro-atherosclerotic profile in patients with FH. Thus, the specific increases in the pro-inflammatory and pro-thrombotic monocytic- and platelet-derived MPs subpopulations indicate that cMPs are not merely markers of cardiovascular risk. Indeed these results in FH patients suggest that cMPs may have a causal role in the progression of atherosclerosis.

Gene expression analysis of circulating endothelial cells in acute myocardial infarction

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Background: Circulating endothelial cells (CECs) line the coronary artery endothelium and are ultimately sloughed into detectable levels during atherosclerotic plaque rupture and myocardial infarction. Comparison of gene expression levels in these cells between those experiencing a myocardial infarction and those with intact coronary artery plaques may potentially identify cell types associated with coronary artery atherosclerotic plaque rupture.

Methods: Two 10 ml EDTA-containing vacutainer tubes were used to collect blood from 21 myocardial infarction patients prior to coronary artery catheterization and 22 age-matched healthy donors. CECs were isolated using the CellSearch system with the CellSearch CEC Profile kit. The total RNAs were isolated from CECs according to standard Trizol method. The quantity and quality of RNA was examined by NanoDrop 1000. 50 ng total RNA was first converted to labeled target cDNA using the Ovation RNA Amplification System V2. Subsequently, 3.75 μg of the purified cDNA underwent a two-step fragmentation and labeling process using the Enzymatic Labeling Module. Targets were hybridized to Affymetrix human U133 Plus 2.0 array. Following hybridization, arrays are washed and stained using standard Affymetrix procedures before scanning on the Affymetrix GeneChip Scanner and data extraction using Expression Console. Each probe set was considered a separate gene. Using the first 12 myocardial infarction subjects and 13 healthy age matched controls a database containing a training collection of approximately 54,000 expression patterns was created. Principal components (PCs) analyses of the CEC gene expression profiles were used to discriminate myocardial infarction subjects from healthy controls. Estimation of classification performance was then carried out in an independent set of 9 myocardial infarction patient and 9 healthy controls.

Results: The amount of variation explained by the first 5 PCs abstracted from the CEC gene expression data significantly exceeded the 4.5% seen in random permutation of this dataset and could be used to accurately discriminate an independent collection of 9 normal donors and 9 MI subjects. The area under the receiver-operating characteristic (ROC) curve for the classifier developed from the PC analysis was 0.9 suggesting that CEC gene expression profiles provide excellent potential for prognostic purposes.

Conclusions: Gene expression profiles isolated from CECs are promising for distinguishing MI events and the molecular signature may be useful for developing an assay for predicting MI.

Assessment of endothelial function allows prediction of the efficiency of thrombolytic therapy in patients with ST-elevation myocardial infarction

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Purpose: The purpose of this work was to evaluate predictors of the efficiency of thrombolytic therapy in patients with ST-elevation myocardial infarction (STEMI).

Methods: We included 1101 patients hospitalized in Hospital with STEMI who underwent thrombolytic therapy. We assessed endothelial function using the brachial artery flow mediated dilation (FMD) test, administered to patients on admission. The efficiency of thrombolytic therapy was estimated according to standard ECG criteria. We collected blood samples before starting the thrombolytic therapy, to determine the levels of high-sensitive C-reactive protein (hs-CRP) (n = 1018). We manufactured a prediction model based on the FMD test and hs-CRP.

Results: We found that the percentages of brachial artery dilation registered with the FMD test were significantly higher in patients with successful thrombolytic therapy (n = 57) than in those with failed thrombolytic therapy (n = 43) (11.63% vs. 47.65%, p<0.001). We included the FMD test and hs-CRP in our model. This model was successful in only 15.7% of patients whose FMD test results were less than 5%. At the same time, thrombolytic therapy was effective in 76.6% of patients with FMD test results in the 5–10% range. Finally, thrombolytic therapy was successful...
in 90.3% of patients with FMD test results greater than 10% (figure 1). Levels of hs-CRP were significantly higher in patients with failed thrombolytic therapy than in those with successful thrombolytic therapy (8.4±10.8 mg/l vs. 2.69±1.34 mg/l; p<0.001). We revealed that there was a significant inverse relationship between levels of hs-CRP and FMD test results (p=0.0006; Spearman ρ = (−0.52)).

Conclusions: The FMD test result and the level of hs-CRP were shown to be predictors of the efficiency of thrombolytic therapy. A significant correlation between these factors was observed.

PROGNOSTIC BIOMARKERS AND ORGAN DYSFUNCTION IN ACUTE CORONARY SYNDROMES

P3594 Prognostic value of admission serum albumin levels in patients treated with primary percutaneous coronary intervention

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Purpose: As a ligand for many endogenous and exogenous compounds, serum albumin accounts for most of the anti-oxidant capacity of plasma and affects pharmacokinetics of many drugs. We sought to investigate whether serum albumin level on admission has a prognostic value in patients with ST elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (p-PCI).

Methods: In a retrospective design, we evaluated 1576 patients treated with p-PCI for STEMI (between January 2006 – December 2008). The patients were divided into two groups according to the admission serum albumin levels, taking the cut-off value of albumin as 3.5 g/dl; i.e.; <3.5 g/dl (n=405) and ≥3.5 g/dl (n=1171). Short- and long-term clinical outcomes were recorded.

Results: Comorbidities such as diabetes mellitus and renal failure were more common and the ratio of subjects with advanced age and C-reactive protein levels were higher in the group with hypoalbuminemia. Postprocedural success with final TIMI grade 3 flow was less common in patients with hypoalbuminemia (83.2% vs. 91.1%, p<0.001). In-hospital death (9.1% vs 2.1%), heart failure (20.7% vs 5.0 vs 9.5% vs 9.5±5.2; p<0.014). In patients with cardiac troponin (91.1%, p=0.0001), 0.75 (p=0.0001) and lower mean hemoglobin values (p<0.001), Three vessel disease (p<0.001) and depression of left ventricular function (p<0.001) were more frequent in these pts, which were less often revascularized (p<0.001). In-hospital mortality (p<0.001) and M6 (p<0.001) were higher in these pts. The AUC’s of CysC, pBNP, CPR and RDW for M6 were respectively 0.84 (p<0.0001), 0.83 (p<0.0001), 0.75 (p<0.0001) and 0.64 (p=0.0036). There was no statistically significant difference between the PP of CysC and pBNP; however, CysC and pBNP had a stronger PP than the CRP and the RDW and had a stronger PP than the CRP and the RDW.

Conclusion: In this population of pts with ACS, the combination of analytic predictors increased the prognostic power. CysC and pBNP appear to be the strongest predictors, followed by CPR and RDW. These results are important in the evaluation of pts with ACS, complementing their risk assessment.

P3595 Younger age and PAI 5G/5G genotype are independently associated with the spontaneous recanalization of the infarct related artery in patients presenting with ST-elevation myocardial infarction


Purpose: Early spontaneous recanalization (SR) has favorable effects on outcomes and preservation of contractile function in patients with ST-elevation myocardial infarction (STEMI). Fibrinolytic activity is partially determined by the 4G/5G polymorphism encoding the promoter region of the gene encoding plasminogen activator inhibitor-1 (PAI-1) enzyme. In this study, we aimed to investigate the relationship of PAI-1 polymorphisms with early SR in patients presenting with STEMI.

Method: A total of 88 patients presenting with STEMI in the first 6 hours of their symptom onset were included in our study after taking written informed consent. Primary percutaneous coronary intervention (PCI) was performed to all patients. DNA isolation was done from collected venous blood samples. PAI-1 genotyping was performed with these samples according to real time PCR method. Post PCI 4th hour electrocardiograms (EKG) were scored due to Selvester method.

Results: Patients with occluded infarct related artery (IRA) (TIMI 0-1 flow) before PCI procedure were called as Group 1 (n=52) and open IRAs (TIMI 2-3 flow) were called as Group 2 (n=36). Group 2 patients were significantly younger (55.3±12.1 vs 60.7±12.2; p<0.041) and had more favorable 4th hour Selvester ECG scores (6.7±5.0 vs 9.5±5.2; p<0.014). In patients with PAI 5G/5G genotype, SR was significantly higher (63.0% vs 37.0%) (Table 1). In the logistic regression analysis, age (OR=0.970 [0.933-1.009 in 95% CI; p<0.05] and PAI 5G/5G genotype (OR=3.571 [9.889-12.920 in 95% CI; p<0.02) were independently associated with the patency of IRA.

Conclusion: PAI 5G/5G genotype and younger age are independently associated with IRA spontaneous patency of IRA in patients presenting with STEMI. Patients with open IRAs have more favorable 4th hour ECG scores. Auto-fibrinolytic activity may be one of the most important mechanisms responsible for the IRA and patients with PAI 5G/5G genotype seem to be luckier than others. Further studies are needed for more precise results.

P3597 Admission glycosylated hemoglobin is a predictor of mortality in non-diabetic patients with ST-segment elevation myocardial infarction treated by thrombolytic therapy

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Purpose: Acute hyperglycemia in diabetic patients presenting with ST-segment elevation myocardial infarction treated by thrombolytic therapy...
elevation myocardial infarction (STEMI) is associated with a poor short and long term prognosis. It is not well established whether this association exists only due to a hyperglycemia as an acute response to stress or whether it is related to a chronic glycometabolic disorder. Our objective was to evaluate the association between this chronic disarray and a worse prognosis in nondiabetic patients with STEMI, using the glycosylated hemoglobin (HbA1c).

Methods: The patients are participants of the Brasilia Heart Study Group, which briefly is a prospective cohort with consecutive patients within 24 hours of admission. STEMI. In this study, 205 patients without diabetes, with HbA1c levels < 5.5% and treated with tenecteplase were included. Patients were observed in a 2-years follow-up, and the primary outcomes observed in this study were early mortality (within the first 30 days of the disease), cardiovascular sudden death and new major coronary events (mainly new myocardial infarction).

Results: Intra-hospital mortality occurred in 4.3% and 7.1% of patients with lower and higher HbA1c levels, respectively (p < 0.03). New myocardial infarction (MI), fatal or nonfatal, occurred in 4.3% and 16%, and sudden cardiovascular death occurred in 4.3% and 17.3% of those with HbA1c lower and higher than 5.7% (P < 0.001).

Conclusions: Our study showed that the admission HbA1c levels for non-diabetic patients with STEMI have a strong prognostic value regarding mortality, both in thrombolyzed patients and in patients undergoing primary angioplasty. This findings demonstrates that the glycemicmetabolic disarray preceding the MI may be involved in the association between glycemia during MI and mortali mortality.

**P3598** Interleukin-6 as a predictor of cardiovascular events in patients with non-ST elevation acute coronary syndrome and troponin-negative

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**Purpose:** Acute coronary syndrome without ST segment elevation (NSTE-ACS) with troponin-negative is a challenging setting in clinical practice. In fact, these patients are considered at low-risk, however they have been shown an intra-hospital mortality as high as 12.7%. The aim of the present study was to explore the value of inflammatory biomarkers such as interleukin-6 and NT-proBNP in the prediction assessment of NSTE-ACS and troponin-negative, and to evaluate whether these biomarkers could improve the predictive performance of the established TIMI risk score.

**Methods:** This is a prospective, observational study in which consecutive patients presenting with NSTE-ACS and troponin-negative were recruited from two University Hospitals. A management according with the current guidelines was performed. TIMI risk score was calculated in all patients. Blood samples were collected on presentation for the determination of IL-6 and NT-proBNP, which were performed using electrochemiluminescence immunoassay (ECLIA) (Cobas® 6000 analyzer, Roche Diagnostics®, Mannheim, Germany). Clinical follow-up at 6 months was recorded. The primary end point was the composite of all-cause mortality, recurrent ACS, non-elective revascularization and/or admission to a coronary care unit. P values were corrected (pC) multiplying by the number of comparisons for new onset of heart failure.

**Results:** A total of 243 patients with NSTE-ACS and troponin-negative were prospectively studied. 35 patients (14.9%) presented adverse clinical events. Those with adverse clinical events were associated with both elevated levels of IL-6 (>12.52 ng/L) (35.3% vs. 16.4%, p=0.01) and NT-proBNP (76.7% vs. 50%, p=0.007). In low risk group, we observed a higher event rate in patients with elevated levels of IL-6 in ACS patients (p=0.042). Moreover, when multivariate adjustment, only IL-6 (>12.52 ng/L) was an independent predictor of adverse outcomes (HR: 2.43 [95CI: 1.05-5.64], p=0.038). The addition of IL-6 and history variables from TIMI risk score in these patients.

**Conclusions:** IL-6 is an independent predictor of adverse events in patients with NSTE-ACS and troponin-negative. Its use identifies a higher risk population in low risk patients according to TIMI risk score. This provides, together with history of IHD, a better discrimination and reclassification that achieved clinical risk variables from TIMI risk score in these patients.

**P3599** Sequential organ failure assessment (sofa) score is superior to multiple biomarkers for the risk stratification in patients with severe chest pain

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**Background:** Patients with chest pain requires urgent risk stratification in emergency room. Multiple biomarkers approach is one of the potential ways to evaluate prognostic information in the risk stratification of patients with acute coronary syndrome (ACS). The objective of the present study was to compare the established intensive care scores, the Sequential Organ Failure Assessment (SOFA) score and biomarkers in patients with respect to hospital mortality and unfavorable cardiac outcome in patients with chest pain.

**Methods:** We performed a prospective, cohort study at three hospitals. The plasma level of high sensitivity C-reactive protein, N-terminal pro-brain natriuretic peptide (NT-pro BNP), myeloperoxidase, white blood cell counts, creatinine, high-sensitivity C-reactive protein (hsCRP), troponin I (cTnI) and NT-proBNP were measured. COX-2 inhibition, elevated myocardial infarction (STEMI) is associated with a poor short and long term prognosis. It is not well established whether this association exists only due to a hyperglycemia as an acute response to stress or whether it is related to a chronic glycometabolic disorder. Our objective was to evaluate the association between this chronic disarray and a worse prognosis in nondiabetic patients with STEMI, using the glycosylated hemoglobin (HbA1c).

Methods: The patients are participants of the Brasilia Heart Study Group, which briefly is a prospective cohort with consecutive patients within 24 hours of admission. STEMI. In this study, 205 patients without diabetes, with HbA1c levels < 5.5% and treated with tenecteplase were included. Patients were observed in a 2-years follow-up, and the primary outcomes observed in this study were early mortality (within the first 30 days of the disease), cardiovascular sudden death and new major coronary events (mainly new myocardial infarction).

Results: Intra-hospital mortality occurred in 4.3% and 7.1% of patients with lower and higher HbA1c levels, respectively (p < 0.03). New myocardial infarction (MI), fatal or nonfatal, occurred in 4.3% and 16%, and sudden cardiovascular death occurred in 4.3% and 17.3% of those with HbA1c lower and higher than 5.7% (P < 0.001).

Conclusions: Our study showed that the admission HbA1c levels for non-diabetic patients with STEMI have a strong prognostic value regarding mortality, both in thrombolyzed patients and in patients undergoing primary angioplasty. This findings demonstrates that the glycemicmetabolic disarray preceding the MI may be involved in the association between glycemia during MI and mortali mortality.

**P3600** The endothelin-1 -974 C>A (rs3087459) and -1394 T>G (rs1800541) polymorphisms are associated with protective role in patients with acute coronary syndrome


**Background:** The inflammation plays an essential role in the development and progression of atherosclerotic lesions. The Endothelin-1 (ET-1) is considered a downstream estrogen gene in the inflammatory process regulation. This gene is a potent vasoconstrictor peptide produced by vascular endothelial cell. The ET-1 have proatherogenic activity and mediates smooth muscle cell proliferation via ET1 receptors, also acts a chemoattractant for monocyte, and induces platelet aggregation and the expression of adhesion molecules. The objective of this study was to test for association between ET1 gene polymorphisms and risk for ACS in Mexican patients.

**Methods:** The ET-1-974 C>A (rs3087459), ET-1-1394 T>G (rs1800541), and ET-1 Glu105Glu (rs5939) single nucleotide polymorphisms were analyzed in 453 patients with ACS and 283 healthy unrelated controls by S exoneuclease TaqMan assays in the Real time PCR. The differences between patients and healthy controls were evaluated by X2 Fisher’s exact test and Woolf method for odds ratio (OR). P values were corrected (pC) multiplying by the number of comparisons for new onset of heart failure.

**Results:** The data obtained showed a significant decreased frequencies of the -974 C allele (pC=0.01, OR=0.64) and -1394 G allele (pC=0.05 and OR=0.73) in ACS patients when compared to healthy controls. In addition, the analysis of the ET-1-1394 T>G showed a moderate decreased of the -1394 G allele (pC=0.05 and OR=0.73) in ACS patients when compared to healthy controls. On the other hand, the analysis of the linkage disequilibrium showed two out of five combinations (TGC and GAG) with significant differences between the study groups. The frequency of these haplotypes were decreased in patients with ACS when compared to controls (p<0.01, OR=0.18 and p=0.01, OR=0.31, respectively).

**Conclusion:** The results suggest that ET-1-974 C>A, ET-1-1394 T>G polymorphisms could be involved in the protective of developing acute coronary syndrome in Mexican patients.

**P3601** Serum adiponectin in patients with STE-elevation myocardial infarction treated with primary PCI: effects on myocardial reperfusion and infarct size

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**Background:** Aim of primary PCI is not only to open epicardial coronary artery, but to achieve optimal tissue reperfusion in STEMI pts. Numerous therapeutic strategies, including mechanical, biochemical and metabolic modulations, are under investigation in order to increase the success of primary PCI. Adiponectin, adipose-derived hormone, is one of them.

**Aim:** To analyze dynamic changes of serum adiponectin in patients with STEMI treated with prim PCI and its potential relation to myocardial reperfusion and infarct size.
Methods: In 90 patients with first anterior STEMI treated with prim PCI, serum adiponectin was measured on admission (before prim PCI), 48th and 7 days after prim PCI. In each patient following parameters were determined: final TIMI flow grade, STEMI treatment with reperfusion therapy (90 min after prim PCI) (marker of myocardial reperfusion) and peak CK-Mb (marker of infarct size).

Results: The highest level of adiponectin was on admission. 48th after PCI adiponectin dropped on the lowest level and on the 7th day it was higher, but did not reach the initial values (7.6±4.3 vs 4.39±3.25 vs 5.61±2.72 ng/mL; ANOVA: F=26.75, p<0.001). Final TIMI flow grade all patients were divided in two groups: group with TIMI flow ≥ 3 and group with suboptimal TIMI flow grade. Patients with suboptimal final TIMI flow had lower values of adiponectin on admission (5.22±3.32 vs 7.75±3.79, p=0.06), on 2nd day (2.41±3.1 vs 4.64±2.25, p=0.006) and 7th day (3.5±1.08 vs 5.77±2.55; p=0.019). In the whole study group adiponectin on admission and on 7th day positively and significantly correlated with percentage of STE recovery (r=0.29, p=0.01). When all patients were divided into two groups based on STE recovery, group with successful tissue reperfusion (ST-E recovery ≥ 50%) had higher levels of adiponectin in all time points compared to group without successful tissue reperfusion (ST-T recovery ≤ 50%) (Adipo 1st day: 8.80±4.02 vs 6.55±2.83; Adipo 2nd day: 5.06±2.43 vs 3.94±1.85; Adipo 7th day 8.54±2.58 vs 4.82±2.17; p<0.01, for all). In the whole study group peak CK-Mb correlated inversely with Adipo 2nd day (r=-0.25, p=0.021) and Adipo 7th day (r=-0.21, p=0.047).

Conclusion: Higher values of adiponectin in patients with ST-elevation myocardial infarction on admission, before PCI, and in the next following days after PCI are associated with higher rate of procedural success, better myocardial reperfusion and smaller infarct size. Whether adjunction therapy with adiponectin could have beneficial effects in these patients remains to be determined.

P3602 Soluble ST2 plasma levels are increased in acute coronary syndromes and predict long-term mortality

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Background: ST2 is an interleukin (IL)-1 receptor family member and is a receptor for IL-33. Elevated soluble ST2 (sST2) has been associated with an adverse short-term and long-term prognosis in non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation MI (STEMI), as well as long-term prognosis in patients with NSTEMI. In the present study we investigated a possible association of sST2 plasma levels and different clinical stages of coronary artery disease (CAD). In addition, we assessed the predictive value of sST2 levels in patients with stable angina, NSTEMI and STEMI.

Methods: We included 373 consecutive patients with angiographically proven CAD of whom 178 had stable angina, 97 had NSTEMI, and 98 had STEMI, respectively. Patients were followed for a mean of 42 months for the occurrence of a combined clinical endpoint (all cause death, MI and rehospitalisation for cardiac disease).

Results: sST2 plasma levels were significantly increased in patients with STEMI (median 453, IQR 313-688 pg/mL) as compared to patients with NSTEMI (269, IQR 157-496 pg/mL; p<0.001). In addition, patients with acute coronary syndromes had significantly higher levels of sST2 as compared to patients with stable CAD (169, IQR 79-260 pg/mL; p<0.001). During follow up, 37 (9.9%) patients died. sST2 plasma levels significantly predicted mortality in the total cohort (p<0.05). Cardiac events occurred in 66 (17.6%) patients. sST2 significantly predicted occurrence of the combined endpoint in patients with STEMI (p=0.003), but not with NSTEMI (p=0.35) or stable CAD (p=0.50).

Conclusions: Plasma levels of sST2 are increased in acute coronary syndromes. In addition, sST2 levels predict mortality in the total cohort and cardiac events specifically in STEMI patients.

P3603 Low T3 syndrome and myocardial damage in patient with ST-elevation myocardial infarction

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An altered thyroid hormone (TH) metabolism known as Low T3 syndrome (LT3S) is a frequent finding in patients with severe illness, including patient with acute myocardial infarction

Aim of this study is to evaluate the relationship between LT3S and the entity of myocardial damage in patients with ST-elevation myocardial infarction (STEMI)

Methods: 1295 patients (male: 73%; mean age: 66.1±12.5 years) admitted for STEMI, were included to early reperfusion therapy were included in this study. Total TH levels were determined in all patients at admission. Myocardial injury was assessed by peak troponin I (Tnl) levels. Brain natriuretic peptide (BNP) and echocardiographic left ventricular ejection fraction (LVEF) were used to describe myocardial dysfunction.

Results: A LT3S (T3 <2.2 pg/ml) at admission was observed in (N=228) 17% of patients. Subjects with LT3S had higher peak Tnl (86.9±88.0 vs 72.9±79.7 ng/mL, p=0.02), basal BNP (690.9±881 vs 218.7±329.5 ng/mL P<0.0001) and peak BNP (1055.4±1509.5 vs 464.0±607.8 ng/mL, P<0.0001) and had a lower ejection fraction (41.5±10.7 vs 44.9±9.5, P<0.0001).

Conclusions: Patients with LT3S have a greater degree of myocardial damage and higher myocardial dysfunction after STEMI. Further studies are needed to study the prognostic significance of LT3S in STEMI and the need for potential therapeutical strategies.
Methods: 289 patients with STEMI who treated primary PCI were enrolled to study. Patients were divided into two groups based upon the TIMI flow grade. No-reflow was defined as TIMI Grade 0, 1 and 2 flows (Group 1). Angiographic success was defined as TIMI 3 flow (Group 2). Uric acid, MPV and hs-CRP were measured. MACE were defined as in-stent thrombosis, non-fatal myocardial infarction and in-hospital mortality.

Results: There were 126 patients (mean age 63±11 and 71% male) in group 1 and 163 patients (mean age 58±12 and 80% male) in group 2. Uric acid, MPV, and hs-CRP levels on admission were higher in group 1 (p < 0.0001 for each). A uric acid level ≥5.4 mg/dl measured on admission had a 77% sensitivity and 70% specificity in predicting no reflow at ROC curve analysis. In-hospital MACE was significantly higher in group 1 (29% vs. 7%, p < 0.0001). At multivariate analyses, high plasma uric acid (OR 2.05, 95% CI 1.49–2.81; p < 0.0001), hs-CRP (OR 1.02, 95% CI 1.01–1.03; p = 0.0007) and MPV (OR 3.09, 95% CI 1.95–4.89; p < 0.0001) levels were independent predictors of no-reflow post primary PCI and uric acid (OR 2.75, 95% CI 1.93–3.94; p < 0.0001), hs-CRP (OR 1.01, 95% CI 1–1.02; p = 0.006) levels, but not MPV, were independent predictors of in-hospital MACE.
B-type natriuretic peptide is an early predictor of acute kidney injury in patients with acute coronary syndromes

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Purpose: The development of acute kidney injury (AKI) during acute coronary syndromes (ACS) is associated with increased morbidity and mortality. Given the slow kinetic of serum creatinine (sCr) changes, AKI is usually detected at least 48 hours after renal injury occurrence, thus precluding any possibility of targeted preventive therapy. Prediction of AKI would improve clinical decision-making and facilitate timely diagnosis and treatment, but specific early markers of AKI are still lacking. In ACS, both BAK and B-type natriuretic peptide (BNP) levels have been shown to be independently associated with cardiac and renal dysfunction. Therefore, we assessed whether BNP, measured at hospital presentation, is able to predict AKI development in ACS patients.

Methods: We measured serum BNP values and sCr in 384 patients with ACS (156 STEMI and 228 NSTEMI) at admission to our coronary care unit (CCU). Then, sCr was measured every day up to discharge. AKI was classified according to RIFLE criteria. BNP increase observed during the CCU stay (Acute Kidney Injury Network [AKIN] criteria): Stage 1 corresponds to an increase in sCr > 0.3 mg/dl from baseline; Stage 2 to increase in sCr > 2 to 3-fold from baseline; Stage 3 to increase in sCr > 3-fold from baseline or sCr > 4.0 mg/dl with an acute increase of at least 0.5 mg/dl, or need for renal replacement therapy (RRT).

Results: Overall, 46 (12%) patients developed AKI during hospitalization. They had a higher in-hospital mortality than patients without AKI (20% vs. 15%, P < 0.001). Of the 46 patients with AKI, 34 (74%) had a Stage 1, 3 (6%) a Stage 2, and 9 (20%) a Stage 3 AKI. BNP levels at hospital admission were higher in patients developing AKI than in those without AKI (575 ± 878 pg/ml vs. 261 ± 477 pg/ml; P < 0.001) and showed a significant gradient according to AKI severity (261 ± 477 pg/ml [No-AKI], 411 ± 478 pg/ml [Stage 1 AKI], and 1040 ± 1467 pg/ml [Stage 2-3 AKI]; P < 0.001). When BNP was evaluated, in terms of capacity to predict AKI, the area under the curve was 0.69 (95% CI 0.609 to 0.765; P < 0.001). The BNP cut-off, able to jointly maximize sensitivity and specificity for prediction of AKI, was 110 pg/ml (sensitivity 78%, specificity 56%).

Conclusions: This study confirms that, in patients with ACS, AKI is associated with increased in-hospital mortality. It also shows that BNP levels measured at hospital presentation seem to predict AKI development. Future studies should investigate whether patients at high-risk of AKI, identified on the basis of early BNP increase, may benefit from a targeted preventive strategy.

Cystatin C in acute coronary syndromes: predictor of prognosis independent of renal function?


Background: The glomerular filtration rate (GFR) is a good predictor of prognosis in patients (pts) with acute coronary syndrome (ACS). Cystatin C (CysC) is a new marker of renal function and appears to be more sensitive than GFR in assessing renal function. Recent studies have suggested that CysC may predict prognosis independently of GFR.

Purpose: To evaluate the prognostic impact of CysC in pts with ACS and normal GFR at admission.

Methods: Prospective study including 773 pts with ACS consecutively admitted to a coronary care unit over 2 years. The plasma concentration of CysC was evaluated on the first 24 h of admission and the GFR was estimated by the MDRD study equation. The pts with GFR > 60 ml/min/1.73m² were excluded. The pts with GFR < 60 ml/min/1.73m² were subdivided into two groups (G) according to the presence of elevated plasma CysC at admission (G1: CysC ≥ 0.95 mg/l; G2: CysC < 0.95 mg/l). The primary endpoint was 6 month mortality (M6).

Results: At admission, 66 pts (10.9%) were stratified in G1 and 541 (81.1%) in G2. Pts with elevated CysC at admission were older (p < 0.001), had higher prevalence of hypertension (p = 0.002) and lower prevalence of smoking (p = 0.007). These pts had more often history of myocardial infarction (MI) (p = 0.023), angina (p = 0.014), stroke (p = 0.001) and atrial fibrillation (p = 0.001). At admission, they had more often non-ST elevation MI (p = 0.01), higher Killip class (p = 0.001), lower mean hemoglobin values (p = 0.003) and higher mean values of C reactive protein and type B natriuretic peptide (p = 0.024 and p = 0.001 respectively). Three vessels disease (p = 0.022) was more frequent in these pts. M6 was higher in pts of G1 (G1 vs. G2: 13.3% vs. 1.6%; p < 0.001).

The elevation of CysC at admission was an independent predictor of M6 in multi-variable analysis (OR=2.8, 95% CI 1.10 to 3.3; p = 0.034).

Conclusion: In this population, elevated CysC on admission was associated with an increase of about four times in the risk of M6. This result can be explained by the detection of mild "renal dysfunction" not detectable by the estimation of GFR. However, it can also be explained by the capacity of CysC in predicting a worse prognosis independently of renal function. In both cases, it allows a better risk stratification and the adoption of more aggressive therapeutic strategies.

The impact of admission serum creatinine on contrast induced nephropathy and 1 year mortality in patients with ST elevation myocardial infarction underwent primary percutaneous coronary intervention

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Purpose: Chronic kidney disease (CKD) is associated with increased risk of adverse cardiovascular events, including contrast induced nephropathy (CIN) after percutaneous coronary intervention (PCI). But, prognostic significance of admission serum creatinine for CIN and mortality in patients with ST elevation myocardial infarction (STEMI) is not known. So, the aim of this study was to evaluate impact of admission serum creatinine on cardiovascular death and CIN in patients with STEMI underwent primary PCI.

Method: We analyzed 325 consecutive patients with STEMI underwent primary PCI. The patients were divided into two groups according to admission serum creatinine level; group I: ≤ 1.2g/dl (n=244, 75.1%), group II: >1.2 g/dl (n=81, 24.9%). Contrast-induced nephropathy was defined as an increase in serum creatinine level >25% or 0.5 mg/dl after 48 hours. We sought CIN and cardiovascular death at 12-month follow-up.

Results: Baseline clinical characteristics were similar between the two groups, except diabetic patients were more frequent in Group I (p=0.008). Group II was associated with a significantly higher rate of CIN (8.4% vs. 26.9%, p < 0.001) and increased in-hospital mortality of 6.6% vs. 18.8% (p < 0.001) compared with Group I. At 12-month follow-up, the death-free survival rate was significantly lower in the group II compared with group I (log rank test p < 0.001). Also, when each serum creatinine group was compared according to presence of CIN, 12-month death-free survival was significantly different between four groups (94.7% vs. 89.7% vs. 78.9% vs. 59.1%, log rank test p < 0.001) (Figure 1).

Conclusion: In STEMI patients treated with primary PCI, increased admission serum creatinine was strongly associated with 12-month mortality and CIN.

Oxygen Preconditioning Prevents Contrast-Induced Nephropathy

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Purpose: Contrast-induced nephropathy (CIN) is one of the independent predictors of long-term mortality in patients undergoing cardiac catheterization (CV angiography). Our preliminary study showed that sufficient oxygenation before the contrast administration did not increase the serum creatinine level. Therefore, oxygen preconditioning have a possibility to prevent kidney injury by improving ischemic condition in parenchyma renis. The purpose of this study was to assess the impact of oxygen preconditioning in preventing CIN for the patients undergoing elective CV angiography.

Methods: We studied 426 consecutive patients undergoing elective CV angiography and eligible patients were randomly assigned either to oxygen preconditioning (n=174) or to control (n=175) group. The oxygen preconditioning was administered 2 liter per minute of nasal pure oxygen from 15 minutes before the cannulation until at the end of procedure. Patient’s arterial blood was examined just before the procedure to assess blood oxygenation, and subsequent blood test at 2 days after the procedure to assess the occurrence of CIN. The primary end point was the incidence of CIN defined as an increase in serum creatinine concentration≥25% or 0.5mg/dl above the baseline level at 2days after CV angiography. The study was registered at UMIN-CTR with the identifier UMIN000007125.
Hepatocyte growth factor – a new marker for prognosis in acute myocardial infarction

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In our previous study, it was shown that hepatocyte growth factor (HGF) in the first few hours of MI (measured by RT-PCR) was significantly increased compared to healthy subjects. The aim of the present study was to investigate whether HGF plasma concentration in the first 24h of STEMI (ST segment elevation myocardial infarction), could be a biomarker for early diagnosis and prognosis of STEMI.

Materials and method: 73 STEMI patients and 11 healthy volunteers. In all the patients, we took blood samples for hHGF two times i.e. at admission to hospital and 24 hours later.

Results: The median value of hHGF in healthy volunteers was 666 pg/ml (576 - 760 pg/ml). In STEMI the highest values of HGF were observed in first measurement (Figure 1). An increase of 1 pg/ml in hHGF level increased STEMI odds ratio by 0.2% (Figure 2).

Conclusions: In acute myocardial infarction, out of known biomarkers, HGF rises the earliest and very promptly returns to normal values.

spouses of individuals with a nonfatal AMI were matched with 131,563 spouses of persons with a nonfatal, non-AMI hospitalization. Those whose spouse died of AMI (compared with a non-AMI cause) had increased use of antidepressants (Figure) and benzodiazepines relative to the year before the event. Those whose spouse had a nonfatal AMI (compared to a non-AMI hospitalization) had increased risk for antidepressant and benzodiazepine initiation (IRR 1.5 vs 1.1, and 6.7 vs 1.3, respectively, p < 0.001). Spouses of fatal AMI patients were also associated with increased risks of depression and suicide. Males whose spouse had a fatal or nonfatal AMI had a relatively increased risk of depression than their female counterparts.

**Figure 1.** Incidence rate ratios for pre-post utilization of antidepressants according to when the individual’s spouse died. The year prior to the event was used as reference.

**Conclusions:** Spouses of those who experience AMIs—both fatal and nonfatal—are at elevated risk for psychological consequences; therefore, the needs of these spouses need also be considered during routine clinical care.

**P3620**

**Age-dependent care and mortality (20 year) of 14,434 myocardial infarction patients: changes from 1985 to 2008**

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**Purpose:** To determine whether age-dependent inequalities in care and outcome changed over a 24 year period for patients admitted with a myocardial infarction (MI).

**Methods:** We examined four age groups (<55, 55-65, 65-75, and >75 years) and treatment and mortality in 14,434 consecutive patients admitted for MI to an intensive coronary care unit from 1985 to 2008. Temporal trend analyses were performed by comparing decades of admission (1985-1990 vs. 1990-2000 vs. 2000-2008).

**Results:** A total of 2040 (14%) of the patients were ≥75 years. Older patients were significantly less likely to receive evidence-based medical care and reperfusion therapy during the last 24 years, although the differences became smaller over time. In 2000-2008, 30-day (adjusted OR 0.28, 95% CI: 0.23-0.34) and 1-year mortality (95% CI: 1.68, 10.17, respectively) were significantly higher in Disaster group than in Non-Disaster group (68% vs. 43%, p < 0.05). Serum creatine kinase (CK)-MB level was significantly higher in Disaster group than in Non-Disaster group (69.9±11.0 vs 74.4±13.1 ng/mL, p < 0.05). Patients prescribed aspirin during the preceeding year (69.9±11.0 vs 74.4±13.1 ng/mL, p < 0.05). The mean age of patients was significantly younger than that of patients in the preceding year (69.9±11.0 vs 74.4±13.1 ng/mL, p < 0.05). Although the number of patients who underwent coronary revascularization was higher in Disaster group than in Non-Disaster group (68% vs. 43%, p < 0.05).

**Conclusions:** The rate of MI among the Disaster group was higher than in the Non-Disaster group. Males whose spouse died were at elevated risk for psychological consequences; therefore, the needs of these patients need also be considered during routine clinical care.

**P3621**

**Increased risk of myocardial infarction after the great East Japan earthquake**

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**Background:** On March 11, 2011, the Pacific coast of Tohoku district, northeast Japan was shocked by the most powerful known earthquake ever to hit Japan. The hospital located in this area struck by the Great East Japan Earthquake has played a central role in the treatment of cardiovascular diseases. Strong psychosocial stress is considered to be a precipitating factor in acute coronary events.

**Objective:** To assess the hypothesis that the incidence of acute myocardial infarction (AMI) and its severity was remarkably heightened after the great earthquake, we performed retrospective analysis of the clinical data which of patients with AMI admitted to our hospital during three-week period between March 11 and March 31, 2011 (Disaster group) by comparing those patients during the corresponding time period of 2010 (Non-Disaster group). Relative risks for AMI during this three-week period, the number of events in the three weeks including and after the earthquake and the three weeks before it in 2011 were compared with the numbers of the events the corresponding weeks in 2010 and 2009.

**Results:** The number of patients with AMI in Disaster group increased by about 3-fold (22 in Disaster group vs 7 in Non-Disaster group). Compared with 2010 of 2009, relative risks for AMI during three-week period in 2011 were 0.6 (95% confidence interval [CI]: 2.35, 15.65), 4.13 (95% CI: 1.68, 10.17, respectively). The mean age of patients was significantly younger than that of patients in the preceding year (69.9±11.0 vs 74.4±13.1 ng/mL, p < 0.05). The year prior to the event was used as reference.

**P3622**

**Long-term prognosis of patients with acute coronary syndrome and non-obstructive coronary artery disease**

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**Purpose:** Data from clinical trials have demonstrated that patients with acute coronary syndrome (ACS) and non-obstructive coronary artery disease (NO-CAD) are at elevated risk for subsequent atherothrombotic events. However, the incidence of ACS in the real world setting has been poorly investigated. The aim of this study was to evaluate the long-term outcome of patients with ACS presenting with non-obstructive CAD (NO-CAD) and the rate of prescription at discharge of aspirin and clopidrogrel according to guideline recommendations.

**Methods:** NO-CAD was defined as a <50% diameter stenosis identified by coronary angiography in any major epicardial artery. An age-matched control group was obtained from all patients presenting with ACS and undergoing percutaneous coronary intervention (PCI) due to obstructive CAD (O-CAD) within the same period. Patients were followed-up for one year. Major adverse cardiac events (MACE), defined as death, recurrent ACS leading to hospitalization, and non-fatal stroke were recorded.

**Results:** A total of 2614 ACS patients were screened, of whom 318 (12%) presented NO-CAD defined according to study criteria. The control group consisted of 688 patients presenting with ACS and O-CAD undergoing PCI. The incidence of MACE at 1-year follow-up was similar among NO-CAD and control group patients (9.7% vs 10.2%, P = NS). After adjusting for baseline characteristics, no difference was found in the rate of one-year MACE among the 2 groups. Aspirin was prescribed in 86.8% of patients with NO-CAD vs 99% of control group patients (p < 0.001). Clopidrogel was prescribed to 54.7% of NO-CAD patients and to 95.4% of control group patients (p < 0.001). Also the rate of prescription of statins was significantly lower among patients with NO-CAD, compared with O-CAD patients (74.2 ± 90.2%, p < 0.001). At 1-year follow-up, premature discontinuation of aspirin and/or thienopyridine was significantly more frequent among patients with NO-CAD compared with patients in the control group (25.8% vs 13.6%, p < 0.001).

**Conclusions:** Among patients with NO-CAD and with O-CAD have a similar high risk for long-term recurrent ischemic events. However, patients with NO-CAD are often undertreated, underscoring the need for aggressive medical management in these patients.
false positive activation for transferred patients with acute aortic dissection: experience from a large acute aortic dissection treatment center

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Purpose: Acute aortic syndrome (AAS) is a medical emergency that requires prompt diagnosis, transfer to a tertiary care facility and medical/surgical intervention. We sought to determine the incidence and etiology of false positive activation for AAS at Cleveland Clinic.

Methods: A total of 150 consecutive patients from our referral network, transferred to our CCU with an ED diagnosis of AAS from March, 2010 to August, 2011, were included. Clinical and imaging data were prospectively collected.

Results: Type A and Type B distribution AAS were diagnosed and confirmed in 63 and 70 patients respectively, and 17 patients (11.3%) had either no aortic pathology or no acute pathology on arrival. Patients with false activation were significantly younger and had a higher incidence of prior cardiovascular surgery (Table 1). Of the 17 false-positives, 5 (29.4%) had a history of aortic surgery or endovascular repair. Fifteen patients were initially misdiagnosed by CT scan and 10 (66.6%) of these patients required repeat imaging with an ECG-gated CT scan to present in the patient with multi-echo diabetic syndrome compared to the 9.7% in hospital mortality observed in the AAS group.

Conclusions: False positive activation for AAS is relatively common and is driven largely by inaccurate non-gated CT imaging. Establishing imaging protocols for suspected AAS and increasing community hospital access to ECG-gated CT scans may reduce the incidence of false positive activation and result in increased efficiency of a regional AAS network.

In-hospital outcomes with acute aortic dissection; multicenter registry analysis from Tokyo CCU network


Aims: Although International Registry of Acute Aortic Dissection (IRAD) evaluated the management and outcomes of Acute Aortic Dissection (AAD), it is still unclear among large cohort of Japanese patients with AAD. Tokyo CCU Network consists of 67 CCU sites in Tokyo, and those cover approximately 13 million people as night population in Tokyo metropolitan area. The aim of this study is to evaluate the in-hospital outcomes of Japanese patients with AAD in Tokyo.

Methods and Results: We analyzed ambulance transported consecutive 833 patients (520 male, aged 67.8±13.4) from Tokyo CCU network data cohort 2007-2009. In this registry, 364 patients were Stanford type A [Non-thrombosed type: 244 (67%), thrombosed type: 120 (33%)] and 469 were type B [Non-thrombosed type: 196 (42%), thrombosed type: 273 (58%)]. In the patients with type A AAD, 72.8% were received surgical treatment and 25.1% were managed conservatively. Among the patients who underwent surgery, 87.8% were operated within 24-hours. In the patients with type B AAD, 13.2% were received surgical treatment and 88.6% were managed conservatively.

In-hospital mortality was 15.7% in type A (Non-thrombosed type: 18.4%, thrombosed type: 10.0%) and 6.0% (Non-thrombosed type: 8.7%, thrombosed type: 4.0%). Especially in type A AAD, in-hospital mortality was 10.9% in patients received surgery and 27.0% in managed conservatively. Major causes of death were due to heart failure, dissection shock and multi-echo diabetic syndrome (A: 131±39mmHg vs. B: 159±39mmHg, p<0.001). Average initial BP was 147±41mmHg, and was different between type A (131±39mmHg vs. B: 159±39mmHg, p<0.001). Hypertension (systolic BP≥150mmHg) was more common in type B (A: 23.1% vs. B: 59.3%, p<0.001), and shock or tamponade (systolic BP<80mmHg) was more frequent in type A (A: 14.0% vs. B: 1.7%, p<0.001). Although initial BP had no relation to survival in type A (Survivor: 131±39mmHg vs. Non-survivor: 128±38mmHg, p=0.54), type B survival showed significantly higher BP in type A (Survivor: 160±39mmHg vs. Non-survivor: 159±37mmHg, p<0.05).

Conclusions: Multi-center registry conducted by Tokyo CCU network demonstrated better outcomes of AAD comparing with previous reports. Initial BP at ambulance dispatch can reflect type of AAD and become potential to predict high-risk cases requiring rapid transport and intensive cardiovascular management.

Hyperacute course of stanford type a acute aortic dissection: study of the patients with cardiopulmonary arrest on arrival

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Background: The natural history of thrombosed type aortic dissection or aortic intramural hematoma (IMH) is still controversial. Thetical courses of acute aortic dissection (AAD) during hyperacute phase before arrival to the hospital have to be clarified.

Methods and Results: Among consecutive 571 patients presenting to our hospital in the state of cardipulmonary arrest on arrival (CPMA)A and excluding injury or suicide from January 2010 to August 2011, 76 patientsunderwent CT study because of massive pericardial effusion detected by echocardiography which was performed for all CPMA patients at emergency room. Of the 76 patients, 41 patients (54%) werediagnosed as Stanford type A AAD. Of them, 21 patients were diagnosed as IMH and the remaining 20 patients as classic type A AAD. Among consecutive 61 alive AAD patients presenting to our hospital during the same period, 27 patients were diagnosed as Stanford type A, of whom 6 patients presented with IMH and 19 patients with ESL. The frequency of cardiac tamponade were higher in IMH than in PSL (6/8.75% vs. 4/19.23%, p=0.0007). The frequency of MIH was higher in CPAO in than in classic type A AAD patients (21/41.51% vs. 8/22.30%, p=0.007).

Conclusions: More than half of the CPAO patients with signifcant pericardial effusion were revealed to have AAD. Of them, thrombosis of MIH was higher than in the previous reports. The prognosis of IMHs not as good as expected.

Pericardial effusion in acute myocardial infarction: new insights from the French regional RICO survey

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Aim: Early post-acute myocardial infarction pericardial effusion are the major pericardial complications. We aimed to analyse the frequency, treatments, characteristics and prognostic significance of pericardial effusion (PE) following acute myocardial infarction.

Methods: From the French regional RICO survey database, all the patients hospitalised between January 1st 2001 and December 31st 2004 for an acute myocardial infarction from the 6 private or public center of Côte d’Or with echocardiographic examination were included in the study. The diagnosis of PE was made by echocardiography, which was performed within 48h after hospital admission. We included patients from pericardial effusion in acute myocardial infarction in the study, and patients without PE were compared at baseline and at follow-up.

Results: During the inclusion period, 8680 patients were included in the study, of whom 135 (1.5%) were diagnosed with PE. Patients with and without PE had similar risk factors, including age and sex ratio and time delays to admission. Interestingly, dyslipidemia and history of MI was less frequent in PE group (respectively 31 vs 45%, p=0.002 and 4 vs 13%, p=0.004). Plasma CRP levels on admission were markedly higher in PE patients (21 vs 6 mg/l, p=0.001). Prior chronic treatments were less frequent in PE group, in particular for aspirin (11 vs 19%, p=0.027), ACE inhibitor (10 vs 16%, p=0.014) and statin (15 vs 23%, p=0.054). Acute treatments were more frequent for BetaBlocker and were more used in patients without PE. Patients with PE were more likely to suffer from STEMI (76 vs 48%, p<0.01), and altered LVEF. Hospital complications such as death, or heart failure (12 vs 7%, p=0.016, 47 vs 38%, p=0.011), and mechanical complications including atrial fibrillation, wall rupture, apical thrombus and mitral regurgitation (respectively 20 vs 9%, p<0.001, 7 vs 5.5%, p=0.011, 8 vs 7.7%, p=0.011, and 8 vs 3%, p=0.03) were more frequent in PE group.

Conclusions: Our large study showed that, although PE is uncommon in the contemporary era of acute MI, this complication is still associated with worse short term prognosis, characterized by high rate of mechanical complications. Our works also suggest a preventive effect of some CV drugs against the development of PE following acute MI.
Acute coronary syndromes in Europe - where do we stand?
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Purpose: The aim of this study was to compare treatment strategies, complications and in-hospital mortality in patients (P) admitted with Acute Coronary Syndromes (ACS) in a Cardiology Department (CD) with the results listed in the ‘Euro Heart Survey - Acute Coronary Syndromes: snapshot 2009’ for the North- and Mediterranean Europe.

Methods: We conducted a retrospective, descriptive and correlational study, basing on a prospective registry, involving 1071 P consecutively admitted with ACS in a CD and data from 2008 to 2009. We evaluated baseline characteristics, strategies and therapeutic procedures, complications and in-hospital mortality. The results were compared with results from the Euro Heart Survey - ACS: ‘Snapshot 2009’. For statistical analysis we used SPSS 13.0.

Results: Table 1 represents the results of the three groups. The mortality rate (3.3% vs 6.1%, p = 0.005) and the end-point composite (death, re-MI or stroke) (4.2% vs 7.2%, p = 0.001) of our CD were lower than those found in the Mediterranean region. The mortality rate (3.3% vs 5%, p = 0.008) and the end-point composite (death, re-MI or stroke) (4.2% vs 7.2%, p = 0.001) of our CD were lower than those found in Northern Europe.

Table 1. Baseline characteristics, treatment strategies, complications and in-hospital mortality in P of our CD in Mediterranean (M) and in Northern Europe (NE)

<table>
<thead>
<tr>
<th>Events and in-hospital mortality</th>
<th>CD</th>
<th>M</th>
<th>NE</th>
<th>Overall (p)CD-NE</th>
<th>CD-NE (p)</th>
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<tr>
<td>STEMI (%)</td>
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<td>PCI, %</td>
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<tr>
<td>Death, re-MI or stroke, %</td>
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<td>Major bleed, %</td>
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<td>1.8</td>
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</table>

Conclusions: 1 - Our population had a cardiovascular risk profile overlapping with that of the Mediterranean region, but showed a lower rate of ischemic events and lower in-hospital mortality. 2 - Despite belonging to the Mediterranean region, this CD had rates of ischemic events and in-hospital mortality, lower than those obtained in the region of Northern Europe.

Relative occurrence and characteristics of type 1 versus type 2 myocardial infarction
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Purpose: The universal 2007 redefinition of myocardial infarction (MI) recommends that non-procedure related Mls should be classified as type 1 or type 2 MI. We wanted to assess the relative occurrence and characteristics of type 1 vs. type 2 MI.

Methods: From January to October 2010 patients (pts) admitted with a suspected MI were considered. Pts with at least one Troponin I (TnI) value tc5.00 ng/L and otherwise fulfilling the 2007 MI criteria were included (symptoms, rise/ fall in Tnl, imaging, ECG). Type 3-5 MI pts were excluded. Tnl was analyzed using Architect c16000 (Abbott Diagnostics). Within 24 hours of inclusion an investigator recapitulated the history. Mls were classified as type 1 or type 2 MI and as ST elevation MI (STEMI) or non-ST elevation MI (NSTEMI). For classifying type 1 vs. type 2 MI specific objective criteria for the mechanisms leading to type 2 MI were used.

Results: 277 pts were included. The rate of type 1 MI was 72% (199 of 277), while 28% had type 2 MI. NSTEMI was more prevalent in type 2 MI (94%; 73 of 78) than in type 1 MI (63%; 125 of 199) (p < 0.001) (Figure 1). Type 2 MI pts were older (74; 12 yrs vs. 71±13 yrs) than type 1 MI (p = 0.042). Type 2 MI pts had higher co-morbidity (DM, heart failure, COPD, PAD, stroke). Contrary, mean peak Tnl values were higher in type 1 MI (1.2±1.4 μg/l) than in type 2 MI (1.0±0.3 μg/l) (p = 0.0028). The most frequent mechanism leading to type 2 MI was respiratory insufficiency: 23% (18 of 78).

Conclusion: The original contribution of this study is its prospective design and use of specific objective criteria for the type 2 MI diagnosis. We show that type 1 MI is nearly 3 times as frequent as type 2 MI. Type 2 MI pts are older, have more co-morbidity and a lower rate of STEMI than type 1 MI pts.

Clinical outcome and impact of glycemia an glycosylated haemoglobin in TIMI risk score: results of a national registry
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Introduction: TIMI risk score is a simple and effective tool for risk stratification in patients (pts) with non-ST segment elevation acute coronary syndromes (NSTE-ACS). High values of glycemia measured at hospital admission (admG) were correlated with a worse clinical outcome in ACS (in diabetic and non diabetic pts). The results for studies about the prognostic value of glycosylated haemoglobin (HbA1c) in ACS are inconsistent.

Purpose: Evaluate the impact of admG and HbA1c in NSTE-ACS, adjusted for TIMI risk score.

Methods: The population of the study included pts with ACS, from a national registry of more than 40 hospital centers. Since 2011 were included in the registry new parameters such the values of admG and HbA1c. In a sample of 1380 pts admitted with NSTE-ACS, 1301 had admG and 935 had HbA1c determinations. Pts were stratified by TIMI risk score in low (0 to 2), intermediate (3-4), and high (5-7) risk groups. For admG the groups were divided in group G1 for admG<140 milligrams per deciliter (mg/dL), G2 140-199 mg/dL, and G3 ≥200 mg/dL. For HbA1c the division was: H1 4.6-5.5%, and H2 ≥6.5%. The endpoint included major cardiovascular events (MACCE): in-hospital mortality, re-infarction, heart failure (Killip class≥2) and stroke.

Results: Pts with higher TIMI risk score had higher rate of MACCE (p<0.05). In G1 there were 14.4% of MACCE, comparing with 23.4% in G2 and 30.8% in G3 (p<0.001). The group H1 had 17.8% of MACCE and H2 had 21.4% (difference not statistically significant, p=0.394). In the presence of TIMI risk score (Table 1), admG still have a statistically significant impact in MACCE (OR 1.64; CI 1.15-2.31; p=0.006 for G2 and OR 2.15, CI 1.14-3.14, p<0.001, for G3). The same was not observed for HbA1c (OR 1.14; CI 0.67-1.95, p=0.635).

Table 1. Group G1 (%) Group G2 (%) Group G3 (%) Group H1 (%) Group H2 (%)

| STEMI (%) | 10.1 | 16.9 | 22.0 | 16.1 | 13.3 |
| PCI (%) | 14.8 | 22.8 | 23.1 | 17.4 | 20.0 |
| TIMI score (5-7) | 25.7 | 30.3 | 43.3 | 23.0 | 23.0 |

Conclusion: In this study, admG was an independent predictor of MACCE, even when adjusted for TIMI risk score. The same was not observed for HbA1c.

Vasospastic angina: is percutaneous coronary intervention a valid option for refractory coronary spasm?
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Aim: Variant angina (VA) accounts for about 2 percent of angina cases. VA is usually well controlled by vasodilator drugs, but 5 to 30 percent of patients are symptomatic despite a maximal vasodilator therapy. There is no consensus treatment for these patients with refractory spasm (RS). In case of focal refractory spasm, stenting has been proposed as an alternative therapeutic strategy. The aim of our study was first to analyse the population of patients with RS looking for potential characteristics associated to failure of the medical treatment. Then we evaluate safety and relevance of the therapeutic option of PCI in case of focal RS.

Methods and results: Between December 2002 and 2011 in our institution, 16941 coronary angiograms were performed followed in 2279 patients by a provocative test. A total of 245 patients have been diagnosed for VA. All were systematically treated with medical therapies including calcium blocking agents and nitrates. 127 (52%) patients were controlled by a provocative test to check for efficacy of the vasodilating agents. While the majority were well controlled...
Gender disparities in management and outcomes of Acute Myocardial Infarction: insights from the euro heart survey Acute Coronary Syndromes III

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Background: Gender differences in quality of care in acute myocardial infarction (AMI) are related to the increased age and more frequent comorbidities in women as compared to men. From the Euro Heart Survey Acute Coronary Syndromes (EHS-ACS) III data, we investigated the gender differences in AMI treatment in Europe in temporal and changes over the two years of the survey.

Methods: In 11,478 patients with AMI, we assessed the rate of reperfusion, coronary angiography, use of aspirin, clopidogrel, beta-blockers, angiotensin-converting enzyme inhibitors, and statins during the acute phase and at discharge. Adjusted gender differences in treatment and in-hospital outcomes, and temporal changes between 2006 and 2008 were assessed.

Results: Women were less often treated with evidence-based treatments, reperfusion and coronary angiography. Adjusted in-hospital mortality was comparable between sexes, but there was a trend towards more bleeding complications in women. Between 2006 and 2008, we observed an increase in the rate of use of effective treatments in both sexes and gender differences were attenuated for aspirin at admission, coronary angiography and reperfusion. Conversely, gender differences increased for discharge aspirin, clopidogrel and statins, which all remained less frequently prescribed in women.

Conclusions: During the EHS-ACS III, management improved in both genders, but the lower levels of progress between Memorial Hospital, Taipei, Taiwan and the European standards considered. These gender differences support the hypotheses that (a) the risk-benefit ratio is evaluated differently in females, particularly as regards bleeding complications, and (b) suboptimal management of female patients persists.

Impact of sedoanaesthesia on length of stay and complications in patients undergoing transfemoral percutaneous aortic valve implantation

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Introduction: Most transcatheter aortic valve implants are performed under general anesthesia and orotracheal intubation. The favourable pharmacokinetics properties of remifentanil make it appropriate for its use as sadoanaesthetic in short invasive procedures. We hypothesized that remifentanil was used as unique sadoanaesthetic during transfemoral aortic valve implantation may reduce length of intensive care unit stay and major complications rate through avoiding general anesthesia and orotracheal intubation.

Patients and methods: Single-center and observational study including 53 consecutive patients (pts) with aortic stenosis rejection for open surgery who underwent transfemoral aortic valve implants under conscious sedation with remifentanil. Baseline clinical profile: Logistic EuroSCORE 14±8%, diabetes 28%, severe chronic obstructive pulmonary disease 28%, ejection fraction<35% (11%), significant mitral regurgitation 28%, coronary artery disease 47%, severe pulmonary hypertension 11%. We analyzed short-term and follow-up variables related to success and complications of the intervention and potential complications of sadoanaesthesia with remifentanil.

Results: All the pts (mean age 82±6 years, 62% males) underwent aortic valve replacement as sadoanaesthetic. The procedural success rate was 98%. One patient required orotracheal intubation. The most common adverse effect of sadoanaesthesia was nausea (11%). There were 2 episodes of respiratory depression quickly solved in a noninvasive manner. The rate of nosocomial pneumonia between non-intubated pts during procedure was 3.8% (2 pts). There were no deaths, severe episodes of hypotension or bradycardia during the intervention. The average stay (range) in the coronary unit was 4.6 (1-48), median 2 days, with a total hospital stay of 10.6 (2-46) days, median 8 days. Mean follow-up was 1.4 years. In-hospital, one-month and cumulative mortality were 6%, 6% and 20%, respectively.

Conclusions: The sadoanaesthesia with isolated remifentanil was safe during transfemoral aortic valve implantation and demonstrated short critical care unit and in-hospital stay with a low incidence of respiratory complications probably because of the avoidance of orotracheal intubation.

Predictors of one-year outcomes in patients with acute coronary syndrome(ACS): insights from Taiwan ACS registry

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Objectives: To evaluate the clinical characteristics, treatment and outcomes of patients with acute coronary syndromes (ACS) in Taiwan.

Methods: Consecutive patients with ACS within 24 hours were prospectively recruited from 39 sites between 2008 and 2010. The disease management data at admission, during in-hospital stay, and one-year follow-up were collected.

Results: Of 3183 patients included, 52.3% of the patients were women. Significantly higher in STEMI and NSTEMI patients with ACS, compared to STEMI patients, whereas CABG was rarely performed (3%). Eighty-two per cent of STEMI patients received reperfusion (primary PCI 97% and thrombolytics 3%). Discharge, 75% of the patients received dual antiplatelet agents, 53% beta-blockers, 60% statins, 63% ACEI/ARB. The mortality rate was 7.5% at one year, higher in NSTEMI (10.1%) than in STEMI (6.1%) (p<0.01). Chronic renal failure, in-hospital bleeding, new-onset atrial fibrillation were the strongest independent predictors of increased death/MI/stroke at one year, while percutaneous coronary intervention, stenting and use of guideline recommended therapies at discharge were shown to be independent predictors of lower one-year adverse outcomes.

Conclusions: ACS Full Spectrum registry is the first large national registry in Taiwan. Rates of secondary prevention medication use in ACS patients were suboptimal. Usage of guideline recommended therapies may further reduce the risk of long-term ischemic events.

A new electrocardiographic criterion to differentiate between takotsubo cardiomyopathy and acute anterior ST-segment elevation myocardial infarction

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Electrocardiographic findings of takotsubo cardiomyopathy (TC) mimic those of acute anterior ST-segment elevation myocardial infarction (AA-STEMI). Several studies examined the electrocardiographic differentiation between TC and AA-STEMI, but those studies did not use the magnitude of ST-segment elevation at the J point which is recommended by the AHA/ACC/HRS guidelines. Accordingly, we retrospectively examined whether electrocardiographic findings, using the magnitude of ST-segment elevation measured at the J point, can differentiate 62 patients with TC from 280 with AA-STEMI. The patients with AA-STEMI were divided into the following subgroups: 140 with a left anterior descending coronary artery (LAD) occlusion proximal to the first diagonal branch (AA-STEMI-P); 20 with an LAD occlusion distal to the first diagonal branch and proximal to the second diagonal branch (AA-STEMI-M); and 20 with an LAD occlusion distal to the second diagonal branch (AA-STEMI-L). TC had a lower peak elevation > 1 mm in lead V1 (19.4%) compared with AA-STEMI (80.4%, p<0.01). AA-STEMI-P (80.7%, p<0.01), AA-STEMI-M (80.0%, p<0.01), and AA-STEMI-L (80%, p<0.01). ST-segment elevation ≥ 1 mm in at least one leads
V3–5 without ST-segment elevation ≥1 mm in lead V1 identified TC, with a sensitivity of 74.2% and a specificity of 80.6%. Furthermore, this criterion could differentiate TC from each subgroup, with a similar diagnostic value. In conclusion, we propose a new and simple electrocardiographic criterion, using the magnitude of ST-segment elevation measured at the J point, to differentiate TC from AA-STEMI, and this criterion had an acceptable diagnostic value. This criterion is necessary to be validated in prospective studies.

**P3635** Sensitivity and specificity of different clinical markers of takotsubo cardiomyopathy

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**Objective:** Takotsubo cardiomyopathy (TC) is characterized by acute, reversible, and transient left ventricular systolic dysfunction mimicking acute coronary syndrome (ACS) without significant stenosis on coronary angiography. The aim of this study was to examine clinical features of TC and ACS, and compare them in order to identify possible markers that may help to discriminate these two similar but different entities.

**Methods:** 46 consecutive patients with TC diagnosis admitted to Cardiology Clinic were enrolled between February 2007 and December 2011. TC was defined by the Mayo Clinic Criteria. All cases were then retrospectively matched with 92 patients of patients with MI according to sex, age and absence of STElevation. ROC curve analysis was used to estimate sensitivity and specificity of different variables as TC diagnostic factors.

**Results:** Unexpected, female sex is associated with TC (HR 2.14, 95% CI 1.25-3.65) as is a recent trigger event, be it an emotional or physical event. Patients with ACS had higher prevalence of hypertension, diabetes mellitus type 2, hypercholesterolemia and smoking habit (all \( p < .05 \)). TC is associated with lower level of ischemia cardiac markers. Admission troponin I levels higher than 4 ng/dL can rule out TC with a sensitivity of 71% and a specificity of 64%. Similarly, CK-MB levels above 14 are associated with ACS with a sensitivity of 64% and a specificity of 76%.

Patients with TC had significant lower EF \( (19\% \pm 3\%) \) when compared with patients with ACS at baseline, and the difference, albeit lower in magnitude, was still significant at discharge \( (-6\% \pm .035) \). Also, mean E wave was higher and mean A wave was lower in patients with TC cardiomyopathy at admission \( (p = .002 \text{ and } p = .012 \text{ respectively}) \), thus producing a positive association between E/A ratio and TC. According to ROC curve analysis, an E/A ratio higher than 1 can be used as a cut-off to predict TC with a sensitivity of 47% and a specificity of 87%. TC was associated with wider QTc \( (47±.04 \text{ vs. } 44±.04 \text{ s; } p = .009) \), whereas QTc between TC and ACS patients were similar at discharge. A QTc \( \geq 0.46 \) can predict TT with similar sensitivity and specificity \( (69\%) \).

**Conclusion:** According to our data, no single marker for TC diagnosis that is both reliable as easily obtainable is currently available. However, a complete risk assessment made up from clinical, laboratoristic, electrocardiographical and echocardiographical markers can rule out TC in a majority of patients.

**CARDIOPULMONARY RESUSCITATION**

**P3636** Who benefits most from extracorporeal cardiopulmonary resuscitation using extracorporeal membrane oxygenation?

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**Purpose:** Extracorporeal cardiopulmonary resuscitation (ECPR) using extracorporeal membrane oxygenation (ECMO) may improve the outcomes in select cardiac arrest patients. However, patients’ selection for ECPR has not yet been established yet. We assessed whether recorded rhythm could be used as a simple predictor of 30-day survival in refractory cardiac arrest patients treated with ECPR.

**Methods:** We retrospectively studied 137 consecutive patients treated with ECPR in 2 tertiary care hospitals between 2004 and 2011. We divided the patients into 3 groups according to their initial recorded cardiac rhythms: patients with asystole (Asystole-group), those with pulseless electrical activity (PEA-group), and those with shockable rhythm (VF2-group). We also divided the patients into 4 groups according to the rhythm recorded when ECMO was initiated: patients with asystole (Asystole2-group), those with PEA (PEA2-group), those with shockable rhythm (VF22-group) and those with non-cardiac arrest (ROSC-group). The primary endpoint was 30-day survival. We plotted a 1-year survival curve to assess the duration of survival by the Kaplan-Meier method, and a stepwise Cox proportional hazards regression analysis was performed to assess the independent predictors of 1-year survival. The variables of which were measured before the initiation of ECMO. The continuous variables are presented as median (interquartile range). \( P < .05 \) was defined as statistically significant.

**Results:** The study included 63 (55–72) year-old patients; 72% of the patients were male, 55% had complicated with acute coronary syndrome, and 46% were out-of-hospital cardiac arrest. The time interval from collapse to the initiation of ECMO was 49 (27–67) min. The 30-day survival rates were 0%, 26%, and 29% for the Asystole- (N = 16), PEA- (N = 56), and VF2- groups (N = 59), respectively \( (P = .005) \). The 30-day survival rates were 0%, 28%, 33%, and 28% for the Asystole2- (N = 31), PEA2- (N = 63), VF22- (N = 25), and ROSC-groups (N = 18), respectively \( (P = .0004) \). Cox proportional hazards regression analysis showed that the initial recorded rhythm was one of the independent predictors of 1-year survival \( (odds ratio 0.47, 95\% \text{ confidence interval } 0.87–0.26, P = .002) \).

**Conclusions:** Patients with asystole as the initial recorded rhythm and those whose rhythm changed to asystole on the initiation of ECMO are less likely to survive even on treatment with assist circulation using ECMO.

**P3637** Who benefits most? Predictors of favourable outcome after survived sudden cardiac arrest and hypothermia treatment

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**Objectives:** Mild therapeutic hypothermia (MTH) has shown improved short- and long-time survival as well as favourable functional outcome after cardiac arrest (CA). The aim of this study was to examine clinical features of MTH and complications of MTH are potential confounders for outcome, especially in non-randomised studies.

**Main Results:** Hypothermia was induced by either invasive or non-invasive surface cooling at 33.0°C core body temperature for 24 h followed by active rewarmin. Mortality and neurological outcome of survivors were determined at hospital discharge and during follow up (median follow up: 2.8 months, range 0-66 months) using the General Performance Category (GPC) score and dichotomized into favourable (GPC1/2) and unfavourable (GPC3-5) outcome. Predictors of outcome were determined by univariable and multivariable logistic regression analysis.

**Main Results:** Having a favourable neurological outcome at follow up were younger age, lower APACHE-Score, absence of diabetes and arterial hypertension in patients history, and congestive heart failure signs at admission (\( p < .002 \)), ventricular fibrillation as initial rhythm, time to defibrillation (\( p = .015 \)), longer period of hospitalization and absence of hypothermia-induced complications (e.g. therapy-necessitating arrhythmias, renal failure, infectious complications, all other \( p < .001 \)). Bystander cardiopulmonary resuscitation, time to re- turn of spontaneous circulation, the cooling method, and time to target temperature were not predictive of outcome.

**Conclusions:** In a large, unselected cohort of cardiac arrest survivors treated with hypothermia, age, initial rhythm, duration of hospitalization and hypothermia-associated complications were the most important predictors of good clinical outcome.

**P3638** Predictors of outcome in patients with ST-elevation myocardial infarction presenting with out of hospital cardiac arrest


**Introduction:** ST elevation myocardial infarction (STEMI) complicated by out of hospital cardiac arrest (OOHCA) is associated with significant mortality. Small observational studies have shown survival benefit with primary percutaneous coronary intervention (pPCI) in this setting. Therefore, increasingly OOHCA patients with evidence of STEMI are either directly conveyed or transferred to pPCI centres for emergency reperfusion. We sought to identify clinical characteristics and predictors of outcome in STEMI complicated by OOHCA in a large patient cohort in the era of pPCI.

**Methods:** Between Jan 2008 and Oct 2011, STEMI admissions to a regional cardiac centre were retrospectively analysed. 128 patients with OOHCA in the context of STEMI were identified. Clinical and procedural data was collected from the UK Myocardial Ischaemia National Audit Project (MINAP) database and patient notes. All cause mortality data was confirmed using the Office of National Statistics mortality database with follow-up ranging from 3 to 44 months.

**Results:** The mean age of patients was 60±14 years, 78.9% were male and 53% were direct admissions via the ambulance service, 47% being transferred from district hospitals. The in-hospital mortality within the cohort was 18% with 105/128 patients surviving with non-cardiovascular discharge. At follow up (10-44 months in 62% patients) 100% of patients who survived to discharge were alive. There were no significant differences in patient demographics, previous cardiac history, arrest rhythm or referral source between patients who survived to discharge compared with those who died. Patients who died had significantly higher incidence of diabetes \( (p = .0029) \), 3-vessel coronary disease \( (p = .0016) \), severe left ventricular (LV) impairment \( (p = .0029) \) and renal dysfunction \( (p = .0005) \). Survivors had significantly higher rates of witnessed arrest \( (p < .0001) \), successful reperfusion of in-
Electrocardiographic disturbances in different target temperature ranges for mild induced hypothermia


Purpose: Mild (32–34°C) therapeutic hypothermia (MTH) improves survival in comatose patients recovered from cardiac arrest (RCA). Some electrocardiographic (ECG) changes have been described in small MTH series and accidental hypothermia. The purpose of this study is to analyze ECG changes and arrhythmias at different MTH target temperatures (TT).

Methods: From 2006 to 2011 all consecutive RCA patients admitted in our coronary care unit (CCU) were included in a prospective registry (87 patients). Different TT were chosen: 33°C (45 patients), 32°C (22) and 34°C (20) following clinician’s criteria. MTH has induced by intravenous cold fluid infusion and maintained by external cooling methods (34%) or by an intravascular cooling system (66%). ECGs were recorded at admission (A), peak MHT (B), and after rewarming (C). ECG telemetry was analyzed by CCU staff for rhythm disturbances. ECGs were blinded and analyzed by 2 independent cardiologists. Variables studied were: rhythm, RR, PR, QRS, QT and QTc intervals; as well as ST segment deviation and T wave amplitude. We analyzed intra-patient variability of ECG intervals and compared ECG interval changes among the 3 TT.

Results: Reversible changes occurred during MTH: a reduction in the heart rate (HR) and prolongation of mean PR, QRS and QTc intervals was found (p<0.05 at 33°C and 34°C, p<0.01 at 32°C). The decreases were 15%, 16%, and 17% for mean PR interval, respectively. A reduction in HR occurred during cooling in lower TT (32°C vs 34°C, p=0.003; and linear trend in 32°C, 33°C, 34°C, p=0.019), resulting in more bradycardias in the 32°C group vs. 34°C (80% vs. 20%, p=0.03; 3 TT comparisons p<0.05). Re-warming caused HR increase, homogeneous among the 3 TT (p=0.28). A total of 40.2% had any arrhythmia different from sinus bradycardia (18.4%) during MTH (non-sustained VT 21.4%, SV tachycardia 10.3%, idioventricular rhythm 5.7%, ventricular fibrillation 3.4% and sustained-VT 1%). No differences in the incidence of arrhythmias were found among different TT. 6 patients (6.9%) had reversible rhythm changes during MTH: 4 patients in sinus rhythm had atrial fibrillation (AF), 1 patient in AF had a rapid idioventricular rhythm and 1 patient in nodal rhythm changed to sinus rhythm. 26% of patients developed Osborn J waves during MTH.

Conclusions: MTH induces reversible changes in ECG intervals (prolongation of PR, QRS, QTc; and HR reduction). Cooling to lower temperatures in the range of MTH did not increase the incidence of arrhythmias or the changes in ECG intervals. Cooling may be more effective for higher bradycardia. Angiography temperature in the range of MTH (32°C to 34°C) was “electrostatically safe” in our registry.

In-hospital outcome of resuscitated from out-of-hospital cardiac arrest patients

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Purpose: Prognosis of patients (pts) with out-of-hospital cardiac arrest (OHCA) continues to be poor. Recent studies suggest that percutaneous coronary inter- vention (PCI) may improve survival. Aim of this study was to determine the indepen-dent predictors of in-hospital outcome in resuscitated OHCA pts without obvious extra-cardiac etiology.

Methods: Clinical characteristics of resuscitated OHCA pts referred to our center in period of 2000 – 2011 were retrospectively reviewed. Information about initial arrest rhythm, delay between the onset of OHCA and recovery of spontaneous circulation (ROSC) and post-ROSC ECG pattern (ST-segment elevation and other ECG patterns) were collected. Therapeutic hypothermia and emergent coronary angiography were performed in selected pts according to clinical judgment. PCI was deemed successful if it resulted in residual stenosis of ≤50% with TIMI 3 grade flow. The primary outcome was survival to hospital discharge with good neurologic recovery. Neurological status was assessed by using the Cerebral Performance Categories (CPC) scale; a CPC score ≤ 2 indicate pts who recovered without major neurological impairment. Right ventricular function delays were “no flow” (4.2±1.6 h, ≤16 minutes), “low flow” (16-25 minutes): the initial rhythm was ventricular fibrillation (VF); ventricular tachycardia (VT) in 39 (63%) pts. Delay between the onset of OHCA and ROSC was ≥ 20 minutes in 28 (45%) pts. On post-ROSC ECG, ST-elevation was present in 20 (32%) pts.

Characteristics and prognostic data of patients treated by mild therapeutic hypothermia for an out-of-hospital cardiac arrest in a cardiac unit


Background: Mild therapeutic hypothermia (MTH) improves the neurological prognosis of out-of-hospital cardiac arrest (OHCA). This study aims at determining the actual characteristics and prognostic elements of patients treated by MTH for an OHCA.

Methods: We retrospectively analyzed data of patients referred to our cardiac intensive care unit during the last 4 years (2008-11) for an OHCA managed by MTH. Characteristics were compared according to the neurological outcome at hospital discharge. A good neurological outcome was defined by a Pittsburg Cerebral Performance Category 1 or 2 (none/mild disability).

Results: 70 patients (age: 59±14; male: 60 (86%) were enrolled. Mean resusci-tation time delays were “no flow” (4.2±1.6 h, ≤16 minutes), “low flow” (16-25 minutes): MTH was performed in 62 pts (86±13 years, 44% female). The initial rhythm was ventricular fibrillation (VF); ventricular tachycardia (VT) in 39 (63%) pts. Delay between the onset of OHCA and ROSC was ≥ 20 minutes in 28 (45%) pts. 20 (32%) pts.

Therapeutic hypothermia and coronary angiography were performed in 12 (19%) and 39 (63%) pts, respectively; successful PCI was performed in 16 (26%) pts. The hospital survival rate with good neurologic recovery was 44%. At univariate analysis, age < 60 years (OR 3.63; 95% CI 1.03-12.94, p=0.044), delay between onset of OHCA and ROSC < 20 minutes (OR 3.17, 95% CI 1.09-9.17, p=0.034), VFVT as initial rhythm (OR 10.67, 95% CI 2.70-42.16, p=0.001) and successful PCI (OR 4.82; 95% CI 1.02-21.17, p=0.046) were related to in-hospital survival. Multivariate analysis, delay between onset of OHCA and ROSC – 20 minutes (OR 5.67, 95% CI 1.44-22.45, p=0.013), VFVT as initial rhythm (OR 12.67, 95% CI 2.71-69.21, p=0.001) and successful PCI (OR 6.39, 95% CI 1.29-31.61, p=0.023) were independently related to in-hospital survival.

Conclusion: Successful PCI is associated with better in-hospital survival in resuscitated OHCA pts without obvious extra-cardiac etiology. This finding supports the use of emergent coronary angiography in all these pts.
Pharmacologically induced hypothermia with Ventricular fibrillation: independent predictors and preserves myocardial function after cardioplegic arrest.

Conclusions: Factors associated with good prognosis are: age, witnessed, short resuscitation delays (“no” and “low” flow), a low dose of adrenaline, angioplasty and a low lactate at the admission.

Purpose: To compare the effects of cannabinoid receptor agonist WIN55,212-2 with mild hypothermia and normothermic control on post-reperfusion myocardial function in a rat model of cardiac arrest.

Methods: Ventricular fibrillation (VF) was induced and untreated for 10 min in adult male Sprague-Dawley rats (400-450 g). Defibrillation was attempted and resuscitated animals were randomized to three groups of ten: (a) normothermia; (b) hypothermia (32°C) and (c) normothermia with WIN55,212-2 intravenous injection after the defibrillation attempt.

Results: WIN55,212-2 administration produced pharmacologic hypothermia (32-34°C) and led to a significantly better recovery of the slope of the left ventricular end-systolic pressure-volume relationship (Des) and Preload recruitable stroke work (PRSW) than hypothermia and normothermia: as percent of baseline 88±13 versus 66±9 g and 85±12 vs 65±11 vs 36±8 respectively (p<0.05). Left ventricular systolic function was expressed by end-diastolic pressure volume relationship (ED-PVR) which was significantly lower after WIN55,212-2 administration compared to the normal temperature group (p<0.01). Left ventricular function describing by the Tau was preserved after WIN55,212-2 treatment but not after normothermia or mild hypothermia (p<0.01). WIN55,212-2 and conventional hypothermia significantly increased phosphorylation of the kinase ERK1 and 2 (2.8±0.4 and 2.5±0.3 or 0.5±0.2 and 0.4±0.1 fold of baseline levels) (p<0.01). Both WIN55,212-2 and hypothermia but not normothermia increased phosphorylation of Akt. This resulted in preserved HEP (p<0.05) and reduced cardiomyocyte apoptotic index (p<0.01) after WIN55,212-2 administration compared to both hypothermia and normothermia.

Conclusions: Pharmacologically induced hypothermia with WIN55,212-2 improves myocardial protection through activation of the pro-survival kinases Akt and ERK1/2 and preserves myocardial function after cardioplogic arrest.

P3643 Pharmacologically induced hypothermia with cannabinoid receptor agonist WIN55,212-2 after cardiac arrest

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Purpose: The present study aimed to investigate the effect of cannabinoid receptor agonist WIN55,212-2 on myocardial protection and restoration of myocardial function in a rat model of cardiac arrest.

Methods: Cardiac arrest was induced in Sprague-Dawley rats. Following 10 minutes of VF, the rats were randomized into three groups: normothermia, hypothermia (32°C), and WIN55,212-2 administration. The effects on myocardial function were assessed through the measurement of cardiac output, left ventricular systolic and diastolic functions, and the expression of pro-survival kinases Akt and ERK1/2.

Results: WIN55,212-2 administration produced pharmacologic hypothermia (32-34°C) and led to a significantly better recovery of the slope of the left ventricular end-systolic pressure-volume relationship (Des) and Preload recruitable stroke work (PRSW) than hypothermia and normothermia: as percent of baseline 88±13 versus 66±9 g and 85±12 vs 65±11 vs 36±8 respectively (p<0.05). Left ventricular systolic function was expressed by end-diastolic pressure volume relationship (ED-PVR) which was significantly lower after WIN55,212-2 administration compared to the normal temperature group (p<0.01). Left ventricular function describing by the Tau was preserved after WIN55,212-2 treatment but not after normothermia or mild hypothermia (p<0.01). WIN55,212-2 and conventional hypothermia significantly increased phosphorylation of the kinase ERK1 and 2 (2.8±0.4 and 2.5±0.3 or 0.5±0.2 and 0.4±0.1 fold of baseline levels) (p<0.01). Both WIN55,212-2 and hypothermia but not normothermia increased phosphorylation of Akt. This resulted in preserved HEP (p<0.05) and reduced cardiomyocyte apoptotic index (p<0.01) after WIN55,212-2 administration compared to both hypothermia and normothermia.

Conclusions: Pharmacologically induced hypothermia with WIN55,212-2 improves myocardial protection through activation of the pro-survival kinases Akt and ERK1/2 and preserves myocardial function after cardioplogic arrest.

P3644 Ventricular fibrillation: independent predictors and clinical outcome in acute coronary syndrome (results from a national registry)

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Introduction: After 40 years of research, a significant portion of the risk of Ventricular Fibrillation (VF) remains unexplained. Most of these studies were made before the "new era" of resuscitation therapy, which many factors were inconsistently associated with VF (younger age, male gender, absence of diabetes, ...).

Purpose: To evaluate the incidence of VF in patients (pts) with acute coronary syndrome (ACS); risk factors for VF; the clinical outcome in pts with VF comparing with pts without this event, both in-hospital (IH) and at 6 months of follow up (Fup); the clinical significance of the diagnosis of infarction with ST segment elevation (STEMI) and ACS without ST segment elevation (non STEMI and unstable angina) in VF; and the statistical importance of the "new era" of reperfusion therapy. Many factors were inconsistently associated with VF (younger age, male gender, absence of diabetes, ...).

Methods: Included pts with ACS, from a national registry of elderly heart failure (HF) patients (≥85 years) are limited. Our objective is to study all cause mortality and prognostic factors in elderly (≥85 years) patients using the Swedish Heart Failure Registry database.

Results: This retrospective study included 16,302 patients (≥75 years) with a mean follow-up of 7 years. The elderly population was further divided into two subgroups: 10,335 patients were 75-84 years and 5,967 patients were ≥85 years. Those without completed data file were excluded. Both univariate and multivariate analyses were performed. The mortality rate was significantly lower in patients 75-84 years of age (14.3%) compared with those ≥85 years (43.1%). In either group had a higher mortality (48.6%) compared with those aged 75-84 years (43.1%). In either group had a higher mortality (48.6%) compared with those aged 75-84 years (43.1%).

Conclusions: Our data from a large elderly heart failure population from real-life demonstrates that the ≥85 years group not only has a higher all cause mortality, but also has distinct underlying prognostic factors being different from ≤85 years.
Sex-specific differences in patients with heart failure. 

The sex-specific aspects of COACH (Coordinating study evaluating Outcomes of Advising and Counseling in Heart failure) (S. Meyer1, T. Jaarsma2, D.J. Van Veldhuisen1, M.H.L. Van Der Wal3, H.L. Hillege1, A.A. Voors1, 1University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; 2Linkoping University, Linkoping, Sweden

Purpose: Sex-related differences in patients with heart failure are not well described.

Methods: Baseline demographic and clinical characteristics, multiple biomarkers, and outcomes were compared between male and female patients included in a nurse-led intervention trial (COACH).

Results: Among 1023 patients, 38% were female. Females showed higher age, BMI, LVEF, chronic hypertension; they more often showed edema and pulmonary congestion and treatment rates were higher for diuretics and antidiuretics but less for ACE-inhibitors compared to males. Total all-cause mortality after 1000 days was 33.3% in females and 39.8% in males (HR=0.81; 95%CI 0.66-0.99, p=0.014). After adjustment for age, renal function, myocardial infarction, LVEF, hypertension, COPD, diastolic blood pressure, and use of ACE-inhibitors, nitrates and statins at discharge, respectively, sex had independent prognostic effects. Females showed lower mortality and admission for HF at 18 months post discharge (HR=0.74; 0.58-0.93, p=0.001) as well as less mortality at 18 months (HR=0.71; 0.53-0.96, p=0.023) and 36 months (HR = 0.75; 0.59 - 0.94, p =0.015), compared to males. In a subset of 567 patients 25 biomarkers were measured at baseline and during follow-up related to inflammation (Pentraxin 3, GDF 15 and TROY), and extracellular matrix remodeling (Syndecan-1 and Periostin), were significantly lower in females compared to males.

Conclusions: Females present differently with heart failure compared with males. Even after adjustment for confounders females have better outcomes. Interestingly, biomarkers related to inflammation and extracellular matrix remodeling were significantly lower in females.

Risk stratification of a population of female elderly patients suffering from chronic heart failure by using ventilatory parameters

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Aim: The prognostic role of cardiopulmonary exercise test (CPX) in elderly women with chronic heart failure has not yet been clarified. We assessed the incremental value of CPX variables for risk stratification in female HF patients able to perform a maximal CPX.

Methods and Results: We prospectively followed up 210 female HF outpatients aged 73 (64-79) years after a symptom limited CPX; 35% had ischemic heart disease and 16% permanent atrial fibrillation, 24% were in NYHA class III, left ventricular ejection fraction (LVEF) was 52 (40-63) %. Peak oxygen consumption (PVO2) was 11.0 [8.7-13.3] ml/kg/min, peak workload was 50 [38-61] watts; the slope of the regression line relating ventilation to CO2 output (VE/VECO2 slope) was 39 [33-45], RER was 1.04 [0.98-1.15]; 38% of patients showed periodic breathing during exercise test (EOB). During a median tracking period of 20 months (7-52), 23 patients (11%) died and 29 were admitted for worsening HF. Using a time-to-first event approach, overall 55 patients (26%) met the combined end-point of all-cause mortality or HF admission. Age, end diastolic volume and EOB were independently associated to all-cause mortality, while NYHA class III, VE/VECO2 slope, and EOB were independent predictors of the composite end-point. When CPX variables were added clinical and echocardiographic parameters outcome prediction significantly improved for both end points (log-likelihood P<0.001). The predictive accuracies of the multivariables models for all-cause mortality and all-cause mortality or HF admission expressed as areas under the ROC curves (AUC), were 0.87 (95%CI 0.80-0.94) and 0.79 (95%CI 0.72-0.87) respectively.

Conclusions: Among elderly female HF patients the CPX derived parameters EOB and VE/VECO2 slope emerged as strong prognostic markers, with additive predictive value to clinical and echocardiographic parameters. The respiratory pattern during CPX represents a key marker of adverse outcome in female HF patients. These findings prospect the utility of comprehensively assessing CPX-derived information to optimize the clinical and prognostic work up of women suffering from HF.
Cardiac resynchronization therapy in the elderly: safety, left ventricular reverse remodeling and the long-term outcome

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Purpose: Despite the firm association between heart failure prevalence and older age, limited data are available on the impact of cardiac resynchronization therapy (CRT) in the elderly. The aim of this study was therefore to evaluate safety, left ventricular (LV) reverse remodeling and long-term outcome after CRT in the elderly.

Methods: A total of 786 consecutive patients (208 elderly: age ≥75 years; 590 non-elderly: age <75 years) who underwent CRT were clinically and echocardiographically evaluated at baseline and 6-month follow-up. In-hospital (within 24h) and follow-up adverse events, including pocket hematoma, LV lead dislodgments and device infection after implantation were reported. During long-term follow-up, cause of death was noted.

Results: Similar incidence of in-hospital (p=0.55) and follow-up adverse events (p=0.98) was observed in elderly and non-elderly patients. At 6-month follow-up, magnitude of LV reverse remodeling was similar in both groups (p=0.65). During long-term follow-up (median 39 months), higher mortality rate (p=0.02) was observed in the elderly. The survival difference, mainly due to non-cardiac cause started 4 yrs after CRT (Figure). In the elderly, multivariable Cox model identified two independent prognostic factors: estimated glomerular filtration rate (eGFR; HR 0.977, p=0.01) and 6-min walk-test (HR 0.996, p=0.01), after adjustment for age, ischemic etiology, diabetes, atrial fibrillation and LV volume.

Conclusion: CRT implantation in elderly patients is as safe as in non-elderly patients. Despite comparable LV reverse remodeling after CRT, all-cause mortality remains higher during long-term follow-up in the elderly, starting after 4 yrs and mainly due to non-cardiac cause. In the elderly, independent prognostic factors were eGFR and 6-min walk-test.

Diabetes mellitus, a serious co-morbidity especially in younger heart failure patients - A report from the Swedish Heart Failure Registry (RiksSvikt)

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Purpose: Patients with diabetes mellitus (DM) are at increased risk for developing heart failure than those without. The prognosis is considered serious but information on long-term outcome from patients representing all day practice is sparse.

Methods: Patients with (n=8837) and without (n=27560) type 2 DM included in the Swedish Heart Failure Registry (RiksSvikt) 2004-2011 were followed for mortality until 30 September 2011 (median 22.5 months). Differences in background characteristics were adjusted for in a stepwise logistic regression model.

Results: Despite that ischemic heart disease was more common in DM patients (60 vs. 45%) coronary angiography (21%) and revascularisation (32%) was underutilised. Left ventricular function expressed as EF did not differ and there were no major differences in evidence based drug treatment. NYHA class III and IV were more common in DM (51 vs. 42%). Kaplan-Meyer curves for mortality are presented in Figure 1. The adjusted and adjusted ORs (95% CI) for mortality were 1.37 (1.31-1.44) and 1.63 (1.52-1.73). DM was a particularly important riskfactor in age groups ≤65 yr (2.26; 1.96-2.60).

Conclusion: Despite a somewhat more aggressive pharmacological treatment, DM increases mortality in heart failure patients, especially in the younger age group, possibly due to too little use of coronary interventions.

Higher body mass index confers better prognosis only in non diabetic heart failure patients

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Background: In the general population obesity and diabetes are associated with an increased cardiovascular risk and mortality. Paradoxically, previous studies have shown that higher body mass index (BMI) predicts better survival in heart failure (HF) patients. We aimed to evaluate how BMI influences mortality in heart failure (HF) patients according to diabetes history.

Materials and Methods: We conducted a retrospective cohort study on 481 ambulatory patients attending a specialized HF clinic between January 2000 and July 2011. Patients with left ventricular systolic dysfunction were included if BMI was available in their first clinic appointment. Demographic data, comorbidities, clinical examination data and laboratory parameters were recorded. Patients were classified according to history of diabetes. Patients were followed up to 5 years and death due to HF was the endpoint under study. A Cox regression analysis was used in the prognostic assessment.

Results: Almost two third of the patients were men and the median population age was 68 yrs: 52.2% of the patients were diabetic. Diabetic patients had significantly more chronic comorbidities: arterial hypertension [131 (72.0%) vs 170 (56.9%) in non-diabetics, p=0.001], dyslipidemia [126 (69.2%) vs 176 (58.9%) in non-diabetics, p=0.023], obesity [55 (30.2%) vs 53 (17.7%) in non-diabetics, p=0.001] and coronary heart disease [90 (50.0%) vs 88 (29.5%) in non-diabetics, p=0.001]. During the follow up, 27 of 299 (13.7%) diabetic patients vs 25 of 182 (9%) non-diabetic ones died from HF, (p=0.107). Higher BMI predicted a better prognosis in the 481 patients under study (HR of 0.94, 95% CI: 0.80-0.96, p value 0.007). Higher BMI was not associated with a better prognosis in the 182 systolic HF patients with concomitant diabetes (HR= 0.97, 95% CI: 0.89-1.05, p=0.440).

Conclusion: The so called obesity paradox might only be true in systolic HF patients without concomitant diabetes. More studies are needed for better refinement of the specific group of HF patients in whom lower BMI should raise concern and clinical attention.

Figure 1. Mortality in patients with heart failure

Conclusion: Despite a somewhat more aggressive pharmacological treatment, DM increases mortality in heart failure patients, especially in the younger age group, possibly due to too little use of coronary interventions.

Adjusted for gender, age, weight, ischemic heart disease, hypertension, atrial fibrillation, pulmonary disease, revascularisation, GFR, blood pressure and pharmacological treatment.
P3653 Prognostic impact of heart failure in patients with diabetes, chronic kidney disease, anemia and preserved ejection fraction

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Purpose: In a cohort of patients with diabetes, chronic kidney disease (CKD), anemia and preserved left ventricular ejection fraction (LVEF) we evaluated the influence of a history of heart failure (HF) on cardiovascular (CV) and renal outcomes.

Methods: TREAT (Trial to Reduce Cardiovascular Events with Aranesp Therapy) enrolled 4338 patients with anemia (hemoglobin ≤ 11 g/dL), CKD (eGFR 20-60 mL/min/1.73 m²) and type 2 diabetes. Of 1236 patients with both baseline LVEF and HF status reported, 917 had a LVEF < 50%. We compared patients with HF-pEF (n=405) to those with similar LVEF but no reported history of HF (n=512) with regards to clinical characteristics and outcomes. (death, HF, myocardial infarction, stroke and end stage renal disease (ESRD)). Baseline characteristics were compared by Wilcoxon rank-sum and Chi squared tests. Event rates were obtained. Multivariate adjusted hazard ratios were calculated with Cox proportional hazard models.

Results: Patients with and without HF were similar with regards to age, sex, BMI, blood pressure, albumin and eGFR. However, coronary heart disease, atrial fibrillation and higher levels of proteinuria were more common in HF-pEF. Those with HF-pEF had a higher risk of death and HF, but there was no difference in the adjusted rates of MI, stroke and ESRD between those with and without a history of HF (Table). However in diet treated patients, there was a U shaped relationship between HbA1c and all-cause deaths after CHF diagnosis was assessed. In this subgroup, as in the overall TREAT, randomization to CONUTS was also associated with increased death (HR; 1.28, 95% CI; 1.19-1.39). The risk of admission due to worsening HF among patients with increased CONUTS was 1.45 (95% confidence intervals [95%CI]; 1.19-1.74) in CONUTS ≥2 patients, and 1-point increase in CONUTS was also associated with increased death (HR; 1.28, 95%CI;1.19-1.39). The risk of admission due to worsening HF among patients with increased CONUTS was higher but was statistically insignificant (as a categorical variable, HR; 1.37, 95%CI; 0.91-1.97, as a continuous variable, HR;1.07, 95%CI; 0.95-1.21).

Conclusions: These results indicate that CONUTS is an independent prognostic factor in Stage-B patients, demonstrating the clinical importance of nutritional assessment in patients in Stage-B.

P3654 HbA1c and mortality in diabetic individuals with heart failure - an retrospective cohort study

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Background: Controversy exists regarding the importance of glycaemic control in patients with type 2 diabetes mellitus (T2DM) and chronic heart failure (HF) based on conflicting reports. We investigated the impact of a single baseline HbA1c on survival in T2DM patients with incident CHF.

Objective: To examine the relationship between the mean of all HbA1c measures after CHF diagnosis and outcome in a large cohort of T2DM patients with incident CHF.

Setting: Retrospective, observational cohort study.

Patients: T2DM patients with incident CHF between 1993 and 2010.

Measurements: A weighted mean HbA1c was calculated using all available HbA1c measures following CHF diagnosis and patients were grouped into five categories of HbA1c (<6%, 6-7%, 7-8%, 8-9% and ≥9%). We subsequently compared survival between mean HbA1c and all-cause deaths after CHF diagnosis was assessed.

Results: 795 patients with T2DM met study criteria. Median follow up of 3.8 years saw 491 (61.8%) deaths. Cox regression model, adjusted for all other significant predictors, with the middle HbA1c category (7%-8%) as the reference, showed a U shaped relationship between HbA1c and outcome. (p=0.91; 95% CI 1.78 (1.26-2.52)); <6%-7%; 1.29 (1.01-1.66) and ≥9% (1.38 (1.03-1.84)). We found a similar relationship in the drug treated sub-group. However in the diet only group, low HbA1c was associated with the lowest risk of death (p=0.17 (0.07-0.39)).

Limitations: Observational design precludes inclusion of all possible confounding variables.

Conclusions: In patients with T2DM and CHF, our observational study shows that in drug treated patients there was a U shaped relationship between HbA1c and mortality with the lowest mortality risk in patients with modest glycaemic control (HbA1c ≤7%-9%). However in diet treated patients, lower HbA1c was associated with lower mortality risk.

P3655 Nutritional status and prognosis of stage-B patients

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Purpose: Poor nutritional status has been recognized as a strong indicator of prognosis in patients with overt heart failure (HF). However, the association between the prognosis and nutritional status is unclear in patients with cardiovascular disease but without HF. We examined the prognostic impact of poor nutritional status using controlling nutritional score (CONUTS; calculated by measuring serum albumin, total cholesterol, and lymphocyte) in Stage-B patients.

Methods: We identified 4,051 patients in Stage-B (mean age: 67.2±12.4 years, male: 71.2%) from our prospective cohort study named the Chronic Heart Failure Analysis and Registry in the Tohoku District-2 (CHART-2). We included CONUTS in multivariable analyses as a categorical variable (CONUTS 0-1 [reference]; N=2,508, CONUTS ≥2; N=1,543) and as a continuous variable.

Results: Mean (median) CONUTS was 1.4 (1.4). Comparing with patients with CONUTS 0-1, those with CONUTS ≥2 were characterized by older age (68.7±12.7, 66.2±12.1), reduced LV ejection fraction (64.1±12, 66±12), and higher BNP level (124±198, 75±105). Multivariable Cox regression model showed that it had a global risk (HR for all-cause death was 1.45 (95% confidence intervals [95%CI];1.19-1.74) in CONUTS ≥2 patients, and 1-point increase in CONUTS was also associated with increased death (HR; 1.28, 95%CI;1.19-1.39).

Conclusions: These results indicate that CONUTS is an independent prognostic factor in Stage-B patients, demonstrating the clinical importance of nutritional assessment in patients in Stage-B.

P3656 Nutritional status and its impact on mortality in patients with heart failure with preserved or depressed systolic function, are there differences?

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Introduction: Malnutrition is an independent prognosis factor of mortality in patients with heart failure. We do not know if the prevalence of malnutrition and its impact on mortality is the same in patients with HF with preserved systolic function (PSF) than in those with ventricular dysfunction (DSF). The aim of our study was to compare the nutritional status and assess their impact on mortality in these two groups of patients.

Methods: For this purpose we analyzed the nutritional status of 208 patients hospitalized for HF. A complete nutritional assessment using anthropometry, biochemical and functional evaluations by the Mini Nutritional Assessment (MNA) test were performed. Its possible independent association with mortality was analyzed by Cox multivariate analysis.

Results: 50% of patients presented HF with depressed systolic function (left ventricular ejection fraction ≤LVEF < 45%). This group presented a lower LVEF (64±5.8 vs 30±6.3 kg/m2, p = 0.002) and higher percentage of ischemic etiology (50.4 vs. 31.2%, p= 0.005) and its mortality was 34% in the group of patients with DSF, and 41%,1% in the group of patients with PSF. This difference was statistically significant (as a categorical variable, HR; 1.37, 95%CI; 0.91-1.97, as a continuous variable, HR;1.07, 95%CI; 0.95-1.21).

Conclusion: These results indicate that CONUTS is an independent prognostic factor in Stage-B patients, demonstrating the clinical importance of nutritional assessment in patients in Stage-B.
was higher in malnourished patients. When we analyzed malnourished patients only, mortality was similar in patients with DSF and PSF (80% vs 73%), log-rank, p = 0.98. In both groups the state of malnutrition with respect to adequate nutrition is an independent predictor of mortality. Thus, in the group of patients with DSF, adjusted hazard rate (Cox multivariate analysis) was 3.2 (CI 95% 1.4–9.9; p = 0.03); in patients with PSF, was 5.47 (95%CI 1.57–18, p = 0.006).

Conclusion: In our series, the nutritional status and the prevalence of malnutrition are not influenced by the presence of ventricular dysfunction. The mortality of malnourished patients does not depend on whether systolic function is preserved or depressed.

**P3657**

The obesity paradox in subjects with and without heart disease in a community-dwelling elderly population: the Bambui Brazil cohort study of aging

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**Purpose:** Understanding the relationship between excessive weight (EW; BMI ≥ 25 kg/m²) and mortality in older adults is critical to supporting clinical decisions. Unexpected findings of longer survival rates in elderly with heart disease (HD) and obesity guidelines should consider these results for recommendations of weight control in older adults.

**Methods:** 1,606 participants entered the study at baseline (1997). Data on mortality until 31st December, 2007 were used in this analysis. BMI was measured at baseline and 5th years of follow-up. Subjects with BMI ≥ 18.5 kg/m² at any time-point were excluded. HD was defined by the presence of both major ECG abnormalities and BNP levels in the highest tertile category. Survival rates were compared by Kaplan-Meier curves between four groups: NW and HD, NW and HD +, EW and HD, - and HD +. Extended Cox models were adjusted for BMI, HD, HD, demographic, clinical, laboratory and lifestyle-related co-variables.

**Results:** During a mean follow-up time of 9.0 (SD 3.1) years, there were 13,339 person-years of follow-up and 457 (32.2%) deaths. Mean age and BMI were 68 (SD 7.0) years and 25.9 kg/m² (SD 4.8), respectively. Survival rates were significantly higher in the EW in comparison to NW groups (p < 0.001; Figure 1). BW was a predictor of mortality (HR 0.960; 95% CI 0.935–0.986) after full-adjustment. Interaction between BMI and HD was not significant (p=0.846).

**Conclusion:** BMI is an independent protective factor in elderly subjects and EW is associated with higher survival rates in subjects with and without HD in comparison to NW. HD and obesity guidelines should consider these results for recommendations of weight control in older adults.

**P3658**

Serum albumin concentration as a predictor of prognosis for the patients with congestive heart failure

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**Purpose:** Undernutrition is common in patients with heart failure. The aim of this study is to evaluate whether the serum albumin concentration can predict the prognosis in the patients with acute decompensated heart failure (ADHF).

**Methods:** 556 patients with ADHF were divided into two groups by the median of serum albumin concentration on admission, low albumin group (≤ 3.6 g/dl, n = 264) and high albumin group (≥ 3.6 g/dl, n = 292). The short-term and long-term prognoses of two groups were investigated retrospectively.

**Results:** In-hospital mortality in low albumin group was significantly higher than in high albumin group (8.7% vs. 3.4%, p = 0.0084). During the mean follow-up periods of 57±219 days, 133 patients (23.9%) died for all cause and 84 patients (15.1%) died for cardiac cause. Long-term prognosis in low albumin group was significantly poorer compared with high albumin group (log-rank, p < 0.0001). The analysis by Cox proportional hazard models revealed that, in the unadjusted model, the risk of death was significantly higher in low albumin group compared with high albumin group (hazard ratio, 2.15; 95% CI, 1.51–3.07; p < 0.0001). The result was the same in the age- and sex-adjusted model (hazard ratio, 1.71; 95% CI, 1.18–2.45; p = 0.0030).

Conclusions: Serum albumin concentration is a useful as a predictor of prognosis for the patients with ADHF.

**P3659**

Prognostic value of bone remodeling in Chronic Heart Failure

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**Purpose:** Patients with chronic heart failure (CHF) have lower bone mineral density, which is related to lower vitamin D status, secondary hyperparathyroidism and bone turnover markers. Our aim was to study prognostic value of bone remodeling and associated parameters in CHF.

**Methods:** We evaluated bone mineral density (BMD, dual-energy X-ray absorptiometry) of lumbar spine (L1-L4) and femur (Neck, Total), serum levels of intact parathyroid hormone (PTH), 25-OH-vitamin D, calcitonin, markers of bone formation (intact osteocalcin - OC) and resorption (C-terminal collagen type I collagen - CTX, osteoprotegerin - OPG), urinary albumin excretion (UAE), glomerular filtration rate (eGFR, MDRD) in prospective study of 82 stable CHF patients ≥ 60 year.

**Results:** Bone mineral density (BMD) in comparison to normal weight (NW; 18.5 kg/m²) patients (15.1%) died for cardiac cause. Long-term prognosis in low albumin group (95% CI: 1.14–9, p = 0.03); in patients with DSF, was 5.47 (95%CI 1.57-18, p = 0.006).

**Conclusion:** Serum albumin concentration is a useful as a predictor of prognosis for the patients with ADHF.

**P3660**

Self-rated health independently predicts survival in patients with heart failure

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**Purpose:** The recently published Cardiac Insufficiency Bisoprolol Study in Elderly (CIBIS-ELD) trial revealed that patients’ self-rated health (SRH) is predictive for adverse events during beta-blocker uptitration in patients with heart failure. This secondary analysis examined the predictive value of SRH for survival after the end of uptitration.

**Methods:** 671 patients (242 women, 36%) aged 72±5 years (mean ± SD) provided information on SRH before and after beta-blocker uptitration in CIBIS-ELD. They were followed up after 1.6-5.6 years. SRH was measured by asking “How do you rate your health in general?”, using a five-point scale (scale: 0–5). The numbers indicating better health: 1=excellent, 2=very good, 3=good, 4=fair, 5=poor.

**Results:** 334 patients (50%) reported fair or poor SRH before or after the uptitration or on both occasions (subgroup SRH<), the others reported excellent,

**Conclusions:** Serum albumin concentration is a useful as a predictor of prognosis for the patients with ADHF.
very good or good SRH at all three time points (SRH+). Patients in group SRH- were older, more often women, had more often preserved ejection fraction and higher NYHA classes. 49 (14.5%) patients in SRH+ and 72 (21.6%) in SRH- died. P=0.02. Mortality in SRH- was independent of whether or not COPD was reported on one or both occasions (P=0.42). In Cox regression adjusting for age, sex, beta-blocker pre-treatment, ventricular function, and NYHA class and heart rate achieved at the end of beta-blocker up titration, SRH was independent of pred- dictive mortality for (SRH- vs SRH+): HR 1.65, 95% CI 1.13 to 2.41, P=0.009.

Conclusions: The simple question of ‘How do you rate your health in general?’ predicts outcomes in our analysis of the to date largest sample of well charac- terised patients with heart failure, even after adjustment for established risk pre- diction covariates. Assessment of SRH should be included in nursing assess- ments of patients with heart failure and stimulate further research into whether SRH can be improved.

P3661 Contemporary prognosis in new york heart association class III-IV heart failure with reduced ejection fraction: who should be referred for advanced therapy?

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Purpose: In heart failure with reduced ejection fraction, drug and device therapy related mortality. However, many patients remain in NYHA class III-IV with poor quality of life and high mortality. The contemporary prognosis, predictors of prog- nosis, and criteria for beginning the evaluation process for heart transplantation and ventricular assist device are unknown.

Methods: We studied 8,764 unique patients with ejection fraction < 40% and NYHA class III-IV registered in the Swedish Heart Failure Registry between 2000 and 2011. Observed all-cause mortality and the influence of patient character- istics were estimated with Kaplan-Meier analysis and uni- and multivariate Cox regression. Excess mortality compared to the overall Swedish population was assessed by relative survival modeling.

Results: Mean±SD age was 73±12 years and 29% were women. One- and 5- year observed mortality was 25% and 62%, and excess mortality was 21% and 49% respectively. The corresponding mortality figures (one-year/5-year) for dif- ferent age groups were as follows: age<60: observed 11/24%, excess 11/31%; age 66-80: observed 21/60%, excess 19/52%; age>80: observed 40/84%, ex- cess 33/68%. Selected independent high risk predictors of mortality are listed in the table.

<table>
<thead>
<tr>
<th>Variable</th>
<th>NYHA I-II</th>
<th>Duration of HF ≤ 3 months</th>
<th>SBP ≤ 120 mm Hg</th>
<th>Creatinine ≤ 1 mg/dl</th>
<th>Hb ≤ 120 g/L</th>
<th>NT-proBNP History of ≤ 2000 ng inotropes</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.61</td>
<td>1.44</td>
<td>2.00</td>
<td>1.78</td>
<td>1.25</td>
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All p-values <0.01; HR, multivariate hazard ratio by Cox regression. NYHA, New York Heart Association; HD, ischemic heart disease; HF, heart failure; SBP, systolic blood pressure; Hb, hemoglobin; NT-proBNP, N-terminal pro brain natriuretic peptide.

Conclusions: Patients with NYHA class III-IV heart failure and ejection fraction < 40% have a poor prognosis and overwhelmingly, mortality is due to heart failure, even in patients up to 80 years old. Patients with one or more high risk predic- tors should be assessed for advanced therapy, such as heart transplantation or destination therapy left ventricular assist device.

P3663 COPD confirmed by spirometry impacts on survival in heart failure

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Purpose: We investigated the prognostic impact of confirmed vs unconfirmed COPD on mortality risk in systolic heart failure (SHF).

Methods: Consecutive outpatients were evaluated 6 months after hospitalization for SHF (left ventricular ejection fraction <40% prior to discharge). Evaluation included clinical signs and symptoms, echocardiography and spirometry. COPD was diagnosed if forced expiratory volume in the first second (FEV1) divided by forced vital capacity (FVC) inhalation remained <0.7 after 100µg fenoterol.

Results: We included 619 patients, meanage 65±12 years, 75% male. COPD was reported in medical records or by the patient in 144 cases (23%). How- ever, COPD was only proven by spirometry in only 32/144 (22%). Further, COPD was newly diagnosed in another 26 subjects. Reported but unconfirmed COPD was associated with higher NYHA classification, smoking, renal dysfunction and higher BNP levels, whereas proven COPD was only related to smoking (all p<0.05). During a median follow-up time of 30 months, 133 patients died (22%). The figure shows the impact of COPD on all-cause death (adjusted for age and sex).

Conclusion: Absence of COPD in medical records and spirometry is associ- ated with better prognosis, whereas COPD if confirmed by spirometry has a pro- nounced impact on mortality risk in SHF. Reported but not confirmed COPD is frequent and indicates a subgroup of patients with intermediate risk mediated by severity of SHF and burden of comorbidities.

P3664 Impact of chronic obstructive pulmonary disease severity on symptoms and prognosis in patients with systolic heart failure

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Background: Systolic heart failure (SHF) and chronic obstructive pulmonary dis-
Low serum total cholesterol level is a surrogate marker of mortality, but not a risk factor, for poor outcome in patients hospitalized with acute heart failure: a report from the Korean Heart Failure Registry

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Background: Hypercholesterolemia is a major risk factor for incident coronary artery disease, and the prevalence of heart failure (HF). The causal relationship between low total cholesterol (TC) levels and poor clinical outcome in patients with acute HF has not been investigated. This study evaluated the effect of cholesterol levels on the long-term outcome in patients hospitalized due to acute HF.

Methods and results: We analyzed a cohort of 2,797 HF patients who were eligible for analysis in 3,200 patients of the Korean Heart Failure Registry. Patients were stratified into quartiles of TC (Q1: <133, Q2: 133-158, Q3: 159-190, and Q4: >190 mg/dL). Propensity score matching was performed with the patients in Q1 and Q4. Patients with lower serum TC had lower blood pressure, lower hemoglobin, lower serum sodium, and higher natriuretic peptide levels than patients with higher TC levels. Low TC was associated with increased risks for death and readmission due to HF; the adjusted hazard ratio (HR) of Q1 compared with Q4 were 1.57 (95% CI 1.30-1.90). However, propensity score matching analysis revealed that low cholesterol itself did not affect outcome (HR=1.12; 95% CI 0.85-1.48).

Conclusions: Low TC is strongly associated with mortality and morbidity in patients with HF. However, low TC seemed to be a secondary result of the patient’s state, rather than an independent risk factor for poor outcome.

Prognostic relevant of plasma aldosterone during renin-angiotensin-aldosterone system inhibition in heart failure patients

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Purpose: A significant subset of patients with heart failure (HF) shows an increase in aldosterone level (aldosterone breakthrough) while on ACE-inhibitors (ACEI), angiotensin receptor blockers (ARBs), and even aldosterone antagonists, but clear data are currently lacking on its impact on patients’ outcome. We thus aimed to assess the prognostic value of plasma aldosterone in HF patients receiving dual renin-angiotensin-aldosterone system (RAAS) antagonism.

Methods: We selected 389 consecutive patients with systolic heart failure (left ventricular ejection fraction ≤35%) admitted to our Cardiology Unit during the period from January 2001 to December 2006. Severity of COPD was defined according to the GOLD classification. There was 37.9% of COPD. Patients’ distribution according to GOLD stages I, II, III and IV were respectively as follows: 51.5%, 37.9%, 7.6% and 3.0%. Seventy-three percent of patients died within 5 years of hospital admission. All patients were then followed-up 6 months with ACEi/ARBs at the maximum tolerated dose and on aldosterone synthase inhibitors.

Results: Persistent elevation of plasma aldosterone levels despite complete RAAS blockade holds significant prognostic value in HF patients and might identify subsets likely needing a tailored, enhanced therapeutic effort, eventually using novel approaches acting on the RAAS, such as direct renin inhibitors or aldosterone synthase inhibitors.

Conclusion: Our results highlight the importance of aldosterone levels monitoring during RAAS blockade for patients hospitalized for acute HF, with potential impact on outcome.

Mortality risk stratification in Chronic Heart Failure patients: an analysis of the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA)

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Background: Classification and Regression Decision Trees (CART) are an attractive method of assigning risk as they are concise, do not rely on model assumptions, are easily understood by clinicians and can be incorporated into software applications.

Methods: Patients from the CORONA study with chronic heart failure due to left ventricular systolic dysfunction (LVEF ≤40%) and ischemic heart disease (IHD) who had a measurement of amino-terminal pro-brain natriuretic peptide (NT-proBNP) were included in this analysis. CARTD were constructed using 1789 randomly selected patients as a training dataset and another 1826 patients as a validation set to stratify patients into those with a low, medium or high mortality (all-cause) at 1-year. Fourteen clinical variables were considered including age, sex and data obtained from the clinical history and examination and standard laboratory measurements. The CARTD were compared with logistic regression (LR) models using ROC curves.

Results: The median age was 72 (IQR: 67-78) years, 75% of patients were men and 10% had died by 1-year. In the CARDT, NT-proBNP was the strongest predictor of mortality. Body mass index (BMI) added a little more information, with further small contributions from creatinine, cholesterol, systolic BP, age and heart rate. Similar predictors were found in LR-models. Using CARDT, 14% of patients with an NT-proBNP >4.57775mmol/L had a one-year mortality of 24.3%, 43% with an NT-proBNP 1.145mg/L had an annual mortality of 5.3% and those with intermediate plasma NT-proBNP concentrations had an annual mortality of 10.5%. Addition of BMI identified only few patients (<10%; 1.7%) who had an NT-proBNP <1.145mg/L but BMI <21.2 with an annual mortality of 14.3%. The CARDT performed similarly to LR-models for predicting mortality (training dataset: ROC area with 95% CI: 0.737 (0.693-0.777) for CARDT and 0.747 (0.717-0.778) for LR; validation dataset: 0.668 (0.626-0.710) for CARDT and 0.683 (0.641-0.726) for LR).

Conclusions: CARDT analysis suggests that NT-proBNP is a useful predictor of outcome in patients with heart failure due to LVD and IHD. Few other variables add clinically useful prognostic information. This could greatly simplify prognostic assessment in this population.

Prognostic impact of high-sensitive troponin T assessment in chronic heart failure and interaction with statin therapy. Results from CORONA

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Background: Circulating levels of cardiac troponins are elevated in chronic heart failure (HF) and related to adverse prognosis. However, the prognostic value of elevated troponin levels in addition to CRP and BNP/NT-proBNP is still debated.

We examined the prognostic value of high-sensitive troponin T (hs-cTnT) in a sub-study involving approximately 30% of participants in the CORONA study (Controlled Rosuvastatin Multinational Trial in HF).

Methods: hs-cTnT as a risk factor for the primary endpoint (cardiovascular [CV] death, non-fatal myocardial infarction, non-fatal stroke; n=356), as well as all-cause mortality (n=366), CV mortality (n=299), death from CHF (n=92) or sudden death (n=170), total- (n=696) or CHF hospitalizations (n=285) was investigated in 1245 patients (≤60 years, New York Heart Association [NYHA] class II-IV, is...
Prevalence, incidence, persistence and resolution of anaemia in patients with heart failure and left ventricular systolic dysfunction and the relationship to outcome

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Background: Most reports of the epidemiology of anaemia and its relationship to prognosis in patients with heart failure come from multi-centre clinical trials (that may be unrepresentative of the epidemiological problem) or hospital discharges but few from unselected hospital out-patients in clinical practice.

Methods: retrospective analysis of patients with suspected heart failure referred to a local clinic underwent a systematic evaluation including prior medical history, symptoms, signs, electro- and echocardiograms, standard haematology and biochemical profiles and amino-terminal pro-brain natriuretic peptide (NT-proBNP). Left ventricular systolic dysfunction (LVSD) was defined as an ejection fraction of <40%. Patients were followed clinically and through electronic record systems. Data are presented for baseline (BL) and 12-month follow-up (FU) visits. The WHO definition for anaemia was used (haemoglobin (Hb) <13 for men; <12 for women).

Results: Of 1693 patients presenting with LVSD and in whom Hb was measured, the median age was 72 (IQR 64-78) years, 26% were women, 67% had ischaemic heart disease, 11% had COPD, 38% were in NYHA class III/IV, 23% in atrial fibrillation. Median (IQR) NT-proBNP was 1753 (725-3961) pg/ml and eGFR 60 (45-73) ml/min/1.73m². At BL, 557 patients (33%) were anaemic according to the WHO definition (433 men; 124 women), of which 174 (10%) were 1.1-2.0 g/dL below. Between BL and FU, 14% of patients were anaemic with <9% of women.

Conclusion: Anaemia is a useful prognostic indicator in heart failure and may be a target for therapy.
Autophagic vacuolization of cardiomyocyte predicts good prognosis in early phase of diluted cardiomyopathy

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Purpose: Autophagic vacuole (AuV) of cardiomyocytes is found in patients with diluted cardiomyopathy (DCM). However, significance of that alteration is still unknown.

Methods: Endomyocardial biopsy (EMB) from left ventricle (LV) was performed for 250 consecutive patients with DCM (54.9 ± 45 and 60 (class 3A), 30 and 45 (class3B) and below 30 ml/min (class 4-5) were separated. Those patients had myofibrillar lysis and AuV in the same cardiomyocytes. Those patients were frequently older and had higher rates of comorbid disease (diabetes, atrial fibrillation and renal insufficiency). Low lymphocyte counts were associated with wider QRS durations, lower ejection fractions, lower blood pressures, natriuretic peptide elevations and hyponatremia. Those patients were less likely to receive evidence-based medications (ACEi/ARBs, β-blockers and MRAs). At median follow-up of 9.9 months, patients with low lymphocyte counts experienced higher rates of ACM (38/182 vs. 22%) and CVM-HFH (51% vs 37%), p = 0.001. After adjusting for baseline clinical risk factors, low lymphocyte count remained a predictor of ACM [HR 1.17 (1.02-1.35), P = 0.026] and CVM-HFH [HR 1.33 (1.01-1.76), P = 0.045].

Conclusions: Low relative lymphocyte count occurs in 25% of patients hospitalized for HF and is an independent predictor of poor outcomes beyond traditional prognostic indicators.

The implication on outcome of CKD-EPI reclassification in patients with chronic renal dysfunction

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Introduction: We recently demonstrated that estimated Glomerular Filtration Rate (eGFR) using Cockcroft-Gault formula is the best among eGFR formulas in predicting prognosis in heart failure (HF) patients. Cystatin-C has emerged as an alternative diagnostic biomarker to assess prognosis in HF.

Objective: To compare the prognostic value of Cystatin-C and eGFR in a HF outpatient population and to assess whether the combination of both improves prognostic accuracy.

Methods: 879 patients (72% men, age 70.7 ± 5.3 years, IQR 65.0-77.2) were studied. Aetiology of HF was mainly ischemic heart disease (52.5%). LVEF was 34% (IQR 26-43). Most patients were in NYHA class II (65.3%) or III (26.2%). Median follow-up was 3.4 years (IQR 1.85-5.05). 316 deaths were recorded. In an adjusted model eGFR and Cystatin-C showed similar prognostic value according to AUC (0.767 and 0.769, respectively). Calibration was similar for both biomarkers (Hosmer-Lemeshow test, P > 0.05). Receiver-operating characteristics curves showed good discriminatory power (C-statistic = 0.75 for eGFR and 0.74 for Cystatin-C). Both biomarkers were significant in Cox regression multivariable analysis (HR 0.99 for eGFR and HR 1.14 for Cystatin-C, p < 0.02 for Cystatin-C, respectively). eGFR and Cystatin-C showed highly sig-
sificant prognostic value as quartiles (figure 1A and 1B). When both variables were incorporated together into the multivariable analysis a very significant in-
teraction was found between them (p<0.001). Remarkably, Cystatin-C value for risk stratification was in ambulatory HF patients. The combination of both mark-
ers improved prognostication only in moderate degrees of renal dysfunction.

**Conclusion:** Cystatin-C and eGFR showed quite similar overall predictive long-
term prognostic value in ambulatory HF patients. The combination of both marks

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**Prognosis - biomarkers**

**P3678**

**Hemoglobin < 12 g/dl in patients with heart failure: marker of an insufficiently treated high-risk patient group and independent risk factor**

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**Background:**

The role of anaemia in patients with heart failure (HF) is not well established. The potential impact of anaemia on prognosis and therapy outcome has been evaluated in a number of small studies. However, the exact role of anaemia in patients with HF is not clearly defined.

**Purpose:**

To determine the impact of anaemia on therapy and prognosis of patients with HF.

**Methods:**

A prospective, observational, multicentre cohort study of consecutive patients with chronic systolic heart failure (CSHF) was conducted. The primary endpoint was all-cause mortality, while the secondary endpoints were hospitalization for acute heart failure or death. The study included 1278 patients from 2010 to 2014.

**Results:**

The prevalence of anaemia was 34.3% at baseline, and the median haemoglobin level was 12.1 g/dl. The Cox regression analysis showed that anaemia was associated with an increased risk of all-cause mortality (HR=1.5, 95% CI 1.2-1.9, p<0.001) and hospitalization for acute heart failure or death (HR=1.4, 95% CI 1.2-1.6, p=0.001). The association between anaemia and the primary endpoint was independent of other risk factors, including age, sex, left ventricular ejection fraction, left ventricular mass, and the presence of comorbidities.

**Conclusion:**

Anaemia is an independent risk factor for all-cause mortality and hospitalization for acute heart failure or death in patients with CSHF. 

**P3679**

**Must NT-proBNP be always included in a multimarker strategy for prognosis in heart failure?**

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**Background:**

Natriuretic peptides are used in the risk stratification of patients with heart failure. The addition of new biomarkers to the NT-proBNP assay may improve the predictive value of this strategy.

**Objectives:**

To assess the utility of the combination of NT-proBNP and other biomarkers in the risk stratification of patients with heart failure.

**Methods:**

A retrospective analysis of 283 patients with heart failure admitted to the Cardiology Department of a university hospital was performed. The primary endpoint was all-cause mortality. The Cox regression analysis was used to assess the independent risk factors.

**Results:**

The median age of the patients was 66 years (IQR 57-72) and 159 (56.1%) were men. The median NT-proBNP level was 997 pg/mL (IQR 503-1928). The addition of other biomarkers increased the predictive value of the NT-proBNP assay. The combination of NT-proBNP and other biomarkers was associated with an increased risk of all-cause mortality (HR=3.7, 95% CI 1.6-8.4, p=0.002) and hospitalization for acute heart failure or death (HR=1.4, 95% CI 1.2-1.6, p=0.001).

**Conclusion:**

The combination of NT-proBNP and other biomarkers increases the predictive value in the risk stratification of patients with heart failure.
biomarkers reflecting different pathophysiological pathways into a multimarker as-
say seems rational and reliable to better stratify the mortality risk.

Objectives: To assess the performance of a multimarker strategy for risk stratifi-
cation in a real-life cohort of ambulatory HF patients.

Patients and methods: We analyzed 876 consecutive outpatients (72% men, median age 70.3 years, most in NYHA class II (65.5%) or III (36.5%)). Median LVEF was 34%. HF etiology was mainly ischemic (52.1%). A combination of biomarkers reflecting myocardial injury (hs-cTnT), myocardial stretch (NT-proBNP) and ventricular fibrosis and remodelling (ST2) was added to established mortality risk factors (age, sex, LVEF, NYHA functional class, diabetes, eGFR, ischemic etiology, sodium, hemoglobin, β-blocker treatment, and ACEI or ARB treatment).

Results: During a median follow-up of 41.4 months, 311 patients died. In the mul-
tivariable Cox regression analysis, all three biomarkers were independent prog-
nosticators (NT-proBNP p = 0.037, hs-cTnT p<0.002 and ST2 p<0.001). The combined addition of hs-cTnT and hs-ST2 to the model yielded good measure-
ments of performance (c-statistic 0.79; integrated discrimination improvement 4.1
[95% CI, 2.5–6.5]; net reclassification index 13.9% [95% CI, 6.2–21.6]). Figure 1 depicts Kaplan-Meier curves according to hs-cTnT and ST2 levels (above or be-
low cut-off points). Reclassification did not benefit NT-proBNP addition into the full model; some indices even worsened with all three biomarkers.

Conclusions: A multimarker strategy seems useful for stratifying risk in chronic heart failure. However, NT-proBNP in addition to new generation biomarkers hs-
cTnT and hs-ST2 had a limited effect on risk stratification.

P3680

Not one month but three month of post-operative BNP level predicts mid-to-long-term prognosis in end stage heart failure patients with left ventricular assist device support
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Background: Brain natriuretic peptide (BNP), secreted from the cardiac ventri-
cle in response to ventricular volume expansion or pressure overload, is widely rec-
ognized as a valuable marker for not only diagnosis, but also prediction of
prognosis of heart failure patients. Implantation of a left ventricular assist device
(LVAD) for patients with severe heart failure unloads a failed left ventricle and dy-
namically lowers BNP level. However, individual patients with LVAD support show
varied levels of the peptide during the period of support and the significance
of changing BNP levels in such patients has not been fully elucidated. In Japan,
heart transplantation candidates generally wait for 2 to 4 years before receiving
heart transplantation and approximately 90% receive an LVAD as a bridge to trans-
plantation. Thus, it is crucial to predict the prognosis of these patients. Herein, we
investigated whether BNP level is a prognostic marker for patients with an LVAD.

Methods: To elucidate the significance of BNP level in patients with an LVAD, we
retrospectively analyzed serial changes in 88 patients who survived for more
than 30 days after receiving an LVAD. BNP levels and other data from laboratory
and physiological examinations were obtained before and serially for up to 24 months
after LVAD implantation. Cox’s proportional hazards model and ROC analysis
were used to determine the optimal cutoff levels to determine mortality in these
LVAD patients.

Results: Seventy-nine patients received a paracorporeal-pulsiatile, 2 an
implantable-pulsiatile, and 7 an implantable-continuous-flow type LVAD. Thirty-
nine died from 34 to 1245 days after implantation (group D). Eleven were suc-
cessfully weaned from LVAD (group R) and 36 underwent cardiac transplantation
in Japan (group J-HTx). The mean period of LVAD support in group J-HTx was
906 days. The mean preoperative BNP level for all patients was 1475 pg/mL, and
then became significantly reduced at 1 month after LVAD implantation, with no
significant differences among the 3 groups. In contrast, BNP levels at 3 month
after implantation were significantly lower in groups R and J-HTx, as compared
to group D. ROC analysis revealed that, a BNP level at 3 months after LVAD im-
plantation greater than 176 pg/mL (specificity = 77%, negative predictive value =
80%) was associated with increased mortality during LVAD support (log-rank test
P<0.001).

Conclusion: Post-operative BNP level at 3 months after LVAD implantation may
be a mid-to-long-term prognostic marker for all-cause mortality in end stage heart
failure patients with LVAD support.

P3681

Prognostic significance of plasma concentrations of mid regional pro-adrenomedullin in patients with suspected chronic heart failure
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Background: Adrenomedullin is a powerful endogenous vasodilator secreted from
the vasculature, heart and other organs. Plasma concentrations
increased in patients with heart failure. Its prognostic value in unselected patients
with suspected chronic heart failure has not been assessed.

Methods: Patients with suspected heart failure referred from the local community
to a specialist clinic were invited to participate. Consenting patients underwent
a systematic evaluation including prior medical history, medications, symptoms,
signs, electro- and echocardiograms, standard haematology and biochemistry
profiles and measurement of stable prohormone fragments, mid-regional pro-
adrenomedullin (MR-proADM) and amino-terminal pro-brain natriuretic peptide (NT-proBNP).

Results: Of 2,260 patients enrolled, the median age was 72 years (IQR: 65 to 78),
787 were women, 1031 had left ventricular systolic dysfunction (LVSD), 412 had a major echo abnormality other than LVSD, 264 had no major echo abnor-
mality but an NT-proBNP – 400ng/L (of whom 84 had atrial fibrillation and 26 had
eGFR <30ml/min) and 556 had none of the above. Median (IQR) MR-proADM
overall was 0.75 (0.57-1.03) nmol/L, and for each of the four sub-groups was 0.81
(0.60-1.11), 0.80 (0.61-1.16), 0.92 (0.65-1.15) and 0.61 (0.49-0.77) nmol/L re-
spectively. Over a median follow-up of 4.9 (IQR: 3.3-7.0) years, 997 patients died,
572 of cardiovascular causes. In univariable analysis, MR-proADM was strongly
related to all-cause, cardiovascular and non-cardiovascular mortality (HR: 2.41
with 95% CI: (2.23-2.61), HR: 2.34 (2.11-2.59) and HR: 2.52 (2.24-2.85) respec-
tively, p<0.001 for all). In a multi-variable Cox regression model, MR-proADM
provided additional prognostic information to 17 standard clinical variables (age, sex, aetiology, diabetes, COPD, symptoms, quality of life, NYHA, BMI, heart rate and rhythm, systolic blood pressure, oedema, severity of ventricular dysfunction, haemoglobin and creatinine and NT-proBNP) for all-cause mortality.

Conclusions: MR-proADM provides complementary information to other pow-
erful prognostic variables in patients with suspected chronic heart failure encoun-
tered in routine clinical practice. Whether it is just a marker of risk or sits on
an important pathway driving the progression of heart failure awaits further study.
Serum markers of collagen turnover predict future shocks in ICD recipients with dilated cardiomyopathy on optimal treatment

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Objectives: We investigated prospectively whether serum markers of collagen turnover could be used as predictors for the occurrence of malignant ventricular arrhythmias in patients with non-ischemic dilated cardiomyopathy (NIDC) implanted with an implantable cardioverter defibrillator (ICD) for primary prevention.

Methods: Serum C-terminal propeptide of collagen type-I (CtIP), C-terminal telopeptide of collagen type-I (CTIP), matrix metalloproteinase (MMP)-1, and tissue inhibitor of matrix metalloproteinases (TIMP)-1 were measured as markers of collagen synthesis and degradation in 70 patients with mildly to moderate symptoms due to NIDC with LV EF <35%, who received an ICD for primary prevention of SCD. Patients were evaluated for any appropriate ICD delivered therapy, whether shock or antitachycardia pacing, during a 1-year follow-up period.

Results: Appropriate device therapies were delivered in 14 of the 70 patients during the follow-up period, with antitachycardia pacing in 2, antitachycardia pacing with shocks in 4, and shocks in 8. Preimplantation MMP-1 levels were significantly higher in patients who had appropriate ICD-delivered therapy than in those who did not have any therapy (27.7±1.6 ng/ml vs. 24.1±2.5 ng/ml, respectively, p<0.001). The same was true for baseline serum concentrations of TIMP-1 and CtIP (9.9±1.4 ng/ml vs. 5.8±1.8 ng/ml, p<0.008 and 0.46±0.19 ng/ml vs. 0.19±0.07 ng/ml, p<0.001, respectively).

Conclusions: Undoubtedly, ECM alterations play a crucial role in the constitution of an arrhythmogenic substrate in NIDC and, given the availability of therapies to prevent fatal ventricular tachyarrhythmias, the quest for factors that have a very good correlation with appropriate ICD discharges in these patients is logical. Our results suggest that markers of collagen turnover as predictors of arrhythmic events in ICD recipients could provide an auxiliary tool in this context.

Prognostic value of serum indoxyl sulfate in patients with nonischemic dilated cardiomyopathy

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Purpose: Elevated serum indoxyl sulfate (IS) has been shown to be an implication of cardiovascular disease. The aims of this study were to determine if serum IS is associated with hemodynamic parameters, and is a possible predictor of cardiac events in patients with nonischemic dilated cardiomyopathy (NDCM).

Methods: Seventy-six NDCM patients in stable condition underwent laboratory measurements, echocardiography, and cardiac catheterization. Serum IS levels were measured using high-performance liquid chromatography. Using a pigtail catheter with a high-fidelity micromanometer, we measured the maximum first derivative of LV pressure (LV dP/dtmax) and the pressure half-time (T½) as an index of contractility and LV saccular relaxation, respectively. All patients were monitored for cardiac events for an average of 82 months. Cardiac events were defined as cardiac death or hospitalization for worsening of heart failure.

Results: The mean serum IS level was 1.04±0.70 ng/ml (range: 0.38 to 4.0 µg/L). Only the LV ejection fraction (LVEF) and brain natriuretic peptide (BNP) levels in the patients were 31.6±10.2% (mean ± SD) and 204±219 pg/mL, respectively. Patients were divided into 2 groups: low IS group: IS <0.9 high IS group: IS ≥0.9 µg/mL based on the median value of serum IS. There were no significant differences in LVEF, LV dP/dtmax and BNP between the 2 groups. However, IS was significantly higher in the high IS group than in the low IS group (P = 0.008), and was an independent determinant for IS. In addition, T½ was significantly longer in the high IS group than in the low IS group (43.8±6.5 ms versus 40.6±7.3 ms, P = 0.024). The probability of event-free survival was lower in the high IS group than in the low IS group by Kaplan-Meier methods (P = 0.014). Moreover, after adjustment for age, sex, BMI, history of PCI, CABG, eGFR, LVEF, diabetes, smoking and common drugs, the CPX-induced increase in h-FABP (HR 3.84, 95% CI 1.52-9.72, P=0.004) remained an independent predictor of cardiac events. (HR = 8.76, 95%CI 1.15-66.94, P = 0.036).

Conclusions: Elevated serum IS may be associated with cardiac dysfunction, especially diastolic function, and consequently increase the incidence of cardiac events in ambulatory patients with NDCM.

Exercise-induced increase in heart fatty acid binding protein (h-FABP) concentrations predicts adverse events in patients with advanced heart failure

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Purpose: We have previously reported that measurement of post-cardiopulmonary exercise (post-CPX) levels of biomarker of cardiomyocyte stress improves prediction of adverse outcomes (AO) in patients with advanced heart failure (HF). We hypothesized that transient ischemia and increased hemodynamic load during CPX might increase the predictive value of h-FABP, a marker of cardiac ischemia and injury.

Methods: We measured plasma levels of h-FABP (Random) in 30 controls and 108 advanced HF patients (NYHA average 2.7±0.6, 47% ischemic, age 54±8) undergoing symptom-limited CPX stress testing. Blood samples were collected before and immediately after CPX. We used a Cox proportional hazard model to examine the association between h-FABP levels and adverse outcomes (death, urgent heart transplant or VAD implantation).

Results: The average follow-up was 17±10 months; 35 patients experienced AO. Median h-FABP concentrations pre and post CPX, and the CPX-induced change were 2.7 (IQR 2.4-3.4), 2.6 (2.3-3.6) and 0.3 (0.1-0.4) ng/ml in controls and 4.3 (3.0-6.0), 4.5 (3.3-6.9) and 0.4 (0.0-1.0) ng/ml in patients. h-FABP levels were significantly higher in patients with ischemic than with non-ischemic etiology of HF both pre- and post-CPX. After adjustment for important clinical covariates including age, gender, BMI, history of PCI, CABG, hypertension, eGFR, LV EF, diabetes, smoking and common drugs, the CPX-induced increase in h-FABP (HR 3.84, 95% CI 1.52-9.72, p=0.004) was the best predictor of AO. HR for the pre- and post-CPX levels (2.04, 0.84-4.93) and post-CPX (1.44, 0.60-3.43) levels lacked statistical significance. Figure shows event-free survival using ROC-optimized cutoff of 0.6 ng/ml for CPX-induced change in h-FABP.

Conclusions: CPX-induced increase in h-FABP predicts AO in advanced HF.
Methods: We used data from 21 heart failure studies included in the Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). Preserved left ventricular ejection fraction (EF) was defined as an EF ≥50%. The outcome was all-cause mortality at 3 years. Pulse pressure was analysed in quintiles in a multi-variable model adjusted for the previously reported MAGGIC prognostic variables (age, gender, ischemic aetiology, atrial fibrillation, hypertension and diabetes).

Results: The 21 studies included 18,037 patients: 14,983 with HF-REF and 3054 with HF-P EF. There were 3621 and 567 deaths amongst HF-REF and HF-P EF patients, respectively, after 3 years follow-up. Pulse pressure was an independent predictor of death in both groups of HF patients (Table 1). Patients with HF-REF in the lowest pulse pressure group had the highest mortality risk compared to all other pulse pressure groups. For patients with HF-P EF this relationship of lowest pulse pressure with highest mortality risk was still present but was less consistent across all pulse pressure groups.

Table 1. Multivariable model by quintiles of pulse pressure - adjusted for the “MAGGIC” variables

<table>
<thead>
<tr>
<th>Pulse pressure</th>
<th>All (n=18,037) (HR, 95% CI)</th>
<th>HF-REF (n=14,983) (HR, 95% CI)</th>
<th>HF-P EF (n=3054) (HR, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-39 mmHg</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>40-48 mmHg</td>
<td>0.72 (0.66-0.80)</td>
<td>0.72 (0.65-0.80)</td>
<td>0.86 (0.58-1.29)</td>
</tr>
<tr>
<td>49-55 mmHg</td>
<td>0.65 (0.59-0.72)</td>
<td>0.67 (0.60-0.74)</td>
<td>0.82 (0.42-0.92)</td>
</tr>
<tr>
<td>56-64 mmHg</td>
<td>0.59 (0.53-0.66)</td>
<td>0.59 (0.53-0.66)</td>
<td>0.70 (0.49-1.01)</td>
</tr>
<tr>
<td>65-68 mmHg</td>
<td>0.62 (0.56-0.68)</td>
<td>0.61 (0.55-0.69)</td>
<td>0.67 (0.47-0.95)</td>
</tr>
<tr>
<td>69-166 mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Pulse pressure is a simple, inexpensive and noninvasive marker of outcome in HF patients. Lower pulse pressure independently predicts mortality in patients with HF-P EF as well as HF-REF.

P3687

The prognostic importance of pulmonary hypertension in acute decompensated heart failure

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Background: Elevated pulmonary arterial pressure has been associated with poor outcome in patients (pts) with heart failure. However, previous studies used invasive hemodynamic measurements. The reliability of Doppler echocardiography to accurately estimate pulmonary pressures has been recently questioned in various patient populations. Therefore, we studied the prognostic significance of echocardiographic estimation of pulmonary artery systolic pressure (PASP) in the setting of acute decompensated heart failure (ADHF).

Methods: We studied 286 pts with ADHF who survived the index hospitalization. PASP was assessed by echocardiography prior to hospital discharge. Pts with moderate or severe mitral regurgitation were excluded. The primary endpoint of the study was all-cause mortality. The relationship between PASP categories and mortality was examined using Cox model, adjusting for age, gender, hypertension, diabetes, estimated GFR, diabetes, hemoglobin, cTn I elevation, BNP levels and LV ejection fraction and discharge medications. The median follow-up was 14 months.

Results: Normal (<35 mmHg), mildly elevated (35-49 mmHg) and moderately-severely elevated (50 mmHg) PASP was present in 61 (16%), 167 (42%) and 61 (16%) patients, respectively. There was a graded association between PASP and mortality (Figure). In a multi-variable Cox model, compared with patients with normal PASP, the adjusted hazard ratio for mortality was 2.3 (95% CI 1.2-4.3, P=0.009) in patients with mildly elevated PASP and 4.0 (95% CI 2.2-7.4, P<0.0001) in pts with moderately-severely elevated PASP.

Conclusions: Although PASP is not an exact measure of pulmonary arterial pressure, it remains a powerful noninvasive hemodynamic indicator of mortality in ADHF.

P3688

Pulmonary vascular gradient: a predictor of prognosis in pulmonary hypertension due to left heart disease

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Purpose: Pulmonary hypertension (PH) is defined by a mean pulmonary artery pressure (mPAP) ≥25 mmHg. The disease can be further classified into pre-capillary PH (pulmonary capillary wedge pressure, PCWP ≤15 mmHg) and post-capillary PH (PCWP >15 mmHg). The driving pressure across the pulmonary circulation is often referred to as the transpulmonary gradient (TPG). In the current guidelines post-capillary PH with a TPG (mPAP – mPCWP) >10 mmHg is labeled as "reactive" or "out-of-proportion" PH, as opposed to what is labeled as "passive" PH, i.e. PH as the consequence of isolated elevation of left ventricular filling pressures. The difference between the diastolic pulmonary artery pressure (dPAP) and mean PCWP theoretically represents the pressure gradient between the major pulmonary arteries and the left atrium, comprising the anatomical space of arterioles, capillaries and pulmonary veins. We refer to this hemodynamic value as pulmonary vascular pressure gradient (PVG), and hypothesize that it reflects resistance created in the vascular compartment affected by classical pulmonary arteriopathy. The aim of this study was to test the prognostic value of PVG in post-capillary PH.

Methods: 3107 all-comers who underwent first diagnostic right and left heart catheterizations at rest were analyzed. 1094 of 2351 complete datasets were from patients post-capillary PH. Patients were followed for a median of 137 months (116 to 154, 25th and 75th percentiles). Cutoffs were determined by ROC analysis. Survival difference was assessed by a Cox-proportional hazards model.

Results: Survival analysis corrected for sex, age, coronary artery disease and creatinine clearance <60 ml/min identified a TPG >12 mmHg as a predictor of death in patients with PH. In patients with "out-of-proportion" PH median survival with a PVG >7mmHg (p=0.010) was worse (78 months) than in matched patients with a PVG >7mmHg (101 months).

Conclusions: Our data show that a PVG threshold of 7mmHg identifies patients with "out-of-proportion" PH who have an increased mortality. PVG may be practically useful for clinical drug trials and facilitate the indication of heart transplantation indications with high pulmonary pressures.

Figure 1. Survival according to PASP category

Figure 1

Targeting pulmonary artery pressures in the treatment of chronic heart failure: insights from the CHAMPION trial

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Purpose: High filling pressures from pulmonary artery (PA) catherization are frequently observed in acute heart failure (HF) patients and predict poor clinical outcome. Access to patient PA pressure (PAP) data beyond the acute setting using an implantable haemodynamic monitoring system may provide a method for identifying and treating high filling pressures in patients at increased risk for decompensation.

Methods: CHAMPION trial was a prospective, multi-center, randomized, single-blind study in 550 patients with NYHA class III HF who had been hospitalized for HF in the previous year. Patients were randomized 1:1 to the treatment group (270) where PAP data were available to physicians or to the control group (280). Over the blinded follow up period (average duration of 15 months), there were 412 HF hospitalizations (HFH) (158 Treatment vs. 254 Control, p=0.0001) and 681 non HFH (338 Treatment vs. 343 Control, p=0.58). All events were adjudicated by a blinded clinical events committee.

Results: The mean PAP at implant was similar in both groups (treatment 31.3±11.1 mmHg vs. control 31.8±10.7 mmHg). During the trial, higher PAP...
Kussmaul physiology is associated with poor survival and pulmonary haemodynamics unfavorable for heart transplantation

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Background: Kussmaul physiology (Kp) describes the absence of an inspiratory fall in right atrial pressure. This study aimed to evaluate the clinical correlates and significance of Kp in patients with heart failure (HF).

Methods: This study included 76 consecutive patients with HF who underwent assessment for heart transplantation. We defined Kp as an inspiratory rise in right atrial pressure on cardiac catheterization to increase specificity. Cardiac function/dimensions were obtained from transthoracic echocardiogram. Peak VO2 and ventilatory efficiency (VE/VCO2 slope) were measured by cardipulmonary exercise testing (ramp protocol). Clinical/laboratory data were used to calculate 1-year survival based on the Seattle Heart Failure Survival Score.

Results: Kp was found in 30 of the 76 patients assessed for transplantation. Age and hypertension were comparable (Age 54±3 vs 51±4 years, mean arterial pressure (MAP) 91±11 vs 89±10 mmHg, p=0.02). Left and right ventricular dimensions and function were worse in patients with Kp, although these were not statistically significant (Table). Kp was associated with restrictive transmural filling pattern (high E/A ratio), adverse pulmonary haemodynamics, functional capacity and 1-year predicted survival. As a direct consequence of adverse pulmonary haemodynamics, 7 of the 30 patients compared to 1 of the 46 patients with and without Kp (P<0.05) were turned down for heart transplantation. Five of the 7 patients with Kp who were turned down for transplantation were also unsuitable for left ventricular assist device (poor right ventricular function).

Conclusion: Kp is common among patients referred for transplantation and identifies patients with adverse pulmonary haemodynamics (precluded heart transplantation in almost 1 in 4 patients) and poorer survival.

Arginine vasopressin increases systemic vascular resistance without impairing pulmonary hemodynamics in patients with vasodilatory cardiogenic shock following acute myocardial infarction

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Objectives: Cardiogenic shock following acute myocardial infarction (AMI) is a frequent cause for in-hospital death after AMI. Current therapeutic options include catecholamine therapy for inotropic and vasopressor support. However, these substances exert substantial side effects. In this context, we studied both the hemodynamic effects and safety of vasopressin therapy for patients with inappropriate vasodilation in cardiogenic shock.

Methods: In the current analysis 35 patients with refractory cardiogenic shock complicating AMI (mean ejection fraction of 29±1.6%) and inappropriate vasodilation (mean arterial pressure = 70±15 mmHg despite high doses of norepinephrine and remifentanil ≥0.5 μg/kg/min) were retrospectively included. Patients received optimal standard care including immediate revascularization. All patients were prospectively treated with a continuous infusion of Vasopressin (2 IE/h). All measurements of invasive hemodynamic parameters, as well as vital organ function and safety parameters, were performed at the time of inclusion and throughout a 72 hours follow-up.

Results: Vasopressin therapy resulted in a significant rise in mean arterial pressure and systemic vascular resistance within two hours and this effect persisted during the following 72 hours. At the same time no decline in cardiac output was observed, despite an increase in systemic vascular resistance. Surprisingly, a respective increase of the pulmonary vascular resistance and mean pulmonary artery pressure could not be demonstrated. In the current analysis 35 patients with refractory cardiogenic shock complicating AMI (mean ejection fraction of 29±1.6%) and inappropriate vasodilation (mean arterial pressure = 70±15 mmHg despite high doses of norepinephrine and remifentanil ≥0.5 μg/kg/min) were retrospectively included. Patients received optimal standard care including immediate revascularization. All patients were prospectively treated with a continuous infusion of Vasopressin (2 IE/h). All measurements of invasive hemodynamic parameters, as well as vital organ function and safety parameters, were performed at the time of inclusion and throughout a 72 hours follow-up.

Purpose: The ratio between E/e' measured by echocardiography is a cornerstone in evaluating the diastolic function at rest. E/e' has shown to correlate to filling pressure at rest when examining the full range of E/e'. However, in the range below 15 the correlation between E/e' and filling pressure is considerably weaker. The purpose of this study was to describe the inverse and non-invasive parameters of filling pressure during exercise in patients with an indeterminate E/e' and an enlarged left atrium (LA).

Methods: Forty patients (age 62±8, 80% male) with fully revascularized AMI and LVEF > 45%, E/e' 8-15 and LA – 34 ml/m², and 10 healthy controls (age 47±6, 70% male) underwent a symptom limited supine bicycle test with simultaneous measurements of heart catheterization and Doppler echocardiography. Hemodynamic parameters and echocardiography was performed before and during exercise.

Results: Resting values for patients and controls, respectively were, LVEF 55±7 vs 63±3% (P = 0.001), E/e' 10.4±1.7 vs 6.3±2.0 (P = 0.001), LA indexed 44±11 vs 35±8 ml/m² (P = 0.005), Stroke Volume 84±29 vs 77±22 ml (P = 0.05), Systemic vascular resistance 957±309 vs 1299±442 mmHg/l (P = 0.005), and Filling Pressure 13.2±4.0 vs 8.1±1.8 mmHg/l (P = 0.001).
The prognostic value of myocardial 123I-MIBG scintigraphy in patients with heart failure: a pooled individual patient data meta-analysis

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**Purpose:** The majority of studies on the prognostic value of myocardial 123I-metabolobenzylguanidine (MIBG) in heart failure (HF) patients used a dichotomous division into low and high cardiac uptake groups. In addition studies often differed substantially in the way increased risk was defined. Therefore the purpose of this study was to derive a more precise estimate of the prognostic significance of myocardial MIBG uptake (i.e. late heart mediodiastinal ratio (H/M)) as a continuous variable in HF.

**Methods:** Published studies were identified via a structured search of all relevant electronic databases. To account for differences in imaging techniques the search was limited to Europe and United States. Original individual patient data were pooled and Kaplan Meier statistics and Cox proportional hazard analyses were performed. The primary outcome was all-cause mortality with cardiac death as a secondary outcome.

**Results:** Six studies with a total of 636 patients, stratifying survival in patients with HF by MIBG, could be retrieved. The majority of patients were male (78%), had a decreased left ventricular ejection fraction (LVEF) (31.1%, ± 12.5%) and a mean late H/M of 1.67 ± 0.47 (1st quintile ≤ 1.32; 2nd to 4th quintile 1.33-1.97, 5th quintile ≥ 1.98). During follow-up (truncated at 60 months, 36.9±20.1 months) there were 83 deaths, including 67 cardiac deaths. Kaplan Meier analysis showed that for both all-cause mortality and cardiac death patients with a late H/M ≤ 1.32 (i.e. 1st quintile) had almost 3 times higher risk of dying compared to the other quintiles (p<0.001). Cox proportional hazard analysis showed that LVEF, age and late H/M were the only independent predictors for all-cause mortality (HR 0.97, 95%CI 0.94-0.99, p<0.001) and 0.401 (95%CI: 0.196-0.821) for LVEF and late H/M respectively.

**Conclusions:** Our results indicate that HF patients with the combination of reduced LVEF, increased age and reduced late H/M are at the highest risk of dying compared to those with a better preserved LVEF and higher late H/M. In addition a late H/M cut-off value can be defined to identify patients who are at the highest risk of dying.
The role of microvolt t-wave alternans (MTWA) in real-world heart failure: prevalence and prognostic importance

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Purpose: Ventricular arrhythmias contribute to the high risk of death in heart failure (HF) and can be treated with an implantable cardioverter-defibrillator (ICD). Micr...