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322: Does rhythm outcome after electric cardioversion of persistent atrial fibrillation influence health related quality of life?

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Purpose: Patients with atrial fibrillation (AF) often report symptoms like exercise intolerance, dyspnoea and fatigue. Recent studies indicate that a rate control strategy, including acceptance of permanent arrhythmia, may be at least as good as a rhythm control strategy in the treatment of patients with AF. The aim of this study was to investigate the impact of rhythm outcome after electrical cardioversion of persistent AF on health related quality of life (HRQoL).

Methods: We studied 105 patients with persistent AF scheduled for electrical cardioversion. Patients with congestive heart failure were excluded from the study. QoL was assessed using the Short Form-36 health survey questionnaire (SF-36) 3-6 weeks before and 3 months after cardioversion.

Results: Patients still in sinus rhythm 3 months after cardioversion (n=36) improved significantly from baseline to end of study regarding the subscales vitality (p=0.006), physical role (p= 0.022) and physical function (p=0.002). In patients with a relapse of AF (n=69), there was no change in scores from baseline to follow-up, apart from a lower score for general health (p= 0.025).

Conclusion: Successful cardioversion of AF and maintained sinus rhythm, as opposed to recurring AF, was associated with improved scores related to physical functions and perceived vitality measured with SF-36.

P437 : A novel method for risk assessment in long QT syndrome mutation carriers: Myocardial mechanical dispersion by tissue Doppler imaging

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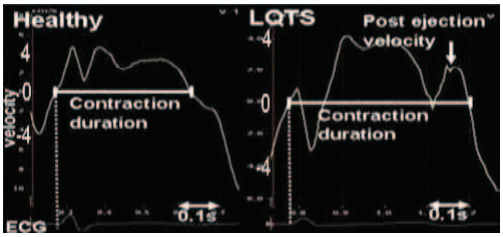
Purpose: Long QT syndrome (LQTS) is characterized by prolonged myocardial action potential which predisposes to life-threatening ventricular arrhythmias. We hypothesized that prolonged action potentials may cause prolonged myocardial contraction by tissue Doppler imaging (TDI). The purpose of this study was to investigate if myocardial mechanical dispersion can be assessed as heterogeneity in myocardial contraction duration and may serve as risk marker in LQTS patients.

Methods: The study population included 65 molecularly defined LQTS mutation carriers (36 with a history of cardiac arrest or syncope and 27 asymptomatic) and 20 healthy control subjects. Myocardial contraction duration and post ejection velocity were assessed by TDI (Fig 1). Standard deviation of contraction duration from the basal LV seg-

ments was calculated as a marker of mechanical dispersion.

Results: Contraction duration was prolonged in LQTS mutation carriers compared to healthy controls (440±70 vs. 360±40ms, p<0.001) and in symptomatic compared to asymptomatic carriers (470±60 vs. 410±60ms, p<0.01). Prolonged contraction duration was better related to severe arrhythmia than QTc (area under curve by ROC analysis 0.73 vs. 0.65). Mechanical dispersion was more pronounced in symptomatic mutation carriers compared to asymptomatic (47±17 vs. 36±18ms, p<0.05). Post ejection velocity was greater in symptomatic compared to asymptomatic carriers (2.4±1.3 vs. 1.3±1.3cm/s, p<0.01).

Conclusion: Mechanical dispersion of myocardial contraction assessed by TDI was increased in LQTS patients. Prolonged contraction duration was superior to QTc for risk assessment in LQTS patients. This new method can be easily implemented in clinical routine and may improve clinical management of LQTS patients.



P490 : Beneficial effects of Celacade immunotherapy among NYHA class II patients with severe systolic dysfunction: data from the ACCLAIM trial

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Background: Some patients with severe systolic dysfunction (LVEF ≤30%) have relatively mild symptoms (NYHA Class II). However, mild symptoms do not necessarily equate to a good prognosis particularly when associated with other predictors of outcome such as a history of recent HF hospitalization. We evaluated the clinical characteristics and response to immunotherapy (IMT) of NYHA class II heart failure patients from the ACCLAIM trial.

Methods: The ACCLAIM trial was a randomized double-blind placebo controlled study of immunotherapy (Celacade system; Vasogen Inc.) in over 2,400 patients. A pre-specified subgroup of 689 (359 IMT; 330 placebo) were NYHA class II with entry criteria including LVEF ≤30%, and prior HF hospitalization or outpatient IV HF therapy within the preceding 12 months.

Results: There were no differences between placebo and Celacade treated groups in baseline characteristics, including age, history of myocardial infarction, mean LVEF, or medication use. In NYHA II patients, IMT significantly reduced the risk of the composite primary endpoint of time to death from all causes or first cardiovascular hospitalization (92 vs. 124 events; hazard ratio 0.61, CI: 0.46 – 0.80, P=0.0003). In contrast, among NYHA III/IV patients (845 IMT; 874 placebo), there was no difference between IMT and placebo groups (307 vs. 305 events; hazard ratio 1.08, CI: 0.92 – 1.27, P=0.33). An examination of prospectively declared ACCLAIM secondary endpoints in the NYHA II subgroup demonstrated a beneficial effect of IMT on a number of outcomes: CV hospitalizations (P=0.001); hospitalization for worsening HF (P=0.016); all-cause death or HF hospitalization (P=0.003); and, all-cause death or all-cause hospitalization (P=0.038).

Conclusion: The results suggest that immunotherapy with Celacade is effective in patients with severe systolic dysfunction but with milder (NYHA class II) symptoms. These observations are consistent with the hypothesis that modulating the immune response to HF can be effective if provided before irreversible fibrosis has developed.

P580 : Plasma levels of sCD40-ligand interact with homocysteine biosynthetic pathway and predict eNOS coupling in human vessels: effects on vascular redox state

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Soluble CD40 ligand (sCD40L), a proinflammatory molecule of the tumor necrosis factor alpha

family released by activated platelets, is a prognostic marker in atherosclerosis, but it is unknown whether sCD40L has direct effects on vascular redox state and endothelial function. Evidence suggests that sCD40L release is associated with plasma total homocysteine (tHCy), that in turn might be associated with other aminoacids of tHCy metabolic pathway, or with folate levels, but the mechanistic importance of these relationships is unclear.

Aim: We determined sCD40L levels, aminoacids in the homocysteine biosynthetic pathway, and vascular superoxide production in patients with atherosclerosis, in order to examine whether plasma tHCy regulates vascular redox by modifying sCD40L release in atherogsclerosis.

Methods: Preoperative plasma sCD40L was determined by ELISA in 138 patients undergoing CABG (aged 66.6±0.6 yrs old). Plasma tHCy, total cystathione, cysteine, methionine, glutathione and 5-methyl-tetrahydrofolate (5-MTHF) were determined by HPLC. Vascular superoxide (O2-) production was determined in saphenous veins obtained during CABG, by lucigenine (5μM) enhanced chemiluminescence +/- NOS inhibitor LNAME (to determine NOS-derived O2-) and after adding NADPH (to determine NADPH-oxidase activity).

Results: sCD40L levels were significantly associated with total vascular O2- (rho=0.349, p=0.009) and LNAME-inhibitable O2- (rho=-0.319, p=0.029), but not with NADPH-induced O2- (rho=-0.112, p=0.423). In bivariate analysis, sCD40L was associated with tHCy (rho=0.317, p=0.0001), cystathione (rho=0.251, p=0.034) and cysteine (rho=0.260, p=0.027), but not with methionine (rho=0.082, p=0.498), glutathione (rho=-0.050, p=0.679) or 5-MTHF (rho=-0.008, p=0.927). In multiple linear regression, plasma tHCy was a predictor of sCD40L (stand. Beta=0.178, p=0.04) independently of 5-MTHF (stand.Beta=0.003, p=0.970).

Conclusions: Plasma total homocysteine, cysteine and cystathione (but not 5-MTHF) are associated with sCD40L levels in patients with coronary atherosclerosis. Importantly, sCD40L is significantly associated with vascular superoxide radical production and eNOS coupling in humans, suggesting that sCD40L may have a central role in the regulation of vascular redox, being a link between homocysteine and atherogenesis.

P606 : Early prediction of tissue viability in acute myocardial infarction by strain Doppler

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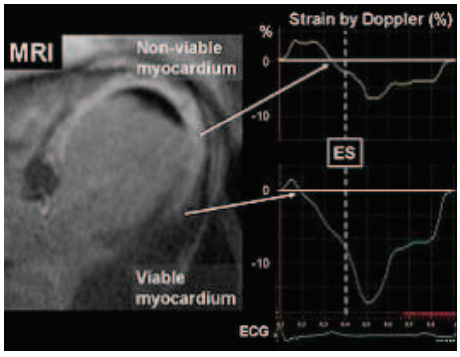
Background: Identification of viable myocardium is vital for treatment strategy during acute myocardial infarction (AMI). The aim was to study if strain Doppler echocardiography (SDE) prior to reperfusion therapy could predict viable myocardium in AMI using cardiac magnetic resonance imaging (CMR) as a reference method.

Methods: Twenty-six patients (60±12 years, 7 women) with AMI who underwent percutaneous coronary intervention (PCI) were examined by SDE immediately prior to PCI. Systolic longitudinal strain and duration of systolic lengthening was analyzed in 16 left ventricular segments. CMR was performed 11±5 months after reperfusion therapy. Scars exceeding 50% of the segment was considered non-viable.

Results: Duration of systolic lengthening in non-viable myocardial segments was 268±122 ms compared to 33±24 ms in viable segments (p<0.0001), with a direct relationship to scar transmurality (r=0.89, p<0.0001). Duration of systolic lengthening longer than 67% (~2/3) of systole (Figure) identified non-viable myocardium by a sensitivity of 90% and a specificity of 93%. Systolic strain was -15±6% in viable segments in contrast to myocardial lengthening in non-viable segments (4±5%, p<0.0001). Systolic strain showed a good correlation with scar transmurality (r=0.74, p<0.0001), but demonstrated equal sensitivity (91%) but lower specificity (82%) to identify viable segments as compared to timing of systolic lengthening.



Conclusion: SDE performed before reperfusion therapy in AMI can identify viable myocardium. Duration of systolic lengthening might be a valuable and easy tool for predicting recovery of myocardial function.

P653 : Circulating osteoprotegerin levels are associated with peripheral vascular intervention and stroke in patients with stable coronary artery disease: the PEACE trial

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Background: Osteoprotegerin (OPG), a member of the tumor necrosis factor receptor superfamily, is a strong prognostic indicator of mortality and heart failure in patients with acute coronary syndromes and post-infarction heart failure. The association between OPG levels and cardiovascular events in patients with stable coronary artery disease (CAD) is unknown.

Methods: The OPG concentration in plasma was determined in 3767 patients (age 63.7±8.2 years, 19% female) with stable CAD and preserved left ventricular (LV) function included in the PEACE trial and related to the incidence of cardiovascular events.

Results: During follow-up (median: 4.8 years) there were 1290 cardiovascular events, defined as a composite of cardiovascular death, nonfatal acute myocardial infarction, unstable angina, coronary revascularization, stroke, new congestive heart failure, cardiac arrhythmias requiring hospitalization, and angioplasty, bypass or aneurysm repair for peripheral vascular disease. There was a significant increase in the cumulative incidence of this composite end-point with increasing OPG levels (hazard ratio (HR) 1.3, 95% CI 1.1-1.4) per unit increase in log OPG; p<0.001), but this association was attenuated and no longer significant after adjustment for conventional risk factors, including LV ejection fraction and contemporary biomarkers, including NT-proBNP. However, prespecified secondary analyses demonstrated that OPG is independently associated with intervention for peripheral vascular disease (HR 1.8; 95% CI 1.2-2.6; p=0.002) and borderline significant for stroke (HR 1.8; 95% CI 1.0-3.0; p=0.05), but not CAD or heart failure events.

Conclusions: Circulating OPG is associated with the incidence of peripheral vascular disease intervention and stroke in patients with stable CAD.

913 : Cytokine profiles in the circulation of mice with heart failure are etiology-dependent

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Objective: Cytokines are upregulated in heart failure, but little is known about cytokine profiles in various etiologies of heart failure. We hypothesised that the diverse etiologies of heart failure lead to distinct cytokine patterns in the circulation.

Methods: Levels of 25 circulating cytokines were studied in three animal models of heart failure. Myocardial hypertrophy of the left and right ventricle was induced in 7-8 weeks old C57BL/6 male mice by banding of the ascending aorta (AB) and pulmonary artery (PB), respectively. Sham-operated mice were used as controls. The inclusion of mice was based on echocardiographic measurements and organ weights, and the AB mice were divided into a failure and non-failure group. Mice with inducible cardiospecific knockout of the sarco(endo)plasmatic reticulum Ca2+-ATPase SERCA2 (SERCA2 KO) were used as a model for cardiomyopathy. Equivalent mice without deletion of the SERCA2 gene were used as controls. Twentyfive cytokines were quantified by Luminex technology in serum samples obtained one week after AB or PB, and four (non-failing phenotype) and seven weeks (failing phenotype) after induction of SERCA2 knockout. P-values < 0.05 were considered significant.

Results: Our main findings were: (I) The level of four cytokines was increased in both the PB group and in the seven week SERCA2 KO failure group. In the non-failing SERCA2 KO group at four weeks, the serum levels of all measured cytokines were unaltered. (II) No increase in circulating cytokines was found in the AB animals regardless of failure or non-failing phenotype. However,

the level of seven cytokines was decreased in the AB failure group. (III) Interleukin (IL)-12p40 and CXCL9 showed altered levels in all models, though with opposite signs, revealing a distinct pattern of these cytokines in the different etiologies.

Conclusion: In heart failure models with right ventricular overload and SERCA2 KO mice with heart failure, we found increased circulating levels of a specific subset of cytokines, suggesting that right ventricular failure with systemic congestion leads to an increase in circulating levels of cytokines. In contrast, in the model with left ventricular pressure overload and hypertrophy, there was no significant increase in the level of any of the measured cytokines. Interestingly, IL-12p40 and CXCL9 showed etiology-specific alterations in the different heart failure models, indicating a role as novel biomarkers.

936 : Interaction between the effects of rosuvastatin and plasma concentrations of NT-proBNP, a post-hoc exploratory analysis from the corona study

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Background and Aim: A declining benefit of statin therapy on cardiovascular outcome with increasing levels of NT-proBNP was reported in the Heart Protection Study (HPS), which included some patients with a history of heart failure (HF). The CORONA trial was a placebo-controlled, double-blind study that compared the effects of rosuvastatin to placebo in patients with HF and left ventricular systolic dysfunction and a wide range of baseline NT-proBNP levels. We investigated the relationship between baseline NT-proBNP and cardiovascular outcomes in this study.

Results: Plasma NT-proBNP (Roche) was measured at baseline in 3,664 patients; mean (SD) age 73+7 years; LVEF 31+7%; 76% men. Patients were grouped according to tertile of NT-proBNP with 868pg/ml (103pmol/L) and 2,347pg/ml (278pmol/L) defining the lower and upper limit of the mid-tertile. In the lowest tertile of NT-proBNP, which overlapped substantially with patients with higher values in the HPS study, the hazard ratio for the primary endpoint (death from cardiovascular causes, non-fatal myocardial infarction or stroke) was 0.65 (95% CI 0.48 to 0.88) and for all-cause mortality was 0.86 (95% CI 0.63 to 1.17) for rosuvastatin compared to placebo. An interaction test between NT-proBNP as a continuous variable and treatment gave a p-value<0.01. The number of cardiovascular (CV) (467 to 303) and HF hospitalisations (191 to 85) were also substantially lower with rosuvastatin. Respective data for the middle tertile were for the primary endpoint 1.06 (95% CI 0.85 to 1.34), for total mortality 1.03 (95% CI 0.83 to 1.29), 559 to 529 CV and 237 to 250 HF hospitalisations; and for the highest tertile 1.00 (95% CI 0.84 to 1.19), 0.93 (0.79 to 1.10), and 802 to 738 CV and 507 to 447 HF hospitalisations.

Conclusion: In this post-hoc exploratory analysis, rosuvastatin reduced fatal and non-fatal cardiovascular events in patients with the lowest tertile of NT-proBNP, an effect as great or greater than that observed in HPS. Rosuvastatin also exerted a substantial reduction in CV and HF hospitalisations in this group. In contrast, there was no difference in cardiovascular outcomes in patients with substantially higher NT-proBNP values. NT-proBNP might define a population of patients with systolic heart failure that benefits from rosuvastatin treatment. NT-proBNP did not identify a group of patients in whom rosuvastatin increased risk.

967 : Glycemic control in diabetes and mortality from ischemic heart disease: twenty years follow-up of the HUNT 1 study in Norway

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Purpose: Diabetes mellitus increases the risk of ischemic heart disease (IHD), but the influence of long-term glucose control is not clear. We compared IHD mortality during twenty years of follow-up in patients with newly diagnosed diabetes with IHD mortality in an age and gender matched group without diabetes. It was assessed whether glycemic control, indicated by annual measurements of HbA1c, modified IHD mortality in the diabetic group.

Methods: In a large population study in Norway (74 914 people in HUNT1), people ≥ 40 years with non-fasting glucose ≥ 8 mmol/L were invited to a

fasting glucose test, and if necessary, an oral glucose tolerance test. Among individuals with confirmed diabetes, 205 consented to participate in a long-term follow-up. 205 age and gender matched individuals without diabetes were selected from the same population. The diabetic subjects were followed with annual HbA1c until death or for a maximum of ten years. For each patient a mean HbA1c value was calculated from the annual measurements. Based on the median of the calculated mean HbA1c values the diabetes group was dichotomized into well or poorly controlled subjects. Ten years after ended HbA1c follow-up, information on causes of death was obtained by linking individual data to the Cause of Death Registry at Statistics Norway. Death from IHD was defined according to the International Classification of Disease. Cox regression analysis was used to estimate hazard ratios (HR) of IHD mortality between the groups.

Results: After adjustment for BMI, blood pressure, smoking status, education, exercise and established cardiovascular disease, patients with diabetes had 60 percent higher risk of fatal IHD (HR 1.61, 95% CI, 0.90-2.87) compared to people without diabetes. In well controlled diabetic persons (mean HbA1c during follow-up<7.38) the risk was only slightly increased compared to the control group (HR, 1.21, 95% CI, 0.61-2.41). Among diabetic subjects with poor glucose control (mean HbA1c >7.38), the risk of fatal IHD was two-fold (HR 2.07, 95% CI, 1.10-3.91).

Conclusion: In persons with newly diagnosed diabetes poor long-term glucose control assessed by annual HbA1c measurements strongly increased the risk of IHD mortality. In diabetic subjects with good long-term glucose control the risk of IHD mortality did not significantly differ from subjects without diabetes. The results indicate that good glucose control is a key to reduce the risk of fatal IHD in patients with diabetes.

P1211 : Non-invasive risk stratification using wedensky modulation to determine cardiac electrical vulnerability late after myocardial infarction

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Introduction: Risk stratification for sudden cardiac death (SCD) remains problematic with reliance on left ventricular ejection fraction (LVEF) which predicts total mortality rather than arrhythmic risk. A novel non-invasive method has been developed that uses Wedensky Modulation (WM) evoked by sub-threshold transthoracic electrical stimulation delivered to every other QRS complex may predict risk of SCD by direct measurement of myocardial electrical vulnerability. This study sought to determine the utility of WM to predict arrhythmic events in patients late after myocardial infarction.

Methods: The study was an international multicentre prospective observational study of post-myocardial infarction patients with ICD implantation. A WM Index (WMI) was computed from differences in the spectro-temporal analysis (frequency/energy) of stimulated vs. non-stimulated beats. Patients were assigned to a WMI-L group (WMI$\leq$ 0.5, n=137) or WMI-H group (WMI > 0.5, n=131). Data were analyzed at 12 months and cumulative ICD-treated arrhythmia event rates for the two WMI groups were compared using Kaplan-Meier estimates.

Results: A total of 268 pts were included with 21 events in the first year for the WMI-L group compared to 37 events in the same time period for the WMI-H group (log-rank $p < 0.01$). Comparing WMI-L to WMI-H, the hazard ratio for event rates was 2.1 at one year (95% CI of 1.2 to 3.6, Wald $p < 0.01$). When stratified both by WMI and LVEF, proportional hazards showed significant differences for cumulative event rates between WMI-L and WMI-H when adjusted for LVEF. However, LVEF did little to separate patients regarding events, either separately or when stratified by WMI.

Conclusions: Wedensky modulation index is a new and important non-invasive test that identifies patients at risk of SCD following myocardial infarction independent of LVEF.

P1224 : Wedensky modulation index and ejection fraction combined provide better risk stratification of post-mi patients

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Introduction: Risk stratification based on ejection fraction (EF) alone is limited. Wedensky Modulation Index (WMI), based on subthreshold transchest electrical stimulation delivered to every other QRS complex, is a novel noninvasive assessment of myocardial vulnerability. We hypothesized that a WMI may have predictive value in patients late after myocardial infarction and provide incremental risk stratification beyond EF to predict best candidates for ICD therapy.

Methods: A WMI was prospectively evaluated along with EF using patient event outcomes. The combination of WMI and EF was evaluated at 8 international centers that included 268 post-myocardial infarction patients with ICD who completed at least one 6-month follow-up over a 12 month period. Patients were placed into two groups: NEG (WMI $\leq$ 0.5 AND EF > 20%, n=119) and POS (WMI > 0.5 OR EF $\leq$ 20%, n=149). Cumulative ICD-treated arrhythmia event rates for the two patient groups were compared using Kaplan-Meier estimates and Cox regression analysis.

Results: There was more than a two-fold increase in the number of events for the POS group versus the NEG group (28% versus 13%, odds ratio = 2.53, p = 0.004). Cox regression analysis determined a > 30% absolute difference in event-free survival over 12 month follow-up between patients with WMI $\leq$ 0.5 and EF > 20% versus WMI > 0.5 and an EF $\leq$ 20% (p = 0.009). Patients with EF > 20% comprised 84% of population; however, when combined with a high WMI, these patients had a 26% event rate and > 15% difference in event-free survival over the 12 months (p = 0.011). Importantly, these results continued to hold when the patient population was restricted to patients with EF $\leq$ 35% (n = N).

Conclusions: WMI adds important incremental prognostic data beyond ejection fraction in patients late after myocardial infarction. High WMI is associated with highest risk of arrhythmic event especially when combined with lower EF and is a non-invasive tool for distinguishing patients at highest arrhythmic event risk who may benefit from ICD therapy.

P1234 : Clustering of multiple biomarkers for the prediction of major cardiovascular events in patients following complicated acute myocardial infarction

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Purpose: A prospective substudy of the OPTIMAAL trial investigated the value of a variety of biomarkers to predict major cardiovascular events in patients following complicated acute myocardial infarction (AMI). The interplay between the families of biomarkers representing different biochemical responses to the index myocardial infarction is complex and further complicated by pre-existing factors related to the extent of cardiovascular disease. A method that groups several of these markers into biologically meaningful clusters could help to highlight the underlying mechanisms as well as identify a “superfamily” representing the best approach to risk stratification in these patients.

Methods: Blood from 236 patients, drawn at a median of 3 days post AMI was analysed. All patients had evidence of heart failure or LV dysfunction. We incorporated all prospectively measured 34 circulating biomarkers of potential predictive value into a single analysis in an attempt to eliminate multicollinearity between these variables. For this purpose variables were grouped in clusters by factor analysis. The predictive value of the clusters for the combined endpoint of CV-death, stroke and reinfarction was tested by multivariate Cox-proportional hazard regression analysis, adjusted for age and renal function.

Results: Factor analysis revealed 5 clusters. Over a mean follow-up time of 30 months 65 events occurred. Only one cluster remained a significant predictor of outcome (p < 0.001). The major contributions for this cluster came from: Mid-regional

pro-ADML (0.76), TNF-receptor (0.70), Pro-Endothelin-1 (0.67), ICTP (0.67), GDF-15 (0.67), C-terminal pro-AVP (0.57), Uric acid (0.54), Chromogranin-A (0.53), MCP-1 (0.48), TIMP-1 (0.47), OPG (0.46) and IL-18 (0.46). Forty-six % (36/79) of patients with the highest tertile of loadings for this cluster reached the combined end-point during follow-up compared to 18% (15/78) in the lowest and 18% (15/79) in the mid tertile (log rank p < 0.001). The cluster containing ANP, mid-portional pro ANP, NT-pro-BNP and CNP lost its predictive value in the multivariate analysis.

Conclusion: Clustering of multiple biomarkers by factor analysis might be an appropriate approach to improve risk stratification and could prove useful in exploring the biological interactions between different biomarkers in cardiovascular disease.

P1268 : Gender differences in Norwegian patients with heart failure

Agewall (Oslo), Brandsaeter (Oslo), Atar (Oslo)

Aims: Recent studies have suggested differences in outcome and treatment between men and women with heart failure. The aim was to study if there were gender differences in the treatment and outcome of real life heart failure patients.

Methods and results: Norwegian Heart Failure Registry was used. Three-thousand-six-hundred-and-thirty-three patients (men, n=2546 (70%), women, n=1087 (30%)) were included in the study from January 2000 to February 2006. Patients were followed up until death or December 31 2006. The male participants were younger, had lower systolic blood pressure and lower cholesterol as compared to the females in the study. The males had lower ejection fraction (EF), and more men than women received ACE-inhibitors, statins and warfarin. Significantly more women received furosemid. Women had a more severe NYHA-classification. Coronary artery disease was the main reason for heart failure for both genders (men: 60%, women 50%) but more men than women had coronary disease and more women than men had hypertensive disease. In a univariate Cox-regression analysis the following parameters were significant predictors of survival: age, systolic blood pressure, atrial fibrillation/flutter, use of ACE-inhibitors, diuretics, beta-blockers, acetylsalicylic acid, and statins, diabetes, stroke, claudication, uric-acid and cholesterol level. Gender was not a significant parameter of survival and there was no significant difference between men and women concerning survival.

Conclusion: There were differences in basic characteristics, medical history and treatment between men and women with heart failure in The Norwegian Heart Failure Registry but there was no gender difference in survival in this group of real life patients with heart failure.

P1280 : Hypertension is associated with asymmetric septal hypertrophy in aortic stenosis (the SEAS study)

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Purpose: Some patients with aortic stenosis (AS) develop asymmetric septal hypertrophy (ASH) that may influence the surgical approach and also is associated with higher postoperative morbidity. Thus further characterisation of patients with AS and ASH is of clinical importance.

Methods: Baseline clinic and echocardiographic data were recorded in 1719 patients (mean age 67±10, 39% women) with asymptomatic AS (average peak transaortic velocity 3.09 m/sec), participating in the Simvastatin Ezetimibe in Aortic Stenosis (SEAS) study evaluating the effect of randomized placebo controlled combined treatment with simvastatin and ezetimibe on progression of AS. The study population was divided according to presence of ASH (interventricular septal/posterior wall thickness ratio >1.5). LV hypertrophy was determined as LV mass/body surface area >104 g/m2 in women and 116 g/m2 in men.

Results: Compared to patients without ASH, patients with ASH (n=381, 22%) had higher left ventricular mass index (g/m2), total peripheral resistance (TPR) and peak transaortic velocity and included more patients with hypertension (all p<0.05), while there was no difference in age, gender distribution, blood pressure, LV ejection fraction or peak LV outflowtract velocity. In logistic regression analysis hypertension was the most important covariate of ASH (table). Combined ASH and LV hypertrophy (asymmetric LV hypertrophy) was present in 130 (34%) of patients with ASH. Asymmetric LV hypertrophy patients had higher systolic blood pressure and pulse pressure, lower LV ejection fraction and larger left atrial diameter, than patients with ASH without LV hypertrophy, but comparable cardiac output. There was no difference in aortic valve area index. In logistic

regression analysis, hypertension was the most important predictor also of asymmetric LV hypertrophy [OR=2.66 (95% CI 1.40-5.07), p=0.03].

Conclusions: ASH in patients with asymptomatic AS is strongly associated with hypertension and increased TPR independently of severity of aortic stenosis.

P1315 : C-reactive protein, infarct size, microvascular obstruction and left ventricular remodeling following acute myocardial infarction

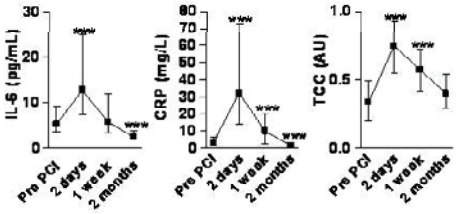
Orn (Stavanger), Manhenke (Stavanger), Ueland (Oslo), Damas (Oslo), Mollnes (Oslo), Edvardsen (Oslo), Aukrust (Oslo), Dickstein (Bergen And Stavanger)

Purpose: Increased C-reactive protein (CRP) levels following myocardial infarction (MI) have been associated with adverse outcome. However, the pathophysiology linking CRP levels with acute myocardial damage is not fully understood. This study assessed the relationship between increased CRP, interleukin-6 (IL-6), terminal complement complex (TCC), infarct size and left ventricular (LV) remodeling following successful primary percutanous coronary intervention (PCI) in patients with first time ST elevation MI (STEMI).

Methods: Forty-two patients admitted with an occluded single vessel at time of angiography were recruited consecutively. Cardiac magnetic resonance (CMR) was used to for serial assessment (2 days, 1 week, 2 months) of infarct size, microvascular obstruction (MO) and LV remodeling. Inflammatory mediators were analyzed before and after PCI.

Results: Our major findings were: (1). Following PCI, there was a marked increase in plasma levels of CRP, closely correlated with an increase in IL-6 and TCC, reaching maximum 2 days after PCI (Figure). (2). CRP two days after PCI was significantly correlated with infarct size and parameters of LV remodeling 2 months after PCI. (3). Patients with persistent MO had significantly higher CRP levels after 2 days and 1 week.

Conclusion: We suggest that the rapid increase in CRP levels in this model of successful revascularization of a single, totally occluded vessel reflects the degree of CRP deposition within the infarcted area. Our findings support a role for CRP-mediated complement activation as both a marker and mediator of myocardial damage following MI.



Median & range, ***p<0.001 vs. pre PCI.

P1342 : Distribution and determinants of very low levels of cardiac troponin T in patients with stable coronary artery disease: the PEACE trial

Omland (Oslo), De Lemos (Dallas / United States of America), Christophi (Washington Dc /United States of America), Rice (Washington Dc /United States of America), Jablonski (Washington Dc /United States of America), Tjora (Lorenskog), Sabatine (Boston / United States of America), Gersh (Rochester /United States of America), Pfeffer (Boston /United States of America), Braunwald (Boston /United States of America)

Background: Most patients with stable coronary artery disease (CAD) have cardiac troponin T (TnT) levels below the detection limit of the conventional assay. The distribution and determinants of very low TnT levels determined with a novel high sensitivity (hs) assay in patients with stable CAD and preserved left ventricular (LV) function is unknown

Methods: The hs-TnT concentration in plasma was determined with a novel assay (Roche Diagnostics) with a detection limit of 0.001 µg/L in 3679 patients (age 63.6±8.2 years, 19% female) with stable CAD and LV ejection fraction > 40% participating in the PEACE trial. Associations between hs-TnT and clinical variables were determined.

Results: Hs-TnT concentrations were greater than the detection limit of 0.001 µg/L in 3594 of patients (97.9%) and ≥ 0.01 µg/L in 782 patients (21%). Median levels of hs-TnT were higher in men than women (0.0063 vs. 0.0046 µg/L, p<0.001) and increased with age (r=0.33; p<0.001). Moreover, higher baseline hs-TnT levels were associated with several conventional risk factors, including history of diabetes mellitus, hypertension, prior stroke, CABG, LV ejection fraction < 50% (p<0.01 for all), as well as with NT-proB-

NP (r=0.30; p<0.001) and estimated glomerular filtration rate (r=-0.16; p<0.001). Hs-TnT levels were lower in patients with prior percutaneous coronary intervention and current smokers. There was no significant association with a history of prior myocardial infarction.

Conclusions: Very low circulating levels of hs-TnT are detectable in the great majority of patients with stable CAD and preserved LV function, suggesting that minor myocardial injury may be an important component of the pathophysiology of chronic as well as acute coronary syndromes. Multiple risk factors are associated with higher hs-TnT concentrations in this population.

P1372 : Lipoprotein components and risk of stroke in the treating to new targets study

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Objectives: The Treating to New Targets (TNT) study has recently provided evidence that further reduction of LDL levels from 2.6 mmol/l to 2.0 mmol/l with 80 mg atorvastatin vs 10 mg atorvastatin lowers stroke rate by an additional 20% to 25% in patients with coronary heart disease. Although randomised trials have clearly shown that cholesterol lowering with statins reduces the incidence of stroke, the association between lipid components and stroke is less clear, especially in those receiving lipid lowering treatment. Therefore, we assessed the relationship between in-trial measurements of lipoprotein components and subsequent risk of stroke in patients on intensive lipid lowering treatment.

Methods: Cox proportional hazards models were used to analyse the association between lipoprotein components and time to first stroke after year 1. Deaths other than from stroke were censored. Two models were used to adjust for potential confounding variables, model 1 with age, gender, smoking, and model 2 with in addition to model 1: history of hypertension, systolic blood pressure, body mass index, glucose and history of diabetes.

Results: When model 1 was used the hazard ratios (95% confidence interval, p value) of 1 standard deviation difference in lipid components for the risk of stroke from year 1 onwards were significant for all lipid components except LDL. After multivariable correction (model 2) HDL, apoA-1, TC/HDL and apoB/apoA-1 were associated with an increased risk of stroke. The apoB/apoA-1 ratio had the strongest association with stroke risk [1.22 (1.07-1.39, p=0.002)], followed by TC/HDL 1.18 (1.04-1.34, p=0.010), apoA-1 0.83 (0.71-0.97, p=0.022) and HDL 0.85 (0.73-1.00, p=0.048).

Conclusions: In high-risk patients receiving optimal lipid lowering treatment the apoB/apoA-1 ratio seems to give the best prediction of stroke incidence, followed by TC/HDL. The association between apoB and LDL was not significant in these patients. Strategies aimed at increasing apoA-1 or HDL could possibly further reduce the incidence of stroke.

P1452 : Daily physical activity related to body fat in an urban sample of children aged 10-13 years

Dencker (Malmo /Sweden), Thorsson (Malmo /Sweden), Karlsson (Malmo / Sweden), Linden (Malmo /Sweden), Wollmer (Malmo /Sweden), Andersen (Oslo)

Purpose: Lack of physical activity is generally thought to be associated with obesity in children. Previous studies have, however, produced conflicting results. This study investigated this relationship with the use of Dual-energy X-ray absorptiometry (DXA) and accelerometers in children aged 10-13 on a population base.

Methods: The study group consisted of 201 children (boys n=114, girls n=87) aged 9.9-13.0 years from a population-based cohort in Malmö, Sweden. A DXA total body scan was performed. Total body fat was measured and calculated as a percentage of body weight (BF%). Daily physical activity was assessed by accelerometers worn around the waist for 4 days. From accelerometer data mean counts/minute were calculated, reflecting general physical activity level.

Results: Number of children that were Tanner stage 1 (n=24), stage 2 (n=90), stage 3 (n=58), and stage 4 (n=29). Mean BF%; 17.5% (range 4.6-48.2%) for boys and 21.71% (6.8-45.0%) for girls.

Since distribution of BF% was skewed a natural logarithm was applied. Pearson correlations, with adjustment for Tanner stage, between general physical activity level and ln BF % (r = -0.07, ns for boys, and r = -0.24 for girls, P<0.05).

Conclusions: In this population-based cohort of children an inverse relationship between percent body fat and daily physical activity level was found for girls, but not for boys. This indicates that low physical activity may be a contributing factor in the development and/or maintenance of obesity in younger girls and perhaps represent one factor for the observed gender differences in the susceptibility for obesity.

1644 : Very low cardiac troponin T concentrations and cardiovascular events in patients with stable coronary artery disease: The PEACE trial

Omland (Oslo), Delemos (Dallas / United States of America), Christophi (Washington Dc /United States of America), Rice (Washington Dc /United States of America), Jablonski (Washington Dc /United States of America), Sabatine (Boston /United States of America), Gersh (Rochester /United States of America), Rouleau (Montreal /Canada), Pfeffer (Boston /United States of America), Braunwald (Boston /United States of America) On behalf: PEACE investigators

Background: Cardiac troponins are strong predictors of future cardiovascular events in patients with acute coronary syndromes (ACS). Most patients with stable coronary artery disease (CAD) have cardiac troponin T (TnT) levels below the detection limit of the conventional assay. Whether very low TnT levels determined with a novel high sensitivity (hs) assay are associated with cardiovascular events is unknown.

Methods: The hs-TnT concentration in plasma was determined with a novel assay with the detection limit of 0.001 µg/L in 3679 patients (age 63.6±8.2 years, 19% female) with stable CAD and preserved left ventricular (LV) function participating in the PEACE trial and related to the incidence of future cardiovascular events.

Results: During follow-up (median: 4.8 years) there were 125 cardiovascular deaths (CVD), 104 fatal or nonfatal new congestive heart failure (CHF), and 233 fatal or nonfatal acute myocardial infarction (AMI) events. Using the lowest category of hs-TnT (<0.004 µg/L in men, <0.003 µg/L in women, corresponding to 26% of patients) as the reference, there was a strong and graded increase in the cumulative incidence of CVD, CHF and AMI with increasing hs-TnT levels. After adjustment for potential confounders, including age, gender, prior AMI, diabetes, stroke, ejection fraction < 50%, estimated glomerular filtration rate, total cholesterol, systolic blood pressure, C-reactive protein, and NT-proBNP, hs-TnT levels >0.01 µg/L (corresponding to 21% of patients) remained independently associated with CVD and CHF, but not AMI (Table).

Conclusions: hs-TnT is strongly and independently associated with CVD and CHF in patients with stable CAD and preserved LV function. In contrast to ACS, in stable CAD hs-TnT is not predominantly a marker of future ischemic events.

1849 : Abnormal myocardial deformation during stress echocardiography is predictive of mortality independent of left ventricular hypertrophy and myocardial ischaemia

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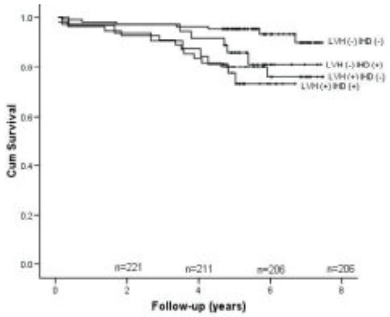
Objective: To investigate whether the incremental value of myocardial deformation during dobutamine stress echocardiography (DSE) for the prediction of mortality is independent of left ventricular hypertrophy (LVH) and myocardial ischaemia.

Methods: 231 consecutive individuals with normal resting left ventricular (LV) function undergoing DSE were studied. LV mass was calculated according to the American Society of Echocardiography (ASE) guidelines and indexed to height(m)2.7 (LVMI). LVH was designated as LVMI≥51g/m2.7. Myocardial ischaemia was defined on the basis of inducible wall motion abnormalities. Customized software was used to measure peak systolic Strain Rate (SR) in 18 myocardial segments and the mean calculated. Individuals were followed for all-cause mortality for a mean of 5.4±1.4 years.

Results: Mean LVMI was 47.6±13.6g/m2.7. 68 patients had ischaemia documented on DSE. In a Cox Proportional Hazards Model the strongest predictor of all-cause mortality was peak systolic SR (HR 4.46, 95%CI 2.45-8.11, p<0.01), exceeding

both LVH (HR 1.82, 95%CI 0.88-3.77, p=0.11) and ischaemia (HR 0.73, 95%CI 0.34-1.54, p=0.4). Peak systolic SR remained the strongest predictor of all-cause mortality after dividing the population into those with ischaemia (n=68, HR 8.96, 95%CI 2.78-28.91, p<0.01), without ischaemia (n=163, HR 3.1, 95%CI 1.49-6.46, p=0.03), with LVH (n=87, HR 2.84, 95%CI 1.36-5.96, p=0.06), and without LVH (n=144, HR 9.65, 95%CI 3.39-27.44, p<0.01). Kaplan-Meier curves were constructed after grouping the data on the basis of the presence and/or absence of LVH and/or ischaemia (p<0.01 overall, figure).

Conclusion: Peak systolic strain rate during dobutamine stress echocardiography is a predictor of all-cause mortality independent of left ventricular hypertrophy and myocardial ischaemia.



P2132 : High density lipoprotein cholesterol, low high density lipoprotein cholesterol and major cardiovascular events among patients with coronary heart disease in the scandinavian simvastatin survival study

Zhang (Whitehouse Station /United States of America), Sazonov (Whitehouse Station /United States of America), Cui (Whitehouse Station /United States of America), Maccubbi (Whitehouse Station /United States of America), Cook (Whitehouse Station /United States of America), Pedersen (Oslo)

Purpose: Many coronary heart disease (CHD) patients fail to attain low density lipoprotein cholesterol (LDL-C) goal despite statin therapy. Over one-third also have low high density lipoprotein cholesterol (HDL-C). We examined the risk of major cardiovascular events (MCEs) including revascularization, in statin treated CHD patients with low HDL-C and elevated LDL-C compared to patients with elevated LDL-C only.

Methods: This is a post-hoc analysis of the 4S, a 5-year trial of simvastatin vs. placebo in CHD patients. Patients from the simvastatin arm with LDL-C ≥100mg/dL at year 1 of treatment were included. Patients with MCEs or with missing LDL-C or HDL-C at year 1 were excluded. MCEs were evaluated over 4 years on average, from year 1 to the end of follow-up. Low HDL-C at year 1 was defined as <40mg/dL for men and <50mg/dL for women. The Cox proportional hazards model, adjusted for gender, baseline history of hypertension, MI, and diabetes, and year 1 age, smoking, LDL-C and triglyceride values, was used to assess the association between low HDL-C in addition to elevated LDL-C and MCEs, compared with elevated LDL-C only. A sensitivity analysis was conducted using the LDL-C cutoff ≥ 130mg/dL.

Results: Among 1450 patients on simvastatin with LDL-C ≥100mg/dL at year 1, 37% had low HDL-C. Compared to patients with elevated LDL-C only, patients with additional low HDL-C were younger, more had diabetes, and had slightly lower LDL-C on average (p<0.05). Overall these patients had higher incidence rate of MCEs (32%) compared to patients with elevated LDL-C only (23%, p<0.0001). Multivariable analysis showed that low HDL-C in addition to elevated LDL-C was associated with a 50% increased risk for MCEs (adjusted hazard ratio (HR) 1.50, 95% CI 1.21, 1.85). In a sensitivity analysis of 566 patients whose LDL-C was ≥130mg/dL, the association diminished (HR 1.05, 95% CI 0.76, 1.44), potentially due to inadequate sample size.

Conclusions: In this post-hoc analysis of simvastatin-treated patients with CHD, low HDL-C levels in addition to elevated LDL-C (≥100 mg/dL) were associated with 50% increased risk for MCEs compared to patients with elevated LDL-C only.

P2136 : Plasma triglycerides and cardiovascular events in the TNT and IDEAL trials of statins in patients with coronary artery disease

Faergeman (Aarhus /Denmark), Holme (Oslo), Larosa (New York / United States of America), Waters (San Francisco /United States of America), Olsson (Linkoping /Sweden), Fayyad (New York /United States of America),

Kastelein (Amsterdam /Netherlands) On behalf: the IDEAL and TNT Steering Committees

Elevated plasma triglycerides (TG) are associated with increased risk of cardiovascular (CV) disease in the general population, but we do not know whether they are associated to risk of recurrence of CV disease in statin-treated patients. To address this issue we have analyzed the databases of the IDEAL (Incremental Decrease in End Points Through Aggressive Lipid Lowering) and TNT (Treat to New Targets) trials, which were comparisons of moderate to high dose therapy (simvastatin 20-40 mg vs. atorvastatin 80 mg/day in IDEAL and atorvastatin 10 mg vs. 80 mg/day in TNT).

In analyses of the pooled IDEAL and TNT cohorts, adjusting for age and sex, risk of any CV event (CVE) increased as a function of increasing TG: patients in the fifth quintile of TG had a 60-70% higher rate of any CVE than patients in the lowest quintile of TG. When the results were adjusted also for HDL-C and apoB/apoA-1, however, results were no longer poolable: TG concentrations did not predict risk in the IDEAL patients, and the relationship of TG to risk was markedly attenuated in the TNT patients, although it remained statistically significant (p = 0.029 for test of trend). Attenuation in the IDEAL data was mostly due to apoB/apoA-1, not to HDL-C, whereas HDL-C and apoB/apoA-1 contributed in approximately equal measure to the disappearance of the effect of TG on risk in the TNT patients. Inclusion of still more variables (diabetes, body mass index, fasting glucose, hypertension and current smoking) wiped out the relationship of TG to risk in both trial populations. Essentially the same results were obtained in patients in whom treatment had reduced LDL-C to targets recommended in various guidelines.

Thus, elevated TG are associated with higher risk of recurrence of CVE in statin-treated patients. The attenuation of this association by other risk factors does not diminish its value as a marker of risk, but it does suggest that reduction of risk cannot necessarily be accomplished by specific triglyceride-lowering therapy.

P2201 : Costimulation blockade induces regulatory T-cells to HESC transplanted into the heart

Genead (Stockholm /Sweden), Grinnemo (Stockholm /Sweden), Danielsson (Stockholm /Sweden), Mansson-Broberg (Stockholm /Sweden), Hovatta (Stockholm /Sweden), Sylven (Stockholm /Sweden), Corbascio (Bergen)

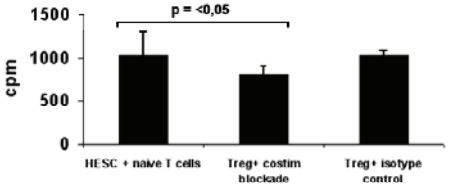
Background: Human embryonic stem cells (HESC) are multipotent and can be differentiated into cardiomyocytes that may be used for cardiomyoplasty. These cells are, however, immunocompetent and a difficulty to overcome is the immune rejection.

Hypothesis: Is it possible to induce long-term immunological tolerance to these cells as an alternative to immunosuppression. Is there a difference between an immunoprivileged organ, the testis and the myocardium?

Methods: SCID mice & immunocompetent C57BL/6 mice treated with triple costimulation blockade (anti-LFA-1, anti-CD40L and CTLA4-Ig) received testicular or myocardial HESC transplants. Mixed leukocyte reaction (MLR) test was used to mimic the clinical setting of HESC transplantation.

Results: All SCID mice with testicular HESC transplants developed teratoma. When SCID mice were transplanted myocardially, only two of five mice developed teratoma-like tumors. C57BL/6 mice with testicular transplants and treated with costimulation blockade all developed teratoma surrounded by CD4+CD25+Foxp3+ T cells, while isotype control treated recipients rejected their grafts. All but one C57BL/6 mice transplanted myocardially and treated with costimulation blockade demonstrated lymphocyte infiltrates one month after transplantation whereas one maintained its graft. Isolation of regulatory T- cells from myocardially transplanted recipients treated with costimulation blockade demonstrated specificity towards HESC and downregulated naive T-cell activation towards HESC (detected by MLR, Fig).

Conclusions: Costimulation blockade is sufficiently robust to induce tolerance to HESC in the immune-privileged environment of the testis but not in the myocardium of immunocomptent mice. This peripheral tolerance seems to be mediated by HESC specific regulatory T-cells.



MLR, mean±SEM, cpm (counts per min).

P2228 : Isolation, expansion, characterisation and transplantation of human fetal cardiomyocyte progenitor cells

Genead (Stockholm /Sweden), Danielsson (Stockholm /Sweden), Wardell (Stockholm /Sweden), Mansson-Broberg (Stockholm /Sweden), Dellgren (Stockholm /Sweden), Corbascio (Bergen), Westgren (Stockholm /Sweden), Sundstom (Stockholm /Sweden), Sylven (Stockholm /Sweden), Grinnemo (Stockholm /Sweden)

Background: Different cardiac stem cell populations have been identified in the heart, namely Lin-/c-Kit+, stem cell antigen 1, side population cells expressing Abcg2, probable first heart field Tbx5+ cells and finally second heart field Islet-1+ cells. The Islet-1+ cells represent true cardiomyocyte progenitor cells that disappear from the human heart in the early postnatal period.

Hypothesis: Islet-1+ & Tbx5+ cells (as markers of both heart fields) are present in human fetal heart and may be expanded and transplanted.

Methods: Cardiomyocytes and their progenitors from human fetal abortion material (gestational age 5-9 weeks) were analysed (immunohistochemistry, EKG by multi-electrode array, MEA), cultured, expanded and transplanted.

Results: Islet-1+ and Tbx5+ cells were present in the human fetal heart (table), where Islet-1+ was present in higher abundance, clustered in the outflow tract, ventricles and the apex and marginally in the atria. Tbx5+ cells were scattered mainly in the ventricles and did not costain for Islet-1. Following isolation, culturing and expansion Islet-1+ cells formed spontaneously beating cardiospheres and monolayer cells. These cells were Nkx2.5+, c-Kit-, Sca-1-, 10-20% Ki67+ & the gap junction protein Connexin 43 was expressed between the cells. Part of the cardiospheres and a majority of the monolayer cells were Troponin T+ while Islet-1+ cells were found in the centre of some of the cardiospheres. The beating cardiospheres exhibited EKG with rate responsive field potentials and after myocardial transplantation to SCID mice they formed stable engraftments, preserving their cardiomyocyte phenotype.

Conclusions: The Islet-1 positive cells and their progeny may be a future tool for cardiomyoplasty.

Isl-1 & Tbx5 cells in human fetal heart

Progenitor cell (count)	Outflow Tract	Left Ventriclar area	Right Ventricler area	Ventricle (LV+RV)	Left atrium tissue	Right atrium tissue	Atria tissue (LA+RA)
Islet-1	67	28	520	548	///	///	2
Tbx5	4	20	7	27	///	///	1

P2600 : Final aggregation response is a more sensitive marker of the effects of P2Y12 receptor antagonists than maximal aggregation response

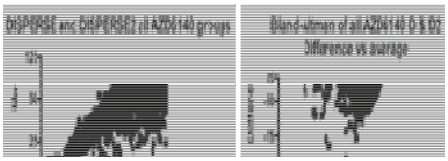
Storey (Sheffield /United Kingdom), Cannon (Boston /United States of America), Harrington (Durham /United States of America), Sandset (Oslo), Heptinstall (Nottingham /United Kingdom), Wickens (Charnwood /United Kingdom), Peters (Wilmington /United States of America), Emanuelsson (Molndal /Sweden), Husted (Aarhus / Denmark)

Background: P2Y12 amplifies and sustains the platelet aggregation (PA) response to ADP, which is initiated by P2Y1. Clopidogrel (CLOP) and AZD6140, the first reversible oral P2Y12 antagonist, block P2Y12 and inhibit PA. Measuring maximal or final PA responses to ADP can assess these effects. To assess the relationship between these measures, we analysed pooled PA data from the DISPERSE and DISPERSE2 clinical trials.

Methods: Effects of CLOP (75 mg once daily) and AZD6140 (50-200 mg twice daily, 400 mg once daily) in patients with stable atherosclerotic disease (DISPERSE, n=200) and non-ST elevation acute coronary syndromes (DISPERSE2 substudy, n=45) were assessed using optical aggregometry and ADP 20 μM. Inhibition of PA (IPA) was measured at multiple time points after drug treatment using maximal (max IPA) and final PA response (final IPA). Correlation (Spearman R) and agreement (Bland-Altman, average vs difference) were analysed by study and treatment (GraphPad Prism).

Results: All analyses showed good correlation between max IPA and final IPA (R=0.65-0.93). Correlation was greatest for CLOP in DISPERSE (R=0.93) and lowest for AZD6140 400 mg once daily in DISPERSE (R=0.65). Agreement fell with increasing IPA and was poorest for regimens that achieved highest IPA, as high final IPA was associated with highly variable and lower max IPA (figure).

Conclusion: There is good correlation between max and final IPA for assessing P2Y12 inhibition. However, max IPA may be limited (in view of a P2Y1-mediated, P2Y12-independent component) so that agreement between both measures is poor at high levels of P2Y12 inhibition. This analysis suggests that final IPA is a more sensitive measure of P2Y12 inhibition than max IPA.



P2647 : Single sheath lead extraction. A single centre experience with 500 pacemaker/ICD lead extractions

Platou (Oslo), Knutsen (Oslo), Heldal (Oslo)

Our centre is serving most of the country of Norway for pacemaker and ICD lead extractions. We have adopted a single sheath technique, a variant of the dilating sheath technique described by Byrd.

Materials and methods: Since we started the service in 1997 to end of December 2007, we have treated 307 patients, median age 65,5 years (range 7-97 years), with 499 leads. Sixty-six percent of the extractions were performed on infections, the rest were elective. Median age of all leads is 5 years (range 0,1 to 27 years). Median age for leads extracted by gentle traction alone is one year (range 0,1 to 16 years). Median age of leads extracted by single sheath technique is 8 years, range 0,3 to 27 years. The single sheath technique was used in 74% of extractions, traction alone 22%, i.v. 'fishing' ('Needles eye' or snares) 2% and double sheath technique in (the first) 9 patients. We start with a gentle traction and then proceed to single sheath technique after applying a locking wire (Cook/Spectranetics/VascoMed). A single Cook polypropylene sheath is mounted with a Cook Pin Vise and is gently pushed down the lead with rapid rotation. When serious resistance is met, the sheath size is increased. In some patients a steel sheath is used to access the subclavia vein.

Results: Complete success has been achieved in 95% of the lead extractions and partial success (ie. removal of all of the lead except the distal 4 cm) has been achieved in 4%. The overall clinical success is 99%. ICD: 55 leads: 100% success, one major complication, resolved without sequelae. Median "sheath-time" (ie. the time the sheath is applied) is 6 min., range 1 to 300 minutes. Complications: Major complications 2,2%, one fatal (0,3%). Minor complications 1%.

Conclusion: The single sheath technique is effective with 99% clinical success. The technique appears to be as quick and effective as powered sheaths (and a lot cheaper). The complication rate of the single sheath technique is low.

P2684 : Strong relationship between the severity of chronic heart failure and the ratio of L-arginine/ asymmetric dimethylarginine (ADMA)

Seljeflot (Oslo), Nilsson (Oslo), Westheim (Oslo), Arnesen (Oslo)

Patients with chronic heart failure (CHF) are known to have abnormal endothelial function. Asymmetric dimethylarginine (ADMA), an important endogenous competitive inhibitor of NO-synthase has been claimed to be a marker of endothelial dysfunction. We investigated the levels L-arginine, the substrate for NO generation and ADMA, as related to the severity of CHF.

Methods: Eighty patients, aged 45-85 years (mean 70), 21% females, with CHF (New York Heart Association function class II-IIIb), all on optimal medical treatment, were included. A 6-min walking test and a bicycle exercise test were performed and fasting blood samples collected for determination of N-terminal pro-brain natriuretic peptide (NT pro-BNP), L-arginine (LArg) and ADMA, the latter with an HPLC-method. Non-parametric statistics and/or logtransformed data were used due to skewed distibuted data.

Results: ADMA was significantly correlated to NT-proBNP ($r=0.237$, $p=0.039$), whereas the LArg/ADMA ratio was inversely correlated to NT-proBNP ($r=-0.354$, $p=0.02$), positively to 6-min walking distance ($r=0.429$, $p<0.001$) and exercise (watt) ($r=0.244$, $p=0.034$), the latters being statistically significant also after adjustment for relevant covariates ($p=0.030$, $p=0.001$ and $p=0.050$, respectively). According to the NYHA-classification, the levels of ADMA were significantly higher in NYHA-III vs -II (medians 0.69 vs 0.65 uM, $p=0.024$), and the LArg/ADMA ratio significantly lower (113 vs 121, $p=0.005$).

Conclusion: The strong relationship between the LArg/ADMA ratio and the severity of CHF assessed both by NT-proBNP, walking capacity and

exercise performance, contributes to increased knowledge of endothelial dysfunction related to the NO-pathway in patients with CHF.

P2744 : Late onset valvular and myocardial dysfunction in Hodgkin lymphoma survivors

Wethal (Oslo), Lund (Oslo), Fossa (Oslo), Kjekshus (Oslo), Edvardsen (Oslo), Pripp (Oslo), Holte (Oslo), Fossa (Oslo)

Background: Hodgkin's lymphoma survivors (HLS) have an elevated risk for cardiovascular diseases that appear several years after radiotherapy. HLS have frequently reported valvular dysfunction and many have received anthracyclines, which increase the risk for cardiomyopathy. Little is known about the progression of valvular dysfunction in HLS and whether anthracyclines negatively affect myocardial function beyond 10 years after treatment.

Methods: A longitudinal follow-up study was performed with 47 patients diagnosed with Hodgkin's lymphoma. Echocardiography was performed in 1993 and again in this study between 2005 and 2007, approximately 9 and 22 years after initial mediastinal radiotherapy. Twenty-seven (57%) of the patients had received treatment with anthracyclines.

Results: The second echocardiograph indicated 38% of the patients had mild to severe aortic stenosis not previously reported. Of those without and with mild valvular regurgitation in 1993, 39% developed moderate regurgitation in the aortic and/or the mitral valve. Of 24 patients with moderate valvular regurgitation in 1993, 33% progressed to severe valvular regurgitation or developed moderate to severe valvular regurgitation in a valve unaffected in 1993. Multiple linear regression analyses demonstrated that use of anthracyclines significantly predicted deterioration in left ventricular function (left ventricular end systolic diameter, B = 0,089 (95% CI: 0,006 – 0,172), p = 0,036; interventricular septum, B = - 0,161 (95% CI: - 0,297 - - 0,025), p = 0,021; left ventricular posterior wall, B = - 0,178 (95% CI: - 0,325 - - 0,031), p = 0,019; and left ventricular end diastolic diameter, B = 0,051 (95% CI: - 0,001 – 0,102), p = 0,053).

Discussion: Severe progression of valvular disease was found in four out of ten HLS ~22 years after radiotherapy despite normal echocardiographic findings after 9 years. Treatment with anthracyclines markedly aggravated left ventricular function at 22 years compared to 9 years after treatment, and compared to those that received mediastinal radiotherapy alone or with adjuvant chemotherapy other than anthracyclines.

P2853 : Neopterin predicts the risk for fatal ischemic heart disease in type 2 diabetes mellitus: results from the HUNT study

Vengen (Trondheim), Dale (Trondheim), Wiseth (Trondheim), Midthjell (Trondheim), Videm (Trondheim)

Purpose: Neopterin is produced by activated monocytes. Activation of the monocyte-macrophage system may contribute to plaque instability in subjects with coronary artery disease. Neopterin has therefore emerged as a novel predictor of coronary events. Hs-CRP, a marker of low-grade inflammation, has traditionally been used in prediction of risk for fatal ischemic heart disease (IHD). However, the predictive value of hs-CRP has been disputed. The aim of this study was to investigate the predictive value of neopterin and hs-CRP on long-term risk for fatal IHD in patients with recently diagnosed diabetes, compared to a matched group of non-diabetic subjects.

Methods: 200 patients with newly detected diabetes and a matched control group without diabetes were selected from HUNT1, a large population study conducted in Norway in 1984–86. Blood was drawn at baseline and frozen serum was stored. The diabetic patients were followed for ten years with annual HbA1c-measurements. Fatal IHD was registered until 2004. Neopterin and hs-CRP concentrations were divided into tertiles, and Cox regression analysis with correction for age, gender, hypertension, body mass index, previous cardiovascular disease, total cholesterol and HbA1c was used to estimate hazard ratios (HR) for fatal IHD.

Results: At baseline hs-CRP was significantly increased in the diabetic compared to the control group ($p < 0.0005$). Baseline neopterin concentrations did not significantly differ between the groups ($p = 0.65$). Neither hs-CRP nor neopterin emerged as significant predictors of fatal IHD in the control group. In the diabetes group neopterin was an independent predictor of fatal IHD (HR 2.7, 95% CI 1.2 – 6.3) whereas hs-CRP did not significantly predict fatal IHD (HR 2.2, 95% CI 0.9-5.3).

Conclusions: Neopterin is a novel and robust predictor of fatal IHD in diabetic patients. In the present study of newly diagnosed diabetic subjects neopterin was a better predictor of fatal IHD than was hs-CRP. This could be caused by neopterin being a more plaque-specific marker, whereas hs-CRP reflects non-specific low-grade inflammation common both for atherosclerosis and diabetes.

P2859 : Oral glucose tolerance testing should not be recommended early after an acute myocardial infarction

Knudsen (Oslo), Seljeflot (Oslo), Eritsland (Oslo), Mangschau (Oslo), Arnesen (Oslo), Andersen (Oslo)

Purpose: A high prevalence of impaired glucose tolerance (IGT) and unknown diabetes mellitus (DM) in patients with cardiovascular disease has been shown in several studies although information on patients with acute ST-elevation myocardial infarction (STEMI) is limited. Recent guidelines recommend an oral glucose tolerance test (OGTT) for detection of abnormal glucose regulation and several investigators have suggested early screening of all patients with acute myocardial infarction with an OGTT. The aims of the present study were to investigate the results of early testing with an OGTT in patients with STEMI and to evaluate the agreement between an OGTT performed early and three months after myocardial infarction.

Methods: Two hundred and two patients (36 women) with STEMI treated by primary PCI (mean age 59 years, SD 11.1) were prospectively enrolled. A standardised OGTT (75 g glucose, glucose measurements in venous plasma) was performed on stable patients before discharge from the CCU (usually within two days of admission) and the test was repeated after three months. The patients were classified according to the WHO criteria as normal glucose tolerance (NGT), impaired fasting glucose (IFG), IGT or DM.

Results: The observed proportion of agreement between OGTT performed early and after three months was only 54% with a poor kappa-value (k=0,15, p<0.001). The prevalence of abnormal glucose regulation (IFG+IGT+DM) was 92 of 202 (45,5%, 95% CI 38,5-52,7%) and 50 of 202 (24,8% 95% CI 19,0-31,3%) at discharge from the CCU and after three months, respectively (Table).

Conclusions: The prevalence of unknown IGT and DM in a STEMI-population is lower than expected. The reproducibility of the OGTT was poor and classification of glucometabolic status should not be performed very early after an acute myocardial infarction.

Table 1. Glucometabolic classification by OGTT at discharge (OGTT1, vertical column), and three months later (OGTT2, horizontal column)

	NGT (OGTT2)	IFG (OGTT2)	IGT (OGTT2)	DM (OGTT2)	Total
NGT (OGTT1)	92	6	11	1	110
IFG (OGTT1)	8	1	1	0	10
IGT (OGTT1)	41	4	11	4	60
DM (OGTT1)	11	0	6	5	22
Total	152	11	29	10	202

P2902 : Correlation between fasting plasma glucose and N-terminal proBNP in a population-based cohort is significant only amongst men and not women

Leosdottir (Malmo /Sweden), Willenheimer (Malmo /Sweden), Hall (Oslo), Tjora (Oslo), Malm (Malmo /Sweden), Melander (Malmo /Sweden), Borgquist (Malmo /Sweden), Nilsson (Malmo / Sweden)

Purpose: Diabetic subjects free from cardiovascular disease have been reported to have higher N-terminal (Nt) proBNP values than non-diabetic controls, suggesting subclinical myocardial dysfunction. A continuous relationship between fasting plasma glucose (FPG) and Nt-proBNP in non-diabetic subjects has also been shown. Gender subanalyses of this relationship are lacking.

Methods: We examined the correlation between FPG and Nt-proBNP in a population-based cohort of 1266 men (M) and 526 women (W) (mean age M: 66.4±6.0 yrs; W: 69.5±5.1 yrs) from the Malmö Preventive Project Re-Examination Study. Linear regression analysis was applied, first in an age- and cystatin C adjusted model, and subsequently adjusting in a backward stepwise selection manner for other relevant covariates: anthropometric measures, blood pressure and heart rate, cardiovascular medication, prevalent atrial fibrillation, prevalent valve disease, history of diabetes and chronic heart failure. All calculations were stratified by gender.

Results: In the age- and cystatin C adjusted model, the correlation between FPG and Nt-proBNP

was significant for men only (M: t-statistic 2.76, p=0.006; W: t-statistic –0.002, p=0.9). In the fully adjusted regression model the correlation remained significant for men (t-statistic 3.21, p= 0.001) and non-significant for women (t-statistic 1.30, p=0.8). The same trend was observed if subjects with a history of diabetes (M: n=338; W: n=116) were excluded (M: t-statistic 3.21, p=0.001; W: t-statistic 1.30; p=0.8).

Conclusions: In this large population-based cohort of middle-aged and elderly subjects, we found a significant positive correlation between fasting plasma glucose and Nt-proBNP but only among men, in all subjects as well as in non-diabetic subjects only. The results indicate a gender difference in the glucometabolic effect on myocardial function in this age-group, which should be further examined.

P2983 : Global strain is superior to mitral annulus displacement to quantify myocardial infarct mass in chronic ischemic heart disease

Gjesdal (Oslo), Vartdal (Oslo), Helle-Valle (Oslo), Lunde (Oslo), Hopp (Oslo), Smith (Oslo), Ihlen (Oslo), Edvardsen (Oslo)

Purpose: Global longitudinal strain (GS) and mitral annulus displacement (MD) are markers of longitudinal LV function. We compared the two method's ability to quantify LV function in patients with myocardial infarct.

Methods: LV infarct mass was measured by late enhancement MRI in 61 patients 9±5 months after a first myocardial infarction (MI). Longitudinal strain was assessed in 16 LV segments by speckle tracking echocardiography and mitral annulus displacement in 6 segments by tissue Doppler imaging. GS and MD were calculated by averaging the segmental values, and were then compared to LV infarct mass by regression analysis and tested for ability to separate small (0-30 g), medium (30-50 g) and large (≥50 g) MI.

Results: GS and MD correlated well with infarct mass (Figure). Myocardial function was progressively lower in patients with larger infarcts as assessed by both methods. Both indices separated large from medium sized MI (*p<0.05, Table), but only GS separated small from medium sized MI ({†}p<0.05).

Conclusions: GS correlates better to infarct mass in patients with MI compared to analysis of mitral annulus displacement. In particular, GS is superior to separate small from medium sized MI.

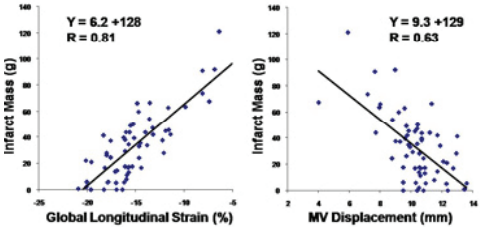
Mean values

	Small (0-30g)	Medium (30-50g)	Large (>50g)
Infarct Mass (g)	13±10	41±5†	74±20*
GS (%)	-17±2	-15±2†	-10±3*
MD (mm)	11±1	10±1	8±2*

*Mean values ± SD by infarct mass. *p≤0.05 vs medium, † p≤0.05 vs small myocardial infarct.*

Correlation plots.

3160 : Contrasting



hemodynamic mechanisms of similar blood pressure reduction with losartan- compared to atenolol-based therapy in the LIFE study

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In the LIFE study, similar blood pressure (BP) reduction occurred with losartan- and atenolol-based therapy, but the impact of different hemodynamic mechanisms by the two BP regimens has not been determined.

Methods: In 960 patients echocardiography was performed at baseline and annually for 4 years to measure stroke index (SI), heart rate, cardiac index (CI), conduit artery stiffness assessed as pulse pressure/stroke index (PP/SI), and total peripheral resistance index (TPRI) assessed from mean BP/CI.

Results: Atenolol- and losartan-based treatment reduced BP similarly (cum. difference in mean brachial BP 0.1 mm Hg). Atenolol increased SI and reduced heart rate more than losartan-based treatment: After 4 years the relative increase in

Table 1

Losartan vs. atenolol	Year 0	Year 1	Year 2	Year 3	Year 4
Stroke index (ml/stroke/m^2)	77.6 vs. 78.0 ns	79.1 vs. 82.1*	79.5 vs. 83.5**	79.1 vs. 83.1**	80.0 vs. 83.2*
Heart rate (bpm)	73.9 vs. 73.7 ns	72.1 vs. 65.1***	71.7 vs. 65.2***	71.5 vs. 65.4***	71.5 vs. 65.2***
Cardiac index (l/min/m^2)	2.78 vs. 2.76 ns	2.81 vs. 2.49***	2.81 vs. 2.55***	2.75 vs. 2.56**	2.84 vs. 2.58***
Total peripheral resistance index (dyn sec cm^{-5} m^2)	3716 vs. 3728 ns	3221 vs. 3599***	3191 vs. 3513***	3189 vs. 3391**	3062 vs. 3377***
Pulse pressure/stroke index (mm Hg/ml/stroke/m^2)	1.90 vs. 1.89 ns	1.61 vs. 1.61 ns	1.59 vs. 1.54 ns	1.56 vs. 1.52 ns	1.48 vs. 1.47 ns

*ns = non significant; *p<0.05; **p<0.01; ***p<0.001.*

SI was 6.7% vs 3.1%, and the reduction in heart rate was 11.5% vs 3.2% by atenolol- and losartan-based treatment, respectively (Table). Because of larger relative reduction in heart rate than increase in SI, CI was reduced and remained below control in the atenolol treated patients while in the losartan group the CI remained unchanged from baseline throughout the treatment period. TPRI was decreased (17.6%) in the losartan group and remained reduced when compared to the atenolol group during the course of the study (after 4 years -9.3%, p<.001). PP/SI was reduced by about 22% (p<.001) in both groups.

Conclusions: Similar BP reduction with losartan vs. atenolol-based treatment in the LIFE study was achieved by contrasting hemodynamic mechanisms, with preserved CI and substantially reduced TPRI with losartan, but reduced CI and lesser TPRI reduction with atenolol. The virtually similar arterial stiffness as shown by identical PP/SI levels in the two study arms suggest that the wider PP in atenolol-treated patients reflects higher SI in addition to possible unmeasured differential effects of the treatments on central BP.

P3387 : Ablation of cardiac serca2 gene in mice affects left atrial but not ventricular dimensions - independent of exercise training

Ericsson (Trondheim), Andersson (Oslo), Amundsen (Trondheim), Torp (Trondheim), Sjaastad (Oslo), Christensen (Oslo), Sejersted (Oslo), Ellingsen (Trondheim)

Purpose: Sarco-endoplasmic reticulum Ca2+ ATPase (SERCA2) and contractile function of cardiomyocytes are intimately linked to aerobic capacity, measured as maximal oxygen uptake (VO2max). Tamoxifen induced deletion of the cardiac Serca2 gene in a new mouse model (SERCA2 KO) gives rise to progressive heart failure within seven weeks. The knockout phenotype shows an increased left atria diameter. Control mice with floxed alleles (SERCA2 FF) are unaffected. Increased cardiac function after exercise training is closely linked to left ventricular function in healthy subjects. A four week training program was set up to determine whether training alters the aerobic capacity in SERCA2 KO mice compared to SERCA2 FF and to investigate left ventricular (LV) dimensions and function in response to training.

Methods: Animals were either subjected to exercise training or remained sedentary. Exercise was performed by treadmill interval running for 1 hour, five days per week, at, 8 min at 85-90% of VO2max, separated by 2 min at low intensity. Running speed was monitored. High-frequency echocardiography (35 MHz) was performed before and after training intervention. Trans-thoracic parasternal long-axis M-mode was used for measuring anterior and posterior wall thickness, left ventricular and left atria diameter. Trained and sedentary SERCA2 FF served as control animals.

Results: VO2max fell by 50% after 4 weeks of exercise training in the SERCA2 KO mice, although running speed was maintained. Sedentary SERCA2 KO reduced their running speed with 25%. Echocardiography showed dilation of the left atrium in SERCA2 KO independent of exercise training. No differences were seen in left ventricle dimensions. Increased right ventricle and lung weights and histology confirmed pulmonary congestion and heart failure in both training and sedentary SERCA2 KO mice. LV dimensions were not affected by the reduced levels of Serca2 protein, independent of exercise training.

Conclusion: Aerobic capacity declines after reduction of SERCA2 protein in myocardium of both sedentary and exercising SERCA2 KO mice. Response to exercise training is altered in SERCA2 KO animals compared to control SERCA2 FF mice. Normal SERCA2 function in the heart seems essential to maintain aerobic capacity. Despite markedly impaired oxygen uptake capacity, training preserves running speed intensity. Ablation of

cardiac Serca2 gene does not seem to affect left ventricular dimensions.

P3622 : Analysis of plaque dimensions and composition in culprit compared to target lesions of acute and stable patients by intravascular ultrasound radiofrequency analysis

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Purpose: To evaluate the plaque composition and plaque classification of culprit (CL) and non-culprit lesions (NCL) of acute coronary syndrome (ACS) patients compared to stable angina (SA) patients by intravascular ultrasound radiofrequency analysis (IVUS-RF).

Methods and results: IVUS-RF lesion segment analysis was performed in 539 patients (ACS: 246pts./ SA: 293pts.). The CL in ACS vs. SA pts. revealed a significant higher plaque burden (54±7.7% vs. 50±8%, p<.0001). Fibrotic (3.21±1.78 vs. 2.64±1.56, p<.0001) and necrotic plaque area (0.92±0.70 vs. 0.70±0.53, p<.0001) were larger in ACS patients. The fibrotic tissue was significantly lower in CL vs. NCL in both patient groups, the necrotic tissue was higher in CL in both patient groups. A higher amount of fibroatheroma (16.6 vs. 13.9%, p=0.0052) and thin cap fibroatheroma (TCFA, 8 vs. 3%, p=.0001) was detected in patients with ACS. Fibrocalcific (FC) lesions were lower in ACS patients (2.2 vs. 5.3%, p=.0001). Significantly more TCFA were detected in CL of ACS patients. FC lesions were significantly higher in SA patients.

Conclusions: The plaque composition of CL in ACS compared to SA pts. is significantly different. Within the patient groups CL and NCL presented also with different plaque composition. In ACS pts. a significantly higher amount of high risk lesions was detected.

P3651 : The maximal level of C-reactive protein increases with age and is correlated to cardiovascular morbidity and mortality

Munk (Stavanger), Melberg (Stavanger), Skadberg (Stavanger), Kvaloy (Stavanger), Larsen (Stavanger)

Background: Elevated levels of C-reactive protein (CRP) are a marker of systemic inflammation and predicts the risk for future cardiovascular events in individuals. We hypothesized that the mean CRP per week analyzed at our hospital is positively correlated to the number of cardiovascular events and death rates in a time dependent manner.

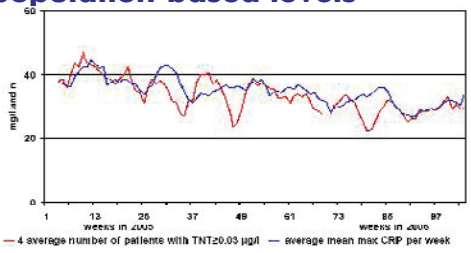
Methods and results: We retrospectively studied the maximal CRP value per individual (n=140,799), 3,497 Troponin T (TNT) values, the number of cardiovascular events and the death rates per week in the population of Southwest Norway over a 2 year periode.

The mean maximal CRP was increasing with age (p<0.001 for trend). The mean, the median and the sum of the maximal CRP per individual were significantly correlated with the number of patients with a TNT≥0.03 µg/l in the same week (R=0.44, R=0.34, R=0.42, respectively, p<0.001). The sum of the maximal CRP per week was significantly correlated to the number of patients admitted with a cardiovascular event 2 weeks later (R=0.22, p=0.027) and to the death rate in the following week (R=0.22, p=0.025).

Conclusions: These results add further proof to the link between inflammation assessed by CRP levels and the prospective development of cardiovascular events and all cause mortality.

Trend lines TNT-pos. patients and mean CRP.

P3655 : Variation in population-based levels of C-reactive protein,



cardiovascular morbidity and all-cause mortality

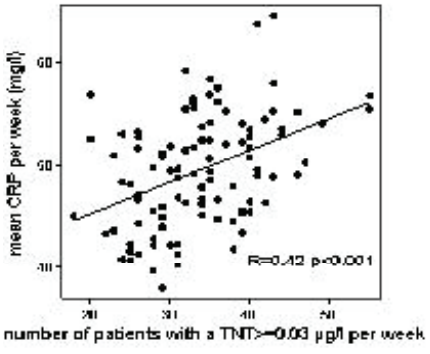
Munk (Stavanger), Melberg (Stavanger), Skadberg (Stavanger), Kvaloy (Stavanger), Larsen (Stavanger)

Background: Large population-based studies link inflammation to the prospective development of cardiovascular events. C-reactive protein (CRP),the most widely used inflammatory marker, has proinflammatory properties acting as a pathogen in atherosclerosis. We hypothesized that the degree of inflammation in the general population assessed by CRP values correlates with the number of cardiovascular events and death rates in a time dependent manner.

Methods and results: We retrospectively studied 272,602 CRP- and 3,497 Troponin T values, the number of cardiovascular events and the death rates in the population of Southern Rogaland, Norway.

The mean, median and sum of CRP values per week were significantly correlated with the number of patients with a TNT≥0.03 µg/l in the same week (R=0.42, R=0.41, R=0.43, respectively, p<0.001 for all analysis). Further, we found a significant correlation between the sum of CRP values per week and the number of patients admitted with a cardiovascular event 2 weeks later (R=0.21, p=0.035). The sum of CRP values per week was significantly correlated to the death rates in the following week (R=0.24, p=0.014).

Conclusions: These findings provide further proof for the hypothesis that inflammation assessed by CRP levels is linked to the prospective development of cardiovascular events and all cause mortality.



Mean CRP and n patients with TNT≥0.03.

P3686 : Differences in risk factor status for Cardiovascular disease between children who performs 30 minutes of vigorous activity per day and those who do not

Dencker (Malmo /Sweden), Thorsson (Malmo /Sweden), Karlsson (Malmo / Sweden), Linden (Malmo /Sweden), Wollmer (Malmo /Sweden), Andersen (Oslo)

Purpose: There are different physical activity recommendation for children, one of them recommend that each child should perform more than 30 minutes of vigorous activity (VPA) per day. This study evaluate if there are differences in risk factor status for Cardiovascular disease between children who performs 30 minutes of VPA or more per day and those who don't.

Methods: Cross-sectional study of 226 children aged 7.9-11.1 years from a middle-class urban area. Abdominal fat mass (AFM) and total body fat mass (TBF) quantified by Dual-Energy X-Ray Absorptiometry, TBF was also calculated as percentage of body mass (BF%). Maximal oxygen uptake (VO2PEAK) was measured during a maximal exercise test. Daily physical activity was assessed by accelerometers for four days, and daily accumulation of VPA was calculated. Resting heart rate (HR) and blood pressure (SBP and DBP) were measured.

Value	Boys (n=125)		p-value	Girls (n=101)		p-value
	<30 min VPA	>30 min VPA		<30 min VPA	>30 min VPA	
	(n=28)	(n=97)		(n=41)	(n=60)	
MVPA (min)	148±32	228±41	<0.001	166±35	207±31	<0.001
VPA (min)	21±8	52±17	<0.001	22±6	43±10	<0.001
TBF (kg)	8.7±7.6	5.7±4.0	0.005	9.9±5.9	7.1±4.4	0.007
BF%	20±12	15±8	0.01	26±9	20±8	<0.001
AFM (kg)	3.5±3.4	2.2±1.7	0.004	4.0±2.7	2.8±2.0	0.01
VO_{2PEAK} (ml/min/kg)	38±8	42±7	0.01	34±6	37±6	0.05
HR (b/min)	82±11	80±11	0.4 ns	87±11	83±9	0.047
SBP (mm hg)	106±6	104±8	0.27 ns	105±9	105±9	0.83 ns
DBP (mm hg)	61±6	59±5	0.048	61±8	60±5	0.53 ns

Results: 78% of boys and 59% of the girls performed 30 minutes of VPA per day or more. Table display results according to performance of 30 minutes of VPA per day or not.

Conclusions: Significant differences were detected in this cohort of children aged 8 to 11 years for

those who achieved 30 minutes of VPA or more per day and those who did not. Children who performed a minimum of 30 minutes of VPA per day were slimmer and had higher fitness level.

P3950 : Connective tissue growth factor (CTGF/CCN2) desensitizes myocardial beta-adrenergic receptor signaling and inhibits isoproterenol induced hypertrophy

Gravning (Oslo), Ahmed (Oslo), Qvigstad (Oslo), Sagave (Oslo), Krobert (Oslo), Edvardsen (Oslo), Valen (Oslo), Skomedal (Oslo), Osnes (Oslo), Attramadal (Oslo)

Background: Under physiological conditions, expression of myocardial CTGF is repressed in the postnatal heart. However, myocardial CTGF is dramatically induced in CHF, a condition associated with diminution of β-adrenergic receptor responsiveness. Accordingly, we aimed to investigate if CTGF is mechanistically involved in desensitization of β-adrenergic receptors in this condition.

Methods and results: Transgenic mice with cardiac-restricted overexpression of CTGF (Tg-CTGF) were generated and compared with nontransgenic littermate control mice (NLC). Stimulation of ventricular muscle strips with increasing concentrations of the β-adrenergic receptor agonist isoproterenol (ISO) revealed substantial attenuation of maximal inotropic response of muscle fibers from Tg-CTGF vs. NLC mice (increase of force 123±14% vs. 427±27%, $p<0.01$). Primary cultures of adult cardiac myocytes from Tg-CTGF hearts exhibited attenuated cAMP synthesis in response to supramaximal concentrations of ISO as compared to those from NLC hearts. Indeed, similar reduction of efficacy of ISO was observed in ventricular muscle strips and isolated cardiac myocytes. Furthermore, no difference in maximal contractile responses upon stimulation with a cAMP analogue (dibutyryl-cAMP) was detected; excluding that downstream signalling pathways and contractile machinery could limit the response. Analysis of [125I]-iodocyanopindolol binding did not disclose alternations in β-adrenergic receptor densities on cardiac myocytes from Tg-CTGF mice versus NLC mice. Real time qPCR analysis of myocardial tissue revealed a three fold upregulation of G-protein receptor kinase 5 (GRK5) in Tg-CTGF hearts, while levels of other cardiac GRKs (2, 3 and 6) were unaltered among the groups. ISO-stimulated cardiac myocytes from Tg-CTGF mice also displayed enhanced ERK-phosphorylation, indicating activation of GRK5 dependent β-arrestin-mediated cytoprotective pathways. Chronic exposure to ISO for 14 days delivered through mini-osmotic pumps, revealed less myocardial hypertrophy in Tg-CTGF mice as compared to NLC mice, and preserved cardiac function as evaluated by echocardiography. Our data provide evidence that β-adrenergic receptors on cardiac myocytes from Tg-CTGF mice are functionally desensitized.

Conclusion: CTGF desensitizes β-adrenergic receptor signaling in the heart, possibly mediated by induction of myocardial GRK5. Functional desensitization of β-adrenergic receptors on cardiac myocytes may contribute to cytoprotection and maintenance of cardiac function. CTGF might be a potent mediator of reduced β-adrenergic responsiveness in CHF.

P4200 : Short- and long-term case fatality in 11.878 patients hospitalized with a first acute myocardial infarction, 1979-2001. The western noway cardiovascular registry

Langoergen (Bergen), Igland (Bergen), Vollset (Bergen), Averina (Tromsoe), Nordrehaug (Bergen), Tell (Bergen), Irgens (Bergen), Nygaard (Bergen)

Purpose: To analyse trends in short- and long-term case fatality after hospitalization for a first episode of acute myocardial infarction (AMI) during 1979-2001.

Methods: Registry data from university hospital during 1972 to 2001 were collected. We censored the first seven years in order to have at least seven years prior to each AMI to exclude subsequent AMIs. The years studied were therefore 1979-2001. The data were linked with the National Causes of Death Registry to obtain information about causes of death and date of death. Case fatality trends were examined over three periods (1979-1985, 1986-1993, 1994-2001) using logistic regression. Trends in long-term survival were examined using Kaplan Meier survival curves.

Results: 7.635 men and 4.243 women with a first AMI were identified. From the first to the last decade mean age at onset for women increased significantly from 73.5 years to 75.2 years. Mean age for men stayed at approximately 66 years.

From the first (1979-1985) to the last (1994-2001) period, crude 28-day case fatality declined from 31.1% to 19.8% in men and from 37.3% to 26.8% in women, whereas crude 10-year case fatality declined from 69.5% to 55.5% in men and from 80.8% to 66.1% in women (both, p –trend < 0.0001). After adjustment for age, OR (95% confidence intervals) for overall 28-day, 1-year and 10 year case fatality comparing the last period with the first period were 0.50 (0.45-0.56), 0.49 (0.44-0.54) and 0.43 (0.37-0.50), respectively. The 10-year case fatality was significantly lower in women than in men (p-sex = 0.0008). When stratifying the patients in two age groups (< and > 60 years), the difference between women and men was only significant in patients aged > 60 years.

Conclusions: Short- and long-term survival after hospitalization for a first AMI improved substantially during the 23 years in both genders. In elderly patients, long-term case fatality was significantly lower in women than men.

P4228 : Sex-based differences in effect of smoking: first acute myocardial infarction occurs more prematurely in women than in men

Grundtvig (Lillehammer), Hagen (Oslo), Reikvam (Oslo)

Purpose: It has been debated but not settled whether there are sex differences in the effects of smoking, implying that smoking increases the risk of heart disease relatively more in women than in men. Women adopted the smoking habit historically later than men and new studies with a more similar tobacco exposure in the two sexes are warranted. We aimed to determine how smoking affects age of onset of first acute myocardial infarction (AMI) in men and women.

Methods: Clinical data on patients with AMI admitted to a regional hospital were prospectively and consecutively entered into a database in the years 1998 to 2005. A total of 1784 patients, 1100 men and 684 women (38.3%), were discharged from or died in hospital with a diagnosis of first AMI. A multivariate regression technique was used to analyse age at first AMI. Smoking history was known for all patients and the variable smoking had the categories “current smoker”, “ex-smoker”, and “non-smoker”.

Results: Unadjusted mean age at the time of hospitalisation for first AMI was 72.3 years for the entire sample, 69.8 years (range 27–98, median 71.7) for men and 76.2 years (range 27–103, median 79.1) for women, a difference of 6.4 years (P < 0.001). In women, the unadjusted mean age was 80.7 years in non-smokers and 66.2 years in current smokers, a difference of 14.4 years (P < 0.001). In men, the mean unadjusted age was 72.2 years in non-smokers and 63.9 years in current smokers, a difference of 8.3 years (P < 0.001). After adjustment for classical risk factors (hypertension, cholesterol levels, diabetes) and patient characteristics (history of angina pectoris and history of stroke), 13.7 years of the age difference in women were attributed to smoking while the corresponding figure in men was 6.2 years.

Conclusion: Smoking caused first AMI to occur significantly more prematurely in women than in men, implying that twice as many years were lost by women smokers as by men smokers. Smoking incurs a strong additional risk in women.

P4232 : Which smokers are most likely to benefit from extended treatment with varenicline?

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Purpose: A trial of an extended course of varenicline has shown that following the initial 12 week treatment period, an additional 12 weeks of medication is effective in preventing relapse in those who had quit. Clinical reasoning suggests that late quitters may be the group which needs extended treatment most. We analysed the data from the original trial to identify patient groups for whom the extended treatment may be of particular benefit.

Methods: The analysis included 1,208 patients who were abstinent for at least the last week of 12 weeks’ treatment with varenicline and were subsequently randomised to continued varenicline or placebo for another 12 weeks. We examined the relationship between the time of the last cigarette and the varenicline versus placebo difference in continuous abstinence rates through weeks 24 and 52. We also examined the influence on varenicline versus placebo differences of baseline patient characteristics including gender, age, BMI, and a range of smoking characteristics.

Results: As expected, with increasing delay in quitting, the success rates declined. Participants

who had their last cigarette at week 11 had lower quit rates at 52 weeks (average of 5.6%) than those who had their last cigarette in week 1 (average of 55%). To test for treatment by quit pattern interaction at 52 weeks, the model included treatment, quit pattern, and treatment by quit pattern (interaction p=0.049). The interaction was not significant at 24 weeks. Patients who did not manage to quit early in treatment benefited more from the extended treatment at the final 52-weeks follow-up point than patients who were continuously abstinent from the first week onwards (OR 1.78 [1.26, 2.52] versus OR 1.1 [0.78, 1.55]), based on a model run for immediate quitters separate from other quitters, that included treatment, BMI, previous quit attempts, and baseline cotinine. None of the baseline variables interacted with treatment which was effective independently of gender, age, amount of smoking or degree of dependence.

Conclusion: Extended treatment with varenicline may be of particular benefit to smokers who did not manage to start abstinence immediately after the target quit date. Smokers who struggle during their quit attempt before achieving abstinence should be preferentially encouraged to use varenicline for an additional 12 weeks.

4449 : Fractional pulse pressure is associated with presence and severity of coronary artery disease

Staal (Stavanger), Nygaard (Bergen), Omvik (Bergen), Gerdts (Bergen)

Background: Ascending aortic pulsatility, quantified by fractional pulse pressure (PPf) has been associated with increased prevalence of coronary artery disease (CAD) in epidemiologic studies. However, less is known about the association between PPf and severity of CAD.

Aim: To describe the association between PPf and angiographic CAD in patients with stable angina pectoris (AP).

Methods: Cardiovascular (CV) risk factors and angiographic findings including invasive blood pressure measurements were recorded in 796 patients (61.8±10.7 years; 31% women) referred for elective coronary angiography due to stable AP in 2003 in a Norwegian University Hospital. PPf was calculated as pulse pressure/mean blood pressure ratio. Univariate and multivariate risks of angiographic significant CAD were evaluated by logistic regression, with PPf quartiles represented as a continuous variable in the models.

Results: Median (interquartile range) PPf was 0.66 (0.53 - 0.77). In univariate logistic regressions, one quartile increment of PPf was associated with Hazard Ratio (HR) 1.26 (1.09-1.46) for presence of CAD and HR 1.22 (1.06-1.41) for 3-vessel disease [both p<0.01]. When adding other well-known CV risk factors in a multivariate model, PPf remained an independent risk factor both for presence and severity of CAD (Table 1).

Conclusion: In patients with stable AP, PPf is associated with presence and severity of CAD, independent of other established CV risk factors.

Table 1. Multivariate logistic regression

Risk factors	Presence of CAD			3 vessel disease		
	HR	95% CI	p	HR	95% CI	p
PPf (quartiles)	1.60	1.24-2.07	0.001	1.28	1.02-1.60	0.03
Age (years)	1.05	1.02-1.07	0.001	1.06	1.03-1.08	<0.001
Gender	6.27	3.42-11.5	<0.001	3.54	1.92-6.51	<0.001
Prior myocardial infarction	8.73	4.15-18.4	<0.001	1.53	1.00-2.35	0.05
Family history	1.98	1.16-3.37	0.01	1.59	1.01-2.51	0.05
Hypercholesterolemia	2.90	1.79-4.70	<0.001	1.23	0.80-1.89	0.34
Ever Smoking	1.80	1.09-2.98	0.02	0.85	0.53-1.35	0.49

HR, Hazard ratio; CI, Confidence Interval. The population is divided according to presence of coronary artery disease (CAD) or not, or 3 vessel disease or not. Additional variables that did not enter the models: Hypertension, diabetes mellitus, body mass index, waist circumference.

4468 : Impact of nurse-based heart failure clinics on drug management and hospital admissions by self monitoring through a common database

Grundtvig (Lillehammer), Gullestad (Oslo), Hole (Aalesund), Flonaes (Asker), Westheim (Oslo)

Purpose: The morbidity and mortality is high in heart failure (HF) patients. The number of hospitalisations is large, and nearly 50% are readmitted within one year following their first hospital admission for HF. The aim was to evaluate the HF medications and the effect on hospitalisations in nurse-based HF clinics by using a common database.

Methods: The HF outpatient clinics were run by specially trained nurses in close co-operations with cardiologists. A database with online registration

was established with the possibility of a hospital to compare treatment with others. The daily dose of diuretic (D) was expressed in furosemide equivalents (bumitanide 1 mg=furosemide 40 mg). Additional 10 mg was added if the patients also used a tiazide. Hospital admissions were measured by comparing both the number of admissions and days stayed in hospital in the 6 month period before and after entering the HF clinic.

Results: A total of 3632 patients (30% females) from 24 hospitals were included between 2000-2006. Their mean age was 70.8+11.8 years. Seventy three percent of the patients had an EF < 40%. Mean heart rate at entry was 73+15 beats per minute and systolic blood pressure 126+ 23 mmHg. Co-morbidities as hypertension, diabetes and chronic obstructive airway disease were common. The medications used at the last registered visit were ACE-I in 73%, angiotensin receptor blocker (ARB) in 14%, betablocker (BB) in 83%, aldosteron antagonist in 27% and D in 87% of the patients. When comparing the first half of the patients to the last half in each centre, the use of ACE-I and ARB`s were unchanged while the use of BB increased from 82% to 89% (p<0.01). The use of D decreased from a mean daily dose of 56 to 51 mg/day (P<0,05). The median (5-95 percentiles) number of hospital admissions were reduced from 1(0-2) to 0 (0-1) (p<0.001), and the median number of days in hospital from 5 (0-21) to 0 (0-2.5) (p< 0.001) in the 6 month periods.

Conclusions: This study shows that the use of evidence based medication improved over time with a reduction in hospital admissions by hospitals monitoring their treatment through a common database.

4515 : High-dose atorvastatin as compared to usual simvastatin treatment is associated with less congestive heart failure in secondary prevention

Strandberg (Oulu /Finland), Tikkanen (Helsinki /Finland), Holme (Oslo) On behalf: The IDEAL Study Group

Purpose: Congestive heart failure (CHF) is an important and costly complication of coronary artery disease. It is obscure whether intensive cholesterol lowering, as compared to usual statin treatment, could more effectively prevent CHF in secondary prevention.

Methods: The Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL) study is a randomized trial with PROBE design comparing “usual” statin treatment (simvastatin 20-40 mg/d, n=4449) with high-dose statin (atorvastatin 80 mg/d, n=4439) in patients with a history of myocardial infarction. The study lasted 5 years and primary results were reported in 2005 showing significant decrease of major cardiovascular events in the atorvastatin group. At baseline, most patients (n= 8351, 94%) had no history of CHF. For the present report we collected all new cases of CHF during trial (blindly reviewed and adjudicated by the end-point classification committee) and related them to the treatment group in: 1) all patients, 2) patients with or without CHF at baseline, and 3) patients with or without in-trial myocardial infarction preceding CHF. We used Cox proportional hazards analyses adjusted for covariates.

Results: During the 5-year trial, there were 222 new hospitalizations for CHF, 123 (2.8%) in the usual statin group and 99 (2.2%) in the high-dose atorvastatin group (hazard ratio [HR] 0.84, 95% CI 0.62-1.05, P=0.11). Of the new CHF cases, 57 and 164 occurred among those with and without CHF at baseline, respectively, and 186 (84%) were not preceded by in-trial myocardial infarction. After adjustments in the whole study cohort (age, sex, baseline cholesterol and HDL-cholesterol, pretrial statin use and baseline history of CHF), high-dose atorvastatin was associated with a 26% reduction of new CHF events as compared to usual statin treatment (HR 0.74, 95% CI 0.57-0.97, P=0.03). Furthermore, high-dose atorvastatin tended to be associated with fewer recurrent CHF events in those with (n=537; adjusted HR 0.61, 95% CI 0.36-1.03, P=0.06) as well as in those without CHF at baseline (n=8351; HR 0.80, 95% 0.59-1.09, P=0.16). Finally, protection by high-dose atorvastatin was observed also when CHF was not preceded by in-trial myocardial infarction (adjusted HR 0.73, 95% CI 0.54-0.97, P=0.03).

Conclusions: Our results provide suggestive evidence that intensive cholesterol lowering with high-dose atorvastatin would be more efficient than usual simvastatin treatment in preventing development of CHF in patients with previous myocardial infarction. This concept needs confirmation in a prespecified randomized controlled clinical trial.

4542 : Biomarkers as predictors of risk in patients

with advanced heart failure. Experiences from CORONA

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Objective: To analyze if the biomarkers NT-proBNP (BNP), hsCRP and apoB/apoA1 can discriminate risk independently of other well known risk factors in patients with advanced systolic heart failure.

Methods: Patients in CORONA with biomarkers available from baseline (n= 3366) were analyzed. Multi-variable Cox regression models were applied to predict the composite primary endpoint of non-fatal MI or stroke or CV death (time to first event; n= 889 events), all-cause mortality (n= 940 deaths) and a composite atherosclerotic endpoint of nonfatal or fatal MI or non-hemorrhagic stroke (n= 288 events). Initially age, sex, ejection fraction (EF), New York Heart Association (NYHA) class, systolic blood pressure (SBP), heart rate (HR), pulse pressure, body mass index (BMI), estimated glomerular filtration rate (eGFR), history of myocardial infarction (MI), diabetes mellitus (DM), hypertension and previous revascularization, atrial fibrillation (AF), smoking status, LDL and HDL cholesterol (C) and triglycerides (TG)) were included; and then the three biomarkers were simultaneously added.

Results: In the initial multi-variable analysis the following variables were significant for the primary endpoint (ordered after Chi-Square value; n denotes negative relationship): EF (n; Chi-Square 31.2; p<0.0001), eGFR (n), BMI (n), DM, NYHA class, heart rate, male sex, age, TG (n), previous revascularization (n), HDL-C (n), previous MI, and SBP (n; the last with Chi-Square 6.3; p= 0.01). For total mortality also in addition LDL-C was significant (n; p= 0.01), but previous MI was removed (p= 0.06). For the atherosclerotic endpoint the following routine variables were significant: previous MI (Chi-square 10.0; p= 0.002), age, HDL-C (n), history of hypertension, NYHA class, heart rate, and AF. After adding the biomarkers risk prediction was improved, with BNP showing a stronger relationship to risk than any other parameter (Chi-square 122 and 97 and 19.8, respectively. apoB/apoA1 was significant for the primary endpoint and total mortality, but hsCRP was not. For the atherosclerotic endpoint, besides BNP, hsCRP was significant (p= 0.008), but NYHA class and HDL-C were removed after adding the biomarkers.

Conclusions: Adding the biomarkers NT-pro-BNP, hsCRP and apoB/apoA1 to routine clinical variables can improve estimating the cardiovascular risk in older patients with advanced systolic heart failure. NT-proBNP in particular added substantial information as regards risk estimation. For the primary endpoint total ChiSquare rose from 284 with the routine variables to 382 when NT-proBNP was added.

P4649 : Exercise-induced abnormal pulmonary arterial pressure response in young athletes. Normal physiology or precursor of endothelial damage?

Moller (Toensberg), Peersen (Toensberg), Fredriksen (Oslo), Holmstrom (Oslo), Thaulow (Oslo)

Introduction: Pulmonary arterial pressure (PAP) is considered to remain nearly unchanged during exercise. Earlier studies have shown an abnormal rise in PAP during exercise in endurance-trained professional athletes.

Methods: A group of 68 healthy volunteers (age 14 to 25 yrs) were studied by cardiopulmonary exercise testing, echocardiography at rest and during supine cycling with target heart rate 160-min. Eight individuals with extremely high (> 2 SD) maximal oxygen uptake were defined as highly endurance-trained athletes (ETA). Their data were compared to 16 age- and gender-matched normal trained individuals (NTI).

Results: At rest, right ventricular performance as measured by tricuspid annulus plane systolic excursion (TAPSE) was equal in both groups (mean 23/23). Exercise peak systolic PAP raised above 50 mmHg in 6 of 8 ETA (mean 48, median 55, range 17 to 66) but only in 1 (51 mmHg) of 16 matched NTI (mean 31, median 31). The difference is statistically significant (p=0.008 [-28.8,-4.8])

Discussion: The mechanism of abnormal PAP elevation in high cardiac output situations may be due to pulmonary blood flow beyond dilative capacity in the pulmonary vascular system. Pressure levels above 35 mmHg are commonly considered to

damage pulmonary endothelium and to be a possible precursor of permanent pulmonary hypertension. Young athletes with abnormal PAP response may have high pressure load in their pulmonary vessels several hours a day for years while maintaining their endurance training program.

Conclusion: Non-professional highly endurance-trained individuals show abnormal pulmonary pressure response during exercise. The common definition of normal range in pulmonary arterial pressure may have to be reconsidered.

P4710 : Cardiac resynchronization therapy in heart failure patients with narrow QRS complexes: results of a PROSPECT sub-study

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Purpose: The current guidelines prescribe cardiac resynchronization therapy (CRT) in patients with severe heart failure (HF), LV ejection fraction ≤ 35% and a wide QRS (≥120 ms). However, patients with narrow QRS complexes might also benefit from CRT. This sub-study of PROSPECT prospectively tested the response to CRT in patients with a narrow QRS duration.

Methods: Fifteen centers in Europe, and 1 in Hong Kong successfully implanted 41 patients with QRS < 130 ms and documented evidence of mechanical dyssynchrony by any of seven pre-defined echocardiographic measures. The age was 63.9±12.5 years (mean ± SD), LVEF was 24.8±5.9%, QRS duration was 108±14 ms, 95.1% were NYHA Class III, 70.7% were male and 48.8% had ischemic etiology of HF. Clinical and echocardiographic parameters were compared (baseline vs. 6 months) and pre-defined criteria were used to assess patient response to CRT at 6 months.

Results: Clinical Composite Score (combination of change in NYHA classification, patient global assessment score and major clinical events) improved in 63.4% of 41 patients. The table reports baseline and 6 months values, and percentage improved on pre-defined criteria for the other parameters.

Conclusions: These preliminary results suggest beneficial effect of CRT in patients with narrow QRS complex and LV dyssynchrony on echocardiography. The majority of patients improved on clinical criteria whereas LVESV did not improve. LVEDD however showed a significant reduction. Larger studies are needed to clearly define the selection criteria to provide CRT-therapy to patients with narrow QRS complexes.

Response parameters and outcome

Response parameter, criterion	N improved (%)	Baseline mean (SD)	6 Month mean (SD)	p-value
NYHA class, improved ≥ 1	31 (75.6%)	3.0 (0.2)	2.2 (0.7)	<0.0001
Hall walk, improved ≥ 10%	22 (61.1%)	315 (130)	385 (126)	0.003
MLHFQ, improved ≥ 9 points	23 (62.2%)	44.1 (20.4)	26.8 (20.2)	<0.0001
LVESV, reduced 15%	10 (27.8%)	174.1 (77.1)	172.7 (81)	0.13
LVEDD, any reduction	17 (68.0%)	6.65 (0.97)	6.31 (1.04)	0.007

LVESV: left ventricular end systolic volume; NYHA: New York Heart Association; MLHFQ: Minnesota Living with Heart Failure Questionnaire; LVEDD: left ventricular end diastolic diameter.

P4734 : Exercise-induced abnormal pulmonary arterial pressure response in adolescents and adults with atrial or ventricular septal defect

Moller (Noetteroey), Pettersen (Oslo), Peersen (Toensberg), Fredriksen (Oslo), Holmstrom (Oslo), Grunig (Heidelberg /Germany), Mereles (Heidelberg /Germany), Thaulow (Oslo)

Introduction: The European Heart Survey on Congenital Heart Disease reported a high prevalence of pulmonary hypertension: 18%/26% in closed ASD/VSD. The study had a selection bias towards difficult cases. Our study aims to examine a representative population-based group of young patients with isolated ASD or VSD. The main focus is pulmonary hypertension or its postulated precursor, abnormal pulmonary pressure response (AR) during exercise.

Methods: The study comprises 50 patients with either isolated VSD or ASD, whose defects were assumed hemodynamically insignificant or surgically closed early in life. The patients were re-

cruited among all patients born between 1982 and 1993 from two regions in Norway. The patients are age- and gender matched against 86 healthy controls. Cardiovascular exercise testing and echocardiography at rest and during supine cycling were performed. During exercise systolic pulmonary arterial pressure (PAP) is monitored by measurement of tricuspid valve regurgitation jet velocity.

Results: Treadmill testing showed normal (Gaussian) distribution of age-corrected maximal oxygen uptake (VO2peak) for both groups. There was a significant ($p<0,001$) lower mean Z-score of VO2peak in the patient group (-1.64, range -5.2 to 1.3) as compared to the normally trained controls (mean -0.12, range -4.5 to 2.0) (figure 5). In patients with surgically closed defects echocardiography at rest showed a significant lower right ventricular performance measured by TAPSE ($p<0.001$, means operated patients/control 15.7/23.0 [-8.6,-6.0]) (figure 6). There were no cases of pulmonary hypertension at rest in the patient group. Exercise echocardiography rendered assessable registrations of tricuspid regurgitation jet velocity in 46/50 patients (92%) and in 83/86 controls (97%). The maximal PAP during exercise was significantly higher in patients compared to controls ($p<0,001$, means patients/controls 39/32 mmHg [3.5, 10.3]) (figure 7). 21 of 46 patients (46%) and 16 of 83 controls (19%) had PAP above 40 mmHg during exercise. Eight patients (17%) but only one control (1%) had PAP above 50mmHg during exercise. The PAP did not differ between genders and no correlation was found between TAPSE at rest and PAP during exercise.

Conclusion: Young patients with small untreated or surgically closed isolated ASD or VSD have lower exercise capacity. Patients with surgically closed defects have lower right ventricular performance than healthy individuals. About one out of five patients has pathologic pulmonary pressure load above 50 mmHg during exercise. The long-term implications of these findings have to be investigated.

P4735 : Moderate altitude conditions may cause hypoxia and abnormal pulmonary arterial pressure response at rest and during exercise in patients with atrial or ventricular septal defect

Moller (Toensberg), Brun (Oslo), Fredriksen (Oslo), Holmstrom (Oslo), Hallen (Oslo), Thaulow (Oslo)

Introduction: Hypoxia and abnormal pulmonary pressure response (AR) during exercise have been observed in healthy individuals. AR has been shown to correlate with susceptibility to high altitude pulmonary edema. It is not known whether moderate altitude can cause or augment these abnormal reactions in numerous patients with minor or surgically closed ventricular septal defect (VSD) or atrial septal defect (ASD) that might have caused increased pulmonary vascular reactivity early in life.

Methods: 11 patients with ASD or VSD (10/11 surgically closed, age 14 to 25 yrs) were examined by echocardiography at rest and during supine cycling at sea level. The patients then rested in a low-pressure chamber for 2 hours at 2500 meters/8200 feet altitude. Oxygen saturation (SpO2), right ventricular performance and pulmonary arterial peak systolic pressure (PAP) were monitored. Exercise echocardiography was repeated before descent.

Results: During exercise at sea level 3 patients showed abnormal PAP response > 40 mmHg (44 to 56), none had hypoxia (mean 98.6%). After 120 minutes resting at moderate altitude mean PAP increased from 24 mmHg at sea level to 32 mmHg, 3 patients showed PAP increase above 40 mmHg (43 to 45), mean SpO2 had fallen to 94% (88 to 98). During altitude exercise mean PAP raised to 49 mmHg, 9 patients showed PAP > 40 mmHg (41 to 63), mean oxygen saturation dropped to 81%, in 3 patients SpO2 decreased below 80% (68 to 79). 2 of these patients had simultaneously hypoxia and pressure increase above 50 mmHg. No patient had symptoms beyond dizziness at rest or fatigue during altitude exercise.

Discussion: Moderate altitude simulates the atmospheric condition in mountainous areas or in pressurised commercial airplanes. Like many other people patients with closed VSD or ASD may be exposed to these conditions for hours (airplane), days or months or even permanently (mountains) with or without physical strain. It is commonly assumed that patients without shunts between pulmonary and systemic circulation would not show major hypoxia or changes in pulmonary vascular resistance.

Conclusion: There might be a significant risk of hypoxia and pulmonary hypertensive reaction in patients with minor or surgically closed ASD or VSD when exposed to moderate altitude. Exercise in altitude seems regularly to provoke or augment abnormal pulmonary vascular resistance despite surgical repair early in life.

P4872 : Cardiology training in Europe: the EBSC Survey 2006

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Background and methods: The European Board for the Speciality of Cardiology (EBSC) strives to harmonize standards in cardiology training in Europe. Therefore the EBSC developed European criteria for accreditation as specialist in cardiology (EHJ; 1996, 17, 996-1000), including a total training duration of 6 years, which includes a common trunk of internal medicine (at least of 2 years). Furthermore a basic cardiology training of at least 3 years will be recommended. Trainees must keep a personal log-book. Each training programme should be assessed at least every 5 years.

To achieve a picture as accurate as possible of cardiology training in Europe EBSC surveyed national authorities in 49 ESC member states containing questions regarding the training in internal medicine, cardiology training and about the infrastructure of training centres.

Results: 27 (55%) of the replying ESC countries, among them 22 EU/EFTA (71% of all EU/EFTA) countries responded. Cardiology as an independent mono-speciality is recognised in 15 (55% of all responders) countries. In further 7 (26%) countries (NOR, PL, AT, SE, BG, BLR, BIH) internal medicine is a prerequisite for a cardiologist. 5 (19%) countries did not answer.

The minimum of two years training in internal medicine (common trunk) is usual in 22 (82%) countries. These criteria are not fulfilled in 4 (15%) countries: 1 year BLR and ES; 1.5 years CZ and FR; no reply: EE.

A minimum of 3 years in cardiology training is obligatory in 22 (82%) countries. 5 (18%) countries have different training durations in cardiology: 2 years in BG, BIH, BLR, LV and PL.

A training logbook is used in all but 5 (18%) countries: DE, FR, ISR, SUI, TR; no reply: GB.

Most countries have an assessment procedure at the end of training in cardiology except of 2 (7%): AT, ES.

Evaluation of training centres (every 5 years) is mandatory in 13 (48%) countries. There is a lack of explicit information of this evaluation process in 14 (52%) countries: TR, FI, PL, BE, GR, ISR, ES, DE, FR, SK, BIH, EE, BLR, SUI.

Conclusion: Within Europe tremendous differences exist in cardiology training. Providing a standardised patient care and free movement of medical specialists within Europe harmonisation and standardisation of the training in cardiology is of utmost urgency and a vital need.

P4959 : Continuous pressure-displacement loop analysis for ischemia detection, a novel technique by use of miniaturized epicardial ultrasound transducer

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To improve myocardial ischemia monitoring after cardiac surgery we have developed a miniature ultrasound transducer for epicardial use. In this study we have tested a prototype transducer and its signal analysis during global hemodynamic changes and regional ischemia.

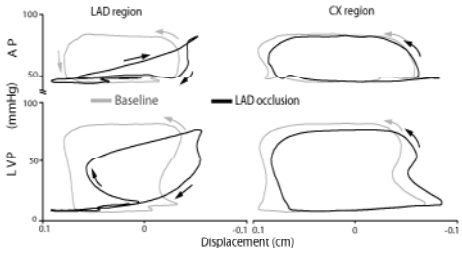
Methods: In an open-chest porcine model we sutured a miniature probe to the epicardium in the left anterior descending artery area (LAD) (n=10), and a second transducer in the circumflex artery area (CX) (n=5). Hemodynamic changes were made by increase/decrease in inotropy and in preload, and during 60 s LAD occlusion. Radial myocardial velocity including peak systolic (S') and postsystolic velocities (PSV) was measured continuously. The integrated velocity curves from the two regions were plotted against the left ventricular (LVP) and the arterial pressure (AP) in pressure-displacement (P-D) loops.

Results: During ischemia, S' decreased (0.9±0.1 to 0.1±0.1 cm/s, $p<0.01$) in LAD region compared to all other interventions. S' in the CX region remained unchanged (0.8±0.1 to 0.8±0.1 cm/s, ns). PSV increased in LAD region during ischemia (-0.1±0.1 to 2.0±0.3 cm/s, $p <0.01$). The LVP-D and the AP-D loop areas became negative in the

LAD region during ischemia (24±0.0 to -10±0.0 mmHg·cm, p=0.01) (Figure), in contrast to positive loop area during global interventions (31±0.0 to 26±0.1 mmHg·cm, ns). In the CX region the areas remained positive during all interventions.

Conclusion: The novel miniature transducer enables continuous real-time detection of ischemia. Importantly, pressure-displacement loops from both LV and arterial pressures provide excellent separation of ischemia from other hemodynamic changes by a qualitative shift of loop area. AP-D-loops may prove useful as a continuous real-time ischemia indicator in clinic.

Pressure vs. radial displacement.



P4969 : Early-diastolic mitral annulus velocity is determined by early-diastolic load

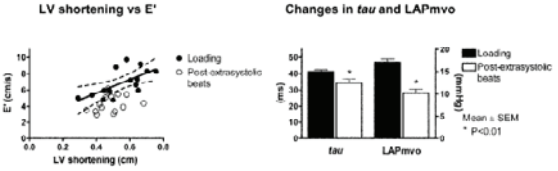
Opdahl (Oslo), Remme (Oslo), Helle-Valle (Oslo), Vartdal (Oslo), Lyseggen (Oslo), Pettersen (Oslo), Edvardsen (Oslo), Smiseth (Oslo)

Background: Peak early-diastolic mitral annulus velocity (E') has been introduced as a marker of LV relaxation. We have shown that long-axis shortening is another determinant of E'. Furthermore, previous observations in isolated muscle experiments have shown that increased load during relaxation (late load) increases myocardial lengthening velocity. Therefore, we hypothesised that left atrial pressure at the time of mitral valve opening (LAPmvo), which represents late load in the intact heart, is another determinant of E'.

Methods: In 15 anaesthetised dogs we measured LAPmvo and time constant of LV relaxation (tau) by micromanometry and E' and long-axis shortening by sonomicrometry. Data were obtained during volume loading and from post-extrasystolic beats.

Results: LAPmvo was 17.1±0.7 (mean ± SEM) during volume loading and 10.3±0.8 mmHg (P<0.01) during post-extrasystolic beats. This difference in LAPmvo was associated with a reduction in E' from 6.9±0.4 to 4.4±0.3 cm/s (P<0.01). Furthermore, we observed a reduction in tau from 41±1 to 34±2 ms (P<0.01), and a downward-shift of the relationship between E' and LV shortening (Figure). Therefore, the decrease in E' during reduced LAPmvo could not be attributed to reduced shortening or slower relaxation.

Conclusions: The present study demonstrates that changes in LAPmvo may account for changes in E'. These results indicate that late load together with LV shortening and LV relaxation are independent determinants of E'. Therefore, E' is not a specific marker of LV relaxation rate.



P5009 : Strain and strain rate by speckle tracking echocardiography predicts coronary occlusion in NSTE-ACS

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Background: Many patients with non ST-elevation acute coronary syndrome (NSTE-ACS) have an occluded coronary artery on coronary angiography (CA). Coronary occlusion often results in substantial infarction and loss of systolic function. Identification of these patients may have considerable impact on treatment and prognosis. We hypothesized that assessment of left ventricular (LV) systolic function by speckle tracking echocardiography (STE) facilitates an early noninvasive identification of coronary occlusion in NSTE-ACS.

Methods: 90 consecutive patients underwent CA 1-3 days after hospitalisation for a first NSTE-ACS. Echocardiography was performed immediately prior to CA. Longitudinal peak systolic

Table of results

	Occlusion	No occlusion	Sensitivity	Spesificity	Cutoff
Peak S (%)	-15.5±3.1	-17.9±2.6	60%	72%	≥-16.7%
Peak SR (s^{-1})	-0.8±0.2	-0.93±0.2	60%	76%	≥-0.89 (s^{-1})
NoS with peak S>-14 (%)	6.3±3.2	2.8±3.0	80%	73%	≥5 segments
Nos with peak SR>-0.8 (s^{-1})	6.6±3.2	3.5±3.3	87%	75%	≥5 segments

Mean values ±SD and ability to identify coronary occlusion in NSTE-ACS.

strain (peak S) and peak systolic strain rate (peak SR) were measured by STE in a 16 LV segments model. Systolic contraction give negative longitudinal S/SR, hence, higher values (closer to or above zero) represent systolic dysfunction. Global values are calculated as mean of analyzed segments. The extent of regional systolic dysfunction was assessed by the number of segments (NoS) with peak S/peak SR above a given cutoff.

Results: 15 patients (17%) had occlusion of a major artery or significantly sized branch on CA. Patients with coronary occlusion had higher values of global Peak S ($p<0.01$), global peak SR ($p=0.015$), and a higher number of segments with peak S or peak SR above cutoff ($p<0.01$). For assessment of regional systolic dysfunction, a cutoff value pr. segment of -14% for peak S and -0.8 s^{-1} for peak SR demonstrated the greatest AUC on ROC analyses. Table displays mean values (±SD), cutoffs and ability to identify coronary occlusion.

Conclusions: STE predicts coronary occlusion in NSTE-ACS patients. Estimating extent of regional systolic dysfunction showed better sensitivity and specificity compared to global parameters. STE may provide valuable additional information for early selection of patients with high risk of developing substantial myocardial infarction in the NSTE-ACS population.