Norske abstrakter presentert i Barcelona

[P3136] Prevalence of lipid disorders in statin treated patients from Sweden, Norway and Denmark: Results from the Dyslipidemia International Study (DYSIS)

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Background: Treatment of lipid abnormalities is a focus in Scandinavia, particularly on low density lipoprotein cholesterol (LDL-C), but also on high density lipoprotein cholesterol (HDL-C) and triglycerides (TG). Sweden, Norway and Denmark use the same guidelines for treating lipid abnormalities and have the same lipid modifying drugs.

Objective: To study the prevalence of dyslipidemia in statin-treated patients in Scandinavia.

Methods: This cross-sectional survey in Scandinavia was part of a 2008 pan-European and Canadian study. Included were 958, 956 and 933, respectively, statin-treated patients 45 year or older seen consecutively in clinic. Patients had used statins for at least 3 months. ESC-Guidelines classified patient risk and defined lipid treatment goals/normal levels.

Table 1. Dyslipidemia rates by ESC risk categories

	Patients with CHD or Diabetes or SCORE risk ≥ 5%		Patients with SCORE risk <5%	
	Men	Women	Men	Women
LDL-C not at goal [%] [≥2.5/2.0 mmol/L (high risk); ≥3.0 mmol/L (low risk)]				
Sweden (n=804)	35.3/66.7	43.6/69.9	31.8	38.5
Norway (n=847)	40.4/70.0	52.4/78.2	34.5	36.6
Denmark (n=889)	36.0/60.7	33.1/59.9	28.9	35.2
TC not at goal [%] [≥4.5/4.0 mmol/L (high risk); ≥5 (low risk)]				
Sweden (n=950)	38.5/63.0	53.1/75.4	40.6	57.0
Norway (n=954)	38.3/59.6	63.9/81.8	41.5	45.5
Denmark (n=911)	37.0/60.0	47.9/72.7	26.1	50.5
Low HDL-C [%] [<1.0 mmol/L (male); <1.2 mmol/L (female)]				
Sweden (n=818)	32.8	24.0	23.8	12.7
Norway (n=919)	29.7	26.9	27.4	16.7
Denmark (n=895)	22.4	17.2	29.5	10.3
Elevated TG [%] [>1.7 mmol/L]				
Sweden (n=802)	42.1	36.1	47.6	30.2
Norway (n=786)	32.6	38.2	50.0	30.8
Denmark (n=866)	36.0	36.3	37.8	29.7

Results: In Sweden 59% were male, the average age was 66 - males and 69 - females. In Norway 57% were male, the average age was 65 - males and 68 - females. In Denmark 56% were male, the average age was 66 - males and 68 - females. (Table)

Conclusion: A large gap between recommendations and practice in patients at high risk of cardiovascular disease remains. More intensive management of dyslipidemia is warranted. Further investigation into the reasons for the variation in reaching treatment goals between Sweden, Norway and Denmark is necessary to explain the numbers presented in this abstract.

[P1274] Combined results and long-term follow-up in NORVIT and WENBIT with 6837 coronary artery disease patients: Homocysteine-lowering B-vitamin treatment does not prevent major cardiovascular events

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Objectives: Observational studies have reported associations between circulating total homocysteine (tHcy) concentration and risk of cardiovascular disease. Oral administration of folic acid and vitamin B12 can lower plasma tHcy levels. Our purpose was to assess the effects of homocysteine-lowering treatment in the Norwegian Vitamin Trial

(NORVIT) and the Western Norway B-vitamin Intervention Trial (WENBIT) by combined analyses of trial results and long-time follow-up of the two study populations.

Methods: A total of 6837 patients, 76.5% male, mean (SD) age 62.3 (11.0) years, with acute myocardial infarction (AMI) or angiographically verified coronary artery disease, were included between December, 1998 and April, 2004. They were randomly assigned to four groups receiving daily oral treatment with 1) folic acid (0.8 mg)/vitamin B12 (0.4 mg)/vitamin B6 (40 mg), 2) folic acid/vitamin B12, 3) vitamin B6 alone or 4) placebo. Otherwise, they were given conventional medical treatment. The primary end point during the intervention was a composite of AMI, thromboembolic stroke or cardiovascular death. The end point during long-time follow-up was cardiovascular death. Estimates of the hazard ratios (HR) and 95% confidence intervals (CI) were obtained using Cox proportional hazard regression with adjustment for trial.

Results: By 1 to 2 months after randomization, plasma tHcy concentration was lowered by median 25% in the groups receiving folic acid/vitamin B12. During in-trial follow-up of median 39 months, the primary end point was experienced by 533 (15.6%) of participants receiving folic acid/vitamin B12 versus 503 (14.7%) of those not receiving such treatment (HR, 1.07; 95% CI, 0.95 to 1.21; P=0.25). The incidence of the separate end points of AMI and thromboembolic stroke did not differ among the groups. During extended long-time follow-up of median 74 months from randomization until September, 2007, a total of 571 (8.4%) of participants died from cardiovascular disease. There was no difference in cardiovascular mortality between groups that had received folic acid/vitamin B12 or not (HR, 1.10; 95% CI, 0.94 to 1.3; P=0.24).

Conclusions: The combined results and long-time follow-up in two large randomized clinical trials with coronary artery disease patients in Norway, are consistent with no beneficial effects of treatment with folic acid/vitamin B12 on major cardiovascular events during intervention or on cardiovascular death during long-time follow-up. Use of homocysteine-lowering B-vitamin supplements as secondary prevention in such patients is not justified.

[P4694] Increased left atrial volume in Norwegian elite football players

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Purpose: Elite athletes in aerobic demanding sports have increased left ventricular (LV) stroke volume (SV) and therefore increased LV volumes, both at rest and during exercise. Left atrial (LA) diameter, measured by echocardiography in one dimension, has been reported moderately enlarged in athletes. To what extent the volume of LA is affected is known only to a minor degree. Thus, the purpose of the present large scale study was to test whether there was an absolute increase in LA volume. We also wanted to test which of the two methods measuring LA size in athletes (LA diameter or LA volume) correlated best to SV.

Methods: As part of the mandatory cardiac screening of elite Norwegian male football players prior to the 2008 season, resting LV SV, end systolic-LA diameter and LA volume (ESV) was measured by two-dimensional echocardiography. All parameters were divided by body surface area (BSA). Blinded measurements were performed on 594 players and 46 matched controls.

Results: There were no significant differences between the groups in age, BSA, body mass index, LV ejection fraction, systolic-, or diastolic blood pressure. Compared to the controls, the football players had markedly higher, and above normal references, LA ESV, 36.8±10.1 vs. 27.8±10.1 ml/m^2 ($p<0.001$). Additionally, they had larger LA diameter, but within normal references, 1.7±0.2 vs. 1.6±0.2 cm/m^2, ($p<0.001$). The athletes also had a significant higher resting SV, 82.3±17.3 vs. 69.3±14.1 ml/beat, ($p<0.001$). Although the LA diameter in the athletes was only 7% larger than LA diameter in the control group, the athletes LA volume was 32% larger than in the controls. The correlation between LA volume and SV ($r=0.44$) was higher than between LA diameter and SV ($r=0.17$).

Conclusions: Athletes have increased LA volume compared to controls. The correlation between LA

volume and SV was markedly higher than between LA diameter and SV. Measurement of LA volume seems to reflect enlargement of LA size more precisely than LA diameter, which may underestimate LA enlargement, as demonstrated in the present study.

[P5606] Efficacy of cardiac resynchronization therapy depends on outcome definitions

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Purpose: The reported response to cardiac resynchronization therapy (CRT) is variable ranging from 50-90%, and we hypothesized that this was due to the various response criteria used. We therefore evaluated response to CRT at 6 and 12 months, and thereafter tested a novel response criterion.

Methods: 81 patients were enrolled. Pre- and postoperatively at 6 and 12 months we evaluated the following definitions of response in our material:

1. 1. NYHA-class (increase by ≥1).
2. 2 and 3. The patients physical and metal function i.e. quality of life, evaluated by the questionnaire short form (SF)-36 (improvement cut-off an increase >3 points).
3. 4. 6 min walk test (increase≥10%).
4. 5. Peak VO2 (increase≥1 ml/kg/min).
5. 6. Left ventricular end systolic volume (LVESV) (reduction≥10%).
6. 7. left ventricular ejection fraction (LVEF)(increase≥5%).
7. 8. N-terminal pro B-type natriuretic peptide (NT-proBNP) (reduction≥20%).

Results: Employing different criteria, response ranged from 31-79% (table 1). A combined definition of response to CRT was predefined as 1) a reduction of LVESV≥10% and 2) either an improvement in NYHA class by 1 or more or an increase in peak VO2≥1 mL/kg/min occured in 42 (52%) and 48 patients (59%) after 6 and 12 months of CRT, respectively.

Response to CRT by different criteria Parameter	% responders at 6 months	% responders at 12 months
NYHA-class improved ≥ 1	70	79
ΔPCS > 3 points	60	63
ΔMCS > 3 points	51	59
Δ6 min hall walk test ≥ 10%	33	31
increased peak VO2 ≥ 1/ml/kg/min	53	56
reduction in ΔLVESV ≥ 10%	61	74
increased LVEF ≥ 5%	52	55
ΔNTproBNP ≥ 20%	62	67

PCS = physical combined score by SF-36, MCS = mental combined score by SF-36.

Conclusions: 52% and 59% were responders to CRT at 6 months and 1 year given a predefined novel endpoint. Different response criteria to CRT gave response rates ranging from 31 to 79%.

[P1295] Serum osteoprotegerin levels and long-term prognosis in patients with stable angina pectoris

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Background and purpose: Osteoprotegerin is a member of the tumor necrosis factor superfamily, and has pleiotropic effects on bone metabolism, endocrine function and the immune system. Serum OPG levels are elevated in cardiovascular disease, and its synthesis within atherosclerotic plaques is hypothesised to be a response to plaque instability. Unstable plaques may, however, occur even in patients with clinically stable angina. We therefore assessed whether OPG predicts thromboembolic events and mortality in such patients.

Methods: Serum samples for OPG analysis were obtained from 1025 patients (mean (SD) age 62 (11) years, 72% men) who underwent elective coronary angiography for clinically stable angina. At inclusion, 443 patients (43%) had 1 or 2 vessel disease, whereas 352 (34%) had 3 vessel disease. OPG levels at baseline were related to the incidence of acute coronary thromboembolic events (fatal and nonfatal acute myocardial infarction (MI), acute hospitalisation for unstable angina pectoris and sudden cardiac death) and to all-cause

mortality. Hazard ratios, HR (95% CI), were estimated using Cox regression.

Results: During a median follow-up of 72 months, 144 patients (14%) experienced an acute coronary thromboembolic event (CTE). A total of 116 patients (11%) died. In crude analysis, OPG predicted both CTE and all-cause mortality. For CTE the HR was 1.27 (1.09-1.47) per quartile increment and 2.03 (1.31-3.14) for decile 10 versus 1-9 of OPG level. For all-cause mortality the HR was 1.61 (1.35-1.92) per quartile increment and 3.38 (2.22-5.14) for decile 10 versus 1-9.

Adjustment for age and gender attenuated the risk estimates. For CTE, the HR was 1.61 (1.01-2.56), and for all-cause mortality the HR was 2.02 (1.28-3.18) for decile 10 versus 1-9.

After additional adjustment for conventional risk factors (hypertension, smoking, diabetes mellitus, history of MI, ejection fraction and CRP levels), there was no significant association between OPG levels and CTE. Nor was there any significant trend over quartiles of OPG in relation to all-cause mortality. However, serum OPG was still a predictor of mortality among patients with levels above the 90th percentile; HR for decile 10 versus 1-9 was 1.87 (1.17-2.99).

Conclusion: In patients with stable angina pectoris, serum OPG is not an independent predictor of acute coronary thromboembolic events. OPG predicts long-term mortality, but this effect is mainly restricted to levels above the 90th percentile.

[5154] Immediate angioplasty compared to standard therapy after thrombolysis for ST-elevation myocardial infarction in areas with very long transfers. Results of the NORDISTEMI study

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Purpose: Thrombolysis remains the treatment of choice for patients with ST-elevation myocardial infarction (STEMI) and long transfer delays to percutaneous coronary intervention (PCI). The optimal treatment following thrombolysis is still debated. The aim of this study was to compare a strategy of immediate transfer for PCI after thrombolysis to a conservative, ischemia-guided approach, in patients living in rural areas with long transfer delays.

Methods: The NORwegian study on DIstrict treatment of STEMI was a randomised, controlled trial in patients with STEMI of less than 6 hours duration and more than 90 minutes expected time delay to PCI, conducted in the South-Eastern part of Norway. The patients were treated with full-dose tenecteplase, aspirin, low molecular weight heparin and clopidogrel, and randomised to immediate transfer for PCI (early invasive group), or initial management in the local hospital with early transfer only if rescue indication or clinical deterioration (conservative group). The primary outcome was a composite of death, reinfarction, stroke or new myocardial ischemia at 12 months, and analysis was by intention to treat. Infarct size estimated at 3 months with SPECT was a secondary outcome. Patient inclusion was finished in April, 2008, and last follow-up is scheduled to April, 2009.

Results: According to power analysis, 266 patients were included in the study. Thrombolysis was given pre-hospitally in 58% of the patients. Time intervals to thrombolysis and to coronary angiography are shown in the table. In the conservative group, 32 patients were sent to rescue PCI. No significant differences in infarct size at 3 months were observed between the two groups (p= 0.29). The result of the primary outcome will be presented.

	Early invasive group	Conservative group
Time from symptom onset to thrombolysis	117 (80-195) min	126 (80-195) min
Time from thrombolysis to angiography	130 (105-155) min	5.5 (0-17.5) days
Transfer distance to PCI centre	158 (129-200) km	180 (132-234) km
Infarct size (% of left ventricle)	7 (0-24)%	6 (0-16)%

The data are given as medians with 25-75 percentiles.

Conclusion: This is the first study evaluating the optimal strategy following thrombolysis in patients with STEMI living in areas with very long transfers to PCI. An early invasive strategy did not reduce infarct size. Final results of the study will be presented.

[P5313] Comparison of left ventricular global strain and left ventricular ejection fraction as determinants of left ventricular injury in patients with acute myocardial infarction

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Purpose: Infarct size is a major determinant of morbidity and mortality following acute myocardial infarction (MI). Early determination of infarct size may identify patients of high risk for adverse left ventricular (LV) remodeling likely to benefit from aggressive pharmacological therapy. The aim of this study was to compare left ventricular ejection fraction (LVEF) and LV global strain by Doppler as predictors of LV infarct size in patients with ST-elevation myocardial infarction (STEMI).

Methods: Strain by Doppler echocardiography and LVEF by echocardiography were assessed within 3 hours of thrombolysis and at discharge in patients with first time STEMI. LV global strain was determined by an average of peak negative strain from 16 segments. LVEF was assessed by the Simpson's biplane method. Both methods were validated against chronic infarct size measured by contrast-enhanced magnetic resonance imaging (ceMRI).

Results: 43 consecutive patients (62±10 years) were included. At the acute assessment following thrombolysis (139±43 minutes), there was a closer correlation between LV global strain and infarct size ($r=0.68$, $p<0.0001$) than between LVEF and infarct size ($r=0.54$, $p<0.0001$). At discharge (10±5 days) there was no difference in the correlation between infarct size and LV global strain ($r=0.78$, $p<0.0001$), and infarct size and LVEF ($r=0.76$, $p<0.0001$). However, global LV strain was better than LVEF for the detection of large (>22% of LV mass) infarctions at both time-points (table), and LV global strain was more reproducible than LVEF.

ROC analysis: LV global strain vs. LVEF Time-point		AUC	Sensitivity (%)	Specificity (%)	Cut-off value (%)
Acute	LV global strain	90	88	83	-16,5
	LVEF	75	88	60	52
Discharge	LV global strain	95	88	94	-16,0
	LVEF	90	88	74	51

Conclusions: In acute STEMI, LV global strain provides a better assessment of infarct size than LVEF. LV global strain may be an emerging tool for the early evaluation of LV function and risk assessment after MI.

[P5501] Circulating osteoprotegerin levels and long-term prognosis in acute ischemic stroke

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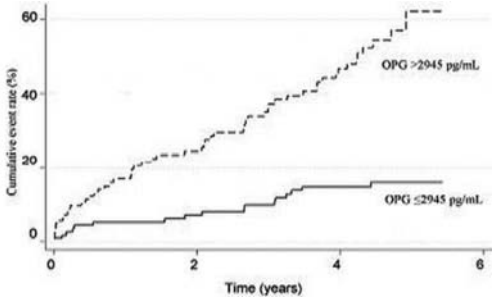
Objectives: To understand whether concentrations osteoprotegerin (OPG) are associated with prognosis in acute ischemic stroke.

Background: Concentrations of OPG have been associated with the presence of vascular and cardiovascular diseases, but the knowledge of this marker in the setting of ischemic stroke is limited.

Methods: In 244 patients with acute ischemic stroke (age 69±13), samples of OPG were obtained serially from debut of symptoms to day 5. The patients were followed for 47 months, with all-cause mortality as the sole end point.

Results: Examination of strata based on time from symptom onset to sample collection did reveal a slight time-dependent difference between day 0 to 5 ($P=0.05$), but in general OPG concentrations were rather stable during the first 6 days of ischemic stroke. Multivariable predictors of OPG values at presentation included hemoglobin ($T=-2.82$; $P=0.005$), creatinine ($T=4.56$; $P<0.001$), age ($T=9.66$; $P<0.001$), active smoking ($T=2.25$; $P=0.025$), and pulse rate ($T=3.23$; $P=.001$). At follow-up 72 patients (29%) had died. OPG concentrations were significantly higher in decedents

patients than in survivors (P=0.0001). Patients with OPG ≤2945 pg/mL at baseline had a significantly improved survival rate on univariate analysis (Figure) (P<0.0001); other time points did not add further prognostic information. In multivariate analysis, after adjustment for age, stroke severity, C-reactive protein levels, troponin T levels, heart- and renal failure, concentrations of OPG independently predicted long-term mortality after stroke (adjusted hazard ratio, 2.3; 95% CI, 1.1 to 4.9; P=0.024).



Conclusions: OPG concentrations measured at admission of acute ischemic stroke are predictive of long-term mortality.

[P4230] Anemia in outpatients with chronic heart failure; prevalence, associated factors and prognostic impact

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Objectives: Anemia is prevalent in patients with chronic heart failure (CHF) and imply worse prognosis. We wanted to assess the prevalence, identify associated factors and determine prognostic impact of anemia in ambulatory patients with CHF.

Methods: Data from 3486 outpatients with CHF of any etiology included consecutively in the Norwegian Heart Failure Registry from October 2000 to March 2006 were studied. Baseline data at time of inclusion were used to identify patients with anemia and to assess associated variables. Anemia was defined as hemoglobin (Hb) < 12 g/l in men and < 11 g/l in women. Data on mortality were available from the national registry. In a logistic regression model anemia was entered as the dependent variable and putative associated factors of anemia were entered as independent variables. Hazard Ration (HR) of anemia was obtained from Cox regression analysis.

Results: The prevalence of anemia was 11.5%. New York Heart Association (NYHA) function class, body mass index (BMI), glomerular filtration rate (GFR), ejection fraction (EF), gender, diabetes mellitus (DM) and cholesterol levels were independently associated with anemia (R^2= 0.08, p<0.001). EF was positively correlated to anemia and anemia was most prevalent in men, no association to medications were found. Crude HR of anemia was 2.05 (95% CI 1.69-2.47, p<0.001), adjusted for age, gender, GFR, NYHA class, BMI and diabetes mellitus HR of anemia was 1.35 (95% CI 1.06-1.72, p=0.016).

Conclusions: Anemia is prevalent in outpatients with heart failure and independently predicates a worse prognosis. Anemia was associated to DM, male gender, renal function and to functional and nutritional status.

[P498] Fast and accurate assessment of left ventricular volumes and ejection fraction by 3D echocardiography

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Introduction: Recent studies have shown that real-time 3D echocardiography gives accurate and reproducible measurements of left ventricular (LV) volume and ejection fraction (EF). We have developed a new software package for semi-automated assessment of LV volume using 3D echocardiography.

Aim: To evaluate the accuracy and repeatability of the new method compared to an offline 3D echo standard.

Methods: LV end-diastolic volumes (EDV), end-systolic volumes (ESV), and EF were measured using the new method in 35 unselected patients referred to echocardiographic examination. These results were compared to a reference, established using a commercially available offline semi-automated analysis tool. Repeated measurements were performed to investigate inter- and intra- observer variability.

Results: Average analysis time of the new method was 141s, significantly shorter than 261s with the offline tool (p<0.001). Bland Altman comparison of the two methods revealed high agreement of measured EDV, ESV, and EF (p=NS) (table), and similar intra-observer variability (p=NS) (table). Inter-observer variability with the new method was significantly lower for EDV and ESV (table).

New method vs. offline reference	EDV [ml]	ESV [ml]	EF [%]
Difference	2.1±21	-0.88±17	1.6±11
Intra-observer variability:			
New method	7.5±6.2	5.5±5.6	3.0±2.7
Offline reference	7.7±7.3	5.0±5.9	2.1±2.0
Inter-observer variability:			
New method	9.0±5.9	5.0±3.6	2.7±2.8
Offline reference	17±6.3*	12±7.7*	3.0±2.1

**Significant difference (p<0.05). All numbers are mean ± 95% limits of agreement.*

Conclusions: The new analysis software gives rapid and reproducible measurements of LV volumes and EF, with good agreement compared to an offline 3D volume quantification tool. This new software package is now fully integrated on a commercially available ultrasound scanner, for fast online LV analysis.

[P824] The chromogranins A and B are regulated differently in the myocardium and circulation during heart failure development; complimentary cardiac biomarkers?

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Purpose: The chromogranins A and B (CgA and CgB) have recently been found to be closely associated with cardiac disease. CgA may serve as a cardiac biomarker independently predicting mortality in heart failure (HF) patients, and CgB was found to modulate development of myocardial hypertrophy in vitro. However, whether CgB is regulated in the myocardium and circulation during HF, and possibly in a similar fashion as CgA, is currently unknown.

Methods: In a post-myocardial infarction (MI) HF mouse model, animals were evaluated by echocardiography before being sacrificed one week post-MI. Gene expression was measured by qRT-PCR and protein levels by Western blotting and radioimmunoassay (RIA). Localization of chromogranin production was assessed by immunohistochemistry. Circulating chromogranin levels were measured with RIA in 80 HF patients recruited mainly from an ambulatory HF clinic and 20 age- and gender-matched healthy control subjects.

Results: CgB production was clearly upregulated in the left ventricle (LV) of HF animals compared to sham animals with a 5.2 fold increase in gene expression (p<0.001), and a 110% and 70% increase in protein levels in the non-infarcted and infarcted part, respectively. CgB mRNA levels in HF animals correlated with animal lung weights (r=0.74, p=0.04). CgB production was unaltered in other tissues investigated, indicating that the myocardium may contribute to circulating CgB levels in HF. CgA gene expression was also upregulated in LV tissue of HF animals (4.8 fold increase, p=0.015), however, there was no significant correlation between myocardial CgA and CgB mRNA levels in neither sham (r=0.57, p=0.14) nor HF animals (r=0.35, p=0.36). By immunohistochemistry we localized production of the chromogranins to cardiomyocytes. Circulating levels of CgB were increased in patients with HF of mainly moderate severity compared to controls (1.69±0.03 vs. 1.52±0.05 nmol/L, p=0.007), and levels increased according to NYHA functional class (test for trend: p=0.03), while CgA levels were not clearly regulated (7.44±0.74 vs. 4.70±0.30 nmol/L, p=0.10). Circulating levels of the chromogranins were only modestly correlated in HF patients (r=0.31, p=0.005), and CgB had superior diagnostic accuracy for diagnosing HF compared to CgA (ROC-AUC 0.70 vs. 0.61).

Conclusion: Myocardial production and circulating concentrations of CgB are increased in proportion to disease severity during HF development. CgB is regulated differently than CgA, another granin protein and established cardiac biomarker, suggesting that the chromogranins may reflect different biological processes in HF.

[P3877] Is there agreement between echocardiography, SPECT and MRI in assessment of LV function after ST-elevation myocardial infarction?

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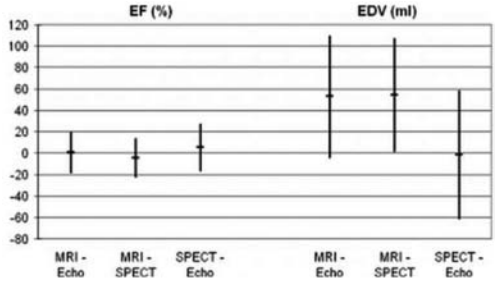
Objectives: Magnetic resonance imaging (MRI) is often considered to be the gold standard in assessing left ventricular function. The aim of this study was to compare left ventricular end diastolic volumes (EDV) and ejection fraction (EF) measured by MRI, single-photon emission computed tomography (SPECT) and echocardiography (Echo) in patients 3 months post-myocardial infarction.

Methods: MRI, SPECT and Echo were performed on the same day 3 months after ST-elevation myocardial infarction (STEMI) in 163 patients participating in the NORwegian DIstrict Study on ST-Elevation Myocardial Infarction (NORDISTEMI).

Results: The figure presents a summary of the Bland-Altman analyses, where each data point shows the mean difference between two methods, and the vertical lines give the limits of agreement (±2 SD). The mean EF measured by each method was almost identical, and less than 5% of the measurements were outside the limits of agreement. The mean EDV, however, was significantly higher by MRI than by Echo (52.7 ml mean difference) and SPECT (54.2 ml mean difference), and the limits of agreement were wider. Echo and SPECT gave practically the same mean EDV on average (1.5 ml difference). 4% of the measurements were outside the limits of agreement. The difference in EDV between MRI and Echo/SPECT increased with increasing volumes.



Conclusion: We find high agreements for EF measured by MRI, SPECT and Echo. The agreement for EDV between MRI and Echo/SPECT is lower which may possibly be caused by different tracing-methods and imaging principles. As echocardiography is preferable from a cost-benefit point of view, further analysis would be needed to clarify the nature of such differences.

[P830] The relationship between the long pentraxin 3 and B-type natriuretic peptide in patients admitted with acute coronary syndromes

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Background: Long pentraxin 3 (PTX3) is a recently identified member of the pentraxin protein family, and elevated plasma levels are found in the acute coronary syndromes (ACS). B-type natriuretic peptide (BNP) is a well known marker of left ventricular dysfunction and heart failure, and it provides prognostic information in patients with ACS. The aim of this study was to assess the relationship between PTX3 and BNP during the first four days of hospitalization in patients admitted with ACS.

Methods: PTX3 was measured in EDTA plasma with a new, high-sensitive ELISA methodology (PPMX, Tokyo, Japan). BNP was analysed in EDTA plasma using the Microparticle Enzyme Immunoassay (MEIA) Abbott AxSYM®. The blood samples were taken on admission and after four days in 358 patients. The study cohort was also divided into subgroups according to their index diagnosis; ST-elevation myocardial infarction (STEMI) or non ST-elevation myocardial infarction (NSTEMI).

Results: The plasma concentrations of PTX3 and BNP increased from day 1 to day 4 for the total

Table1. PTX3 and BNP following hospitalization in TnT positive (>0.05 ng/mL) chest pain patients	Admission	Day 4	Wilcoxon paired test
	Median marker values (interquartile range)	Median marker values (interquartile range)	p-value
PTX3 (ng/mL)			
Total group (n=358)	6.95 (4.35 – 11.30)	7.83 (5.61 – 11.20)	0.014
STEMI (n=l92)	6.54 (4.07 – 9.69)	7.69 (5.71 – 10.92)	0.012
NSTEMI (n=166)	7.12 (4.62 – 12.50)	8.00 (5.41 – 11.78)	0.251
BNP (pg/mL)			
Total group (n=358)	133.0 (43.0 – 416.0)	194.0 (80.0 – 499.0)	<0.001
STEMI (n=l92)	57.0 (30.0 – 210.0)	169.0 (85.5 – 348.3)	<0.001
NSTEMI (n=166)	204.5 (65.0 – 507.5)	229.0 (74.0 – 616.0)	0.025

group, STEMI and NSTEMI subgroups (Table). PTX3 and BNP were correlated to each other for the total group, STEMI and NSTEMI subgroups at admission (R= 0.334 (p<0.001), R= 0.340 (p<0.001) and R = 0.322 (p<0.001), respectively), and on day 4 (R= 0.526 (p<0.001), R=0.511 (p<0.001) and R= 0.552 (p<0.001), respectively).

Conclusion: PTX3 and BNP levels increase significantly from day 1 to day 4 and are strongly correlated for patients admitted with ACS.

[P5465] Combined effect of resting heart rate and physical activity on ischaemic heart disease: mortality follow-up in a population study

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Purpose: Resting heart rate is positively associated with the risk of cardiovascular death, but in women, the data are sparse and inconsistent. It is not known if the effect of resting heart rate could be modified by physical activity.

Methods: In a cohort of 24 999 men and 25 089 women who were free from cardiovascular disease at baseline, we used Cox proportional hazard models to estimate adjusted relative risks of death from ischaemic heart disease related to resting heart rate measured at baseline. We also assessed the combined effect of resting heart rate and self-reported physical activity on the risk of death from ischaemic heart disease.

Results: During 18 years of follow-up, there was a stronger positive association of resting heart rate with deaths from ischaemic heart disease than for cardiovascular deaths as a whole, and the effects were particularly clear in women younger than 70 years at baseline. For each increment of 10 heart beats per minute, risk of death from ischaemic heart disease was 18 percent higher in women younger than 70 years (p for trend <0.001), and 4 percent higher among women 70 years or older (p for trend, 0.43). Among men, there was a corresponding 10 percent higher risk in the younger (p for trend, 0.004), and 11 percent higher risk in the older age group (p for trend, 0.01) per increment of 10 heart beats per minute. Among women, the risk associated with high resting heart rate was substantially attenuated among those who reported high level of physical activity, whereas in men, there was no clear indication that physical activity could modify the effect of resting heart rate.

Conclusion: Resting heart rate is positively associated with the risk of death from ischaemic heart disease, and among women, the results suggest that by engaging in physical activity, the risk associated with a high resting heart rate may be substantially reduced.

[P2277] The correlation of the long pentraxin 3 (PTX3) to lipids in patients hospitalized with acute chest pain

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Background: The long pentraxin 3 (PTX3) is a recently identified member of the pentraxin protein family that also includes C-reactive protein. PTX3 is produced by the major cell types involved in atherosclerotic lesions in response to inflammatory stimuli, and elevated plasma levels are found in the acute coronary syndromes (ACS). However, currently available clinical data on the relation of PTX3 to lipids in a population hospitalized with acute chest pain is sparse. The aim of this study was to assess these variables.

Table 1. The relationship between PTX3 and lipids for patients hospitalized with acute chest pain	B (p-value)			R	Multiple regression model p-value
Groups	Total cholesterol	HDL cholesterol	Triglycerides		
All patients (n=795)	-1.10 (<0.001)	0.67 (0.304)	-0.42 (0.066)	0.213	<0.001

HDL cholesterol, high-density lipoprotein cholesterol.

Methods: PTX3 was measured with a new, high-sensitive ELISA method (PPMX, Tokyo, Japan) in EDTA plasma in admission samples from 795 patients. The patients were followed for 24 months for clinical outcome. A multiple regression model was fitted for the total population.

Results: PTX3 was related to total cholesterol but not to high-density lipoprotein cholesterol or triglycerides for the total population (r= 0.213, p<0.001) (Table I).

Conclusion: In patients with acute chest pain PTX3 is correlated with total cholesterol.

[P865(W)] Isolated systolic hypertension in patients with asymptomatic aortic stenosis (a SEAS substudy)

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Background: Isolated systolic hypertension (ISH) and aortic stenosis (AS) are both associated with left ventricular (LV) hypertrophy and higher risk of cardiovascular advents. Less is known about patients with combined ISH and asymptomatic AS.

Design and methods: Baseline blood pressures and echocardiographic LV structure was assessed in 1719 patients with asymptomatic AS randomized in the Simvastatin Ezetimibe in Aortic Stenosis (SEAS) study. LV hypertrophy was defined as LV mass/$m^{2.7}$ ≥46.7/$m^{2.7}$ in women and ≥ 49.2mg/$m^{2.7}$ in men. ISH was defined as systolic blood pressure ≥140 mmHg and diastolic blood pressure <90 mm Hg (n=670) measured at baseline, and was compared to the rest of the patients (n=1049) including 489 patients with non-ISH hypertension.

Results: ISH patients were older, included more women, had more often aortic regurgitation, a history of hypertension and received more often antihypertensive treatment, while severity of AS and body mass index did not differ between the groups. ISH patients also had lower systemic arterial compliance, larger LV mass index and a higher prevalence of LV hypertrophy, mostly of eccentric type. LV ejection fraction did not differ between the groups. In logistic regression, ISH was independently associated with higher age, lower systemic arterial compliance and higher prevalence of LV hypertrophy and aortic regurgitation (Table). In a similar model replacing LV hypertrophy with LV geometry using normal geometry as reference, only eccentric hypertrophy was associated with ISH (Odds ratio 1.48, 95% confidence interval 1.13-1.93, p<0.05)

Associations of ISH in asymptomatic AS Variables	Odds ratio	95% Confidence Intervals	Sign.
Aortic regurgitation	1.55	1.24-1.93	<0.001
Age (1 SD change)	1.46	1.30-1.64	<0.001
Treatment of hypertension	1.35	0.86-2.01	0.18
Left ventricular hypertrophy	1.32	1.05-1.67	<0.05
History of hypertension	0.98	0.63-1.5	0.92
Transaortic maximum velocity (1 SD change)	0.98	0.88-1.09	0.67
Systemic arterial compliance (1 SD change)	0.67	0.59-0.76	<0.001

Conclusion: In asymptomatic AS, ISH may be a marker of more advanced cardiovascular disease.

[P2969] The value of calprotectin as a prognostic marker of cardiovascular risk in acute chest pain

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Background: Calprotectin is a heterodimeric calcium-binding protein abundantly present in the cytoplasm of neutrophils, and it is released upon cell activation. Elevated levels of Calprotectin, as well as high-sensitive C-reactive protein (hsCRP) and B-type natriuretic peptide (BNP) are found in patients with acute coronary syndrome (ACS). The aim of this study was to assess the value of

Calprotectin as compared to BNP and hsCRP as a prognostic marker of cardiovascular risk within 24 months following hospitalization for acute chest pain.

Methods: Calprotectin was measured in EDTA plasma using the Calprest® ELISA kit. The blood samples were taken on admission in 785 patients. For statistical analysis, the study cohort was divided into quartiles according to Calprotectin levels. A Cox regression model was fitted which included standard risk measures.

Results: At 24 months follow-up, 121 of the 785 patients included in the multivariable model had died and 93 patients had suffered a recurrent non-fatal Troponin T positive event. The hazard ratio (HR) for patients with Calprotectin, BNP or hsCRP concentrations in the highest quartile (Q4) as compared to those with concentrations in the lowest quartile (Q1) for all-cause death were 0.31, 4.00 and 0.87 (p=0.752, p=0.005 and 0.666), respectively. Concerning recurrent non-fatal Troponin T positive events the HR were 1.07, 1.81 and 2.57 (p=0.830, p=0.124 and p=0.007), respectively.

Conclusion: Calprotectin was not found to be a predictor of clinical outcome in patients with acute chest pain. However, BNP was significantly associated with fatal outcome only, whereas hsCRP only predicted non-fatal cardiac events.

[293] Randomized comparison of percutaneous left ventricular assist device with open chest cardiac massage and surgical left ventricular assist device in ischemic cardiac arrest

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Purpose: A percutaneous left ventricular assist device (LVAD) may maintain blood flow to vital organs and prevent myocardial and cerebral ischemia during cardiac arrest and may be useful by supplementing chest compressions during treatment of patients with cardiac arrest in the catheterization laboratory. We compared a percutaneous LVAD, with open chest cardiac compressions (OCCM), and with a surgical LVAD during ischemic cardiac arrest in a randomized experimental model.

Methods: Transit-time flowmetry probes were placed around the pulmonary artery (Cardiac Output) and both carotid arteries (CA). Myocardial ischemia was induced by coronary ligature and ventricular fibrillation (VF) was induced by diathermia. Perfusion was measured by microspheres. Defibrillation was attempted after 20 minutes of VF.

Results: After 3 minutes of VF, Cardiac Output in the OCCM group was 1129mL/min vs. 1169 mL/min in the percutaneous LVAD- and 570 mL/min in the surgical LVAD group (P<0.05 for surgical LVAD vs. others).

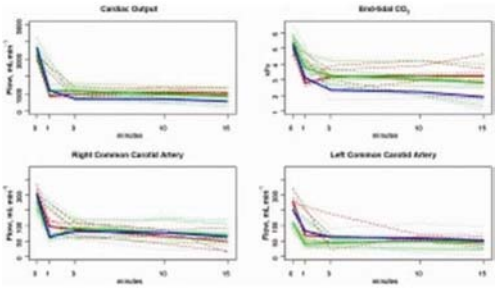
Right common carotid artery flow was 86mL/min for OCCM, 98 mL/min for percutaneous- and 79 mL/min for surgical LVAD (P=NS).

End-tidal CO2 was 3.3 kPa in OCCM, 3.2 kPa in percutaneous-, and 2.3 kPa in surgical LVAD (P<0.05 for surgical LVAD vs. others).

Epicardial perfusion was 0.33 mL/g/min for OCCM vs 0.62 mL/g/min for both LVADs (P<0.05 LVADs vs. OCCM).

Return of spontaneous circulation after defibrillation at 20 minutes was not different between groups (P=0.27).

Cardiac Output, et CO2 and carotid flow



Conclusion: A percutaneous LVAD can achieve hemodynamics comparable to open chest cardiac massage during cardiac arrest in an experimental model.

[P1468] CRP and MCP-1 - independent predictors of previously unknown abnormal glucose regulation in patients with acute STEMI

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Purpose: Inflammation plays an important role in both cardiovascular disease and diabetes. Previous studies have shown that poor glycemic control is associated with high circulating levels of the chemokine monocyte chemoattractant protein-1 (MCP-1). Furthermore, MCP-1 seems to be related to coronary heart disease and future cardiovascular events. C-reactive protein (CRP) increases during the first days after a revascularised ST-elevation myocardial infarction (STEMI) and is also associated with hyperglycaemia, insulin resistance and type 2-diabetes.

The aims of the study were to assess the ability of circulating levels of CRP and MCP-1 measured in-hospital to predict abnormal glucose regulation (AGR) in patients with acute STEMI without previously known diabetes. AGR was defined by an oral glucose tolerance test (OGTT) 3 months after the acute STEMI.

Methods: CRP and MCP-1 were measured in fasting blood samples from 201 patients within 24 hours after a primary percutaneous coronary intervention (PCI) treated STEMI. Three months later the patients performed a standardised 75 g OGTT. The patients were categorized according to the World Health Organisation criteria as normal glucose regulation, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and type 2-diabetes. AGR was defined as the sum of IFG, IGT, and type 2-diabetes. The analyses were performed in an explanatory strategy. Continuous variables were categorised into quartiles. A linear trend analyses across the groups selected the cut off point of the 25th and 75th percentile, respectively. The Mantel-Haenzel method was used to quantify confounders and highlight effect modifiers. Adjustment for multiconfounders was done using a logistic model.

Results: Median (25th, 75th percentiles) of CRP and MCP-1 levels were 12.0 (6.4, 33.1) mg/L and 222 (190, 272) pg/mL, respectively. After adjustment for established cardiovascular risk factors, age and serum-cTroponinT, CRP levels > the 75th percentile was independently predicting AGR at 3 months with an adjusted OR of 3.24, p=0.002. Triglycerides was an effect modifier on the association between high levels of MCP-1 and AGR and the adjusted OR for high MCP-1 levels was 8.06, p=0.007 when patients with high triglycerides (≥1.8 mmol/l, highest quartile) were excluded.

Conclusions: High levels of circulating CRP and MCP-1 measured in patients the first morning after a PCI treated acute STEMI were independently of each other, associated with abnormal glucose regulation defined by an OGTT performed 3 months later.

[P2122] Effect of thrombolysis with immediate transport to PCI vs. thrombolysis with ischemia-guided strategy on left ventricular function in ST-elevation myocardial infarction

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Objectives: Treatment of acute ST-elevation myocardial infarction (STEMI) with prehospital or in-hospital thrombolysis is widely used in rural areas with long transfer delays to invasive centers. In this setting it is unclear which treatment strategy that best preserves left ventricular function. In the NORDISTEMI study (NORwegian Study on DIstrict Treatment of ST-Elevation Myocardial Infarction) we aimed to test the hypothesis that thrombolysis with immediate transport to percutaneous coronary intervention (PCI) results in better preserved left ventricular function compared to a more conservative, ischemia-guided strategy.

Methods: 266 patients with STEMI of less than 6 hours duration and more than 90 minutes time delay to PCI were randomized to thrombolysis followed by PCI or thrombolysis followed by concervative strategy. Ejection fraction (EF), end systolic volume (ESV) and end diastolic volume (EDV) in the two treatment strategies were assessed by echocardiography, magnetic resonance imaging (MRI) and single-photon emission computed tomography (SPECT) when clinically feasible, three months after the myocardial infarction.

Results: EF ranged from 55 to 65% with the three different methods, but was literally identical in the two treatment strategies (table). ESV and EDV

were also the same in the two treatment stategies. The median EDV (ml) in the conservative and in the early invasive strategy measured with echocardiography, MRI and SPECT was 108 vs. 106 (p=0.76), 157 vs. 162 (p=0.41) and 101 vs. 104 (p=0.34), respectively.

Table. Ejection Fraction after 3 months Ejection Fraction	Conservative strategy	Early invasive strategy	p-value
Echocardiography (n=191)	55 (49.5-62.5)	55 (49-62)	0.70
MRI (n=178)	57 (53-63)	57 (49-65)	0.87
SPECT (n=241)	65 (55-71)	63 (51-70)	0.41

Conclusion: Ejection fraction and left ventricular volumes assessed with echocardiography, MRI and SPECT three months post-myocardial infarction did not differ between the two treatment strategies. Our data suggest that, in patients with STEMI, an early invasive strategy following thrombolysis does not preserve left ventricular function better than a conservative strategy.

[P4634] Effects of radiotherapy on arteries within and outside the radiation field in Hodgkin's lymphoma survivors

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Purpose: Hodgkin's lymphoma survivors (HLSs) treated with mediastinal radiotherapy are at an increased risk of developing coronary artery disease. Radiotherapy is associated with premature arterial stenoses within the radiation field. The aim was to perform a comparative study between the extension and amount of calcium deposits in the coronary and great arteries within the radiation field related to peripheral endothelial dysfunction in HLSs.

Methods: Forty-seven HLSs treated with mediastinal radiotherapy at the median age of 26 (range 14 – 42) years were included. The observation time was 22 (18 – 27) years. The radiation dose was 40 (27 – 44) Gy. Thirty-nine patients were treated with mantle field and the remaining 8 had mediastinal field only. We registered i) verified coronary artery disease (CAD; all treated with PCI or bypass surgery) ii) coronary calcium score with the use of a multi detector CT scanner, iii)widespread calcifications defined as calcium deposits in the internal carotid artery and/or carotid bifurcation as well as at the level of aorta and the branching of the great vessels demonstrated by CT collum angiography iv) peripheral endothelial function in arms and legs using strain-gauge plethysmography and finally v) markers of inflammation (CRP) and endothelial dysfunction (von Willebrand factor; vWF).

Results: 7 patients had CAD and additionally 18 had widespread calcifications. Coronary calcium volume score was 439 (8 – 2057) in patients with verified CAD and 68 (0 – 767) in patients without ($p = 0.022$). Median coronary calcium score was 183 (16 – 2057) among patients with widespread calcification demonstrated by CT collum angiography compared to 25 (0 – 415) in those without ($p < 0.001$). Widespread calcifications were associated with a reduced peak reactive hyperemia (strain-gauge plethysmography) in the arm, median 35.3 (range 25.3 – 50.6) mL/min/100 mL tissue versus 27.9 (20.8 – 53.5) mL/min/100 mL tissue, $p = 0.003$. vWF was increased in the subjects with widespread calcifications, median 106 (range 37 – 160) versus 83 (72 – 225, $p = 0.015$). vWF correlated also negatively with peak reactive hyperemia in the arm ($r = - 0.30$, $p = 0.042$). CRP did not discriminate between subgroups but was generally elevated in HLSs (2.20 (0.20 – 43) mg/L).

Conclusion: Radiotherapy induces calcium deposits in all arterial vessels within the radiation field. These changes are associated with impaired endothelial function outside the radiation field and elevation of vWF. Impaired endothelial function may be a marker of a phenotype vulnerable to early arterial calcification after radiotherapy

[P3811] Percutaneous left ventricular assist device may prevent acute cerebral ischemia during ventricular fibrillation

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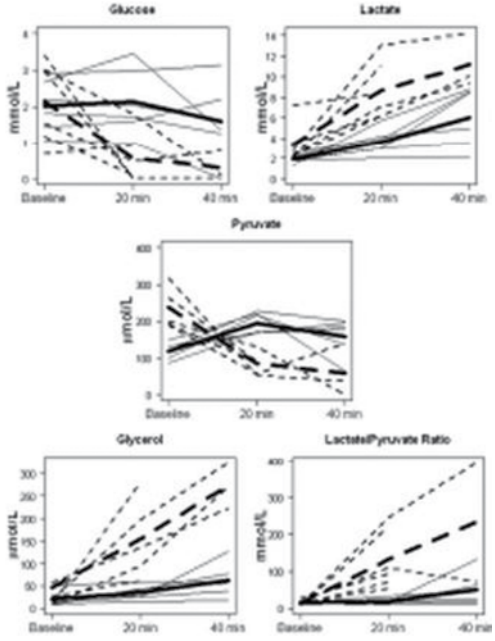
Purpose: A percutaneous left ventricular assist device allows perfusion of vital organs in cardiac arrest without concomitant chest compressions. We assessed assisted circulation during ventricular

fibrillation with microspheres injections and continuous end tidal CO2 monitoring and used cerebral microdialysis to detect ischemia in the brain.

Methods: 12 anesthesized pigs had microdialysis and pressure catheters implanted via craniotomy. A percutaneous left ventricular assist device was deployed transfemorally. VF was induced by angioplasty-balloon occlusion of the LAD.

Results: Microdialysis samples (glucose, pyruvate, lactate, glycerol) at Baseline, 20, and 40 minutes of VF with assisted circulation were analyzed. Tissue perfusion was measured with microspheres injections. In predicted survivors (end-tidal CO2 values at 20 minutes above 1.3 kPa), microdialysis showed no significant changes in mean Lactate/Pyruvate ratio at 20 or 40 minutes (P=NS to Baseline). At 40 minutes only lactate showed significant change (P<0.05 to baseline). Microspheres confirmed blood flow to the brain at 57% and myocardium at 72% of baseline after 15 minutes (P<0.05), declining to 22% and 40% after 45 minutes respectively (P=NS). In predicted non-survivors (end tidal CO2 below 1.3 kPa at 20 minutes) all had flow by microspheres below 1% of Baseline values during VF and also microdialysis at 20 and 40 minutes was consistent with cerebral ischemia (all P<0.05).



Figur 1. Cerebral Microdialysis Results

Conclusions: A percutaneous LVAD may prevent ischemic cerebral injury during VF. Cerebral and coronary perfusion is indicated by end tidal CO2.

[P3333] Impact of atrial fibrillation on inflammatory and fibrinolytic variables in the elderly

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Purpose: Atrial fibrillation (AF) is associated with inflammation and a prothrombotic state, however it is still unclear whether this is independent of ageing and comorbidity. The objective of this study was to investigate the impact of AF on circulating levels of inflammatory and fibrinolytic markers in a 75-year-old general population.

Methods: All 75-year-old citizens in Asker and Baerum counties in Norway were invited to participate in a prevalence study of AF. Blood samples were collected at rest from 63 subjects with AF and a gender-matched control group of 126 subjects in sinus rhythm. C-reactive protein (CRP), tumour necrosis factor alpha (TNFa), interleukin-6 (IL-6), monocyte chemoattractant protein-1 (MCP-1), P-selectin, CD40 Ligand, tissue plasminogen activator antigen (tPA ag) and plasminogen activator inhibitor-1 (PAI-1) activity were analysed using commercially available assays.

Results: Subjects with AF had higher levels of IL-6 (median 3.07 pg/mL (interquartile range 2.11, 4.36) vs. 2.26 (1.70, 3.26); p=0.002) and PAI-1 activity (12.9 U/mL (6.6, 17.1) vs. 9.0 (4.6, 14.0); p=0.005). No difference was found for the other markers. The presence of AF was still significantly associated with higher levels of IL-6 and PAI-1 activity after adjusting for body mass index and the presence of heart failure, coronary heart disease and hypertension (p=0.028 and p=0.007, respectively).

Conclusion: AF was independently associated with higher levels of IL-6 and PAI-1 activity. Thus, there is evidence of a proinflammatory state and reduced fibrinolysis also in this stable, out-of-hospital group of 75-year-old AF patients.

[P4679] Interaction between inflammation and blood viscosity predicts cardiovascular mortality. A 26-year follow-up study among apparently healthy middle-aged men

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Purpose: Inflammation and increased blood viscosity are associated with increased risk of cardiovascular (CV) mortality. Erythrocyte sedimentation rate (ESR) and Hematocrit (Hct) both influence blood viscosity whereas the first also is a marker of inflammation. Little is known about how ESR and Hct interact with each other on long term CV mortality risk. We aimed to investigate the interaction between baseline ESR and Hct as predictors of CV mortality after 26 years among apparently healthy middle aged men.

Methods: 2014 men aged 40 to 59 were examined in 1972 to 1975. Hct was measured in a random subsample of 488 men. The association between ESR, Hct and CV mortality was studied in these 488 men over a period of 26 years. Risk estimation was made in Cox proportional hazards and adjusted for age, smoking, systolic blood pressure, total serum cholesterol, and physical fitness.

Results: The highest quartile of Hct was associated with a 2.44-fold increased risk of dying from CV disease (95% confidence interval (CI) 1.37 to 4.35) compared to the lowest quartile. Of the 488 men, 265 had an ESR >6 m/h (median). The adjusted CV mortality risk was 3.05-fold (95% CI 1.49 to 6.23) in the highest quartile of Hct versus the lowest quartile of Hct among these men. This association was not observed among the 223 men with ESR <6 mm/h.

Conclusion: Our data suggest that high Hct is independently associated with increased long term risk of CV mortality in apparently healthy middle-aged men. This association was exclusively confined to subjects with ESR above median. Inflammation may potentiate untoward CV effects of blood viscosity.

Risk of cardiovascular mortality Quartiles	ESR<6				ESR≥6			
	CV deaths/n	HR	CI 95%	p	CV deaths/n	HR	95%CI	p
Q1	4/34	1.00	–	–	15/95	1.00	–	–
Q2	15/61	1.70	0.55-5.28	0.43	18/74	1.83	0.91-3.69	0.09
Q3	8/60	0.90	0.26-3.16	0.87	16/58	1.71	0.84-3.48	0.14
Q4	15/68	1.63	0.52-5.09	0.40	16/38	3.05	1.49-6.23	0.0025

Numbers of CV deaths and subjects (n) within each quartile (Q1-Q4) of hematocrit and the adjusted hazard ratio (HR) compared to the quartile with the lowest hematocrit (Q1). Data are shown separately for individuals with an erythrocyte sedimentation rate (ESR) below and above median (6 mm/h).

[P1732] TNF-alpha antagonists improve arterial stiffness in patients with inflammatory arthropathies: Results from a controlled study

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Purpose: The chronic inflammatory state of rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) contributes to the accelerated atherosclerosis associated with these diseases. The aim of this comparative study was to evaluate the effect of one year treatment with Tumor Necrosis Factor (TNF)-α antagonists on arterial stiffness in patients with RA, AS and PsA.

Methods: 36 patients (RA=15, AS=14 and PsA=7) who started with anti-TNF-α therapy (adalimumab=11, etanercept=16, infliximab=9) and a non-treatment group of 16 patients (RA=9, AS=5 and PsA=2) underwent measurements of aortic Pulse Wave Velocity (aPWV) and Augmentation Index (AIx) at baseline and after one year (Sphygmocor). Patients in the non-treatment group had the same indications for anti-TNF-α therapy, but had to postpone their initiation due to positive Mantoux-test or planned operations.

Results: Mean (SD) age in the treatment/control group was 46.2 (12.2)/49.0 (14.1) years, 42.9/50.0% (p=0.63) were females and disease duration was 11.0 (9.6)/11.6 (10.1) years. Patients who started anti-TNF-α therapy had a significant decrease in aPWV whereas the patients in the control group had no change. AIx did not change in any

of the groups. CRP and Disease Activity Score 28 joints (DAS28) were significantly reduced in the treatment group but did not change in the control group.

Baseline and change in key variables	Baseline			Change		
	Anti-TNF	Control	p-value	Anti-TNF	Control	p-value
	(n=36)	(n=16)		(n=36)	(n=16)	
PWV m/s	7.5	7.3	0.64	-0.53	0.08	0.001
AIx %	20.5	23.0	0.41	0.1	0.2	0.95
CRP mg/l	12.5	10.9	0.73	-8.63	0.88	0.001
DAS28*	3.92	4.20	0.47	-1.10	-0.20	0.02
MAP** mmHg	98.5	95.9	0.78	-3.2	-2.7	0.85
HR b/min	64	65	0.93	-0.3	1.4	0.45

**RA patients only, **Mean Arterial Pressure.*

Conclusion: The present study shows for the first time in a comparative design that long term anti-TNF-α therapy improves aPWV in patients with RA, AS and PsA. These findings lend support to the idea that the atherosclerotic process is amenable to pharmacologic intervention.

[P2281] Smokers benefit more from early invasive treatment of acute myocardial infarction than non-smokers

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Purpose: The aim of this study was to investigate whether a previously shown survival benefit of early invasive treatment of acute myocardial infarction (AMI) may differ according to smoking status.

Methods: Prospective observational cohort study on consecutive patients admitted for AMI in 2003 (conservative cohort) (n = 311) and 2006 (invasive cohort) (n = 307). Patients were subdivided into current smokers at admission, including those who stopped within the last 3 months, and non-smokers (including ex-smokers). Statistics: Cox proportional hazards regression analysis.

Results: A total of 27% (invasive cohort) and 32% (conservative cohort) of the patients were categorized as current smokers, respectively. Current smokers had a 72% increased risk (HR 1.72, 95% CI 1.08-2.68, p = 0.021) for death after one year, adjusted for treatment cohort, age, gender, prior AMI, prior stroke, and diabetes. Smokers and non-smokers in the invasive cohort had a 70% and 30% lower one-year mortality compared with the conservative cohort, respectively (Kaplan-Meier plots are presented in the figure). Non-smokers were significantly older than smokers both in the conservative (median age 77 vs. 60 years, p<0.001) and invasive cohort (median age 79 vs. 58 years, p = 0.001). We found a significant interaction (p = 0.039) between treatment cohort and smoking status supporting a larger survival benefit in smokers.

Figur 1. Survival according to smoking status

Conclusions: The survival benefit following introduction of early invasive management of unselected AMI patients was higher among smokers than non-smokers.

[P1410] Reverse remodeling of the left ventricle during the early phase after relief of pressure overload in a mouse model

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Purpose: Chronic pressure overload due to aortic stenosis (AS) induces concentric myocardial remodeling with hypertrophy, fibrosis and reduced cardiac function. Patients with excessive remodeling carry a particular peri-operative risk when treated with aortic valve replacement (AVR). AVR leads to reverse remodeling, with regression of hypertrophy and fibrosis. The mechanisms regulating reverse remodeling remain unknown. The aim of this study was to study reverse remodeling after relief of pressure overload in a mouse model of aortic banding-debanding and if possible identify mediators regulating the reverse remodeling process.

Methods: A novel mouse model with banding-debanding of the ascending aorta and echocardiographic evaluation up till 14 days after debanding was established. To avoid confounding effects, mice with signs of heart failure were excluded from the study. Myocardial gene expression was examined using Affymetrix microarray 4 weeks following aortic banding and 3 days after debanding. Regulation of functional gene groups was assessed using the topGO software. The findings were verified by RT-PCR. Quantitative measurements of myocardial collagen were performed

by HPLC of hydroxyproline and by Western blot analysis of collagen subtypes.

Results: Aortic banding increased left ventricular weight by 44%, with reduction to sham level by 14 days after debanding. The gene ontology group "extracellular matrix structural constituent" and in particular the collagen genes were most significantly regulated following debanding. These genes were up-regulated after aortic banding and reduced back to sham levels 3 days after debanding. Myocardial collagen content was 2.3-fold increased after banding, and remained increased by 1.6-fold and 1.7-fold at 3 days and 7 days following debanding. There was a shift in collagen subtypes from collagen type III following 4 weeks of banding to type I at 3 days and type VIII at 7 days after debanding. Active mediators regulating reverse remodeling were not identified. However, we found that following debanding the balance between pro- and anti-remodeling factors was shifted in favour of anti-remodeling factors.

Conclusions: Regression of extracellular matrix gene expression was the most significant alteration on the gene level during the early phase of reverse remodeling. After debanding, the collagen protein content remained increased, with an isoform shift which might affect the biomechanical properties of the myocardium. Reverse remodeling seems to be regulated by a balance shift favouring anti-remodeling factors.

[148] Natriuretic peptide testing for long-term risk assessment following acute ischemic stroke

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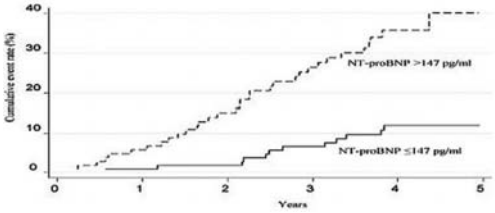
Background: The acute-phase levels of B-type natriuretic peptide and the N-terminal fragment of the BNP prohormone (NT-proBNP) have been associated with mortality when measured in patients with an ischemic stroke, whereas the longer-term value of NT-proBNP for chronic prognostication following ischemic stroke are limited.

Methods: Two hundred and sixteen patients (mean age, 67±13) with acute ischemic stroke were seen 6 months after index event. All patients underwent a structured interview and measurements of plasma NT-proBNP. Follow-uped was 45 months, with all-cause mortality as the clinical end point.

Results: The median NT-proBNP concentration for the whole group of patients was 147 pg/mL (10th to 90th percentile, 37 to 869 pg/ml). At follow-up 45 patients (21%) had died. NT-proBNP concentrations were significantly higher in decedents (308 pg/ml (10th to 90th percentile, 74 to 2279 pg/ml)) than in the 171 survivors (132 pg/ml (10th to 90th percentile, 35 to 570 pg/ml); P<0.001). Patients with NT-proBNP ≤147 pg/ml had a significantly improved survival rate on univariate analysis (Figure 1) (Log rank, P<0.001). In multivariate analysis after adjustment for age, stroke severity, heart- and renal failure, levels of NT-proBNP were an independent predictor of mortality later than 6 months after stroke (adjusted hazard ratio, 1.5; 95% CI, 1.1 to 1.9; P=0.005).



Conclusion: NT-proBNP concentrations measured during the stable phase after acute ischemic stroke are strongly predictive of long-term mortality.

[1116] Myocardial mechanical dispersion in long QT syndrome identifies individuals with high risk for cardiac arrhythmias

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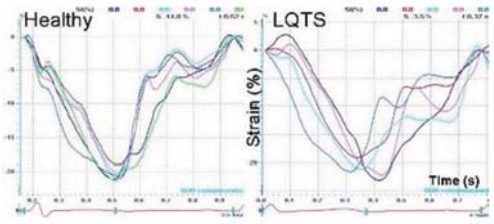
Purpose: Long QT syndrome (LQTS) predisposes to life-threatening ventricular arrhythmias. Prolonged action potentials in LQTS may cause prolonged myocardial contraction which can be assessed by strain echocardiography. We hypothesized that heterogeneity in myocardial contraction duration measured as myocardial mechanical dispersion can serve as a risk marker in LQTS patients.

Methods: We included 87 genotyped LQTS mutation carriers and 20 healthy control subjects. 45 mutations carriers had a history of cardiac arrest or syncope and 42 were asymptomatic. Myocardial contraction duration was assessed as time to peak strain. Standard deviation of contraction duration from the 6 basal LV segments was calculated as a marker of mechanical dispersion.

Results: Contraction duration was prolonged in LQTS mutation carriers compared to healthy controls (430±50 vs. 370±40ms, p<0.001) and in symptomatic compared to asymptomatic carriers (440±50 vs. 410±40ms, p=0.001). The longest contraction duration was predominantly localized in the interventricular septum in symptomatic mutation carriers (p=0.02). Mechanical dispersion was more pronounced in symptomatic mutation carriers compared to asymptomatic (67±22 vs. 34±15ms, p<0.001). The figure shows representative strain traces from a healthy individual with homogeneous contraction duration and a LQTS-patient with mechanical dispersion. Mechanical dispersion was better related to severe arrhythmia than QTc (AUC by ROC analysis 0.92 (95%CI 0.86-0.98) vs. 0.73 (95%CI 0.62-0.83)).



Conclusions: Mechanical dispersion of myocardial contraction assessed by strain echocardiography was increased in LQTS mutation carriers and was superior to QTc in identifying those with cardiac events.

[P2175] Myocardial ejection velocities and strain underestimate electrical dyssynchrony during left bundle branch block (LBBB)

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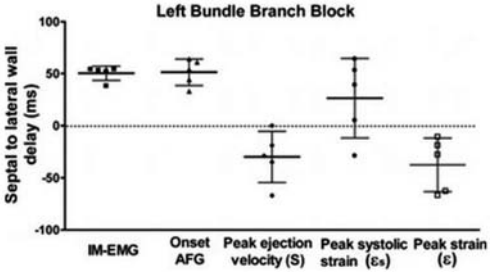
Background: The clinical value of assessing LV intraventricular dyssynchrony prior to cardiac resynchronization therapy is controversial. This study investigated if peak myocardial ejection velocity (S), peak systolic strain (εs) and peak strain including post systole (ε) reflect electrical conduction delay in LBBB.

Methods: In 5 anaesthetized dogs with LV micromanometers we measured myocardial segment lengths by sonomicrometry and intramyocardial-EMGs (IM-EMG) by implanted electrodes. Onset of R in IM-EMG defined onset of regional electrical activation, and reference method for onset of "true" mechanical activation was first sign of active force generation (AFG) by LV pressure-segment length loop analysis. Time delay for lateral wall with respect to septum was quantified for each index during LBBB induced by RF-ablation.

Results: During LBBB there was marked delay in electrical activation of the lateral wall by 50±7 ms (mean±SD) and similar delay in mechanical activation measured as onset AFG by 51±13 ms (p=NS). Mechanical activation measured as S, εs and ε, however, showed time delays of -30±25, 26±38 and -38±26 ms, respectively, indicating that these indices underestimated electrical dyssynchrony (Figure 1). Furthermore, peak S and peak εs suggested erroneously that the lateral wall was activated prior to septum. Similar finding were found by echocardiography.



Conclusions: As predicted, LBBB was associated with marked delay in electrical activation between the LV lateral wall and septum and similar delay in true mechanical activation. Velocity and strain indices, however, were inaccurate measures of electrical delay, suggesting that these indices may lead to erroneous conclusions regarding magnitude of electrical delay and direction of the electrical activation sequence in LBBB.

[292] Moderate hypothermia induces severe diastolic changes in a porcine model

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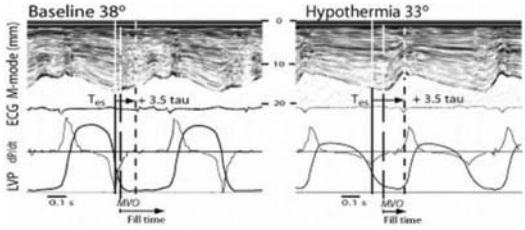
Purpose: Hypothermia is used in patients after cardiac arrest for neuroprotection. The associated cardiac effects in diastole are not well described. We have studied the effects of hypothermia on left ventricular (LV) diastolic function in a porcine model.

Methods: 6 anesthetized pigs were cooled from 38° to 33°C. Using micromanometer we measured LV pressure and the time constant (tau) of LV isovolumic pressure decay. Systolic duration was calculated from R on ECG to time of dP/dtmin (Tes). Isovolumic relaxation (IVR) was calculated from Tes to mitral valve opening (MVO), and filling time from MVO to R on ECG. Duration of the relaxation was calculated from Tes as 3.5 times tau. LV volume was measured by echocardiography. Registrations (mean ± SEM) were made during atrial pacing at 100 beats/min.

Results: Systolic duration increased (P=0.01) while stroke volume decreased from 48±1 to 40±2 ml, P=0.01. This was accompanied by a marked decrease in diastolic duration (285±30 to 185±6ms, P=0.01), also shown by M-mode (Figure). IVR increased (41±3 to 91±8 ms, P=0.02) and filling time decreased from 226±9 to 87±9ms (P=0.01). Tau increased from 30±2 to 54±3ms (P=0.01). Relaxation time increased as fraction of diastolic duration from 0.4±0.1 to 1.1±0.1 (P=0.01), indicating that relaxation was not completed before next systole. LV EDP was unchanged while EDV decreased from 72±3 to 63±2 ml, P=0.04.



Conclusions: Moderate hypothermia induced a significant decrease in diastolic filling time and prolonged relaxation. The shift in end-diastolic pressure-volume relation is consistent with a stiffer myocardium due to incomplete relaxation. These findings suggest that diastolic dysfunction may be an important contributor to reduced stroke volume during hypothermia.

[5224] Long term results after intracoronary injection of autologous mononuclear bone marrow cells in acute myocardial infarction. The ASTAMI study

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Background: In randomized-controlled trials on the effects of intracoronary infusion of autologous mononuclear bone marrow cells (mBMCs) in acute myocardial infarction (AMI), results on change in LVEF after 4-6 months vary. Data on long term safety and efficacy are scarce. We present a 3 year follow-up of the ASTAMI study.

Methods: 100 patients with ST-elevation AMI treated with primary PCI on LAD were randomized to either intracoronary injection of autologous mBMCs (n=50) or control (n=50). 68 mill. (median) mBMCs were injected 4-8 days after the infarction. Results after 6 and 12 months have been reported previously. We re-examined the patients with MRI, echocardiography and exercise testing 3,2±0,2 (mean±SD) years after randomization.

Results: The rate of adverse events was low, with no significant difference between groups. By MRI and echocardiography, left ventricular volumes, infarct size and global systolic function were similar between groups at baseline. No significant effects of mBMC therapy were found. The mBMC treated patients had significantly larger improvement in exercise time than the control group, but change in peak VO2 did not differ.

Values are mean ± SD. † 2-3 weeks after randomization. [a]Respiratory exchange ratio. [b]p-value for difference between groups in change over time (mixed model regression). *p<0.05 for intragroup change from baseline.

Conclusion: Intracoronary mBMC therapy in AMI appears to be safe. A modest beneficial effect on exercise capacity is indicated by the larger increase in exercise time in the mBMC group, but no significant effects were identified on predefined endpoints during 3 years follow-up.

	Baseline		6 months		3 years		p-value[b]
	mBMC	Control	mBMC	Control	mBMC	Control	
MRI: EDV (ml)	162±46†	165±47†	153±54	162±45	163±64	165±58	0.60
MRI: LVEF (%)	54.8±13.6†	53.5±11.6†	56.0±14.6	58.0±11.5	54.9±13.2	55.2±10.6	0.18
MRI: Infarct size (%)	21.9±12.8†	22.1±13.9†	20.8±11.6	19.6±12.5	17.6±9.9*	16.2±9.9*	0.37
Echo: EDV (ml)	136±31	132±35	145±42*	143±45*	138±44	139±50	0.39
Echo: LVEF (%)	45.7±9.4	46.9±9.6	48.8±10.7*	49.0±9.5	47.5±9.0*	46.8±8.6	0.87
Exercise time (min)	8.6±2.8†	8.8±2.6†	10.6±3.2*	9.9±2.9*	10.1±2.7*	9.4±2.6*	0.05
Peak VO_2 (ml/kg/min)	19.8±6.4†	18.8±6.5†	22.4±7.2*	20.9±6.3*	22.4±6.8*	22.1±6.5*	0.75
Peak RER[a]	1.13±0.08†	1.12±0.07†	1.13±0.07	1.12±0.07	1.16±0.06*	1.16±0.06*	0.93

[P4617] Increased CRP early in the RA disease course predicts cardiovascular disease and arterial stiffness. 15-year follow-up of the EURIDISS cohort

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Background: Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular disease.

Objectives: To explore whether early inflammatory markers of RA disease activity could predict cardiovascular disease and levels of the augmentation index (AIx), a surrogate markers of cardiovascular disease.

Patients and Methods: 238 patients with RA of maximum 4 years duration, mean age (SD) 51.9 years at inclusion, were included in the EURIDISS cohort in 1992. Comprehensive baseline clinical and radiographic data were collected. At the 15-year follow-up patients reported cardiovascular disease and AIx was measured. A composite variable (CVD) was constructed, defined as the occurrence of hypertension, angina, cardiac disease, stroke or myocardial infarction after inclusion in the study in 1992. CVD was the dependent variable of the logistic regression model. Adjusted univariate and multivariate linear regression were performed with AIx as the dependent variable.

Results: Of 108 participants at the 15- year follow-up, 44 reported cardiovascular disease. 102 patients had acceptable AIx recordings. Baseline RA disease duration, high sensitivity C- reactive protein (hsCRP) and scores of Stanford Health Assessment questionnaire (HAQ) predicted both CVD and increased AIx after 15 years, when entered separately into the adjusted univariate model. In addition the Ritchie index predicted CVD and use of methotrexate predicted increased AIx in adjusted univariate models (table). In the multivariate model, disease duration and HAQ remained significant predictors of CVD, (Ritchie score was a confounder of HAQ), whereas baseline CRP levels predicted AIx.

Conclusion: This study finds that inflammation early in the disease course is associated with an increased occurrence of self-reported CVD and with increased arterial stiffness 15 years later.

Table 1. Baseline predictors of cardiovascular disease and AIx Dependent variable

	Cardiovascular disease					Augmentation index				
	Model 1	Model 2	Model 3	Model 4	Final model	Model 1	Model 2	Model 3	Model 4	Final model
Baseline variable	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)	β (CI)	β (CI)	β (CI)	β (CI)	β (CI)
	p	p	p	p	p	p	p	p	p	p
Disease duration	1.87 (1.25- 2.80)				1.63 (1.07-2.48)	1.23 (0.17-2.28)				
	0.002				0.002	0.02				
HsCRP		1.05 (1.01-1.10)					0.16 (0.05-0.27)			0.16 (0.05-0.27)
		0.02					0.005			0.005
HAQ score			5.47 (2.13-14.05)		3.32 (0.97-11.40)			3.00 (0.71-5.26)		
			<0.001		0.06			0.01		
Ritchie score				1.14 (1.04-1.24)	1.04 (0.92-1.16)					
				0.003	0.53					
Methotrexate user									3.55 (0.43-6.67)	
									0.03	

[P5570] High sensitive CRP as a risk marker for progression of aortic stenosis and coronary artery disease in patients with aortic stenosis

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Background: The Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) trial investigated the effect of simvastatin/ezetimibe vs. placebo in patients with asymptomatic mild to moderate aortic stenosis (AS), at low risk for atherosclerotic disease. This post-hoc analysis evaluates prediction of clinical outcome by high sensitive CRP (HsCRP) in patients with AS.

Methods: Data from1,618 patients (mean age 68±10 years, 39% women) randomized to active or placebo therapy and with CRP-measurements at baseline and at 1 year of follow-up. Mean baseline CRP: 4.27±8.2 mg/l, mean baseline LDL-cholesterol 3.55±0.89 mmol/l, were analyzed with regard to baseline risk markers for atherosclerotic disease against clinical outcome over a median follow-up of 52.2 months, adjusting for age, sex, time-varying systolic blood pressure, smoking and history of hypertension in multiple regression analysis.

Results: Aortic valve events (AVE [aortic valve replacement and heart failure due to progression of AS], n=536) were predicted by logHsCRP, HR=1.17 per baseline 1SD (95%CI: 1.07-1.27), p<0.001. Ischemic cardiovascular events (ICE [myocardial infarction, stroke, cardiovascular (CV) death, hospitalization for unstable angina and coronary revascularization], n=282) were predicted by logHsCRP, HR=1.13 per 1SD (95%CI: 1.01-1.27), p<0.038. Baseline logHsCRP did not predict cardiovascular death (n=91), myocardial infarction (n=49) or stroke (n= 59). However, time-varying reduction of HsCRP by 1 SD was associated with 21-39% reduction in the associated endpoints (Table) independent of simvastatin/ezetimibe treatment, age, gender, smoking and time-varying systolic blood pressure.

Time-varying:	HR	95%CI	P
Aortic valve events	0.79	(0.73-0.85)	<0.001
Ischemic cardiovascular events	0.76	(0.68-0.85)	<0.001
Cardiovascular death	0.76	(0.63-0.73)	0.009
Myocardial infarction	0.73	(0.54-1.00)	0.046
Stroke	0.73	(0.40-0.75)	0.031

Conclusion: Baseline HsCRP independently predicted AVE and ICE independent of covariates. In addition, reduction in time-varying HsCRP was associated with a significant reduction in clinical endpoints, indicating that reducing HsCRP might be a treatment goal in patients with mild to moderate AS.

[P3884] High resolution speckle tracking dobutamine echocardiography reveals heterogeneous responses in myocardial layers. Partial wall deformation predicts flow reduction and contractile reserve

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Background: Dobutamine-stress- echocardiography can be used to identify hypoperfused and viable myocardium. Lately it has been recommended to refine the method by strain imaging. Using Speckle-tracking in ultrasound opens for high spatial resolution and analyses in three dimensions. However, the possibility to place the region of interest (ROI) into different layers of the myocardium creates a potential problem with obtaining standardization in heterogeneously responding layers. We therefore aimed to investigate myocardial strain in four layers at hypoperfusion and with dobutamine challenge. Our hypothesis was that the different layers of the myocardium would deform

markedly heterogeneously and thus a new definition of normally responding and dysfunctional myocardium would be needed.

Methods: In 10 anesthetized open chest pigs the left anterior descending artery (LAD) was constricted to a constant stenosis with an initial flow-reduction (FR) of about 35%. Fluorescent microspheres were used to measure tissue flow. High-resolution-echocardiography was performed epicardially to calculate strain in 4 myocardial layers and in radial, longitudinal and transversal direction using a speckle-tracking software. Images were obtained at rest, at LAD-constriction and at hypoperfusion combined with dobutamine-stress.

Results: A resting gradient across the myocardium with highest values in the subendocardium was found in all directions, being most pronounced in the radial direction. Additionally, there was a good correlation between FR and strain reduction in all dimensions of the three inner layers. Dobutamine-stress increased strain varyingly in the three inner layers, most subendocardially in radial direction and in mid-and subendocardial layers in longitudinal and transversal direction.

Conclusion: Strain axes, flow reductions and dobutamine-stress induce varying responses of the different layers of the myocardium. Therefore, standardization and definition of normal and pathological strain responses, will have to take into account detailed specification of strain axes and region of interest (ROI).

[P5678] High prevalence of sleep disordered breathing in a general heart failure population, especially in patients with preserved systolic function

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Purpose: Sleep disordered breathing (SDB) seems to be common in heart failure patients with reduced left ventricular ejection fraction (LVEF). However, the prevalence of SDB in a general heart failure population including patients with preserved LVEF is still unknown. In this study we evaluated the prevalence of SDB in a single centre outpatient heart failure clinic.

Methods: Outpatients with clinically stable chronic heart failure in New York Heart Association (NYHA) functional class II-IV and on standard medical therapy were consecutively enrolled from our heart failure clinic. All subjects underwent an in-home overnight sleep study with a 10-channel recording device. Current guidelines were used for scoring of respiratory events.

Results: We included 105 patients with a mean age of 62±10 years and mean LVEF of 38±13%. Beta-blockers and ACE-inhibitors / ARBs were used by 89% and 92%, respectively. Among these patients, 70% had SDB (43% obstructive sleep apnea and 27% central apnea with Cheyne Stokes respiration). Preserved LVEF was found in 38 patients in our cohort, and in these patients SDB was observed in 76% of the cases. Patients with preserved LVEF had significantly more obstructive sleep apnea and hypertension (Table 1).

Clinical characteristics of patients	Reduced LVEF (n=67)	Preserved LVEF (n=38)	p value
Obstructive sleep apnea n	23 (34%)	23 (60%)	p = 0,01
Central sleep apnea n	22 (33%)	6 (16%)	p = 0,06
LVEF %*	29±8	52±5	p < 0,01
Hypertension n	18 (27%)	22 (58%)	p = 0,02
Atrial fibrillation n	23 (34%)	18 (47%)	p = 0,19
Body Mass Index (kg/m^2)*	28,7±5,2	31,0±4,7	ns

**Values expressed as mean ± SD.*

Conclusion: SDB remains common in a general heart failure population. High prevalence of SDB may be especially relevant in the patients with preserved LVEF, where referring to a sleep specialist should be considered.

[P3865] Global strain is a strong predictor of infarct size in patients hospitalized with NSTEMI

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Background: Reduction of infarct size through acute reperfusion therapy has improved prognosis after myocardial infarction (MI). Patients with non ST-segment elevation MI (NSTEMI) are rarely eligble for acute reperfusion therapy. However, a fraction of these patients develop substantial MI. We hypothesized that echocardiographic parameters of left ventricular (LV) systolic function correlate to infarct size in NSTEMI, and enable identification of patients at risk of developing substantial MI in absence of acute reperfusion therapy.

Methods: 47 patients with NSTEMI were examined by echocardiography prior to revascularization, 1-3 days after hospitalization for acute chest pain. Longitudinal peak negative systolic strain by speckle tracking echocardiography and wall motion score were assessed in a 16 segments LV model. Segmental values were averaged to obtain global strain (GS) and wall motion score index (WMSI). Ejection fraction (EF) was calculated. Final infarct size was determined by late enhancement magnetic resonance imaging after 9±3 (mean ± s.d.) months. ROC analyses were used to determine sensitivity and specificity for detection of infarct size >12% of total LV mass, which is associated with adverse prognosis.

Results: Median infarct size was 5%, (interquartile range 2 – 12%). 12 patients (26%) had infarct size > 12% of LV mass. GS, WMSI and EF all correlated to infarct size (p<0.001). Table displays correlation coefficients (R), and results from ROC analysis of the different parameters' ability to identify infarct size > 12% of LV mass.

Table of results	R	AUC	Sensitivity	Specificity	Cut-off
GS	0.72	0.96	92%	97%	-13.7%
WMSI	0.74	0.91	83%	77%	1.25
EF	-0.56	0.80	67%	80%	50%

Table displays correlation coefficients (R), area under the curve (AUC) on ROC analyses, sensitivity and specificity for detection of infarct size > 12% of LV mass.

Conclusion: All echocardiographic parameters of LV systolic function correlated to final infarct size in patients with NSTEMI. Global strain in particular demonstrated excellent ability to identify substantial MI, and is a potential new marker for risk stratification of patients with NSTEMI.

[P4106] Estimation of pressure recovery at different levels of the ascending aorta impact on assessment of aortic stenosis severity (A SEAS substudy)

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Background: Downstream pressure recovery (PR) in the ascending aorta affects transvalvular pressure gradient measurement and calculation of aortic valve area by continuity equation in patients with aortic stenosis (AS). Influence of the aortic level used for calculation of PR and PR corrected aortic valve area index (AVAI) assessed as energy loss index (ELI), has not been evaluated in a large series of AS patients.

Methods: PR was calculated from inner aortic diameter measured at levels of sinus of Valsalva, sinotubular junction and tubular aorta 1 cm distal to the sinotubular junction in 1481 patients with asymptomatic AS included in the Simvastatin and Ezitimibe in Aortic Stenosis (SEAS) study (mean age 67±10, 39% women, 51% hypertensive). PR and ELI were calculated by previously published equations. Severe AS was defined as ELI <0.55cm^2/m^2.

Results: Aortic diameter at sinus of Valsalva, sinotubular junctional and tubular aorta differed significantly (all p≤0.001). PR and ELI were significantly higher when based on aortic diameter at sinotubular junction. Severe AS was diagnosed in 17.2% of patients using sinotubular junctional diameter, compared to 19.7% and 20% when using sinus of Valsalva or tubular aortic diameter (p<0.01). 36 patients (12.6%) were re-classified from non-severe to severe AS by using sinus of Valsalva compared to junctional diameter and similar 40 patients (13.8%) were re-classified from non-severe to severe AS by using tubular compared to junctional diameter.

Variables	Sinus of Valsalva	Sinotubular junction	Tubular aorta
Diameter (cm)	3.08±0.44*§	2.82±0.42§	3.11±0.47
PR (mmHg)	5.14±1.97*	5.88±2.27§	5.07±1.98
ELI (cm^2/m^2)	0.84±0.38*	0.89±0.45§	0.84±0.38
Severe AS (n, %)	286 (19.7)*	250 (17.2)§	290 (20.0)

Diameter, PR, ELI and prevalence of severe AS at different levels of the ascending aorta. * p<0.001 vs. sintotubular level, § p≤0.001 vs. tubular aortic level.*

Conclusion: Assessment of PR and severity of AS using PR adjusted AVAI (ELI) differed significantly by the level of the ascending aorta used for calculation of PR. The number of patients classified as severe by ELI was significantly higher when PR was calculated at sinus of Valsalva or tubular aorta compared to sinotubular junction. Standardisation is important in future studies of PR.

[5053] Endurance training improve cardiomyocyte function, restore calcium handling and reduce diastolic calcium leak in cardiomyocytes from mice with transgenic overexpression of CaMKII

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Purpose: The cytosolic calcium/calmodulin-dependent protein kinase IIδ (CaMKIIδC) phosphorylates several central proteins related to calcium handling. Transgenic (TG) over-expression of CaMKIIδC causes depressed cardiac function, altered calcium handling and increased diastolic sarcoplamic reticulum (SR) calcium leak. The later may be a central trigger for delayed after depolarisation and ventricular arrhythmias in heart failure. Endurance training increases also the activity of CaMKIIδC in healthy mice, but in contrast to individuals with heart disease, this improves cardiac performance.

We hypothesised that endurance training improves calcium handling and reduces diastolic SR calcium leak in TG mice with over-expression of CaMKIIδC and heart failure.

Methods: We compared TG mice exhibiting a 3-fold increase in CaMKIIδC activity (n=8), with wild type (WT) controls (n=8). Four CaMKIIδC TG mice underwent high intensity endurance training 5 days per week over 12 weeks. Calcium handling and diastolic SR calcium leak were measured in Fura-2AM loaded cardiomyocytes.

Results: CaMKIIδC TG mice had decreased cardiomyocyte shortening (3.3±1.8% in TG vs. 6.2±1.2% in WT, P<0.01), which was restored to levels of WT control by endurance training (5.9±1.3% in TG trained). Twitch calcium transient amplitude was lower (Fura-2AM ratio in TG was 0.09±0.03 vs. 0.18±0.02 in WT, P<0.01) and time to 50% twitch calcium release was slower (25±2ms in TG vs. 15±1ms in WT, P<0.05). Reduced calcium amplitude in sedentary TG mice may partly be explained by a reduced SR calcium content, demonstrated by reduced caffeine-induced calcium transients. Endurance training increased twitch calcium-amplitude to levels of WT control (Fura-2AM ratio 0.15±0.02 in TG trained), which may be a result of an also restored SR calcium content. SR calcium leak over the RyR was significantly larger in TG mice (19±3% of total SR calcium vs. 5±2% in WT, P<0.01). Endurance training reduced diastolic SR calcium leak to levels of WT control (4±2%, P<0.01). After inhibition of CaMKIIδC, by autocamtide-2-related inhibitory peptide, the increased SR calcium leak in sedentary TG was abolished, while trained TG and WT control mice remained unaffected. The protein kinase inhibitor A, H89, did not affect SR calcium leak in any groups.

Conclusion: Endurance training improved cardiomyocyte function and calcium handling in mice with TG over-expression of CaMKIIδC. Increased diastolic SR calcium leak, that may trigger ventricular arrhythmias, was completely abolished after endurance training.

[128] Does telephone follow-up after discharge for acute myocardial infarction reduce anxiety and depression? A randomized controlled trial

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Background: Following discharge from hospital for acute myocardial infarction patients many patients experience stress and have unmet information needs. In a context where existing follow-up services are poorly developed, we previously demonstrated that a telephone follow-up intervention after discharge from hospital, showed positive effects after 6 months on the physical dimension of health related quality of life (HRQOL). No long term effects on physical or mental HRQOL were found.

Purpose: To assess whether the telephone follow-up intervention has short- and longterm effects on symptoms of anxiety and depression using the HADS scale 3, 6, 12 and 18 months after discharge. Further to compare patients levels of anxiety and depression to levels in the normal population.

Method: Out of 413 screened patients with a diagnosis of acute myocardial infarction, 288 patients consented to participate, and were randomized to an intervention (n= 156) or a control group (n=

132). The intervention group received weekly telephone follow-up by a nurse the first four weeks after discharge, thereafter in week 6, 8, 12 and 24, in addition to the standard post discharge follow-up of the control group. Endpoint data on the HADS was collected through mailed questionnaires. Reference population data were obtained from the Nord-Trøndelag Health Study (HUNT) 1995-97.

Results: There were no baseline difference between the groups, or any effects of the intervention on the HADS subscales at each of the different measurement points 3, 6, 12 and 18 months after discharge. Analysing both groups together, 20% and 14% of AMI patients reported high levels of anxiety and depressive symptoms at baseline, respectively. Comparing to reference population at baseline AMI patients were more anxious, but not more depressed ($p<0.001$ and $p=0.092$), respectively. After 3–18 months, AMI patients' levels of anxiety and depression were not higher than levels in the reference population.

Conclusion: This study demonstrates that the telephone follow-up intervention had no effects on symptoms of anxiety and depression. However, the potential for improvement was less than anticipated, as patients after 3 months did not have more symptoms of anxiety or depression than the reference population. The results indicate a reduced psychological morbidity among acute myocardial infarction patients compared to levels reported in research a decade ago.

[5163] Discordant relationship between lipid-lowering changes and reduction of ischemic cardiovascular events (ICE) among patients with more severe aortic stenosis (AS) in the SEAS trial

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Purpose: LDL-C lowering is associated with the reduction of CHD risk and major cardiovascular events. In the SEAS trial, treatment with 40mg simvastatin (S) and 10mg ezetimibe (E) reduced LDL-C by 50% and ICE risk by 22% compared with placebo in the full cohort of patients with AS. Based on other studies, a larger reduction of ICE risk might have been expected for the degree of lipid-lowering achieved. In this post-hoc analysis, relationships between reductions in ICE risk and changes in lipoprotein components (LC) were examined among tertiles of patients, sorted by the degree of AS as assessed by jet velocity (JV) at baseline.

Method: SEAS patients included in the analysis (n=1570) were those who at year 1 had complete data on JV, LDL-C, HDL-C and Apo B and had not yet experienced an ICE. Relationships between on-treatment measurements of LC at year 1 and time to subsequent occurrence of ICE were assessed in JV tertiles using a Cox model. Observed and predicted ICE risk reductions were also compared.

Results: Decreases in LC (LDL-C, non-HDL-C, ApoB, TC/HDL-C) after 1 year of treatment with E+S were significantly associated with lower ICE risk in the two lower JV tertiles ($p<0.05$-<0.001). ApoB and non-HDL-C were the best predictors of ICE risk in the lower two tertiles. In contrast, changes in LC were not associated with ICE risk in patients with more severe AS in tertile 3. In JV tertiles 1 and 2, ICE risk decreased by 47% and 36% respectively at year 1; these reductions were reasonably well-predicted by all LC. LC were not associated with ICE reduction in tertile 3. The observed relationships with LDL-C and ICE risk reduction in tertiles 1 and 2 were consistent with data from the Cholesterol Treatment Trialists' (CTT) meta-analysis of statin trials. Based on the 21% reduction in major vascular events per mmol/l change in LDL-C reported in CTT, an approximate 38% reduction in ICE risk would be expected for the 2.05 mmol/l LDL-C decrease at 1 year with E+S compared to placebo in this analysis of SEAS patients. This 38% estimate is highly consistent with the observed ICE risk reductions in tertiles 1 and 2, but discordant with that in the tertile of patients with the most severe AS.

Conclusion: The observed reductions of ICE risk among patients with less severe AS, as indicated by the lower baseline JV (tertiles 1 and 2), were consistent with the risk reduction that would be expected based upon actual LC changes with E+S. The lack of a significant relationship between change in LC and ICE risk in tertile 3 may be due to confounding of ICE by cardiovascular events associated with severe AS.

[3776] A sequence variant in the ZFHX3 gene on chromosome 16p22 associates with atrial fibrillation and ischemic stroke

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Introduction: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in humans and a cause of substantial morbidity and increased mortality. We have previously, through a genome-wide association study, reported on two sequence variants on chromosome 4q25 that confer risk of AF. The 4q25 locus has since been found to be significantly associated with ischemic stroke, with the strongest risk for cardioembolic stroke. In the attempt to discover additional variants that associate with AF, we have expanded our genome-wide association scan by increasing samples with a broad AF phenotype.

Methods: After quality filtering, 304,226 SNPs were tested individually in a sample of 2,385 Icelandic patients with AF and/or atrial flutter (AFl) and 33,752 Icelandic population controls, genotyped with the Illumina HumanHap300 or HumanHapCNV370 bead chips. Of the top ten SNPs, seven represented the previously discovered signal on chromosome 4q25. The remaining three SNPs were genotyped in three replication sample sets of European descent, from Iceland (989 cases and 2,027 controls), Norway (725 cases and 725 controls) and the United States (735 cases and 729 controls).

Results: A sequence variant, rs7193343-T in the ZFHX3 gene on chromosome 16p22, showed genome-wide significant association with AF in the combined Icelandic sample set and this association was replicated nominally in the non-Icelandic samples with constant direction of the effect. In the combined analysis of all sample sets the odds ratio (OR) for this variant was 1.21 (95% CI: 1.14-1.29) with a corresponding P value of $P=1.4\times10^{-10}$. This variant does not associate with hypertension, coronary artery disease, or obesity which are all known risk factors for AF. The population frequency of this sequence variant is 20% in the Icelandic control set. Combined analyses of the datasets also showed association between rs 7193343-T and ischemic stroke (OR 1.11, 95% CI: 1.04-1.17, P=0.00054).

Conclusions: A sequence variant in the ZFHX3 gene on chromosome 16p22 confers risk of both common AF and ischemic stroke in populations of European descent. This is the second reported locus with a common sequence variant that associates with AF and has been replicated in several populations. These findings are further evidence of an important genetic contribution to the pathogenesis of this complex arrhythmia.

[P4523] Ck-mb mass contrary to the cardiac troponins has long-term prognostic value after routine coronary angioplasty in low-risk patients with stable angina

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Objectives: The long-term prognostic value (> 5 years) of elevated cardiac biomarkers after elective coronary angioplasty is yet not clear. Most previous studies have included high risk, unstable patients. The aim of this study was to determine the prognostic value of CK-MB mass versus the cardiac troponins after PCI in low-risk patients with stable angina.

Methods: 208 consecutive patients undergoing elective PCI were included in the final analysis. Blood samples were drawn just before and 1-3 hours, 4-8 hours after the procedure and the next morning. Patients with elevated baseline values were excluded. Using a cut-off value of 3 times the reference, patients with high and low values (=controls) of CK-MB mass, cardiac troponin T (TnT) and troponin I (TnI) were compared. No patient developed new Q-waves on ECG. The median follow up time was 82 months (equalising 1500 -2000 patient years).

Results: None of the patients died during the procedure or within the first 30 days after angioplasty, confirming a low risk cohort. All cause mortality, readmission for acute coronary syndromes and target lesion revascularisation were more frequent in patients with high CK-MB, 42.9% vs 22.2%,

P=0.049. There was no significant difference in event-free survival in patients with high and low values of TnT (P=0.205) and TnI (P=0.314).

Conclusions: CK-MB mass but not the cardiac troponins (values ≥3 times the reference) is associated with reduced long-term event-free survival after elective angiopolasty in low-risk patients with stable angina.

[P4527] CK-MB mass but not the cardiac troponins has long-term prognostic value after cardiac surgery in low-risk patients with stable angina

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Objectives: The long-term prognostic value (> 5 years) of elevated cardiac biomarkers after elective cardiac surgery is not clear. Most previous studies have included high risk, unstable patients. The aim of this study was to determine the prognostic value of the cardiac troponins vs CK-MB mass after elective cardiac surgery in low-risk patients with stable angina.

Methods: A total of 204 consecutive patients undergoing cardiac surgery were included in the final analysis. Blood samples were drawn just before and 1-3, and 4-8 h hours after the procedure, thereafter every morning for 3 days. Patients with elevated baseline values were excluded. Using a cut-off value of 5 times the reference, patients with high and low values (=controls) of CK-MB mass, cardiac troponin T (TnT) and troponin I (TnI) were compared. None developed new Q-waves on ECG. The median follow up time was 95 months (equalising 1500-2000 patient years).

Results: All cause mortality and readmission for acute coronary syndromes were more frequent in the high CK-MB group (30.6% vs 16.8%, P=0.025), as were target vessel revascularisation (18.6% vs 5.0%, P=0.002). The corresponding P-values in the CABG subgroup were P=0.043 and P<0.001. In a multivariate logistic regression analysis, high CK-MB (P=0.014) and ejection fraction (P=0.003) were the only variables independently related to a reduced event-free survival. There was no significant difference event-free survival in patients with high and low values of TnT (P=0.223) and TnI (P=0.200).

Conclusions: CK-MB mass but not the cardiac troponins (values ≥5 times the reference) is associated with reduced long-term event-free survival after elective cardiac surgery in low-risk patients with stable angina.

[P1481] Calcium intake is independently associated with increased arterial stiffness: results from a cross-sectional follow-up study of two rheumatoid arthritis cohorts

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Background: A recent placebo controlled randomized trial found that intake of oral calcium in healthy older women was associated with an increased risk of cardiovascular events over a 5 -year observation period. Furthermore, bone resorption has been suggested to be an independent predictor of arterial wall thickening in patients with RA.

Objective: To investigate the association between bone loss, calcium intake and levels of the augmentation index (AIx) and pulse wave velocity (PWV), two arterial stiffness measurements and surrogate markers of cardiovascular disease.

Materials and Method: Arterial stiffness measurements were performed on 144 patients with RA. A study-nurse performed clinical examinations, BMD measurements and asked the patient to fill out a questionnaire. Linear regression models were constructed with AIx and PWV as the dependent

Table 1. Predictors of arterial stiffness Dependent variable

	PWV m/s β (CI)		AIx β (CI)	
Predicting variable	Univariate models	Multivariate model	Univariate models	Multivariate model
HRT	0.16 (-0.39-0.70)		1.08 (-1.69-3.85)	
Bisphoshonates	0.61 (-0.16-1.39)		3.04 (-0.44-6.52)	
D vitamins ever/never	0.26 (-0.25-0.77)		3.30 (0.76-5.85)*	
Calcium ever/never	0.43 (-0.05-0.90)	0.44 (-0.03-0.90)	3.75 (1.35-6.14)*	3.75 (1.35-6.14)*
Total hip BMD	-1.06 (-3.20-1.08)		-6.97 (-18.25-4.31)	
Lumbar BMD	-052 (-2.34-1.31)		-5.30 (-14.49-3.90)	
Fractures	0.17 (-0.35-0.70)		0.55 (-2.08-3.17)	
Male:				
Pre-menopausal:	0-0.11 (-0.87-0.32)		3.39 (-0.31-7.09)	
Post-menopausal:	-0.28 (-0.87-0.32)		3.63 (0.06-7.19)*	

*$p<0.05$.

variables. The univariate models were adjusted for age, sex, mean arterial pressure, heart- rate, body mass index and use of anti-hypertensive drugs. Predictors that were significant at the p≤0.01 level were entered into at multivariate model with possible confounders.

Results: Calcium supplementation was associated with significantly higher levels of AIx (p=0.02) and near-significant increased PWV (p=0.06) in both univariate and multivariate models (Table). Vitamin D and menopausal status were associated with higher levels of AIx in the basic analysis, but not in the multivariate model.

Conclusion: Calcium supplementation was associated with increased arterial stiffness in this cohort of patients with RA. Residual confounding cannot be ruled-out.

[P5362] Assessment of myocardial function by different ultrasound systems and speckle tracking software. Are conventional strain values feasible?

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Purpose: Myocardial strain by two-dimensional speckle echocardiography (2DSE) is a new quantitative technique for objective assessment of myocardial function. Looking forward to the future clinical application of 2DSE, it is important to know whether vendor diversity of commercially available speckle tracking software can be used indifferently for myocardial strain analysis. This study compares two different ultrasound systems using their manufacturers specific speckle software for assessment of myocardial strain in a healthy population.

Methods: 24 healthy subjects (age: 38±9, 60% male) underwent two 2D echocardiograms within the same day using different cardiac ultrasound systems: Vivid 7 (GE Ultrasound, Horten Norway) and Artida 4D (Toshiba Medical Systems). Standard apical views and short-axis planes of the left ventricle (LV) were obtained in each subject with a frame-rate range of 60±20frames/s. Global and regional longitudinal, radial and circumferential strain values were analysed using the respective speckle tracking software: 2D-strain EchoPac PC v.7.0.1.,GE Healthcare, Horten, Norway; and 2D Wall Motion Tracking, Toshiba Medical Systems. Global strain values were estimated as the average of regional LV strain values. Agreement between the two systems was assessed by Bland and Altman method.

Results: Mean LV ejection fraction was 58±7%. Images were acquired using both systems under similar heart rate (64±10vs.68±9, p=ns). Global longitudinal, radial and circumferential strain was -21.21±2.3, 45.5±7.9 and -22.43±3.4 respectively for Vivid and -21.3±2.5, 42.6±8.9 and -24.30±4.8 when using Toshiba. Limits of agreement between both speckle tracking software were narrower for global longitudinal strain (-2.73-3.19) than for radial and circumferential strain (-1.94-8.06 and -1.1-5.7 intervals respectively).

Conclusions: Two different available cardiac ultrasound systems, Vivid and Toshiba, appear to be comparable when quantifying LV function by speckle tracking. Of the parameters analysed, longitudinal myocardial strain is more robust than radial or circumferential strain for quantitative assessment of myocardial function when using either speckle tracking software.

[P5707] Aerobic interval training improves myocardial function more than moderate intensity training in essential hypertension

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Background: Physical activity improves myocardial function, as well as reduces blood pressure. Aim: Compare the effect of different training intensities on left ventricular (LV) systolic and diastolic function, evaluated by 2D ultrasound, tissue Doppler (TDI) and blood-pool indices.

Methods: 64 patients (mean age 52±7.9, 27 women) with essential hypertension grade I and II, without medication were included for exercise training three times a week for 12 weeks. The patients were randomized into three groups: Aerobic interval training (AIT) at 95% of peak heart rate (HR), isocaloric moderate continuous training (MIT) at 70% of peak HR and a control group (CG) who received standard advice regard-

Table 1	AIT			MIT			CTR		
	Before	After	P-value	Before	After	P-value	Before	After	P-value
	N=22	N=17		N=20	N=16		N=22	N=18	
EF %	58.0	64.5	<0.01	59.5	61.0	0.25	59.0	58.0	0.50
CO l/min	4.53	5.15	<0.01	4.45	5.02	0.09	5.30	4.90	0.11
SV ml	72.0	80.0	0.02	68.5	71.0	0.48	75.5	72.0	0.29
S' cm/s	7.29	8.54	<0.01	8.28	8.77	0.04	7.92	8.63	0.53
E' cm/s	8.06	9.26	<0.01	8.93	8.62	0.42	8.70	8.27	0.24
IVRT ms	96.5	81.0	0.02	91.0	89.0	0.59	102.0	97.0	0.12
HR	66	68	0.39	68	73	0.04	72	70	0.35
BP mmHg	154	141	<0.01	151	147	0.05	154	155	0.66

P values are for within-group changes.

ing physical activity without training supervision. Baseline and final measurements were ejection fraction (EF), stroke volume (SV), cardiac output (CO), mitral annulus systolic (S') and diastolic (E') tissue velocities and flow velocities in LVOT (S) and mitral early (E) and Late (A) flow velocity, with isovolumic relaxation time (IVRT) and E wave deceleration time Dec-T.

Results: Results are given in table 1, as on-treatment results, i.e. corrected for drop out and drop in. There were no changes in S, E, A, E/A or Dec T. There was a small decrease in E/E', from 9.4 to 8.3 ($p< 0.01$), but as this was within normal range, and solely due to increased E', it is doubtful that it reflects reduction in filling pressure.

Conclusion: Exercise is an effective treatment to improve cardiac function in a hypertensive population. Training intensity matters, as aerobic interval training was more efficient to improve both systolic and diastolic function as well as reducing blood pressure.

[P3802] Aerobic interval training decreases blood pressure more than moderate intensity training in patients with essential hypertension

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Background: Physical exercise reduces blood pressure (BP) in patients with essential hypertension. The aim of this study was to compare the effect of different training intensities on blood pressure in essential hypertension.

Methods: The study included 89 patients (mean age 52±7.8 years, 40 women) with essential hypertension grade I and II without medication for exercise training three times a week for 12 weeks. The patients were randomized into three groups: Aerobic interval training (AIT) at 95% of peak heart rate (HR), isocaloric moderate continuous training (MIT) at 70% of peak HR and a control group (CG) who received standard advice regarding physical activity without training supervision. Baseline and final measurements included 24 hour ambulatory BP, maximal oxygen uptake (VO2max), endothelial function measured as flow mediated dilatation of the brachial artery, echocardiography for cardiac output (CO) and peripheral resistance (R) measurements and cholesterol (Hdl).

Results: Results are given in table 1, as on-treatment results, i.e. corrected for drop out and drop in. AIT was superior to MIT in all measurements. However, both training modalities significantly reduced BP, increased VO2 max and increased Hdl cholesterol.

Table 1	AIT			MIT			CG		
	Before	After	P-value	Before	After	P-value	Before	After	P-value
	(n=31)	(n=27)		(n=28)	(n=24)		(n=30)	(n=30)	
Sys Bp (mmHg)	154	141	<0.001	151	147	0.048	154	155	0.66
Dia Bp (mmHg)	94	87	<0.001	92	88	0.022	92	92	0.92
HR, mean	73	69	0.001	72	72	0.91	74	75	0.41
VO_{2max} (ml/kg/min)	36.5	41.7	<0.001	34.0	35.8	0.003	34.5	36.0	0.058
CO (l/min)	4.53	5.15	0.028	4.45	5.02	0.085	5.30	4.90	0.11
R	26.2	21.2	0.002	26.5	23.1	0.058	22.6	23.4	0.55
Hdl cholesterol (mmol/L)	1.41	1.48	0.036	1.49	1.52	0.044	1.60	1.58	0.48
Endothelial function (% dilatation)	6.12	10.07	0.002	6.54	7.05	0.69	8.29	8.97	0.39

P values are for within-group changes.

Conclusion: Exercise is effective in reducing blood pressure in a hypertensive population. Training intensity matters, as aerobic interval training was more efficient in reducing blood pressure, mean heart rate and the peripheral resistance, as well as reducing several cardiovascular risk factors among patients with essential hypertension. These findings may have important clinical implications

[P4864] ADMA levels as measure of endothelial dysfunction are increased in elderly patients with atrial fibrillation

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The prevalence of atrial fibrillation (AF) is increasing. Several independent risk factors for AF have been identified, however, the importance of endothelial dysfunction is still not clarified.

The aim of the present study was to evaluate the levels of L-arginine, the substrate for nitric oxide (NO) and the asymmetric dimethylarginine (ADMA), an endogenous inhibitor of NO-synthase, as related to the presence (or absence) of AF.

Material and methods: This is a case control study consisting of 75-year old subjects with permanent AF (n=62) and control subjects in sinus rhythm (n=124), matched for gender. Clinical data were obtained and fasting blood samples were collected at study entrance. EDTA-plasma was used for L-arginine and ADMA analyses, performed by an HPLC-method. Statistics: Group differences were compared by t-test and Chi-square was used for trend analysis through quartiles. Multiple regression models were performed for estimation of independency.

Results: Means (SD) are given. Levels of ADMA were elevated in AF vs controls (0.69 (0.13) vs 0.62 (0.12) umol/L, $p<0.001$) and the L-arginine/ADMA ratios were lower (114 (23) vs 124 (27), $p=0.015$), still significant after adjustment for relevant covariates (creatinine, hypertension, body mass index, diabetes, ischemic heart disease, LDL-cholesterol) ($p=0.007$ and $p=0.037$, respectively). When dividing the ADMA levels into quartiles there was a significant trend for having AF with increasing levels of ADMA ($p=0.001$) with a clear cut-off at the 25th percentile (<0.54umol/L), giving an OR for having AF of 7.16 (95% CI 2.43-21.09) ($p<0.001$) with higher levels. A similar inverse trend was seen for the L-arginine/ADMA ratio.

Conclusion: Elevated levels of ADMA are significantly predicting the presence of atrial fibrillation in the elderly, elucidating the importance of endothelial dysfunction in such patients.

[P3391] Depressed contractile function, SERCA-activity and reduced T-tubule density in myocytes isolated from the free left ventricular wall from patients with post-infarction heart failure

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Purpose: Most cellular and molecular data for depressed cardiac function in man comes from well-established animal models and biopsies from transplant hearts (end-stage heart failure). These studies suggest impaired SERCA-2 activity and reduced T-tubule density as central mechanisms behind a failing heart. The aim of the present study was to determine SERCA-function in tissue samples, and contractile function, calcium handling and T-tubule density in cardiomyocytes isolated from free left ventricular wall in patients with- and without post-infarction heart failure (post-MI HF-patients) undergoing coronary artery bypass graft (CABG).

Methods: 10 (63±6 years) patients without myocardial infarction and an EF>50 and 10 (69±5 years) post-MI HF-patients with EF<30 (NYHA 2-4) scheduled for CAGB were included. Small muscle biopsies were taken during the surgery. One small sample was processed for measurements of SERCA-activity whereas one was used for enzymatic cell isolation and one saved for molecular analysis. Tissue and cardiomyocytes were studied using fluorescence and confocal imaging.

Results: Cardiomyocyte shortening was similar between groups at 0.5Hz (i.e. 30 beats/min), but in contrast to cardiomyocytes from heart with normal EF, we found a negative shortening-frequency relation in cardiomyocytes from failing hearts. At 2 Hz stimulation, cardiomyocyte shortening was clearly depressed ($p<0.001$) in post-MI HF. Diastolic calcium was increased ($p<0.01$), calcium amplitude ~45% lower, and time to peak contraction and time to relaxation were slower at all stimulation frequencies ($p<0.01$) in cardiomyocytes from post-MI HF-patients. Synchrony of calcium release is closely linked to the density and

organization of T-tubules in the cardiomyocyte. We found that the T-tubule density was reduced by ~35% in myocytes from post-MI HF patients, which may contribute to the slower time to calcium release and lower amplitude. The rate of calcium removal via SERCA was 35% slower in tissue from post-MI HF-patients ($p<0.01$), which may explain the prolonged time to calcium removal and time to relenghtening in cardiomyocytes from failing hearts.

Conclusion: This study demonstrate that patients selected for CAGB with post-MI HF have impaired cardiomyocyte function and depressed calcium handling. Reduced T-tubule density contributes to reduced calcium release and hence reduced cardiomyocyte shortening. Impaired SERCA function influence upon calcium removal and thereby relaxation during diastole. The findings substantiate that impaired SERCA-2 function and reduced T-tubule density is central mechanisms behind heart failure.

[P5366] High risk patients for cardiac arrhythmia after myocardial infarction can be identified by left ventricular global strain

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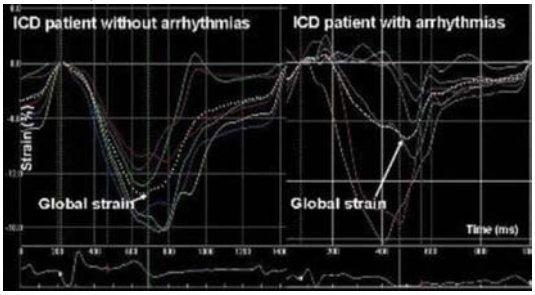
Purpose: Left ventricular ejection fraction (EF) is currently used as the primary parameter to select patients for ICD therapy after myocardial infarction (MI). Myocardial strain by echocardiography can accurately quantify regional myocardial function. We aimed to investigate if myocardial strain is a better marker of susceptibility for ventricular arrhythmias than EF in patients after myocardial infarction.

Methods: We included 65 patients with an ICD according to secondary prevention criteria post MI. After 3.8±3.5 years follow up, 30 had no and 35 patients had one or more recorded arrhythmias requiring appropriate ICD therapy. Strain measurements were assessed by speckle tracking echocardiography. The average value of peak systolic strain in a 16 LV segments model was assessed as global LV strain.

Results: EF did not discriminate ICD patients with arrhythmias from those without (39±10% vs. 40±11%, P=0.81). Left ventricular end diastolic (LVEDV) and end systolic volumes (LVESV) were not significantly different between arrhythmic and non-arrhythmic patients (LVEDV 173±63ml vs. 159±54ml, P=0.34 and LVESV 107±49ml vs. 98±45ml, P=0.41). Global LV strain was lower in the arrhythmic patients compared to the non-arrhythmic (-10.5±4.4% vs. 13.3±4.0%, P=0.01). Figure demonstrates reduced global strain in an ICD patient with recorded arrhythmias (right panel) compared to an ICD patient without recorded arrhythmias.



Conclusion: Global LV strain by echocardiography was superior compared to EF in identifying further arrhythmias in post MI patients.

[P2945] Aerobic interval training versus strength training as a treatment for the metabolic syndrome

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Background: Physical inactivity and overweight is strongly associated with an increased risk for developing metabolic syndrome. The syndrome is characterized by a cluster of risk factors for cardiovascular disease and mortality such as increased blood pressure, impaired glycemic control, excess of abdominal fat and dyslipidemia. Regular physical activity and increased fitness can improve several metabolic factors and reduce the risk of developing cardiovascular diseases, however the optimal training regime to treat metabolic syndrome and its associated cardiovascular abnormalities remain undefined.

Methods: Forty subjects were randomized and stratified by gender and age to either aerobic interval training (AIT, n=11), strength training (ST, n=10), combination of aerobic interval training and strength training (COM, n=9), or a control group (n=10). Training was performed 3 times per week for 12 weeks, and risk factors comprising

the metabolic syndrome were measured before and after the intervention in all four groups.

Results: AIT significantly increase VO2peak (from 146.2±34.2 to 156.5±36.9 ml/lbm-075/min^{-1}) whereas ST, COM and the control group increased maximal strength (45%, 46% and 12%, respectively). AIT significantly reduced triglyceride levels (from 2.27±0.97 to 1.83±0.76 mmol/l) systolic blood pressure (from 140±14.6 134.2±12 mmHG) and diastolic blood pressure (from 89±8.1 to 85±5.5 mmHG). Only ST reduced waist circumference significantly (from 111.5±10.8 to 110±11 cm). Endothelial function measured as flow mediated dilution (FMD) was significantly improved in all three training groups (24%, 26% and 36% for AIT, ST and COM group, respectively). There was no change in weight, fasting plasma glucose, high density lipo-protein or insulin C-peptid in either group.

Conclusion: Although all three training regimes improved abnormalities associated with the metabolic syndrome, AIT for 12 weeks was superior to both strength training and a combination of interval and strength training for improving risk factors defining metabolic syndrome. Three out of the six risk factors identifying the metabolic syndrome were significantly improved after 12 weeks of aerobic interval training.

[P482] Head to head comparison of the reproducibility of different measures of systolic left ventricular function

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Objectives: 1) To compare the interobserver reproducibility of new and traditional measures of the left ventricular (LV) global and regional systolic function. 2) To compare interobserver reproducibility of the same measures in separate recordings (interobserver) vs. repeated analyses of single datasets (intra- and interanalyzer).

Methods: Two experienced sonographers separately performed a complete echo/Doppler study on ten healthy subjects. All recordings were analyzed and reanalyzed by both sonographers (20 recordings and 50 analyzes). The following variables were measured: Ejection fraction (EF) by biplane Simpson, left ventricular outflow tract peak velocity (LVOT peak), global and segmental LV end systolic strain (Ses) and peak strain rate (SRs) by 2D speckle tracking, systolic annulus velocity by pulsed wave tissue Doppler (S') and systolic M-mode annulus excursion (MAE).

Results: Mean, coefficient of repeatability (COR) and mean error (absolute difference divided by the mean) are shown in table 1. Interobserver mean error was significantly lower for MAE (p=0.018). Mean error of segmental Ses and SRs was significantly higher than all the global measures (p<0.001 for all). The overall interanalyzer and intraanalyzer mean error based on single datasets was 23% (p=0.002) and 37% (p<0.001) lower than the mean error calculated by separate recordings and analyzes done by a different sonographer.

Table 1 Method	Mean inter-observer	COR inter-observer	Mean error inter-observer	Mean error inter-analyzer	Mean error intra-analyzer
LVOT peak	1,0 m/s	±0,2 m/s	9,8%	2,9%	3,2%
Global S_{es}	-0,21	±0,02	5,7%	6,3%	3,4%
Global SR_s	-1,14 s^{-1}	±0,21 s^{-1}	9,4%	4,5%	5,0%
S'	9,1 cm/s	±1,7 cm/s	8,5%	3,3%	2,1%
MAE	16,9 mm	±1,6 mm	3,6%	2,8%	2,9%
EF	0,59	±0,07	5,6%	6,0%	4,9%
Segmental S_{es}	-0,21	±0,07	14,2%	12,3%	11,0%
Segmental SR_s	-1,12 s^{-1}	±0,51 s^{-1}	17,4%	11,9%	8,6%

Conclusion: 1) MAE showed better interobserver reproducibility than other traditional and newer measures of LV systolic function. 2) Repeated analyses of the same recordings underestimates the true -clinically relevant- interobserver variability by approximately 30% for most measures of LV function.

[P2245] The role of conventional risk factors in explaining residual risk in statin-treated post myocardial infarction patients. Results from the IDEAL study

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Background: We have previously described significant relations between Apolipoprotein B (apoB), apoB/apoA1 ratio and non-HDL-cholesterol and cardiovascular events (CVE) in statin-treated pa-

tients reaching the goals of 2.0 and 2.5 mmol/L in the IDEAL study.

Methods: Patients were allocated to either 20 to 40 mg of simvastatin (n=4449) or atorvastatin 80 mg (n=4439) daily for 5 years. The study had an open-label randomized design (PROBE) and had no run-in phase. In this post-hoc subanalysis, for subjects who reached the LDL-C goals of 2.5 mmol/L or 2.0 mmol/L at 3 and 6 months, risk factors for CVE were investigated by Cox regression analysis including sex, age, systolic blood pressure, coronary heart failure at baseline, hypertension, diabetes, smoking, and prior statin use, and each of mean apoB, mean apoB/apoA1 and mean non-HDL at months 3 and 6. In addition, net reclassification analysis (NRI) was performed by logistic regression with cross-classification of CVE risk into 4 groups based on a model including apoB/apoA-1 and excluding it over and above the adjustment factors defined above. A similar analysis was performed by comparing the model with and without smoking.

Results: For subjects who reached LDL goals of <2.5 mmol/L, apoB, apoB/ApoA1 and non-HDL-C significantly predicted CVE risk. The hazard ratios (HR) and 95% confidence intervals of 1 standard deviation increase in apoB, apoB/apoA1 and non-HDL were: 1.13 (1.06-1.21), 1.16 (1.09-1.23), and 1.11 (1.04-1.19), respectively. Neither inclusion of the apoB/apoA1 ratio or inclusion of smoking over and above the standard factors had much influence on the NRI for CVE. For apoB/apoA-1, the index was 2.6% for goal <2.5 mmol/L, and 2.0% for goal <2.0 mmol/L. Similar numbers for smoking were 2.3% and 1.9%.

Conclusion: For subjects who reached LDL goal, even though there are are still significant relations between conventional risk factors and outcome in post myocardial infarction patients, on-study apoB/apoA1 did not provide further prediction of CVEmeasured by NRI. This does not diminish the need of paying attention to these factors in long term cardiovascular prevention. The causes of the residual risk in statin treated patients in a 5-year perspective may be related to more short-term factors such as thrombogenic and inflammatory factors or to other lipoproteins e.g. HDL.

[P1414] Overexpression of myocardial CCN2/CTGF prevents heart failure and improves survival after myocardial infartion

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Background: Myocardial CCN2/CTGF - connective tissue growth factor is robustly induced in experimental and human heart failure (HF). Yet, its role in the pathophysiologic mechanisms of HF remains unresolved.

Methods and Results: To elucidate the role of myocardial CTGF in HF, transgenic mice with cardiac-restricted overexpression of CTGF (Tg-CTGF) were employed and compared with non-transgenic controls (NLC). Myocardial infarction was induced by ligation of the left coronary artery in Tg-CTGF (n=22) and NLC mice (n=21). Sham-operated animals underwent the same procedure without ligation of the artery. All mice were followed for 4 weeks in order to investigate the development of HF. Area at risk was estimated in a separate group of animals, harvested immediately after ligation and perfused with Evans blue dye. Area at risk was similar among Tg-CTGF and NLC mice (42.7±1.6%, n=8 vs 40.4±2.1%, n=8, p=0.39). During follow-up, significant improvement of survival was found in Tg-CTGF mice (63.6% vs. 38.1%, p<0.05). In vivo pressure-volume analysis performed after 4 weeks displayed preserved cardiac performance in Tg-CTGF mice, as measured by dp/dt, end-diastolic pressure and cardiac output. End-point analysis revealed attenuation of cardiac hypertrophy in Tg-CTGF mice vs NLC mice (Heart weight/body weight ratio; 5.3±0.2mg/g, n=14 vs 8.0±0.9mg/g, n=9, p<0.05). Consistently, markers of myocardial remodelling, i.e. BNP and β-myosin heavy chain, measured by real-time qPCR, were significantly less up-regulated in Tg-CTGF than NLC hearts. Concentration-effect curves of isoproterenol-stimulated contractility in myocardial strips uncovered marked attenuation of inotropic responses in Tg-CTGF hearts (increase of maximal contractility; 123±14% vs. 427±27%, p<0.01). Selective upregulation of G-protein receptor kinase 5 (GRK5) in cardiac myocytes of Tg-CTGF hearts were found and confirmed as the mediator of this functional desensitization. Western blot analysis also revealed activation of salvage kinase pathways in Tg-CTGF

hearts, evident as increased phosphorylation of AKT (Ser 473) and GSK-3β (Ser 9). Interestingly, induction of myocardial collagen contents four weeks after myocardial infarction, determined by quantitative HPLC of hydroxyproline, was lower in Tg-CTGF mice than in NLC mice.

Conclusion: This study uncovers novel, unexpected properties of CTGF as cardioprotective factor in ischemic HF. Myocardial CTGF prevents development of HF and improves survival after myocardial infarction, possibly due to activation of salvage kinase pathways and inhibited neurohumoral stimulation of the heart.

[P2965] Cardiac troponin I at 24 or 48 Hours predicts infarct size in patients with STEMI as determined by cardiac magnetic resonance imaging. A FIRE-substudy

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Purpose: i) To determine the correlation of single-point cardiac troponin I (cTnI) and infarct size as measured by cardiac magnetic resonance (CMR) imaging at 5 days and 4 months; ii) To define predictors of infarct size above or below median at 4 months in a binary logistic regression analysis including early CMR estimated infarct size.

Methods: A post-hoc analysis of the F.I.R.E. (FX06 in Ischemia-REperfusion injury) trial. 234 patients were randomised presenting with acute ST elevation myocardial infarction (STEMI) and receiving primary percutaneous coronary intervention within 6 hours from onset of symptoms. cTnI sampling at 24 (cTnI24) and 48 (cTnI48) hours. Infarct size was measured by contrast enhanced CMR examination at 5-7 days and 4 months. Association between two variables was calculated by Spearman rank correlation. Binary logistic regression analysis for determining independent predictors (adjusting for BMI, age, and gender).

Results: Median infarct size as % of left ventricle (IQR): 5 days: 17.2% (8.4;28.2); 4 months: 13.4%(6;24). Median cTnI (IQR): 24 hours: 45.7 ng/ml (15.9;77.4); 48 hours: 17.7 ng/ml (9.2;35.5).

Spearman's rho for infarct size at 5 days: 0.605 (cTnI24) and 0.665 (cTnI48). Spearman's rho for infarct size at 4 months: 0.687 (cTnI24) and 0.711 (cTnI48). Results of binary regression analysis presented in table.

Table 1. Binary logistic regression analysis of independent predictors of infarct size above or below median at 4 months	β-coeffi-cient	OR (95% CI)	P-value
Non-anterior location	- 0.946	0.388 (0.136 - 1.106)	0.249
$cTnI_{24}$	0.029	1.030 (1.013 - 1.047)	< 0.001
Early infarct size	0.136	1.146 (1.082 - 1.214)	< 0.001

Conclusion: We here report a strong correlation between early, single-point cTnI measurements and infarct size as determined by state-of-the art CMR imaging. There was considerable shrinkage of IS during the follow-up period, which could explain why correlations with cTnI were generally better at 4 months than at 5 days. Moreover, our results suggest that single-point cTnI is an independent predictor of infarct size above or below median at 4 months in a model including early CMR estimated infarct size.

[P3803] Aerobic fitness relates to blood pressure in a healthy adult population

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Purpose: Aerobic fitness is suggested to be a continuum from health to disease, with important influence on a variety of known risk factors. Direct objective measurement of aerobic fitness (VO2max) was included in the third wave of the Health Study in Nord-Trøndelag. It is not established whether there is a close relationship between aerobic fitness and blood pressure. Hence, the aim of the present study was to examine how aerobic fitness related to blood pressure in a healthy adult population.

Methods: Between June and December 2007 2355 participants ≥20 years of age completed a maximal treadmill test finding VO2max (alternatively, VO-2peak). In addition, height, weight and blood pressure was measured. We calculated adjusted mean blood pressures and odds ratios (OR) for having high blood pressure across gender-specific tertiles of aerobic fitness.

Results: After adjustment for age and body mass index (BMI), men and women in the low fitness group had significantly higher blood pressures than those with high fitness. A significant inverse gradient across fitness groups was observed for systolic blood pressure (SBP, p-trend <0.05), diastolic blood pressure (DBP, p-trend <0.05) and mean arterial pressure (MAP, p-trend <0.01) in men, and for SBP (p-trend <0.01) and MAP (p-trend <0.05) in women. Compared to high aerobic fitness, low fitness was associated with increased odds of having high blood pressure, independent of age and BMI (OR, 2.3; 95% CI, 1.4-3.9 in men, and OR, 2.5; 95% CI, 1.1-5.7 in women).

Conclusions: Blood pressure was inversely related to aerobic fitness in these data. The adverse effects of aging and high BMI on blood pressure were attenuated in those with high aerobic fitness. Hence, people with a moderate to high aerobic fitness level may be protected against high blood pressure, thus having reduced risk of cardiovascular disease, the latter being especially important in elderly or overweight/obese.

Table 1. Parameters	Group 1	Group 2	Group 3	Group 4
	(none LVH + normal LVEDP) (n=20)	(LVH + normal LVEDP) (n=23)	(none LVH + LVEDP>15) (n=20)	(LVH + LVEDP>15) (n=24)
Radial_S_value_(%)	27±15	21±12*	21±13*	22±13*
Radial_SRs_value_(1/s)	2.30±0.86	2.04±0.83*†	2.41±0.78	2.07±0.90*†
Radial_SRe_value_(1/s)	-2.21±1.04	-1.83±0.76*†	-2.45±0.97	-1.89±1.00*†
Circ_S _value_(%)	-22±9	-23±10	-22±10	-23±9
Circ_SRs_value_(1/s)	-2.15±0.76	-2.06±0.70	-2.07±0.7	-1.97±0.71°
Circ_SRe_value_(1/s)	2.21±1.07	2.44±1.08	2.33±1.06	2.06±0.83°
Long_S _value_(%)	-20±5	-19±5	-19±6	-20±6
Long_SRs_value_(1/s)	-1.36±0.44	-1.25±0.46*	-1.31±0.45	-1.21±0.45*†
Long_SRe_value_(1/s)	1.59±0.75	1.35±0.68*†	1.59±0.77	1.38±0.74*†

**p < 0.05 vs. group 1, °p < 0.05 vs. group 2, † p < 0.05 vs. group 3.*

[P4923] Patterns of regional myocardial dysfunction in patients with hypertensive heart disease: an ultrasound speckle tracking study

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Aim of the study was asses the effect of left ventricular hypertrophy (LVH) on regional myocardial function.

Methods: Eighty-seven patients with normal coronary angiograms and ejection fraction >55% underwent echocardiograpic examination and were divided according to left ventricular mass index (LVMI) and left ventricular enddiastolic pressure (LVEDP) as following:

1. normal, 2. LVH + LVEDP <15 mmHg, 3. none LVH + LVEDP >15 mmHg, 4. LVH + LVEDP >15 mmHg. LVH was defined as: LVMI >115 g/m^{2}BSA for men and >95 g/m^{2}BSA for woman.

Greyscale cine-loops were obtained from three apical views (four-chamber, two-chamber, apical long axis) and two short axis planes (basal and mid) of the left ventricle. Based on two-dimensional ultrasound speckle tracking the absolute value (value) and the time to peak value (time) of the following parameters were extracted in longitudinal (long), radial (rad) and circumferential direction: strain (S), systolic (SRs) and diastolic strain rate (SRe). The parameters are expressed as mean values between all left ventricular segments.

Results: Results are displayed in Table 1. LVMI correlates significant with Long_S_value (r=-0.18; p<0.001), Long_SRs_value (r=-0.19; p<0.001), Long_SRe_value (r=-0.15; p<0.001), Long_S_time (r=0.29; p<0.001), Long_SRs_time (r=0.11; p<0.001) and Long_SRe_time (r=0.25; p<0.001).

Conclusions: (1) Systolic and diastolic parameters (SRs, SRe) of longitudinal and radial deformation are reduced in both groups with higher LVMI irrespective of LVEDP. (2) Radial function was only impaired in group 4. (3) The time to peak values of longitudinal deformation parameters are significantly prolonged with increasing LVMI.

[P5701] Effects of statin therapy according to plasma high sensitivity C-reactive protein concentration in the Controlled Rosuvastatin Multinational Trial in Heart Failure trial (CORONA)

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Purpose: We examined whether the anti-inflammatory action of statins may be of benefit in heart failure (HF) a state characterized by inflammation and in which low cholesterol is associated with worse outcomes.

Methods: 10 mg rosuvastatin daily was compared to placebo in patients with ischemic systolic HF according to baseline high sensitivity C reactive protein (hs-CRP) <2.0 mg/L (placebo=779, rosuvastatin=777) or ≥2.0 mg/L (placebo=1694, rosuvastatin=1711). The primary outcome was cardiovascular death, non-fatal myocardial infarction or stroke.

Results: Baseline LDL was the same in both hs-CRP groups and rosuvastatin reduced LDL by 45% in both groups. Median hs-CRP was 1.10 mg/L in the lower hs-CRP group and 5.60 mg/L in the higher group with a net change of -22% in the high group and -33% in the low group. In the high hs-CRP group, 548 (14.0 per 100 patient years of follow-up) placebo-treated and 498 (12.2) rosuvastatin-treated patients had a primary endpoint (placebo: rosuvastatin hazard ratio [HR]0.87; 95%CI 0.77-0.98). In the low hs-CRP group 175 (8.9) placebo-treated and 188 (9.8) rosuvastatin-treated patients experienced this outcome (HR 1.09,0.89-1.34); interaction p=0.062. The corresponding numbers of deaths were: 581 (14.1) placebo-treated and 532 (12.6) rosuvastatin-treated patients in the high hs-CRP group (HR 0.89,0.79-1.00). In the low hs-CRP group: 170 (8.3) placebo-treated and 192 (9.7) rosuvastatin-treated patients died (HR 1.17,0.95-1.43); interaction p = 0.026.

Conclusion: Elevated hs-CRP concentrations are associated with worse outcomes in HF. We found a significant interaction between hs-CRP and the effect of rosuvastatin whereby rosuvastatin treatment was associated with better outcomes in patients with hs-CRP ≥2.0 mg/L.

[P4848] Post-cardioversion P wave duration is inversely related to the atrial fibrillatory rate and does not predict sinus rhythm maintenance in the CAPRAF study

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Introduction: Shortened atrial refractoriness and reduced conduction velocity, both essential components of reentrant wavelength that affects atrial fibrillatory rate (AFR), have been linked to the maintenance of atrial fibrillation (AF). However, association between AFR and post-cardioversion P-wave duration have not been studied in patients. For this purpose, a post hoc subanalysis of the randomized, placebo-controlled CAPRAF (Candesartan in the Prevention of Relapsing Atrial Fibrillation) trial was performed.

Methods: AFR and P-wave duration were assessed from surface ECG at the day of cardioversion in 108 patients with persistent AF. Class I and III antiarrhythmic drugs were not allowed. AFR prior to cardioversion was determined from ECG lead V1 using spatiotemporal QRST cancellation and time–frequency analysis. P-wave duration was obtained from P-wave triggered signal-averaged orthogonal ECG 4 hours after cardioversion. Primary study endpoint was recurrence of AF at 6 months.

Results: Post-cardioversion P-wave duration was prolonged (160±21 ms) and positively correlated with age ($r = 0.401$; $p < 0.001$) and left atrial diameter ($r = 0.382$; $p < 0.001$). Conversely, AFR was negatively correlated to age ($r = - 0.314$; $p = 0.002$) and left atrial diameter ($r = -0.231$; $p = 0.023$). P-wave duration was inversely related to the atrial fibrillatory rate (AFR=390±57 fibrillations per minute; $r = 0.247$; $p = 0.014$). However, the inverse relation between P-wave duration and AFR was lost when adjusting for age and left atrial diameter. P-wave duration was not predictive of AF recurrence.

Conclusion: Post-cardioversion P wave duration did not predict sinus rhythm maintenance. Age and left atrial dimensions are important determinants of both P wave duration and AFR. The association between the prolongation of P wave duration and AFR slowing is a new finding that characterizes the arrhythmia substrate and motivates further studies in patients with other clinical types of AF.

[4970] Effects of frequency of exercise for improving aerobic capacity: training and de-training

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Background: Aerobic exercise performed as interval training is an effective way of improving maximal aerobic capacity (VO2max). We have previously shown that high-intensity exercise performed 2-3 times per week is superior to moderate exercise for improving VO2max when total exercise volume is equalized. This is valid both within highly trained individuals as well as in different patient groups. The aim of the present study was to investigate the rate of adaptation of VO2max in young, healthy individuals performing exercise at either high frequency or moderate training frequency. We hypothesised that improvements of VO2max could be achieved to the same extent when exercising at high frequency compared to moderate frequency.

Methods: Nineteen healthy students (23.5±2.0 yrs) carried out a total of 24 exercise sessions at either 3 times per week for 8 weeks, or 8 times per week for 3 weeks. All training was carried out as uphill treadmill running using heart rate monitors. VO2max was measured initially and after every 8th exercise session. During the de-training period, VO2max was measured 4, 14 and 24 day post exercise, and thereafter every second week over a total period of two months.

Results: The moderate frequency group increased VO2max by 6.0±2.7 ml/kg/min ($p<0.001$) and the high frequency group by 4.1±3.1 ml/kg/min ($p=0.002$). Using the linear model with correction for baseline value, we found however no differences between the groups regarding the magnitude of elevating VO2max ($p=0.36$). Interestingly, while the moderate frequency group reached the highest measured VO2max-value 4 days post training, the high frequency group reached the peak value 14 days post training. This elevation was sustained 24 days post training in the high frequency group ($p=0.413$), while the moderate frequency group showed declined VO2max compared to peak level at this time point ($p<0.001$).

Conclusions: Improvements of VO2max after high-intensity aerobic interval training could be accomplished in reduced time with high frequency training compared to normal frequency training. VO2max may boost after ending a high-intensive, high frequency training programme, and this over-compensation may be sustained for over three weeks without training.

[P2288] Prediction of cardiovascular events by MMP-9 in elderly men

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Purpose: Matrix metalloproteinase-9 (MMP-9) is thought to play a crucial role in the progression of atherosclerosis. Experimental data suggests interactions between MMPs and lipid metabolism, triglyceride hydrolysation and adipocyte maturation. We investigated the importance of MMP-9, its inhibitor tissue inhibitor of matrix metalloproteinases-1 (TIMP-1) and MMP-9/TIMP-1- ratio on cardiovascular events in elderly men at high risk for cardiovascular disease with respect to lipid levels.

Methods: We prospectively studied 563 elderly men at high risk for cardiovascular disease. The variables were measured at inclusion and cardiovascular events were recorded over 3 years. MMP-9 levels were grouped by quartiles and related to cardiovascular event rate.

Results: Cardiovascular events were recorded in 68 individuals. Higher circulating levels of MMP-9 ($p = 0.046$) but not triglycerides, total cholesterol, HDL, LDL or oxidised LDL were associated with cardiovascular events. Univariate regression revealed a significant association between higher MMP-9 levels (>75th percentile; 543 ng/ml) and cardiovascular events (OR 1.93; CI 1.13-2.30; $p = 0.016$). When calculated in a multivariate model, the significance was lost (adjusted OR 1.59; CI 0.90-2.78; $p = 0.108$). Analysing MMP-9 together with plasma lipid levels, it appeared that elevated MMP-9 levels are stronger predictors of cardiovascular events (OR 3.69; CI 1.67-8.19; $p=0.001$) in individuals with hypertriglyceridaemia (>1.7 mmol/l). In a multivariate regression model, the prediction of cardiovascular events by MMP-9 was still significant in patients with hypertriglyceridaemia (adjusted OR 3.17; CI 1.33 - 7.55; $p = 0.009$).

Conclusions: MMP-9 is associated with cardiovascular events in elderly men. In the presence of hypertriglyceridaemia, elevated MMP-9 levels (>543 ng/ml) are a strong predictor of cardiovas-

cular events. Even though not suitable as an independent marker for atherosclerosis, taking into account hypertriglyceridaemia, MMP-9 could be a useful tool to identify elderly men at particular high risk for cardiovascular events.

[P866] Association of pulse pressure with new-onset atrial fibrillation in hypertensive patients with ECG left ventricular hypertrophy: the LIFE study

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Objective: Atrial fibrillation (AF) is associated with increased cardiovascular events, and the incidence of new-onset AF is increased by hypertension. Antihypertensive treatment reduces new-onset AF, and treatment with the angiotensin receptor blocker losartan is more effective than the beta-1 selective blocker atenolol in this respect. To assess whether arterial stiffening influences the risk of developing AF, we examined whether pulse pressure predicted new-onset AF in the Losartan Intervention For Endpoint reduction in Hypertension (LIFE) study, independent of mean arterial pressure as time-varying covariates.

Methods: In LIFE, a double-blinded, randomized, parallel-group study, 9,193 hypertensive patients (46% men; mean age 67 yrs, blood pressure 174/98 mmHg after placebo run-in) with ECG-documented left ventricular hypertrophy (LVH), randomized to once daily losartan- or atenolol-based antihypertensive therapy were followed for a mean of 4.9 years. At baseline 8,831 patients had neither a history of AF nor AF by ECG Minnesota coding, and were at risk of developing this condition during the study.

Results: ECG confirmed new-onset AF in 353 patients. Univariate Cox analyses showed that time-varying heart rate, systolic blood pressure and pulse pressure as well as baseline Cornell product ECG LVH, weight, height, total cholesterol, urine albumin/creatinine ratio, age, male gender, Caucasian ethnicity, prior congestive heart failure and Framingham risk score significantly predicted subsequent new AF. Multivariate Cox regression analyses showed that time-varying pulse pressure or systolic blood pressure, age, male gender, treatment allocation, time-varying heart rate and time-varying ECG LVH independently predicted new-onset AF. Pulse pressure was an equally strong predictor of new onset AF as systolic blood pressure (HR [95% CI] 1.13 [1.05-1.22] per 10 mmHg, p = 0.001 vs. 1.10 [1.04-1.17] per 10 mmHg, p = 0.002). The mean arterial blood pressure did not reach significance as predictor of new-onset AF in the univariate (HR 1.10 [0.99, 1.22] per 10 mmHg, p=0.064) or in the multivariate (HR 1.10 [0.99, 1.21] per 10 mmHg, p=0.066) Cox analyses.

Conclusions: After taking into account effects of age, gender, heart rate and ECG LVH, pulse pressure was more strongly associated than mean arterial pressure with subsequent new AF in hypertensive patients with ECG LVH. Systolic blood pressure and pulse pressure were equally strong predictors of new onset AF in this model.

[P5426] Diabetes and palpitations are risk factors of atrial fibrillation. The Tromso study

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Purpose: To study the incidence of atrial fibrillation in a large, general population, with focus on risk factor identification.

Methods: The study population comprised 16 220 women and 15 234 men, aged 20 to 97 years (mean 41 years) who attended population health surveys in 1986 or 1994. The subjects were free from atrial fibrillation at baseline. Attendance rate was 76%. Information on symptoms of palpitations during the previous year, diabetes, cardiovascular disease, anti-hypertensive treatment, smoking habits, and coffee and alcohol consumption was obtained from self-administered questionnaires. Blood pressure, blood lipids, pulse,

height and weight were measured, and body mass index (BMI) was calculated. Incident cases of atrial fibrillation were identified through linkage to hospital and national diagnosis registries, with end of follow-up on Dec. 31, 2004. All cases of atrial fibrillation were validated by physicians. Electrocardiograms were studied when necessary. Age adjustment of the incidence rates was done by the direct method with the total cohort as standard population. Multiple-adjusted relative risks (RR) were obtained by Cox proportional hazards analysis.

Results: The mean follow-up time was 12.9 years, and 406 women and 503 men with atrial fibrillation were identified during follow-up. Overall age-adjusted incidence of atrial fibrillation was 1.7 per 1000 person-years in women and 2.8 per 1000 person-years in men ($p<0.0001$). In multivariable analysis, diabetes was positively related to atrial fibrillation in both women (RR 4.46, 95% CI 3.05-6.51) and men (RR 1.88, 95% CI 1.17-3.03). Palpitations were also a significant risk factor in both sexes (RR in women 1.94, 95% CI 1.54-2.44, and RR in men 2.14, 95% CI 1.74-2.63). Systolic blood pressure and anti-hypertensive treatment were significant predictors of atrial fibrillation in both sexes, while BMI was related to atrial fibrillation in men only.

Conclusion: In this prospective, population-based study, diabetes and a history of palpitations were associated with increased risk of atrial fibrillation in both sexes.

[P5679] Apolipoprotein E genotypes are associated with lipid levels and CRP but not outcomes in heart failure

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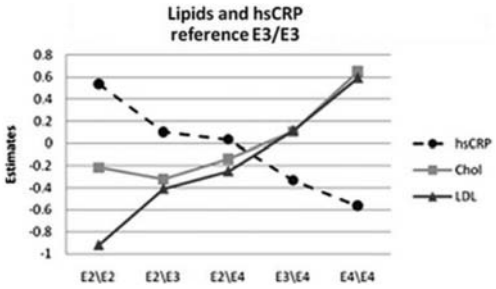
Purpose: Variations in the APOE gene has been consistently associated with lipid levels, coronary artery disease (CAD) and cognitive decline. APOE is also considered a frailty gene with average mortality risk throughout adulthood lower in ε2 and higher in ε4 carriers. But invoking a common pathway to explain the pleiotropic effects of APOE has been difficult. It is likely that the APOE associations may influenced by comorbidities and pharmacotherapy.

Methods: We tested the association of APOE genotypes on lipid levels, hsCRP and cardiovascular outcomes in 3276 elderly patients with heart failure who participated in the CORONA trial. APOE genotypes were inferred from rs429358 and rs7412 polymorphisms. The reference genotype was ε3/ε3. Adjustment for centre did not influence the results significantly.

Results: The frequency of ε2,ε3, ε4 were 8%,81% and 12% respectively. ε4 carriers had significantly lower BMI, hsCRP and higher total cholesterol and LDL cholesterol (figure). Compared with ε3/ε3, the variant APOE genotypes showed no significant excess risk for the all-cause and cardiovascular events.



Conclusions: In elderly patients with heart failure APOE genotype distribution showed no survivor bias. The association of high risk CRP and lipid profiles to low risk APOE genotypes in heart failure patients may partly explain the absence of relationship to outcomes.

[P1717] Presence of radial discoordination during ejection phase is a major determinant for reverse remodeling after cardiac resynchronization therapy

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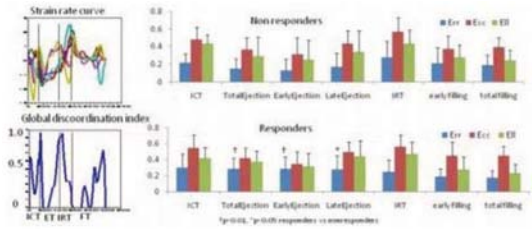
Background: Mechanism of reverse remodeling by cardiac resynchronization therapy (CRT)is yet to be examined.

Methods: Fifty-seven patients with advanced heart failure (Age 69.2±10.6, Male 33/57, Ischemic 20/57, Sinus rhythm 52/57, LVEDV 199.5±55.3ml, EF 24.6±5.81%, QRS 154.1±26.7ms) underwent CRT. At pre and 3 -6 months post CRT, echocardiography (GE, Vivid7, Norway) was obtained. Radial/circumferential/longitudinal strain curve were obtained by speckle tracking analysis of two dimensional echocardiogram from mid short axis view and apical four chamber view. Global discoordination index (GDI=ISR/(GSR+ISR), where ISR (internal strain rate)=$\int(\Sigma|S'(n)|-|\Sigma S'(n)|)dt)/2$, GSR=global strain rate) as a function of time was calculated for spatial nonuniformity. Standard deviation of time to 10, 20, 50, 80, 100% of peak strain as systolic asynchrony and time to 30% completion of lengthening as diastolic asynchrony on each strain curves were calculated for temporal nonuniformity.Reduction of LVESV>15% is defined as responder.

Results: None of the temporal nonuniformity parameters showed significant difference between responders and nonresponders. As regards spatial nonuniformity, only radial discoordination index during ejection phase showed significant difference (GDI during total ejection phase, 0.14±0.11 vs 0.28±0.13, p<0.005). Circumfenrential/longitudinal discoordination index were not significantly different between two groups. Comparison among discoordination in each axis showed radially more coordinated (p<0.01) and circumferentially/longitudinally more discoordinated deformation in both groups.



Conclusion: CRT responders showed more radially discoordinated deformation than non responders. Both groups showed more circumferential and longitudinal discoordination to similar degree.

[P2084] Correlation of inhibition of platelet aggregation after clopidogrel with post discharge bleeding events: assessment by different bleeding classifications

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Background: Data from ACS trials and registries suggest a link between increased risk of bleeding and cardiovascular mortality. However, the potential association of bleeding risk and the inhibition of platelet aggregation (IPA) is not established. It may play a critical role for the safety of more aggressive platelet inhibition, or/and individual tailoring of antiplatelet strategies. We correlated (IPA) with bleeding events assessed by TIMI-, GUSTO-, and BleedScore™ scales in a large cohort of patients with coronary artery disease (CAD) and ischemic stroke (IS) treated with chronic low dose aspirin plus clopidogrel.

Methods: We conducted secondary post-hoc analyses of 5μM ADP-induced IPA and bleeding complications assessed by TIMI, GUSTO, and BleedScore™ scales in a dataset consisting of patients with documented CAD (n=246) and previous IS (n=117).

Results: Demographic characteristic differ substantially dependent on the underlying vascular disease, however IPA and bleeding risks were similar between CAD and IS. All three bleeding scales adequately captured serious hemorrhagic events, where the TIMI scale was the most exclusive, while BleedScore™ was the most inclusive. Over half of all patients experienced superficial event(s), most commonly occurring during 2-3 distinct bleeding episodes. There was no correlation between IPA and duration of antiplatelet therapy. IPA above 50% strongly predicts minor (r2 =0.583), but not severe (r2 =0.109) bleeding events.

Conclusion: Chronic oral combination antiplatelet regimens are associated with a very high (56.5-

60.7%) prevalence of superficial bleeding episodes. We postulate that in trials and registries, these hemorrhages are grossly underestimated. The role of such frequent mild complications for the overall benefit of antiplatelet therapy is entirely unknown, as is their effect on compliance. While IPA is well suited for defining the risk of minor complications, more serious bleeding events cannot be predicted.

[5083] COPD predicts mortality in CHF: the Norwegian Heart Failure Registry

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Purpose: Chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) are two commonly encountered clinical conditions that often coexist and share tobacco as a common risk factor. There is very little data evaluating the prognostic impact of COPD in patients with CHF. Thus, the aim of the present study is to evaluate the prognostic impact of COPD on CHF patients.

Methods and results: The Norwegian Heart Failure Registry was used. COPD status was available for four-thousand-one-hundred-and-thirty-two patients (4132) (COPD, n=699 (17%); no COPD, n=3433 (83%)) from 22 hospitals, included from January 2000 to February 2008. Patients were followed up until death or December 2008. Females (29%) were equally represented in the two groups. Coronary artery disease was the main reason for heart failure in both groups (57% vs. 56%). At baseline COPD patients were older (71 vs. 70; P=0.0550), more likely to be smokers and to be diabetic. They had a higher heart rate and were less often on beta-blockers. They were more often on diuretics and aldosterone antagonists but had a lower creatinine. COPD patients presented more often in sinus rhythm and were less often on warfarin. Despite that left ventricular ejection fraction (LVEF) was distributed equally in both groups, COPD patients were more likely to be in New York Heart Association (NYHA) class III or IV (COPD, 63%; No COPD, 51%; P<0.0001). In the univariate analysis, COPD was a predictor of death of borderline significance (non adjusted hazard ratio (HR) for death, 1.16; 95% CI, 1.000 to 1.352; P=0.05) but it gained significance in the multivariate analysis (adjusted HR, 1.181; 95% CI, 1.009 to 1.382; P=0.0385). Other independent predictors of death were age, creatinine, NYHA Class - III/IV (adjusted HR, 1.427; 95% CI, 1.252 to 1.627; P <0.0001) and diabetes. Higher systolic blood pressure at baseline had a protective effect. Beta-blockers at baseline did not influence outcome.

Conclusion: COPD is independently associated with a poorer vital prognostic in patients with heart failure. COPD patients are overrated in terms of NYHA class in comparison with other heart failure patients with similar LVEF. Nonetheless, NYHA class remains the strongest predictor of death in these patients.

[P5685] Prognostic importance of co-enzyme Q10 in heart failure and interaction with statin therapy in the controlled rosuvastatin Multinational trial in heart failure trial (CORONA)

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Purpose: Co-enzyme Q10 (CoQ10) is an essential co-factor in mitochondrial oxidative phosphorylation and a lipophilic antioxidant. Statin therapy reduces CoQ10 synthesis and CoQ10 depletion has been suggested to be harmful in heart failure (HF). We investigated the prognostic importance of CoQ10 in patients with ischaemic systolic HF randomized to treatment with placebo (n=600) or rosuvastatin (n=591) 10 mg once daily in a substudy of CORONA.

Methods: The prognostic importance of baseline plasma CoQ10 concentration was tested in all patients randomized and in patients randomized to placebo and rosuvastatin separately, using multivariable model incorporating demographic characteristics, physiological measurements, co-morbidity and NT proBNP. Tests for interaction between treatment and baseline CoQ10 were also carried out (examining tertiles of CoQ10 and CoQ10 as a continuous variable).

Results: Patients in the lowest CoQ10 tertile were older, in a higher NYHA class, had more atrial fibrillation, a higher NT proBNP and lower lipids and eGFR. Although patients with a low CoQ10 had worse outcomes, low CoQ10 was not an independent predictor of worse prognosis in the multivariable analyses. Rosuvastatin reduced plasma CoQ10 concentration. Rosuvastatin treatment was associated with better outcomes than placebo treatment in patients with a baseline CoQ10 in the upper two tertiles but worse outcomes in those with CoQ10 in the lowest tertile (table). Tests for interaction between baseline CoQ10 concentration and treatment were of borderline significance – tertile analysis p=0.24 and analysis with CoQ10 as a continuous variable p=0.06.

Death rate per 100 patient years follow-up CoQ_{10} Tertile*	Placebo	Rosuva-statin	Adjusted HR (95% CI)
I	14.1	17.1	1.19 (0.86, 1.66)
II	11.8	9.2	0.82 (0.56, 1.22)
III	9.6	9.2	0.90 (0.61,1.34)

**Tertile I = lowest CoQ_{10} concentration.*

Conclusion: Plasma CoQ10 concentration is a marker of the severity of HF but is not an independent predictor of outcome. There may be an interaction between CoQ10 concentration and the effect of statins in HF.

[P3306] Left ventricular mechanical dispersion predicts ventricular arrhythmia in patients after myocardial infarction

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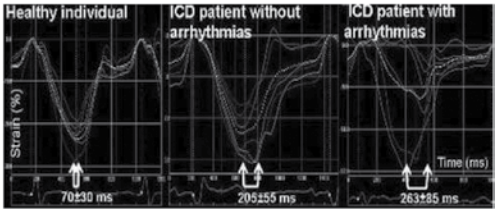
Purpose: Electrical dispersion in infarcted myocardium facilitates ventricular arrhythmia. Electrical dispersion leads to mechanical dispersion (heterogeneous contraction pattern) which can be assessed by myocardial strain echocardiography. We therefore hypothesized that mechanical dispersion by myocardial strain can predict risk for ventricular arrhythmias in patients after myocardial infarction (MI).

Methods: We prospectively included 33 post MI patients with ICD implanted according to secondary prevention criteria. After 1.7±0.8 years follow up, 20 had no and 13 patients had one or more arrhythmic events requiring appropriate ICD therapy. Healthy individuals (n=21) served as a control group. Contraction duration was measured as the time from ECG Q/start R to maximum LV shortening by strain. Standard deviation (SD) of contraction duration in a 16 LV segment model was calculated as a parameter of mechanical dispersion.

Results: EF did not discriminate ICD patients with arrhythmias from those without (38±8% vs. 38±13%, ns). ICD patients showed increased mechanical dispersion compared to healthy individuals (68±19ms vs. 22±10ms, P<0.001). Mechanical dispersion was significantly more pronounced in ICD patients with arrhythmia compared to those without (76±20ms vs. 61±15ms, P=0.03). Figure displays increased mechanical dispersion (right panel) in an ICD patient with recorded arrhythmic events. Arrows indicate difference between longest and shortest contraction duration.



Conclusions: Cardiac mechanical dispersion assessed by strain echocardiography was present in post MI patients compared to healthy individuals. Increased mechanical dispersion predicted further ventricular arrhythmias in post MI patients.

[P1438] Isoform-specific activation of NFAT signalling in ANGII and NA-stimulated neonatal cardiomyocytes of mice

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A fundamental mechanism involved in cardiac hypertrophy and subsequent heart failure is sympathetic adrenergic hyperactivity accompanied by activation of the renin-angiotensin system, in which noradrenaline (NA) and angiotensin II (ANGII) are primary effectors mediating hypertrophic, apoptotic and fibrotic events in the heart. As NA and ANGII have been shown to affect intracellular calcium in cardiomyocytes, we hypothesize that the calcium-sensitive calcineurin-Nuclear Factor of Activated T-cell (NFAT) signalling pathway is activated downstream of these factors. More specifically, our aim was to investigate isoform-specific activation of NFATs in ANGII and NA-mediat-

ed hypertrophy. The NFAT transcription factors have previously been shown to be important in the regulation of pathological hypertrophy in cardiomyocytes, and it is likely that each of the four isoforms, termed c1-c4, play specific roles in this regulation. However, little is known about the endogenous protein expression of the NFATs in cardiomyocytes, their differential regulation or their possible role in ANGII or NA signalling.

We have stimulated neonatal ventriculocytes from C57/B6 mice for 5, 10, 15 or 30 minutes or 24 hours with 1 µM ANGII or 100 µM NA. NFAT activity was quantified on Western blots using specific antibodies against the phosphorylated, inactive form of the isoforms.

Our results show that both ANGII and NA regulate the activity of NFATc4 and NFATc1, however neither of them regulate the activity of NFATc2 or NFATc3. More specifically, after 24 hours, the level of pNFATc4 was reduced by 31 and 19% by ANGII and NA stimulation, respectively. Similarly, pNFATc1 was reduced by 11 and 16% (n=4). ANGII reduced the level of pNFATc4 by 43% already after 10 minutes of stimulation and pNFATc1 by 41% after 30 minutes, while NA reduced pNFATc4 by 22% after 30 minutes of stimulation (n=3).

To our knowledge, we are the first to show isoform-specific activation of endogenous NFATs in isolated cardiomyocytes and we here demonstrate that the NFAT signalling system is controlled by both ANGII and NA. As today's main therapies for heart failure aim at antagonizing the adrenergic and renin-angiotensin systems, understanding their molecular mechanisms of action is of clinical importance, and our data indicate that ANGII and NA act partly through activation of the NFAT signalling system.

[2774] Non-invasive Wedensky Modulation of T- & RT-wave accurately predicts arrhythmic events

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Background & Objectives: Wedensky Modulation (WM) is based on subthreshold transthoracic electrical stimulation. The WM Index (WMIR) measured within R-waves accurately predicts arrhythmic events. We hypothesized WM Index measured within T-waves (WMIT) would accurately predict arrhyth-mic events.

Methods: WMIT index was prospectively evaluated post-hoc using patient ECG data. 268 post-myocardial infarction (post-MI) patients with ICD implantation had at least one 6 month follow-up com-pleted. Patients were placed into the WMIT-L group (WMIT≤0.5, n=203) or the WMIT-H group (WMIT>0.5, n=65). Cumulative ICD-treated arrhythmia event rates for the two WMIT groups were com-pared using Kaplan-Meier estimates.

Results: 36 first-year events (18%) for the WMIT-L group compared to 22 first-year events (34%) for the WMIT-H group yielded log-rank p=0.01. Comparing WMIT-L to WMIT-H, the hazard ratio for event rates was =1.9 at one year (95% CI of 1.1 to 3.3, Cox p<0.02). WMIT was significantly different from WMIR regarding future cardiac-related events prediction (p<0.0001). When combined with WMI study results to form an R-wave/T-wave index (WMIRT) the event rate prediction significantly improves, raising the sensitivity from 64% (WMIR) and 38% (WMIT) to 81%. The event rate for the WMIRT-L group (WMIRT≤0.5, n=106) was 10% compared to the event rate of 29% for the WMIRT-H group (WMIR>0.5, n=162).

Conclusion: Post-MI patients with a high WMIT may have significantly increased risk of life-threatening arrhythmia when compared to patients with a low index.

[159] Is it necessary to perform echocardiography in hypertensive patients with electrocardiographic left ventricular hypertrophy: The LIFE study?

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Background: Characteristics of hypertensive patients with left ventricular hypertrophy (LVH) diagnosed by electrocardiogram (ECG), echocardiogram (echo) or both are uncertain.

Methods: Baseline clinical, ECG and echo data and occurrence of the pre-specified composite primary study end-point (cardiovascular death, stroke and myocardial infarction) and hospitalized heart failure (a secondary endpoint) during 4.8 years randomized losartan- or atenolol-based treatment were recorded in 832 hypertensive patients aged 55-80 (mean 66) years in the LIFE echocardiography substudy. LVH was diagnosed by ECG Sokolow Lyon and Cornell product criteria and as LV mass/body surface area >116 g/m^2 in men and >104 g/m^2 in women.

Results: 156 patients had LVH only on ECG, 143 only on echo and 533 had LVH on both ECG and echo. Compared to patients with ECG LVH alone, patients with both ECG and echo LVH were older, more obese, had higher systolic blood pressure and included more women and patients with history of ischemic heart disease, and fewer African Americans (all p<0.05). Patients with combined ECG and echo LVH had larger echo left atrial diameter, higher end-systolic wall stress, lower LV ejection fraction and stress-corrected midwall shortening, and included more patients with aortic valve regurgitation. Incidence of the primary study endpoint did not differ among groups with echo and/or ECG LVH during 4.8 years follow-up, while incidence of hospitalized heart failure was 3.5 times higher in patients with both ECG and echo LVH (p<0.05). In Cox regression analysis, baseline combined ECG and echo LVH predicted hospitalization for heart failure [HR 3.46 (95% CI 1.20-10.01), p=0.022] independent of gender, study treatment and time-varying systolic blood pressure.

Conclusion: Performing echocardiography in hypertensive patients with ECG LVH helps identify patients with lower LV systolic function and higher risk for hospitalized heart failure.

[P3912] Normal reference ranges for atrial volumes and ejection fractions with real-time 3-dimensional echocardiography

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Purpose: Obtain normal reference ranges and intraobserver variability for left (L) and (R) atrial (A) volume indexes (VI) and ejection fractions (EF) with real-time 3-dimensional echocardiography (RT3DE) without the use of offline analyses.

Methods: RT3DE measurements of atrial volumes and EF were performed in 159 carefully screened healthy participants aged 29-79 years, considered free from clinical and subclinical diseases based upon a comprehensive screening visit including 2-dimensional echocardiography (2DE). The normal range was calculated as mean ± 2 standard deviations (SD) for maximal (max) and minimum (min) atrial VIs and EFs. In 23 participants selected at random two examinations were performed with a mean interval of five days for the assessment of intraobserver variability expressed as coefficient of variability (CV). The CV was calculated as SD of the difference divided by the mean of the variable under consideration.

Results: The normal ranges for left and right atrial volume indexes and EFs are presented in the table. The CVs for intraobserver variability were 9% for max LAVI, 21% for min LAVI, and 13% for LAEF. The respective CVs for RAVIs and RAEF were 8%, 14%, and 12%.

Table 1	Males, n=75	Females, n=84	Total study group, n=159
Max LAVI, ml/m^2	15-42	15-39	15-42
Min LAVI, ml/m^2	6-20	5-18	5-19
LAEF, %	46-77	44-80	45-79
Max RAVI, ml/m^2	18-50	17-41	18-47
Min RAVI, ml/m^2	7-22	5-18	5-20
RAEF, %	46-74	48-83	46-80

Normal ranges for left and right atrial volume indexes and EFs.

Conclusions: In view of the increasing awareness of the clinical importance and prognostic impact of atrial enlargement and decreased contractility, the normal ranges provided may be regarded as a useful tool in daily practice with a new, fast and fairly reproducible method.

[P3395] Increased sensitivity to ischemia in an early diabetic cardiomyopathy: the role of calcium handling

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Diabetic cardiomyopathy is characterized by early-onset diastolic dysfunction and late-onset systolic dysfunction. However, little is known about the mechanisms underlying the response of the diabetic myocardium to ischemia.

Aim: To study the left ventricular (LV) dysfunction and the role of calcium handling in infarcted diabetic mice in an early stage of diabetic cardiomyopathy.

Methods and Results: A cohort of male diabetic db/db and age-matched nondiabetic control mice at 10 wk of age was randomly assigned into Sham and myocardial infarction (MI) groups. MI was induced by coronary ligation. Standard echocardiography and tissue Doppler imaging were performed by high-resolution in-vivo imaging system, and diastolic sarcoplasmic reticulum (SR) calcium leak was measured in isolated cardiomyocytes using fluorescence microscope. One month after MI, 75% of the nondiabetic mice survived vs. 55% of the MI diabetic mice (p=0.04). LV dilatation was observed in MI diabetic mice compared to nondiabetic (p=0.03). Peak systolic tissue velocity (Sm) was 28% lower in MI diabetic mice than in nondiabetic group (nondiabetic: 19±1 vs. 17±2mm/s; diabetic: 18±2 vs. 13±2*mm/s, * p=0.05, for Sham and MI, respectively). Peak early diastolic tissue velocity (Em) was decreased in both Sham and MI diabetic mice (17±2* and 16±4* vs. 25±3 and 25±4 mm/s, * p<0.05, respectively). Diastolic SR calcium leak was unchanged in 10-wk diabetic mice compared with nondiabetic mice. However, increased diastolic SR calcium leak was observed in MI diabetic mice relative to MI nondiabetic mice.

Conclusion: The altered calcium homeostasis is an important determinant of sensitivity to ischemia and of loss of the ventricular function in the early stage of diabetic heart disease in diabetic mice. The identification of the cellular early damage could facilitate proper interventions and provide protection against development of diabetic cardiomyopathy in the later stages of the disease.

[P1674] Increased production of CXCL16 in experimental and clinical heart failure; a possible role in extracellular matrix remodeling

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Background: Although both experimental and clinical studies indicate a role for inflammation in the development of myocardial failure, knowledge about the production and functional role of the different inflammatory actors in heart failure (HF) remains incomplete. Based on its combined role in inflammation and vascular remodeling, we hypothesized a role for CXCL16 in the pathogenesis of HF.

Methods and Results: Our main findings were: (i) Patients with chronic HF (n=188) had significantly raised plasma levels of CXCL16 as compared with healthy controls (n=20), that significantly correlated with the degree of disease severity. (ii) Left ventricular (LV) tissue from patients with severe HF (n=8) showed enhanced production of CXCL16 compared to non-failing LV (n=6) as assessed by Western blotting. (iii) In mice exposed to pressure overload we found enhanced CXCL16 mRNA levels in the LV, with particularly high levels in those with decompensated hypertrophy. In mice with post-myocardial infarction (post-MI) HF, expression of CXCL16 was increased both in the infarcted and the non-infarcted areas of LV 3 and 7 days after coronary artery ligation, indicating early onset of increased CXCL16 production. The increase in CXCL16 in the tissue at 7 days post-MI was associated with increased CXCL16 levels both in cardiomyocytes and in non-cardiomyocytes (i.e., endothelial cells and fibroblasts). (iv) In vitro experiments showed that CXCL16 induces enhanced protein synthesis in neonatal rat cardiomyocytes, and promotes proliferation and matrix metalloproteinase (MMP) activity in myocardial fibroblasts accompanied by a significant increase in gelatinolytic activity. Furthermore, CXCL16 induced increased MMP activity in cardiomyocytes, primarily reflecting increased MMP-2 levels. (v) Using specific inhibitors in cell experiments, we showed that the effect of CXCL16 on fibroblasts involved activation of the c-Jun N-terminal kinases.

Conclusion: We demonstrate enhanced myocardial expression of CXCL16 in both experimental and clinical HF. The combined effect of CXCL16 on cardiomyocytes and myocardial fibroblasts suggest a role for CXCL16 in extracellular matrix remodeling and ultimately also in the development of HF.

[243] Increased levels of cytokines, vasoactive peptides, and growth factors in alveolar macrophages in heart failure

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Purpose: Pathophysiologic interactions between the heart and the lungs in heart failure (HF) are well recognised. Increased circulating levels of vasoactive peptides and cytokines known to be synthesised in the heart in HF may directly affect the lungs and potentially also vice versa. The purpose of the present study was to investigate whether expression of different factors known to be increased in the myocardium and/or the circulation in HF is also increased in alveolar macrophages in HF.

Methods: Twenty-two non-smoking HF patients (NYHA functional class II-IV) and 16 healthy controls were included in the study. Lung function and diffusion capacity were investigated by spirometry and DLCO, respectively. Induced sputum was performed after inhalation of hypertonic saline, and alveolar macrophages were isolated from the sputum by use of magnetic microbeads. Gene expression was examined in alveolar macrophages and in peripheral blood by real-time RT-PCR.

Results: Lung function and diffusion capacity were reduced in HF patients compared to controls with significantly lower FVC (88±4 vs. 112±3% of predicted value), FEV1 (84±4 vs. 104±3% of predicted value), and DLCO (69±4 vs. 101±3% of predicted value) ($P<0.05$ for all). Real-time RT-PCR demonstrated increased mRNA levels of several important cytokines, chemokines, vasoactive peptides, and growth factors in alveolar macrophages from HF patients compared to controls ($P<0.05$): endothelin-1 (1.8-fold), adrenomedullin (10-fold), TNFα (2.3-fold), IL-1β (3.9-fold), IL-6 (12-fold), MCP-1 (2.2-fold), IL-8 (4.2-fold), activin A (10.5-fold), and CTGF (3.2-fold). MIP-1α mRNA levels were not altered in HF. A similar increase in mRNA levels was not found in peripheral blood, indicating that the increase in gene expression is taking place in the lungs and is not a result of induction in monocytes in the circulation before entering the pulmonary compartment. mRNA levels of adrenomedullin, IL-6, MCP-1, IL-8, and CTGF in alveolar macrophages from HF patients displayed a negative correlation to left ventricular ejection fraction ($P<0.05$).

Conclusions: Several important cytokines, chemokines, vasoactive peptides, and growth factors are induced in alveolar macrophages in human HF. Further studies should clarify whether this induction affects pulmonary remodelling and whether the increased synthesis of these factors is reflected by increased release to the circulation and thus potentially may affect the failing myocardium.

[2049] Normal values for diastolic strain rate from combined speckle tracking and Doppler tissue imaging. Preliminary data from the HUNT3-study

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Purpose: Strain rate imaging is becoming a widely published method for quantifying both systolic and diastolic left ventricular (LV) function. The aim of the study is to establish normal values for global diastolic strain rate.

Methods: 1296 persons aged 20 to 89 which participated in the HUNT 3 study was randomised to echocardiographic examination which included colour tissue Doppler imaging Personell were eligible for inclution if they were without known heart diseases, diabetes or treated hypertension. 31 were excluded after echocardiographic examination.

Post-prosessing analysis was performed with a semi-automatic software with segmentation of the myocardium and tracking along ultrasound beam with tissue Doppler and tracking perpendicular to the ultrasound beam with speckle tracking. Segments with poor data quality were discarded manually. An 18 segment LV model was used. 22770 segments were analysed. Global diastolic strain rate was calculated as the average of accepted segments for E and A respectively. 98,9% had segments accepted for global strain rate measurement.

Results: The over all longitudinal diastolic strain rate E and A (s^{-1}) was (SD) 1,29 (0,29) and 0,98 (0,23).

Participants were divided into 3 age groups: <40, 40-59 and >60 years. In females longitudinal diastolic strain rate E (s^{-1}) was (SD) 1,56 (0,24), 1,36 (0,25) and 1,08 (0,20) respectively and in males 1,41 (0,23), 1,21 (0,22) and 1,03 (0,23). There was a very highly significant decrease of strain rate E with increasing age with p<0,0001 between all adjacent age groups. Mean strain rate E was higher in female groups than in male and the significance of difference between genders was very highly significant with p<0,0001.

Longitudinal strain rate A (s^{-1}) in females was 0,83 (0,17), 0,98 (0,22) and 1,37 (0,29) respectively. The increase in mean strain rate A with increasing age was very highly significant with p<0,0001 between adjacent age groups, but there was no significant difference between genders.

Conclusions: The study presents preliminary normal values for global diastolic strain rate E and A for both genders. Mean strain rate E decreases significantly with increasing age and is significant higher in females than in males. Mean strain rate A increases significantly with increasing age but there is no significant difference between genders. In all age groups there is a significant variability for both diastolic strain rate E and A which has to be taken into account in individual clinical decision making.

Abbreviations: LV - Left ventricle

SD - Standard deviation

[P4100] Prognostic value of inappropriate left ventricular mass in severe aortic stenosis

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Objectives: To define the prognostic impact of inappropriate left ventricular mass (iLVM) in patients with severe aortic stenosis (AS).

Background: In some patients with AS left ventricular (LV) myocardial growth exceeds individual needs to compensate LV hemodynamic load. This condition, named "iLVM", is a powerful marker of cardiovascular events in patients with arterial hypertension. How it influences prognosis in patients with AS is yet unknown.

Methods: We analyzed clinical and echocardiographic data from 200 patients (75±11 years, 54% hypertensive) with severe AS defined as valve area < 1 cm^2 and mean trans-aortic gradient > 40 mmHg. Patients were followed for 21±18 months. iLVM was diagnosed by echocardiography when the measured LV mass exceeded 28% of the expected value predicted from height, sex and stroke work.

Results: Event-free survival with end-points defined as death or aortic valve replacement or hospitalization for non-fatal myocardial infarction or heart failure in the 119 patients with appropriate and 81 (40%) with iLVM was 71 vs 54% at 1 year, 50 vs 27% at 3 years, and 38 vs 10% at 5-year follow up, respectively (all p < 0.02). Cox proportional hazard analysis identified iLVM as a strong predictor of adverse outcome independent of NYHA functional class, diabetes, transaortic valve peak gradient and extent of valvular calcification. Impact of iLVM on prognosis was significant both in asymptomatic and symptomatic patients. Among patients with LV hypertrophy, those with iLVM had a risk of adverse events 3.2-fold higher than counterparts with appropriate LV mass.

Conclusions: iLVM is common in patients with severe AS and has a negative influence on outcome, independent of severity of valve disease, diabetes and functional status. In patients with traditional LV hypertrophy, iLVM provides additional prognostic information.

[P509] Improved left- and right ventricular function after exercise training in COPD patients

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Objective: In general, patients with cardiovascular disease obtain more beneficial cardiac and fitness adaptation from aerobic interval training

(AIT) than moderate continuous exercise training (MCT). However, this has not been studied in chronic obstructive pulmonary disease (COPD) patients were lung ventilation is a clear limitation to exercise capacity. The aim of this study was to determine the effects of AIT Vs. MCT on cardiac function and fitness level in COPD patients.

Methods: 17 patients with COPD (65±7 years, 13 men) with FEV1 52.8±11 (% pred), FEV1% FVC 44±11 (% pred) and a smoking history of 34±9 packyears were randomly assigned to MCT (n = 7; 70% of peak heart rate (HR) for 47 minutes) or AIT (n= 10; 95% of peak HR for 4x4 minutes) 3/week/12 weeks.

17 age- and sex-matched healthy individuals served as reference group. Spirometry, maximal oxygen uptake (VO2max) and echocardiography were examined before and after the intervention period.

Results: Both AIT and MCT increased VO2max and work economy by 7% and 10% ($p<0.02$). Right and left ventricle systolic function was significantly lower in the COPD patients and improved by both modes of exercise training compared to controls (Table). Exercise training did not change, resting and peak HR, blood pressure, FEV1 and did not improve diastolic function.

Table 1. Echocardiographic variables	Control	AIT pre	AIT post	P-value	MCT pre	MCT post	P-value
SV ml	86	69.9	81.3	0.038	63.3	76.3	0.043
LVOT Vmax m/s	1.0	0.93	1.01	0.033	0.85	0.95	0.018
CO l/min	5.3	4.3	5.2	0.035	4.3	4.9	0.049
LV S' cm/s	8.0	6.8	8.0	0.005	6.9	8.1	0.018
LV E' cm/s	8.8	7.6	8.3	0.11	8.9	9.8	0.11
TAPSE mm		22.3	25.9	0.005	21.0	24.4	0.028
RV S' cm/s	14.1	12.5	14.4	0.017	12.1	13.9	0.027
RV Global SR s^{-1}		-1.34	-1.69	0.008	-1.48	-1.70	0.028

SV - stroke volume, LV - left ventricular, LVOT - LV outflow tract, RV - right ventricular, S' - tissue Doppler systolic velocity, E' - tissue Doppler early diastolic velocity, TAPSE - tricuspid annular plane systolic excursion, SR - strain rate.

Conclusion: Both exercise regimens improved systolic cardiac function, despite moderate effect on physical fitness. In contrast to other patient groups studied, exercise intensity seems not to be important to achieve beneficial cardiac effects in COPD patients.

[P863] Impact of stroke volume on cardiovascular events in hypertensive patients with electrocardiographic left ventricular hypertrophy. A LIFE substudy

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Background: Left ventricular (LV) geometric patterns carry different cardiovascular (CV) risk in hypertensive patients with electrocardiographic LV hypertrophy. We hypothesized that this difference may be mediated by different stroke volume (SV).

Methods: To test this hypothesis, the association between LV SV and combined CV death, stroke and myocardial infarction, the pre-specified primary study end-point, was assessed in Cox regression analysis using data from baseline and annual follow-up visits in 939 patients during 4.8 years of randomized losartan- or atenolol-based treatment in the Losartan Intervention For Endpoint reduction in hypertension (LIFE) echocardiography substudy.

Results: During follow-up, a total of 105 primary end-points occurred. At baseline, lower LV SV was associated with smaller body size, female gender, lower LV mass, higher relative wall thickness and more concentric LV geometry (all $p<0.01$). In time-varying multivariable Cox-regression analysis, lower in-treatment LV SV was independently associated with higher risk of CV events (HR 1.55 per 1 SD lower SV [1.25-1.91] $p<0.001$) while no significant associations with in-treatment concentric geometry nor systolic blood pressure were found (Table).

Variable	Hazard ratio	95% Confidence interval	p
Stroke volume* (per 1 SD lower)	1.55	1.25-1.91	<0.001
Relative wall thickness*	1.42	0.71-2.84	0.325
LV mass index* (per 1 SD higher)	1.34	1.14-1.57	<0.001
Systolic blood pressure* (per 1 SD lower)	1.22	0.99-1.49	0.061
Randomized losartan treatment	1.08	0.73-1.61	0.692
Framingham risk score at baseline	1.05	1.03-1.07	<0.001

**In treatment levels.*

Conclusion: In hypertensive patients with electrocardiographic LV hypertrophy participating in the LIFE echocardiography substudy, the relation between LV geometry and prognosis is partly explained by lower SV predicting higher risk of CV events.

[P4205] NT-proBNP keeps its predictive ability during several years of follow-up

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Objective: To analyze the importance of the biomarker NT-proBNP (BNP) by time of follow up after adjustment of other well-known risk factors in patients with stable advanced systolic heart failure.

Methods: Patients in CORONA with BNP available from baseline (n= 3366) were analyzed. The hazard function of death from heart failure (and of other events) was estimated by Poisson models as a continuous function of time in study and BNP together with other risk variables. The event hazard was of the form $\exp(\beta 0+\beta 1 \cdot x1+.+\beta k \cdot xk)$, where β0, β1, etc, were constants and x1, x2, etc, were the values of the variables. More precisely the time in study was modeled by connected linear pieces in specified intervals and interaction between logBNP and time in order to investigate whether the predictive power changed (decreased) with time. Endpoints were all-cause mortality (n= 940 deaths) and for death due to worsening of heart failure (n= 230 deaths). The HR for a difference in logBNP of one standard deviation was calculated by time of follow up. The HR for EF is given for a difference of 5%. The following variables at baseline have been used in the model: logBNP, ejection fraction (EF), diabetes mellitus (DM), age, sex, New York Heart Association (NYHA) class, hypertension and MI. Median follow up time was 32.8 months.

Results: logBNP was the strongest predictor of outcome both early and later during follow up. In the first six months of follow the HR for all cause mortality was 2.7 decreasing to 1.6 after 3 years with both $p<0.001$, for EF the figures were 1.2 $p=0.003$ and n.s. See figure below. Corresponding figures for death due to worsening of heart failure was 3.6 and 2.0 with both $p<0.001$, and 1.3 $p=0.007$ and 1.1 $p=0.04$, respectively.

Comments Neither a conventional Cox proportional hazards model nor a time dependent Cox regression model allow for the type of modeling we have done. The Cox model gives a strait line approximation of the curves.

Conclusions: Adding the biomarkers NT-pro-BNP to routine clinical variables can improve the prediction of cardiovascular risk in older patients with advanced systolic heart failure. NT-proBNP added substantial information as regards risk estimation in both short term and long time prediction. Interestingly, even a three-year-old BNP carries a stronger risk for death than a recent measurement of EF.

[1015] Impact of alcohol and smoking habits on the risk of new-onset atrial fibrillation in hypertensive patients with ecg left ventricular hypertrophy: the life study

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Objective: Atrial fibrillation (AF) is associated with increased cardiovascular events and the incidence of new-onset AF is increased by hypertension. Antihypertensive treatment reduces new-onset AF and treatment with the angiotensin receptor blocker losartan is more effective than the beta-1 selective blocker atenolol in this respect.

However, it is unclear how smoking and alcohol intake influence the risk of new AF during treatment which we assessed in the Losartan Intervention For Endpoint reduction in Hypertension (LIFE) study.

Methods: In LIFE, a double-blinded, randomized, parallel-group study, 9,193 hypertensive patients (46% men; mean age 67 yrs, average blood pressure 174/98 mmHg after placebo run-in) with ECG-documented left ventricular hypertrophy (LVH), randomized to once daily losartan- or atenolol-based antihypertensive therapy were followed for a mean of 4.9 years. At baseline 8,831 patients had neither a history of AF nor AF by ECG Minnesota coding, and were thus at risk of developing this condition during the study.

Results: ECG confirmed new-onset AF in 353 patients. New-onset AF occurred in 5.7% (n = 20) of patients with alcohol intake > 10 units/week vs. 3.9% (n = 333) patients with lower or no alcohol intake. Univariate Cox analyses showed that time-varying heart rate and systolic blood pressure, and baseline Cornell product ECG LVH, weight, height, total cholesterol, urine albumin/creatinine ratio, age, male gender, Caucasian ethnicity, prior congestive heart failure and Framingham risk score significantly predicted subsequent new AF. Intake of alcohol >10 units/week was predictive of AF in univariate Cox analysis, HR (95% CI) 1.6 (1.0, 2.5) p=0.042. Multivariate Cox regression analyses showed that age, male gender, time-varying systolic blood pressure, time-varying Cornell voltage-duration, time-varying heart rate, treatment allocation, and intake of alcohol >10 units/week (HR 1.8 (1.2, 2.9), p = 0.009) independently predicted new-onset AF.

Trend for impact of smoking was cancelled out in the Cox multivariate analyses, and there was no significant interaction between high alcohol intake and smoking.

Conclusions: High intake of alcohol was associated with an increased risk of new-onset AF maybe due to volume changes or to direct toxic effects on the left atrium. However, smoking habits did not influence the risk of new-onset AF in these hypertensive patients with ECG LVH.

[1100] Osteoprotegerin predicts long-term all-cause mortality in patients with chronic heart failure

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Purpose: Numerousreports confirm a pathogenic role for tumor necrosis factor (TNF)α in thedevelopment and progression of heart failure (HF).We have shown thatosteoprotegerin (OPG), a member of the TNF superfamily, may be implicated inthe pathogenesis of HF and that OPG levels are predictive of survival in patients withpost-infarction HF. However, prognostic data in patients with chronic HF arelacking.

Methods: The importance of plasma OPGas a risk factor for the primary endpoint (cardiovascular death, nonfatalmyocardial infarction, nonfatal stroke; events, n=411) and for all-causemortality (events, n=424) was investigated in a total of 1464 patients at least60 years of age [mean age 72±7 (SD), 341 (23%) women], in NYHA class II-IV, with ischaemic systolic HF receiving optimal pharmacologicaltherapy in the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA) population, randomly assigned to receive 10 mg rosuvastatin or placebopr day and followed for a median 32.8 months.

Results: OPG was strongly related to age, and patients in Tertile 1of OPG were at much lower risk than in those in Tertile 3. In multi-variableanalyses, OPG as a continuous variable, added no clear significant predictiveinformation for the risk estimation of the primary endpoint, beyond demographic,clinical and biochemical variables (left ventricular ejection fraction, NYHAclass, age, body mass index, diabetes, sex, intermittent claudication, heartrate, serum creatinine and apoA1), [HR1.05 (1.00-1.10), p=0.058]. However, OPG added independent predictiveinformation for all-cause mortality [HR 1.09 (1.04-1.14), p<0.001]. The primaryendpoint and total mortality were reduced by rosuvastatin in Tertile 1 of OPG [OPG<5420pg/ml;Cox adjusted HR 0.67 (0.45-0.99), p= 0.047, and 0.65 (0.43-0.98), p=0.038,respectively], but not in Tertile 2 or 3, interactionby treatment comparing the three OPG Tertiles showed p=0.076.

Conclusion: Circulating OPG is predictive of all-causemortality in patients with advanced chronic systolic HF of ischemic aetiologyindependently of conventional risk markers.

[P2223] Humoral changes, expression of endothelial selection ligands and bubble grade following SCUBA (self contained underwater breathing apparatus) dive

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SCUBA (S) diving has diverse risk to health. The decompression sickness (DCS) is initiated by gas bubbles. Since CD15 and CD15s are leukocytes antigens recognised as ligands by endothelial selectins, we assumed they could be markers for impaired vasodilatation following diving. Aim: To evaluate humoral changes, expression of endothelial selection ligands (CD15 and CD15s on leukocytes) and formation of gas bubbles following open sea S dive.

Methods: We performed an analysis of peripheral blood samples to detect the leukocytes that carries CD15 and CD15s and flow cytometry analysis of CD15 and CD15s to estimate any alteration in the membrane expression of those markers. The blood samples of 8 divers were collected 30 mins before and 50 mins after a dive to 54 m for 20 mins bottom time. The number of gas bubbles in the heart was monitored by ultrasound (according to Eftedal-Brubakk method).

Results: Gas bubbles were observed in the right side of the heart in all 8 divers. The maximal mean bubble grade was 1.9±1.9 bubbles/cm^2. There was a significant increase in total white blood cells after the dive (before 6.4±1.6:after 8.0±1.9 (x10 9/l) and neutrophils (3.8±1.4:5.7±1.9), the monocytes slightly but not significantly increased (0.3±0.2:0.4±0.2), while lymphocytes significantly decreased (2.3±0.5:1.8±0.6). There were no significant changes in the red blood cells and platelet counts. There was a significant increase in LDH (175.3±39.5: 206.1±44.8 (IU/l)), CK (158.0±55.1:242.3±75.4), CKMB fraction (4.0±2.1:11.3±2.1), Na (137±1.0:139.5±1.1 (μM)) and decrease in K (4.8±0.2:4.3±0.3). There were no significant changes in glucose, laktate, CRP and troponin. The proportion of CD15+monocyte increased significantly after the dive (before dive 38.4±19.3 (mean±SD):after 67±34.2 ($P<0.01$; t-test) as well as the CD15s monocyte (CD15s high) (3.2±1.4:6.7±4.0 ($P<0.05$; t-test). The expression of the CD15 and CD15s was continously low on lymphocites (CD3+CD19+).There were no correlation between CD15+monocyte expression and average bubble formation ($r=-0.56$; $P=0.17$), as well as with CD15s+monocytes ($r=0.43$;$P=0.29$).

Conclusion: The study suggests that biochemical changes, induced by SCUBA diving, primarily activate existing monocytes, rather that increase their number. The significant change of CD15+ monocytes and CD15s+high monocytes is not critical for bubble formation but may be involved in endothelial dysfunction. In addition, there were signs of muscle injury what supports the idea that inflammation may be part of decompression injury. The specific mechanisms involved in bubble formation await further examination.

[P2088] The frequency and intra-individual variation of clopidogrel non-responsiveness over time as measured by VerifyNow in patients with stable coronary heart disease

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Evaluation of in vitro treatment effect of clopidogrel has lately been given large attention, and different laboratory methods are now available for this purpose.

Aims and Methods: We investigated the frequency and stability of clopidogrel non-responsiveness in patients with stable coronary heart disease by use of the VerifyNow P2Y12 method. The method gives results both in platelet reaction units (PRU) and as %-inhibition. Patients on chronic single aspirin treatment (160 mg/d) were randomized to continue on aspirin or change to clopidogrel 75 mg/d. Follow-up time for laboratory assessements were 1 month and 1 year. All blood samples were drawn in fasting condition 24 hour after the last intake of medication.

The cut-off for response was defined as the 95%/5% percentile of all patients tested when

being on aspirin (n=227, mean age 62 yrs, 78% male), giving PRU value ≥170 and %-inhibition ≤24% to be non-responders.

Results: After 1 month on clopidogrel (n=89) the mean PRU-level was 144 (SD 69) and %-inhibition 43 (SD 25). After 1 year blood samples from 70 patients on clopidogrel were available and the mean PRU-level was 154 (SD 79) and %-inhibition 35 (SD 28), significantly different from 1 month (p=0.050 and p=0.013, respectively). The frequency of non-responders defined with PRU and % inhibition was 35% and 28%, respectively at 1 month and 43% and 41% respectively at 1 year. To evaluate the intra-individual variation of non-responsiveness over time we performed an agreement calculation, which shows an agreement of 67% when using the PRU with kappa =0.321 (p=0.001) and 77% with kappa =0.504 (p<0.001) when using the % inhibition, judged to be fair or moderate.

In conclusion, the frequency of clopidogrel non-responsiveness evaluated by the VerfyNow P2Y12 method is considerable, in agreement with data obtained with other methods. The intra-individual variation over time, although significant agreement, indicate that precaution has to be taken when judging the individual response. The concequences for clinical outcome is under investigation.

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