

# NORSKE ABSTRACTS PRESENTERT I STOCKHOLM

## **P425 : Asymptomatic arrhythmogenic right ventricular cardiomyopathy mutation carriers have impaired biventricular function by myocardial strain**

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**Purpose:** Life threatening arrhythmias can occur prior to apparent ventricular dysfunction in arrhythmogenic right ventricular cardiomyopathy (ARVC) mutation carriers. Myocardial strain by echocardiography is a sensitive tool for assessing ventricular function. The purpose of this study was to investigate right (RV) and left ventricular (LV) function by strain in asymptomatic ARVC mutation carriers not fulfilling current ARVC criteria.

**Methods:** We included 21 individuals (age 39±20 years) positive for an ARVC related mutation (18 Plakophilin2 and 3 Desmoplakin) diagnosed by family genetic screening. 20 age matched healthy individuals served as control group. Strain measurements were assessed by speckle tracking echocardiography. RV strain was calculated in a 6 segment model and LV global strain in a 16 segment model.

**Results:** ARVC mutation carriers had significantly reduced strain in RV compared to healthy individuals (-21.8±3.5% vs. -24.5±3.3%, p=0.01). In addition, LV strain was significantly reduced in mutation carriers compared to healthy individuals (-20.4±1.6% vs. -22.4±2.6%, p<0.01). LVEF did not differ between ARVC mutation carriers and healthy (63±4% vs. 65±5%, p=0.21).

**Conclusions:** Asymptomatic ARVC mutation carriers with no signs of the disease by current diagnostic guidelines had significantly reduced biventricular function assessed by strain echocardiography although LVEF was normal.

Reduced RV and LV strains indicate subclinical cardiac dysfunction in asymptomatic ARVC mutation carriers and that strain echocardiography may be helpful in decisions regarding preventive treatment.

## **P431 : Type of fibrosis predicts serious events in patients with obstructive hypertrophic cardiomyopathy**

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**Purpose:** Myocardial scarring (fibrosis) is an established pathophysiological feature associated with markers of sudden cardiac death (SCD) in patients with hypertrophic cardiomyopathy (HCM). The aim of this study was to describe the associations between pericellular and replacement-type fibrosis, serious events and risk factors for SCD in HCM-patients undergoing septal myectomy.

**Methods:** Twenty-four HCM-patients (54.2% men; mean age 58.0±10.4 years) underwent risk stratification for SCD followed by septal myectomy. Risk factors for SCD: prior cardiac arrest; family history of SCD; unexplained syncope; non-sustained ventricular tachycardia (nsVT); abnormal blood pressure response; hypertrophy ≥ 30 mm. Degree of pericellular and replacement fibrosis was determined (percentage of total specimen) on histopathology of surgical specimen. Patients with earlier myocardial infarction were excluded.

**Results:** Maximal interventricular septal thickness was 1.9±0.3 cm, intraventricular gradient was 57±23 mmHg, NYHA classification was 2.9±0.4 and CCS classification was 1.7±1.1. Patients with events (prior cardiac arrest, nsVT,

unexplained syncope) had significantly higher median percentage area of pericellular fibrosis than patients without events (30.0, range 17-62 v. 8.0, range 0-60,  $P=0.0094$ , Mann Whitney (Figure)). Patients with one or two risk factors had significantly higher mean percentage area of pericellular fibrosis than patients with no risk factors ( $26.9 \pm 23.8$  v.  $9.9 \pm 6.2$ ,  $P=0.034$ , unpaired t-test). Replacement fibrosis was not associated with events or with risk factors.

**Conclusion:** There is an association between increased area of pericellular fibrosis and serious events and risk factors for SCD in patients with obstructive HCM.

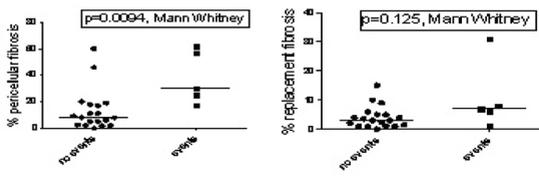


FIG Pericellular and replacement fibrosis

## P473 : Systolic and postsystolic velocities quantify low grade myocardial ischaemia by a miniaturized epicardial ultrasonic sensor

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**Background:** Early detection of myocardial ischaemia during heart surgery is essential to preserve ventricular function. More sensitive methods for continuous assessment of myocardial function are required. We tested a miniatur-

ized epicardial ultrasonic transducer for detection of graded myocardial ischaemia.

**Methods:** Coronary bypass from left internal mammary artery (LIMA) to left anterior descending coronary artery (LAD) was performed in six pigs to regulate coronary perfusion. Intermittent ischaemia was induced by reducing LIMA-flow to 75%, 50% and 25% for 5 min. Sub-endocardial peak systolic ( $V_{sys}$ ) and postsystolic ( $V_{pst}$ ) velocities were continuously obtained by two miniaturized epicardial ultrasonic transducers ( $\varnothing=5\text{mm}$ ) in the LAD and circumflex (Cx) area. In addition, radial strain was calculated as 2D strain by echocardiography. Left ventricular peak (LVP) and end-diastolic pressure (LVEDP) were measured with a micromanometer. Values are given as median (interquartile range).

**Results:** During all levels of flow reduction  $V_{sys}$  decreased significantly ( $p<0.05$ ) from baseline, while  $V_{pst}$  increased at 50% and 25% flow ( $p<0.05$ ) (fig.1A). These findings correlate with systolic ( $R=0.89$ ,  $p<0.01$ ) and postsystolic ( $R=0.64$ ,  $p<0.01$ ) radial strain. No changes were seen in the Cx area. Moderate flow reduction (75% and 50%) did not affect hemodynamic parameters, but a small decrease in LVP ( $p<0.05$ ) was seen when flow was reduced to 25% (fig.1B).

**Conclusion:** Mild and moderate myocardial ischaemia can be quantified by tissue velocity measurements from epicardial ultrasonic sensors. The findings are promising for continuously real-time monitoring of myocardial function during heart surgery, and with further miniaturizing of the sensor, also in the postoperative period.

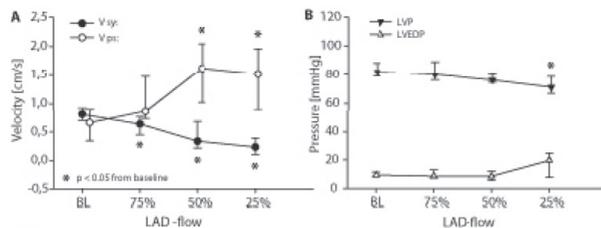


Figure 1. Data shown at baseline (BL) and after 5 min of reduced coronary flow to 75%, 50% and 25%. A. Myocardial peak systolic velocity ( $V_{sys}$ ) and peak postsystolic velocities ( $V_{pst}$ ), obtained from a miniaturized ultrasonic probe in the supply area of left anterior descending coronary artery (LAD). B. Left ventricular end-diastolic pressure (LVEDP) and LV peak pressure (LVP) measured with a micromanometer. Data is presented as median and interquartile range.

## P631 : Phosphorylation of syndecan-4 acts as a molecular switch of the pro-hypertrophic calcineurin-NFAT signalling pathway in the myocardium

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**Background:** Myocardial hypertrophy and heart failure develop in response to pressure overload, however, the signalling processes involved are poorly understood. We have previously linked syndecan-4, a transmembrane proteoglycan localized to focal adhesions and costameres in cardiomyocytes, to pathological myocardial hypertrophy. In brief, mice lacking syndecan-4 do not develop concentric hypertrophy after aortic banding. In the present study we demonstrate a crucial role for phosphorylation of syndecan-4 in regulating the central pro-hypertrophic calcineurin-Nuclear Factor of Activated T-cell (NFAT) signalling pathway in the myocardium.

**Methods/Results:** Pull-down experiments showed that recombinant calcineurin binds directly to syndecan-4. Immunoprecipitations showed that the association between endogenous calcineurin, its activator calmodulin and syndecan-4 was stronger in pressure-overloaded murine hearts, compared to sham. The syndecan-4 cytoplasmic domain is 28 amino acids long and composed of three regions; C1 and C2 are conserved between the four syndecans, while the V-region is specific for each of them. Peptide array experiments showed that calcineurin interacts with the V-region of syndecan-4 through its autoinhibitory domain. Phosphorylation of serine 179 (pS179) in C1 has previously been shown to be important for protein associations. We demonstrate that pS179 is reduced in patients with aortic stenosis and in pressure-overloaded murine hearts, compared to controls. More calcineurin immunoprecipitated with non-phosphorylated syndecan-4 than with pS179, indicating that reduced pS179 in syndecan-4 is involved in the hypertrophic response. Similarly, pull-down with pS179 or peptides mimicking constitutive pS179 (S179D/E) resulted in reduced binding of calcineurin. Activation of NFATc4 occurred in HEK293 cells transfected with a mutant mimick-

ing minimally phosphorylated S179 (S179A) whereas S179D/E mutations did not. Finally, we recently found that overexpression of calcineurin in HEK293 reduces pS179, indicating that calcineurin regulates its own binding and activation.

**Conclusions:** Our results indicate that in a pressure-overloaded heart, serine 179 in syndecan-4 is dephosphorylated by calcineurin, and calcineurin binds to the intracellular V-region through its autoinhibitory domain. Increased binding of calcineurin to syndecan-4 results in activation of NFATc4, a well-known pro-hypertrophic transcription factor. Conclusively, these data suggest a crucial role for phosphorylation of syndecan-4 and the syndecan-4-calcineurin interaction in development of myocardial hypertrophy.

## **P667 : Maintained increased proximal aortic stiffness 6 months after pre-eclamptic pregnancy**

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**Purpose:** Pre-eclampsia (PE) occurs in 3-10% of all pregnancies. The adaptation of the systemic arterial tree in these patients have not been well described. We performed a comparison of systemic arterial properties in women with PE in third trimester and at 6 months postpartum (PP), with women with normal pregnancy (NP) and follow-up as control.

**Methods:** 35 women (33±6 years) with PE and 65 (33±1 years) with NP were studied. Aortic root pressure and flow were obtained by calibrated right subclavian artery pulse trace, and aortic annular Doppler blood flow recordings. Systemic arterial properties were described by total arterial compliance (C), arterial elastance (end systolic pressure/stroke volume, Ea) characteristic impedance (parameter of proximal aortic stiffness, Z0), and peripheral arterial resistance (R). Parameters were estimated both by use of a 4-element Windkessel (WK) model

	At termNP	6 mo PPNP	At termPE	6 mo PPPE	P Δ (ΔNP vs ΔPE)
Mean arterial pressure (mmHg)	85±7	86±7.3	115±10*#	98±12#	<0.001
Heart rate (beats/min)	77±10*	66±7	75±10	70±11#	0.005
Cardiac output (L/min)	5.8±1.1*	4.9±0.9	6.4±1.2*#	5.4±1.2#	0.70
R (mmHg/(ml/s))	0.92±0.23*	1.10±0.29	1.13±0.24#	1.13±0.27	0.04
Z <sub>0</sub> WK (mmHg/(ml/ms))	65±24	68±22	85±32#	75±21#	0.06
Z <sub>0</sub> FD (mmHg/(ml/ms))	45±23*	50±21	64±32#	55±25#	0.003
C WK (ml/mmHg)	1.55±0.46*	1.40±0.45	1.34±0.40#	1.38±0.50	0.17
C PPM (ml/mmHg)	1.21±0.33	1.14±0.30	0.96±0.25	1.07±0.32#	0.06
Ea (mmHg/ml)	1.19±0.28	1.27±0.28	1.48±0.32#	1.43±0.37#	0.30

\*p<0.05 vs 6 months, #p<0.05 vs normal pregnancy. FD = frequency domain, PPM = pulse pressure method.

and by Fourier analysis of central aortic pressure and flow data.

**Results:** In PE pregnancy at term, Z<sub>0</sub>, Ea and R was higher and C was lower than in NP indicating a higher vascular resistance from the proximal aorta to the peripheral resistance vessels in PE. Although Z<sub>0</sub> was significantly reduced and C was increased in the PE group at 6 months PP, R was unchanged. Neither Z<sub>0</sub>, C, nor R attained normal values after PE pregnancy.

**Conclusion:** PE is characterized by a maintained elevated arterial proximal and peripheral resistance and lower compliance during and after pregnancy. The alterations in blood pressure cannot be explained changes in R, but is likely related to changes in Z<sub>0</sub> and C.

## Results

(Table)

## P757 : Symptoms in atrial fibrillation are related to oxygen uptake at anaerobic threshold

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**Purpose:** Exercise hyperpnea normally occurs after the anaerobic threshold in response to increased production of lactic acid. We hypothesized that symptoms and health-related quality of life (HRQoL) scores were associated with exercise capacity both at the anaerobic threshold and at peak oxygen uptake (VO<sub>2</sub> peak) in patients with permanent atrial fibrillation (AF).

**Methods:** 75 year-old patients with permanent AF, recruited from the general population, underwent maximal treadmill cardiopulmonary exercise testing, measuring VO<sub>2</sub> peak. The oxygen uptake (VO<sub>2</sub>) at anaerobic threshold was assessed by the modified V-slope method. The participants filled in the arrhythmia-specific questionnaire Symptom Checklist Frequency and Severity, where higher scores denote more or worse symptoms, in addition to the generic HRQoL questionnaire SF-36 where higher scores represent better HRQoL. SF-36 score results were pooled into a Physical Component Summary score (PCS) and a Mental Component Summary score (MCS). A similar program was also applied to 75 year-old subjects in sinus rhythm.

**Results:** AF patients (n=27) had VO<sub>2</sub> peak (mean ± SD) 22.7±5.5 ml/kg/min. VO<sub>2</sub> at the anaerobic threshold was 16.6±3.2 ml/kg/min. AF patients had PCS median (25th, 75th percentile) 41 (31, 51), MCS 56 (42, 61), Symptom frequency score 16 (9, 21) and Symptom Severity score 12 (8, 18). In AF patients Symptom frequency and Symptom severity scores were strongest related to VO<sub>2</sub> at the anaerobic threshold, and PCS score was related to VO<sub>2</sub> peak (Table 1). In 70 subjects with sinus rhythm PCS score was related both to VO<sub>2</sub> peak and VO<sub>2</sub> at the anaerobic threshold. (Table)

**Conclusion:** Symptoms in patients with permanent AF were related to the oxygen uptake at the anaerobic threshold, whereas physical HRQoL score was more related to maximal exercise capacity.

## P791 : Moderate hypothermia causes increased left ventricular wall stiffness and delayed filling in a porcine model

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Table 1. Spearman correlations

		Symptom frequency	Symptom severity	PCS
Atrial fibrillation	VO <sub>2</sub> at AT	- 0.62, p=0.006	- 0.64, p=0.006	0.41, p=0.102
	VO <sub>2</sub> peak	- 0.49, p=0.016	- 0.41, p=0.049	0.55, p=0.006
Sinus rhythm	VO <sub>2</sub> at AT	-0.22, p=0.078	-0.24, p=0.064	0.46, p<0.001
	VO <sub>2</sub> peak	-0.22, p=0.069	-0.19, p=0.132	0.49, p<0.001

VO<sub>2</sub> = oxygen uptake (ml/kg/min). AT = anaerobic threshold. PCS = SF-36 physical component summary score.

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**Introduction:** Hypothermia is used for neuroprotection in patients after cardiac arrest. However, hypothermia at 33°C also affects myocardial function. To elucidate these effects we studied myocardial function during hypothermia in a porcine model, with particular focus on diastolic dysfunction.

**Methods:** 8 anesthetized open chest pigs were cooled from baseline (38°C) to hypothermia (33°C). Left ventricle pressure (LVP) was measured with a micromanometer, and LV dP/dt as well as time constant ( $\tau$ ) of LV relaxation were calculated. Diastolic duration was measured from dP/dt<sub>min</sub> to following R on ECG and isovolumic relaxation time (IVRt) from dP/dt<sub>min</sub> to mitral valve opening. End diastolic (EDV) and stroke volumes (SV) were measured by 2D echocardiography. Transmitral flow velocities were obtained by echo/Doppler, and velocity time integral (VTI) of the E and A filling waves calculated as a measure of filling volume. Due to E-A fusion in some animals at 33° C, early diastolic filling was defined as the percentage of VTI occurring before following P on ECG. LV wall stiffness (KLV) was calculated from continuous pressure/m-mode recordings. Measurements were obtained at 38° and 33°C.

**Results:** Heart rate decreased during hypothermia, from 91±11 (mean±SD) to 79±9 beats per minute (p<0.05, paired t-test). Peak LVP decreased (85±12 to 68±11 mmHg, p<0.05), as did LV dP/dt<sub>max</sub> (P<0.05). SV and EDV were unchanged. Diastolic duration decreased (311±76 to 281±93 ms, p<0.05) while IVRt was prolonged at 33° (40±8 to 72±22 ms, p<0.05), resulting in a decreased filling time (274±62 to 219±66 s, p<0.05).  $\tau$  increased from 31±4 to 59±10 ms (p<0.05). E was reduced (0.7±0.1 to 0.5±0.2, p<0.05) while A increased (0.5±0.1 to 0.6±0.1, p<0.05), inverting the E/A ratio at 33°C (p<0.05). During normothermia, 67% of the SV entered LV early and E was completed before P in all animals. In contrast, during hypothermia early

LV filling was reduced to 33% of SV, and E not being completed before P on ECG in any animal., KLV increased indicating a stiffer LV wall in hypothermia (0.5±0.1 to

0.6±0.1 mm/mmHg, p<0.05).

**Conclusion:** Hypothermia resulted in a substantial decrease in LV diastolic filling time, whereas stroke volume was preserved in our model. We observed a marked reduction in early diastolic filling, consistent with shift from early- to late diastolic filling due to delayed LV relaxation and increased wall stiffness. Our findings during hypothermia suggest a compromised LV filling, more dependent on atrial contribution and a slower heart rate.

## P1092 : Complications and arrhythmia after percutaneous transluminal septal myocardial ablation (PTSMA). Results from Scandinavian HOCM Database

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**Background:** Due to the risk of PTSMA-related complications, myectomy maintains the gold standard for treatment of severely symptomatic patients with hypertrophic obstructive cardiomyopathy (HOCM). We analyzed the peri-procedural complications, arrhythmia and survival after PTSMA in the Scandinavian HOCM Database.

**Methods and results:** A total of 238 HOCM patients (age 60±14 years) were referred for 263 PTSMA procedures from 1999 to 2009 in



**Conclusion:** Our findings suggest a potential role for Stromelysin-1 both as a very early marker of LV remodelling and as an active participant in the healing and remodelling process following STEMI.

## **PI153 : Ticagrelor versus clopidogrel in patients with Acute Coronary Syndromes intended for a non-invasive management in the PLATO trial**

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**Purpose:** The potential benefit of potent dual anti platelet therapy have not been well studied in patients with acute coronary syndromes (ACS) intended for a management with a non- invasive strategy. Ticagrelor compared to clopidogrel reduced the primary composite endpoint of cardiovascular death, myocardial infarction and stroke with similar major bleeding rates through 12 months in the PLATelet inhibition and patient Outcomes (PLATO) trial.

**Methods:** Of the 18,624 patients hospitalized for ACS (with or without ST elevation) in the PLATelet inhibition and patient Outcomes (PLATO) trial, 5,216 (28%) were at the time of randomization specified as planned for a non-invasive management.

**Results:** Despite intended initial non-invasive management, coronary angiography was performed during the initial hospitalization in 2183 of 5216 patients (41.9%), PCI in 1065 (20.4%) and CABG in 226 (4.3%). Cumulatively, 40% of the patients underwent a revascularization procedure by the end of the trial follow-up. The incidence of the primary composite endpoint was reduced with ticagrelor vs. clopidogrel (12.0% vs. 14.3%, hazard ratio HR, 0.85; 95% confidence interval [CI], (0.73 - 1.00); P=0.045) and overall mortality was also reduced to (6.1% vs. 8.2% HR 0.75 (0.61 - 0.93), p=0.01. The incidence of

PLATO-defined total major bleeding was numerically higher with ticagrelor vs. clopidogrel, but was not statistically different (11.9% vs. 10.3%, HR 1.17; 95% CI (0.98 - 1.39), p=0.08). Of all patients who underwent coronary angiography during hospitalization, significant coronary disease was found in 596 patients (89%). Patients with no significant disease had numerically lower event rates compared to patients who were discovered with significant disease and the primary composite event rate was numerically lower in the ticagrelor group compared to the clopidogrel group, 14 (3.65%) v.s 22 (6.46%). Total mortality and major bleeding in these patients also occurred numerically less frequently in the ticagrelor group (9 (2.3%) vs. 15 (4.3%) and 7 (2.4%) vs. 20 (7.6%) respectively.

**Conclusion:** In NSTEMI ACS patients initially intended for non invasive management, the results with ticagrelor vs. clopidogrel were similar to the overall PLATO trial results indicating the broad benefits of intensified P2Y12 inhibition for patients with ACS across management strategies.

## **PI1439 : Cost-effectiveness of an early invasive versus conservative strategy in ST-elevation myocardial infarction treated with thrombolysis**

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**Purpose:** The health benefits and optimal timing of invasive treatment after thrombolysis is not established. In the NORwegian study on District treatment of ST-Elevation Myocardial Infarction (NORDISTEMI), a strategy with early transfer for percutaneous coronary intervention (PCI) after thrombolysis was compared to a conservative, ischemia-guided strategy in patients living in areas with long transfer distances to an invasive centre. The clinical outcomes of the study have been published recently, showing a reduction in the composite of death, reinfarction and stroke with the early invasive strategy. The aim of this substudy was to explore the health-related quality of life (HRQoL) and cost consequences of replacing conservative treatment with early angioplasty.

**Methods:** Patients with STEMI of < 6 h duration and >90 min transfer delays to PCI were treated with thrombolysis and randomised to either

early invasive (n=134) or conservative (n= 132) strategy. The HRQoL (Sintonen 15D) and use of health resources were assessed at baseline, 1, 3, 7 and 12 months follow-up. Data on in-patient care, out-patient care, transportations, pharmaceuticals and work absenteeism were collected. The costs of in-patient care were based on a detailed hospital accounting system. Other costs were based on fee schedules and market prices. Costs were analysed in a societal perspective and on the basis of intention-to-treat analysis. Bootstrapping with 1000 replications was used to test for differences.

**Results:** In total, 266 patients were randomised. Complete data on costs and HRQoL was available in 259 patients. The unadjusted mean differences in the number of quality adjusted life years (QALYs) as well as total costs after 12 months are shown in the table. When adjusting for the difference in baseline HRQoL, the mean difference in QALYs was reduced to 0.008 (95%CI= -0.027, 0.043).

	Early invasive	Conservative	Mean difference (95% CI)
Quality of life,baseline values	0.913	0.902	0.011 (-0,011,0.033)
QALYS	0.885	0.870	0.016 (-0.023,0.055)
Total costs (€)	19047	17861	1185 (-1683,4167)

**Conclusion:** There was no significant difference in health related quality of life or costs between early invasive and conservative strategy in STEMI patients treated with thrombolysis.

## P1454 : Coronary artery bypass graft patients experience unmet physical and psychosocial symptoms during their early rehabilitation. Results from the intervention group in a randomized controlled trial

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**Background:** Patients' experiences after CABG reveal unmet physical, psychological and educational needs after surgery. Foremost are symptoms of anxiety and depression that significantly predict increased morbidity and mortality. A structured information and psychological supportive psycho-educative method to perform health education and teaching coping skills are warranted.

**Purpose:** To implement an individualized intervention that explores the CABG patients`

symptoms, and promotes symptom management in the early rehabilitation.

**Method:** A randomized controlled trial recruited 101 patients (n = 101) to a home-based intervention at 2 and 4 weeks after surgery. The psycho-educative intervention consisted of an intervention protocol with 7 predefined themes known to be important. The narrative interviews were analyzed using thematic content analysis before sub-themes were quantified to give a background on how often specific experiences were addressed in the interviews.

**Results:** A total of 93 patients completed the intervention. Patients` experiences revealed 16 sub themes related to the 7 predefined themes. 1. Physical theme: postoperative pain (84% at 2 weeks/66% at 4 weeks), assessment of surgical site (55%/53%), numb feeling at chest surgery site (23%/22%), physical activity/exercise (almost 100%) and issues with compression stocking (7%/13%). 2. Prescribed discharge medication theme: uncertainty about

medications (15%/12%). 3. Anxiety and/or depression themes: living alone (12%/5%), changed sleep pattern (11%/9%), irritability "short fuse" (15%/7%), postoperative complications (16%/13%), security of grafts after CABG (10%/15%), return to work (13%/3%) and driving a car (7%/15%). 5. Sexuality theme: impotence (erectile dysfunction) (20% at 4 weeks). 7. Open themes: discharge phase (15% at 2 weeks) and missing link to hospital (6%/28%).

**Conclusion:** This study indicates the need to extend hospitals` discharge care for CABG patients to the first month after surgery for specific symptoms to enhance the patients` symptom management.

## P1470 : Intravenous ferric carboxymaltose improves quality of life in patients with chronic heart failure and iron deficiency regardless the presence of anaemia: an analysis from the FAIR-HF study

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**Background:** Patients with chronic heart failure (CHF) show impaired health-related quality of life (HRQoL), and iron deficiency may contribute to this.

**Aims and methods:** We evaluated the effect of iron repletion using intravenous ferric carboxymaltose (FCM) on HRQoL of iron-deficient CHF patients. The FAIR-HF trial randomized 459 CHF patients with impaired left ventricular ejection fraction and iron deficiency to FCM or placebo (2:1). HRQoL was assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the generic EQ-5D questionnaire (Visual Analogue Scale [VAS]) at baseline and after 4, 12, and 24 weeks of therapy. In both, higher scores indicate better HRQoL.

**Results:** Baseline HRQoL directly correlated with serum ferritin and percent transferrin saturation ( $r=0.11-0.18$ ,  $p<0.05$  for all) and FCM significantly improved HRQoL measures at all time points (see table). This effect was observed regardless of anaemia status ( $p$ -values for interaction: 0.93 [VAS] and 0.66 [KCCQ overall score]). (Table)

**Conclusions:** Intravenous FCM resulted in significant improvements in HRQoL during 24 weeks of therapy. The positive effects were seen after 4 weeks of treatment and were independent of anaemia status.

## P1480 : Does telephone follow-up after discharge for acute myocardial infarction affect patient experience with hospital care?

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**Background:** Patient experience assessments are increasingly used to describe health care from the patient's point of view and evaluate outcome of health care. In a context where existing follow-up services were poorly developed, we have previously demonstrated that a telephone follow-up intervention after discharge from hospital, showed positive effects after 6 months on the primary endpoint, the physical dimension of health related quality of life. No long term effects on physical or mental health related quality of life were found.

**Purpose:** To assess whether the telephone follow-up intervention improved patient's experience of quality of hospital care and analyse what factors are associated with satisfaction/dissatisfaction with hospital care.

**Method:** Out of 413 screened patients with a diagnosis of acute myocardial infarction, 288 patients consented to participate, and were randomized to an intervention or a control group. 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 in this study was collected through mailed questionnaires six weeks after discharge using the Patient

QoL at baseline and changes with therapy

	Baseline (mean±SD)		% Change from baseline					
	Placebo	FCM	week 4		week 12		week 24	
			Placebo	FCM	Placebo	FCM	Placebo	FCM
EQ-5D VAS	54.1±15.2	54.3±17.1	1.5	11.0 <sup>‡</sup>	4.4	14.5 <sup>‡</sup>	6.3	16.8 <sup>‡</sup>
KCCQ-OS	52.5±17.2	52.4±19.6	6.7	17.9 <sup>‡</sup>	8.8	23.3 <sup>‡</sup>	11.8	24.4 <sup>‡</sup>
KCCQ-CS	55.4±17.4	55.5±20.0	5.6	18.7 <sup>‡</sup>	6.0	22.9 <sup>‡</sup>	7.0	21.6 <sup>‡</sup>
KCCQ-TS	58.9±18.5	58.9±20.9	4.6	15.8 <sup>‡</sup>	5.6	19.7 <sup>‡</sup>	7.1	19.3 <sup>‡</sup>
KCCQ Domain Scores								
Physical limitation	51.9±19.9	52.1±22.6	4.4	15.7 <sup>‡</sup>	6.4	20.1 <sup>‡</sup>	8.7	20.5 <sup>‡</sup>
Symptom stability	52.5±14.7	53.7±17.0	3.0	23.6 <sup>‡</sup>	3.2	26.4 <sup>‡</sup>	8.6	24.6 <sup>‡</sup>
Symptom frequency	57.7±20.9	58.6±22.5	7.1	17.2 <sup>‡</sup>	5.5	20.5 <sup>‡</sup>	8.0	19.6 <sup>‡</sup>
Symptom Burden	60.2±17.8	59.3±21.0	3.5	18.2 <sup>‡</sup>	5.5	22.4 <sup>‡</sup>	5.5	21.1 <sup>‡</sup>
Self-efficacy	63.5±25.7	63.6±24.3	9.0	10.8	6.8	14.0 <sup>‡</sup>	9.4	15.2
QoL	48.0±21.3	47.4±22.1	7.5	18.3 <sup>‡</sup>	9.4	28.0 <sup>‡</sup>	14.1	31.2 <sup>‡</sup>
Social limitation	50.9±23.3	51.3±25.7	8.0	20.0 <sup>‡</sup>	14.1	23.6 <sup>*</sup>	16.7	25.5

\* $P<0.05$ ; <sup>‡</sup>  $P<0.01$ ; <sup>‡</sup>  $P<0.001$  all vs placebo.OS: overall score; CS: clinical summary; TS: total symptom.

Experiences Questionnaire and a questionnaire assessing perception of received information.

**Results:** There were no significant differences between the intervention- and control group on the ten summated rating scales in the Patient Experiences Questionnaire. Patients in the intervention group to a smaller extent experienced that there were need to improve information and follow-up after discharge, compared to the control group. Further, they experienced lack of information after discharge to a significant smaller extent. Factors associated with satisfaction/dissatisfaction with hospital care are to be presented and discussed.

**Conclusion:** The telephone follow-up intervention did not affect the patient's experience of hospital health care. However, the telephone follow-up contributed positively to satisfaction with follow-up and reduced the information needs experienced after discharge. Predictors of satisfaction/dissatisfaction with hospital care are identified.

## P1584 : Malignant arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy are related to right ventricular mechanical dispersion

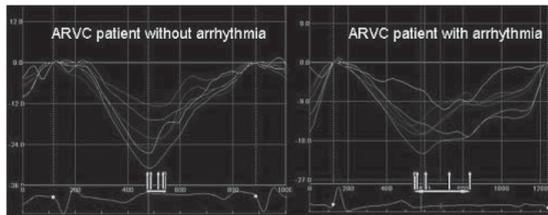
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**Background:** Life-threatening ventricular arrhythmias are frequent in arrhythmogenic right ventricular cardiomyopathy (ARVC). Electrical dispersion is a well known trigger of arrhythmias in these patients and may result in mechanical dispersion (heterogeneous contraction) which can be assessed by strain echocardiography. We hypothesised that mechanical dispersion by myocardial strain can predict risk for ventricular arrhythmia in patients with ARVC.

**Methods:** We included 59 patients with ARVC diagnosis based on clinical criteria (n=36) or genetic mutation criteria (n=23). Ventricular arrhythmia was documented in 36 (61%) patients.

ARVC related mutations were confirmed in 43 (73%) patients, (37 PKP2, 5 DSP and 1 RYR2). Mutation was not found in 16 (27%) patients. Strain was assessed by speckle tracking echocardiography. Contraction duration (CD) was measured as time from onset R on ECG to maximum right ventricular (RV) shortening by strain. Standard deviation (SD) of CD was calculated as a parameter of mechanical dispersion, in a 6 RV segment model.

**Results:** Patients with arrhythmias had decreased RV function by strain ( $-19 \pm 7\%$ ) compared to those without ( $-24 \pm 5\%$ ,  $p < 0.05$ ). RV mechanical dispersion in patients with arrhythmias was substantially increased compared to those without ( $53 \pm 25\text{ms}$  vs  $33 \pm 20\text{ms}$ ,  $p < 0.05$ ). Fig. shows increased mechanical dispersion in an ARVC patient with arrhythmias.



**Conclusion:** RV mechanical dispersion assessed by strain was increased and RV strain was decreased in ARVC patients with arrhythmias. These novel markers may become important tools in risk stratification of ARVC patients.

FIG Mechanical dispersion in ARVC patients

## P1629 : Cardiac Troponin T as a predictor of long time survival after cardiac resynchronization therapy

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**Aims:** Predicting response to cardiac resynchronization therapy (CRT) is challenging. High sensitive cardiac Troponin T (hsTnT) might predict response to CRT and identify patients at a high risk of experiencing severe cardiovascular events. We investigated whether baseline levels of hsTnT were associated with response to CRT and with severe cardiovascular events after long term follow-up.

**Methods:** 81 consecutive patients were included according to the current guidelines for cardiac resynchronization therapy. Biochemical, functional, and clinical parameters were assessed at baseline and at 3, 6 and 12 months follow up (FU), and mortality/cardiac transplantation after 46±6 months FU was investigated. Cardiac magnetic resonance imaging (MRI) and echocardiography were used to assess left ventricular function including viability and remodeling.

**Results:** 75 patients completed 12 months FU and after a follow-up of 46±6 months a total of 15 patients died, 13 of these from cardiovascular causes and 7 underwent heart transplantation. Baseline hsTnT < 15ng/L predicted response to CRT and was associated with a more favourable outcome with regard to severe cardiovascular events. Multivariate analysis found that presence of transmural scar tissue/fibrosis on MRI, use of statins and relatively lower ejection fraction on echocardiography were independently associated with higher concentrations of hsTnT at baseline. There was a strong correlation between hsTnT and NT-proBNP

**Conclusions:** HsTnT levels were elevated in the majority of HF patients that were scheduled for CRT. HsTnT levels predicted response to CRT as well long time survival. CRT is associated with a significant reduction in hsTnT concentration.

## PI1667 : Left ventricular function assessed by global strain in Hodgkin's lymphoma long-term survivors after adjuvant anthracycline chemotherapy- a two-dimensional speckle tracking echocardiographic study

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**Purpose:** Anthracycline therapy is associated with cardiovascular morbidity and mortality. There are, however, limited studies for long-term follow up of myocardial function in adult Hodgkin's lymphoma survivors receiving adjuvant anthracycline. Two-dimensional speckle tracking echocardiography (2D-STE) is an accurate angle-independent modality for quantification of regional and global left ventricular (LV) function. The aim of the present study was to investigate the long-term impact of adjuvant anthracycline therapy on left ventricular systolic function.

**Method:** Echocardiography was performed in 47 Hodgkin's lymphoma survivors 22±2 years following successful mediastinal radiotherapy with (n=27) or without (n=20) adjuvant anthracycline treatment, and in 20 healthy controls. LV function was assessed by left ventricular ejection fraction (LVEF) and global longitudinal strain, calculated as the average of peak systolic strain by 2D-STE in a 16 segments LV model.

**Results:** Both patient groups received similar dosage of radiation (41±3Gy vs. 41±1Gy, ns). Patients with adjuvant anthracycline treatment received a total dose of 313±92 mg/m<sup>2</sup>. Global longitudinal strain was reduced in patients receiving combined anthracycline and mediastinal radiation therapy compared to those receiving radiotherapy alone (-16.1±1.9% vs. -17.5±1.7%, p<0.05), and both groups had reduced strain compared to healthy controls (-20.4±1.7%, both p<0.05). LVEF did not separate between the patient groups (55±8% vs. 56±6%, ns), but patients had reduced function compared to controls (62±5%, both p<0.05).

**Conclusions:** Myocardial function was reduced in Hodgkin's lymphoma survivors two decades after successful treatment, indicating irreversible myocardial impairment. Patients receiving adjuvant anthracycline chemotherapy had additional negative long-term effect on left ventricular systolic function. Global longitudinal strain is an excellent tool for assessment of LV dysfunction following anthracycline therapy.

## 1839 : Influence of long-term vs. short-term endurance training in old males on left ventricular function

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**Purpose:** Myocardial function decreases with age. We hypothesised that aerobic interval training (AIT) improves diastolic function and lifelong endurance training ameliorate age-associated reduced myocardial function.

**Methods:** 10 old sedate males (72±1 yrs) performed AIT (4x4minutes) at 90% of maximal heart rate 3 times/week/12 weeks and results were compared with 11 male master athletes (MA) (74±2 yrs) and 10 young males (24±2 yrs). Echocardiography, including tissue Doppler, was recorded at rest and during submaximal bicycle exercise.

**Results:** End-diastolic volume (EDV) increased by 22% in the old group after intervention, but was still higher among the MA and young. The MA had a higher stroke volume (SV) both at rest and at exercise compared to the other groups. After intervention the elderly increased systolic

and early diastolic tissue velocity during exercise. (Table)

**Conclusion:** 12 weeks of AIT induced a significant improvement in diastolic function at rest and exercise among elderly. However, exercise training only partially improved diastolic function as age related diastolic changes were found both in sedentary and MA. MA compensated the reduced diastolic function by a higher EDV and SV, but 12 weeks of training was insufficient for the sedentary old to reach the same EDV.

## 1984 : Secretoneurin is a novel peptide increased in the myocardium and circulation in heart failure with cardioprotective properties

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Table 1. Old sedate vs. master athletes vs young

	Old (n=10)		Master Athletes (n=11)	Young (n=10)	P-value			
	Pre intervention	Post intervention			Master vs. old pre	Master vs. old post	Master vs. young	Old post vs. young
VO <sub>2max</sub> , ml/min/kg	35.0±5.0	39.0±7.2**	49.5±4.5	56.0±5.5	<0.01	0.01	<0.01	<0.01
Heart rate	69±8	59±7**	53±8	57±6	0.003	0.02	0.6	0.82
EDV, ml	102±13	124±15**	142±21	136±19	<0.01	0.02	0.5	<0.01
SV, ml	79±13	87±11**	102±16	85±22	0.002	0.003	0.001	0.5
E/A	0.89±0.2	1.18±0.24**	1.33±0.70	2.14±0.63	0.07	0.55	0.01	<0.01
Em, cm/s	6.9±1.5	7.5±1.3 ns	9.0±2.1	15.7±2.2	0.03	0.20	<0.01	<0.01
Sm, cm/s	7.3±0.8	7.6±1.1 ns	8.2±1.60	9.2±1.4	0.10	0.30	0.10	0.01
SV <sub>submax</sub> , ml	88±16	106±20**	132±26	100±21	<0.01	0.02	<0.01	0.25
Em <sub>submax</sub> , cm/s	12.2±2.1	13.7±2.2*	14.4±1.4	13.5±1.9	0.03	0.05	0.23	0.20
Sm <sub>submax</sub> , cm/s	8.4±1.5	10.8±1.6**	11.9±1.2	14.1±1.1	<0.01	0.20	<0.01	<0.01

\*p<0.05, \*\*p<0.01, ns, non-significant; VO<sub>2max</sub>, maximal oxygen uptake; EDV, end diastolic volume; SV, stroke volume; E/A, early/late mitral flow velocity; Em, early diastolic tissue velocity; Sm, systolic tissue velocity, submax, submaximal exercise.

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**Purpose:** Secretoneurin (SN) is a 33 amino acid peptide from the granin protein family. Chromogranin A (CgA), the principal member of the granin protein family, is regulated during heart failure (HF) development, and we hypothesized that SN would also be increased and play a pathophysiological role in HF.

**Methods:** SN production, levels, and localization were examined in a post-myocardial infarction (MI) HF mouse model. mRNA levels were measured by qRT-PCR, protein levels by radioimmunoassay (RIA) and immunoblotting, and localization assessed by immunohistochemistry. Plasma SN and CgA levels in 58 patients with chronic, stable HF recruited from an outpatient HF clinic were compared to levels in 20 age- and gender-matched healthy control subjects. Effect of SN on cardiomyocyte apoptosis and ischemia/reperfusion injury was also investigated.

**Results:** Pro-SN mRNA levels were 11.5 fold upregulated in the left ventricle (LV) of HF animals compared to sham-operated animals ( $p < 0.001$ ). This was a greater relative increase than observed for LV BNP (5.8 fold increase) and CgA (4.8 fold increase) mRNA levels. SN protein levels were also increased in the non-infarcted (35%) and infarcted region (85%) of the LV in HF animals. Furthermore, processing of pro-SN to shorter, functionally active SN fragments was enhanced in the myocardium of HF animals. In contrast, SN levels were not increased in lungs, spleen, liver, gastrointestinal tract or skeletal muscle in HF. Myocardial SN production was confined to the cardiomyocytes. Patients with chronic, stable HF of mainly moderate severity had increased circulating SN levels compared to control subjects ( $0.17 \pm 0.01$  vs.  $0.12 \pm 0.01$  nmol/L,  $p < 0.001$ ), and SN levels were superior to CgA, a proposed HF biomarker, for diagnosing HF (ROC-AUC 0.84 vs. 0.57,  $p = 0.001$ ). Adding SN to the perfusate in a global ischemia model of the isolated perfused rat heart reduced ischemia/reperfusion injury by 30% ( $p < 0.05$ ). SN also increased Erk1/2 and Stat3 phosphorylation in cardiomyocytes after short-term stimulation, and protected against hydrogen peroxide-induced cardiomyocyte apoptosis in vitro.

**Conclusion:** SN is regulated in the myocardium and circulation in HF, activates protective intracellular signaling pathways and has cardioprotective properties during myocardial ischemia and cardiomyocyte stress. SN may represent a novel endogenous protective agent in HF and a putative new cardiac biomarker.

## 1986 : Myocardial connective tissue growth factor (CCN2/CTGF) attenuates left ventricular remodeling after myocardial infarction and prevents ischemic heart failure

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**Purpose:** Myocardial CCN2/CTGF - connective tissue growth factor is induced in experimental models of heart failure as well as in human heart failure. However, its pathophysiological role in the development of ischemic heart failure remains unresolved.

**Methods:** Transgenic mice with cardiac-restricted overexpression of CTGF (Tg-CTGF) were compared with nontransgenic littermate control mice (NLC). Myocardial infarction (MI) was induced by ligation of the left coronary artery in Tg-CTGF ( $n = 22$ ) and NLC mice ( $n = 21$ ) and left ventricular (LV) remodeling and cardiac function was assessed after 4 weeks. Area at risk was estimated in a separate group of animals after perfusion with Evans blue dye, and was similar among Tg-CTGF and NLC mice. In addition, serum levels of CTGF (s-CTGF) were measured in 42 patients admitted to hospital for ST-elevation myocardial infarction (MI), 2 days, 1 week, 2 months and 1 year after percutaneous coronary intervention (PCI). Cardiac magnetic resonance imaging was performed at the same time points to determine infarct size and LV ejection fraction (EF).

**Results:** During the 4 weeks follow-up, there was significantly better survival in Tg-CTGF mice as compared to NLC mice; 63.6% vs. 38.1%,  $p < 0.05$ . In vivo pressure-volume analysis after 4 weeks displayed preserved cardiac performance in Tg-CTGF mice, as measured by dp/dt max,

LV end-diastolic and end-systolic pressure as well as cardiac output, and end-point analysis after excision of the hearts revealed attenuation of cardiac hypertrophy and pulmonary congestion in Tg-CTGF mice vs NLC mice (Heart weight/body weight ratio;  $5.3 \pm 0.2 \text{ mg/g}$ ,  $n=14$  vs  $8.0 \pm 0.9 \text{ mg/g}$ ,  $n=9$ ,  $p < 0.05$ ). Also, markers of myocardial remodeling, i.e. myocardial BNP and beta-myosin heavy chain mRNA levels, measured by real time qPCR analysis, were significantly less up-regulated in Tg-CTGF than in NLC hearts. Interestingly, in patients in which s-CTGF levels increased from day 2 after PCI until 2 months after PCI ( $n=21$ ), infarct healing was significantly improved and LV remodeling attenuated one year after the ischemic event. Consistently, EF was also significantly higher in these patients after one year, as compared to patients with unaltered or decreased s-CTGF levels ( $n=21$ ).

**Conclusion:** CTGF prevents development of experimental ischemic heart failure in mice, and increase in s-CTGF levels in patients after MI is associated with attenuated LV remodeling and improved cardiac function. These results may indicate cardioprotective effects of CTGF in ischemic heart failure.

### 2003 : The athletes heart: different training responses in African and Caucasian male elite football players

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**Purpose:** Previous studies have shown that male Caucasian athletes have increased LV mass and more marked eccentric remodelling of LV compared to non-athletes. Others have shown that Africans compared to Caucasians, are even more exposed to such structural changes. Thus, the aim of this study was to test these issues in a large scale study, and to investigate if there were

any other differences between Caucasian and African athletes in the remodelling of the four heart chambers in response to training.

**Methods:** As a part of the mandatory heart screening, 555 male elite football players (509 Caucasians and 46 Africans) and 46 Caucasian controls were examined: End-diastolic LV internal diameter (LVlDd), LV septal (IVSd) and posterior wall (LVPWd) thickness were measured by M-mode in parasternal long axis view, and LV mass was calculated by the equation  $(0.8 \times (1.04[(LVlDd + LVPWd + IVSd)^3 - (LVlDd)^3]) + 0.6g)$ , and the relative wall thickness (RWT) by  $(2 \times LVPWd / LVlDd)$ .  $115 \text{ g/m}^2$  was considered as upper normal limit. LV end-diastolic volume (LVedV) and end-systolic left atrial volume (LAesV) were calculated by Simpsons' s and area-length methods, respectively. End-diastolic area of the right ventricle (RVedA) and end-systolic area of the right atrium (RAesA) were also measured. Body mass index (BMI) and body surface area (BSA) were calculated. All echo measurements were performed blinded.

**Results:** There were no significant differences in age, BMI, BSA or blood pressure between the groups. 37 of the football players had a LV mass/BSA above  $115 \text{ g/m}^2$ . (Table)

**Conclusion:** Caucasian athletes had a larger increase of both LV and RV size than the Africans, while LA and RA increased similarly. Moreover, there were no significant difference in LV mass between Africans and Caucasians, but African athletes had markedly more concentric remodelled LV than the Caucasian athletes, which again showed a more concentric LV than the controls.

### 2025 : Regional and diastolic function improves after acute myocardial infarction treated with acute PCI, but is not influenced by injection of autologous mononuclear bone marrow cells. An ASTAMI sub-study

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	LV mass (g)	RWT	LV edV (ml)	LA esV (ml)	RVedA (cm <sup>2</sup> )	RAesA (cm <sup>2</sup> )
Caucasian Controls, n=46	149.7±35.6 <sup>‡</sup>	0.31±0.06 <sup>‡</sup>	124.7±23.9 <sup>†</sup>	55.6±20.0 <sup>‡</sup>	24.2±4.0 <sup>†</sup>	17.6±3.9 <sup>‡</sup>
Caucasian athletes, n=509	181.6±34.4 <sup>*</sup>	0.33±0.06 <sup>*‡</sup>	146.9±27.8 <sup>*‡</sup>	73.6±20.8 <sup>*</sup>	27.5±4.9 <sup>*‡</sup>	21.5±3.9 <sup>*</sup>
African athletes, n=46	181.3±37.5 <sup>*</sup>	0.37±0.06 <sup>*†</sup>	131.1±24.1 <sup>†</sup>	72.2±20.5 <sup>*</sup>	24.8±3.8 <sup>†</sup>	21.6±3.7 <sup>*</sup>

<sup>\*</sup> $p < 0.005$  vs. controls, <sup>†</sup> $p < 0.005$  vs. Caucasian athletes, <sup>‡</sup> $p < 0.005$  vs. African athletes.

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**Purpose:** To investigate the long term effects of intracoronary injection of autologous mononuclear bone marrow cells (mBMCs) on regional and diastolic left ventricular (LV) function in acute myocardial infarction.

**Methods:** In the Autologous Stem cell Transplantation in Acute Myocardial Infarction (ASTAMI) study, 100 patients with anterior wall ST-elevation myocardial infarction treated with acute PCI were randomized to receive intracoronary injection of mBMCs or not. Transthoracic echocardiography (GE Vingmed Vivid 7) was performed at baseline, 3, 6, 12 months and 3 years. Peak negative systolic strain ( $\epsilon_s$ ) was measured by speckle tracking in a 16 segment model of the LV. Segments were classified as LAD territory (6 segments) or remote (10 segments). Diastolic function was evaluated by Doppler mitral valve and pulmonary vein flow patterns, and mitral annular velocities.

**Results** (table): There were no significant differences between groups in LV ejection fraction, regional function by strain, or diastolic function during 3 years follow-up. Both groups improved global and regional LV function during the first 3 months after AMI, without further change.

**Conclusion:** Both groups in ASTAMI experienced recovery of global, regional and diastolic left ventricular function, as expected in AMI after acute PCI with best medical care. We did not find any additional beneficial effect of intracoronary mBMC injection.

## P2250 : Germany lags behind other European Countries and Canada in LDL-cholesterol goal achievement according to existing guidelines: results of the Dyslipidemia International Study

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**Background:** Chronic statin treatment is well established for patients with dyslipidemia and high risk for subsequent cardiovascular events and its use is widespread in clinical practice. However, many patients do not achieve recommended lipid targets in clinical practice.

**Methods:** Between June 2008 and February 2009, 2,987 primary care physicians, cardiologists, endocrinologists and internists in 11 European countries and Canada enrolled 22,063 consecutive statin-treated outpatients into DYSIS (Dyslipidemia International Study) to assess the prevalence of dyslipidemia on chronic statin treatment. ESC recommendations were used to classify patient's risk and define the LDL-C goal. We compared the level of LDL-C goal achievement in Germany with other European countries and Canada.

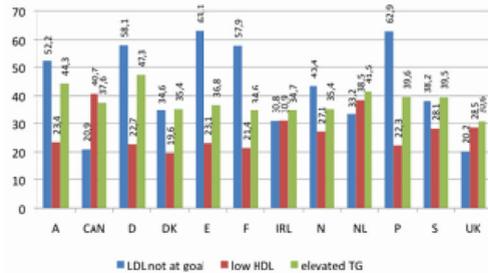
**Results:** Germany enrolled 4260 patients (19.3%). Patients in Germany were older (67 vs 65 years), more often obese (BMI >30 kg/m<sup>2</sup>: 35.4% vs 33.0%), more often had manifest ischemic heart disease (46.1% vs 34.5%), cerebrovascular disease (12.7 vs 8.8%), peripheral artery disease (13.0% vs 9.6%) and diabetes (45.7% vs 37.5%). Most of

	Baseline		3 years		p-value*
	mBMC	Control	mBMC	Control	
LVEF (%)	45.7±9.4	46.9±9.6	47.5±9.0 <sup>†</sup>	46.8±8.6	0.87
WMSI	1.78±0.22	1.75±0.19	1.57±0.34 <sup>†</sup>	1.58±0.29 <sup>†</sup>	0.48
$\epsilon_s$ (global)%	-13.0±3.1	-13.1±2.4	-15.1±3.3 <sup>†</sup>	-15.5±3.5 <sup>†</sup>	0.75
$\epsilon_s$ (LAD) %	-9.7±3.9	-9.9±3.5	-12.2±4.0 <sup>†</sup>	-12.8±4.4 <sup>†</sup>	0.45
$\epsilon_s$ (remote) %	-14.9±3.1	-14.9±2.5	-16.9±3.2 <sup>†</sup>	-17.1±3.3 <sup>†</sup>	0.93
E/A- ratio	1.24±0.53	1.23±0.54	0.99±0.31 <sup>†</sup>	1.01±0.37 <sup>†</sup>	0.65
EdecT (ms)	161±43	176±57	194±43 <sup>†</sup>	211±56 <sup>†</sup>	0.37
E/E'	14.7±4.7	14.8±5.1	12.9±3.8 <sup>†</sup>	11.9±4.2 <sup>†</sup>	0.31

Mean ± SD. \*p-value for difference in change over time between groups (treatment effect) by mixed model linear regression analysis on all available data (baseline, 3, 6, 12 and 36 months). <sup>†</sup> p<0,05 for change from baseline within group.

the patients in Germany received simvastatin (84.0% vs 39.5%).

**Conclusion:** Despite an even larger cardiovascular risk profile of patients, Germany had one of the highest rates of patients not at recommended LDL-C goal under chronic statin treatment. In addition, a substantial number of patients in Germany had abnormal levels of HDL-C and triglycerides. These results demonstrate the gap between guideline recommendations and clinical practice and the need for a more intensive and comprehensive lipid management in this population.



Dyslipidemia despite statin treatment

## P2251 : Predictors of LDL-cholesterol goal achievement in secondary prevention in Europe and Canada: results of the Dyslipidemia International Study

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**Background:** The majority of patients with dyslipidemia are currently treated with a statin. However, many patients do not achieve recommended lipid targets, and persistent lipid abnormalities will continue to contribute to cardiovascular risk in statin-treated patients.

**Methods:** Between June 2008 and February 2009, 2,987 primary care physicians, cardiologists, endocrinologists and internists in 11 European countries and Canada enrolled 22,063 consecutive statin-treated outpatients into DYSIS (Dyslipidemia International Study) to assess the prevalence of dyslipidemia on chronic statin treatment. ESC recommendations were used to classify patient's risk and define the LDL-C goal. We determined predictors of LDL-C goal achievement in clinical practice.

**Results:** Overall nearly half of all patients had LDL-cholesterol not at goal (48.5%). (Table)

**Conclusion:** Patients with already known ischemic heart disease, cerebrovascular disease or diabetes were more likely to achieve the recommended LDL-C goal. Treatment with higher statin dosages, with ezetimibe and treatment by internists/cardiologists/diabetologists were independent predictors of better LDL-C goal achievement in clinical practice.

Covariates	OR (95% CI)	Pr > ChiSquare
More likely to achieve LDL-C goal		
Statin dose: >80 mg/day Simvastatin equivalent	2.84 (2.50-3.24)	<0.0001
Statin dose: 20-40 mg/day Simvastatin equivalent	1.86 (1.69-2.05)	<0.0001
Ischemic heart disease	1.54 (1.44-1.65)	<0.0001
Diabetes mellitus	1.51 (1.41-1.61)	<0.0001
Specialists	1.35 (1.26-1.44)	<0.0001
Ezetimibe	1.25 (1.13-1.39)	<0.0001
BMI ≥30 kg/m <sup>2</sup> (obesity)	1.24 (1.16-1.33)	<0.0001
Age ≥70 years	1.22 (1.15-1.31)	<0.0001
Cerebrovascular disease	1.22 (1.10-1.36)	0.0002
Less likely to achieve LDL-C goal		
1st grade fam. hist. of premature CVD	0.91 (0.85-0.97)	0.0046
Peripheral artery disease	0.87 (0.79-0.96)	0.0079
Sedentary lifestyle	0.86 (0.81-0.91)	<0.0001
Alcohol consumpt. >2 units/week	0.84 (0.78-0.89)	<0.0001
Heart failure	0.80 (0.71-0.89)	<0.0001
Female	0.76 (0.71-0.81)	<0.0001

## P2258 : Peptic ulcer prevention by esomeprazole 20 mg and 40 mg once daily in patients taking low-dose acetylsalicylic acid for secondary cardiovascular prevention

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**Background:** Low-dose acetylsalicylic acid (ASA) is a mainstay of secondary cardiovascular (CV) disease management, but may be associated with peptic ulcers (PU) and adverse upper gastrointestinal (GI) symptoms, which may interrupt low-dose ASA treatment adherence. This post-hoc analysis of the OBERON study (NCT00441727; 204 centres in 20 countries) assessed the efficacy of esomeprazole 20 and 40mg once daily (od) in reduction of PU (gastric/duodenal) among patients (pts) taking low-dose ASA (75–325mg) for secondary CV prevention.

**Methods:** Helicobacter pylori-negative (at screening visit) secondary CV prevention patients receiving low-dose ASA with  $\geq 1$  of the following criteria were included: age  $\geq 65$ y;  $\geq 18$ y with history of PU;  $\geq 60$ y with stable coronary artery disease or upper GI symptoms and  $\geq 5$  peptic erosions, or low-dose ASA use begun within 1 month of study entry. Pts with reflux esophagitis (Los Angeles grade C or D), previous ulcer complications or PU at baseline endoscopy, or continual use of nonsteroidal anti-inflammatory drugs were excluded. Pts were randomized to esomeprazole 20 or 40 mg od, or placebo for 26 wks. Endoscopy-confirmed PU at weeks 8 and 26 or upon withdrawal were analysed overall, and in a further subset of secondary CV prevention patients taking ASA 75–100mg. Upper GI symptoms were also assessed by Reflux Disease Questionnaire (RDQ).

**Results:** Overall, 1257 evaluable pts (58.2% men, mean age 63.8yrs) used low-dose ASA for secondary CV prevention. Of these, 968 (77%) used ASA in the range of 75–100mg. Esomeprazole 20 and 40mg od significantly reduced the frequency of PU at 26 wks, relative to placebo, among secondary CV pts overall, and in the group taking ASA 75–100mg ( $p \leq 0.0002$  for all comparisons; Table). Esomeprazole 20 and 40mg significantly reduced the frequency of gastric and duodenal ulcers compared to placebo and also reduced the occurrence of upper GI symptoms. (Table)

**Conclusions:** Esomeprazole 20 and 40mg od is effective in preventing the occurrence of PU as well as upper GI symptoms in pts who take low-dose ASA for secondary CV prevention, including those pts using ASA within the 75–100mg range.

## P2317 : Attainment of cholesterol goals with Fenofibrate 160 mg/Pravastatin 40 mg Therapy in Type 2 Diabetic patients with combined hyperlipidemia in primary prevention, not at goal on Simvastatin 20 mg

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**Purpose:** Patients with type 2 diabetes (T2D) often require combination therapy to achieve goals of LDL-cholesterol (LDL-C) and non HDL-cholesterol (non-HDL-C). This study evaluated the efficacy of Fenofibrate (F) 160 mg/Pravastatin (P) 40 mg fixed dose combination in T2D patients without cardiovascular disease and not at goals on Simvastatin (S) 20 mg.

**Methods:** This was a multicenter, randomized, double-blind, parallel group study. After a 6-week run-in period on S20 mg, 291 patients with non-HDL-C  $\geq 130$  mg/dL or LDL-C  $\geq 100$  mg/dL and triglycerides (TG)  $\geq 150$  mg/dL, but  $\leq 600$  mg/dL were randomized for a 12-week treatment period to the F160 mg/P40 mg fixed-dose combination or S20 mg, followed by a 12-week open-label period where all patients received the F160 mg/P40 mg combination therapy. The primary efficacy comparison was the mean percent changes in non-HDL-C. Secondary end-points included achievements of non-HDL-C and LDL-C targets.

**Results:** F160 mg/P40 mg combination therapy resulted in significantly greater decrease in non-HDL-C (-12.9% (F160 mg/P40 mg) vs -6.8% (S20 mg);  $p=0.008$ ). No difference was found between groups on LDL-C levels. At the 12-week endpoint, the proportions of patients achieving the non-HDL-C target ( $< 130$  mg/dL) were 42.4% in the F160 mg/P40 mg group and 24.1% in the S20 mg group ( $p=0.001$ ). No significant difference was found in the proportion of patients having attained the LDL-C targets ( $< 100$  mg/dL) (34.0% in the F160 mg/P40 mg group vs 27.6% in the S20 mg group;  $p=0.24$ ). Combined non-HDL-C and LDL-C target at 12-week was achieved more frequently by patients treated with the F160 mg/P40 mg combination (28.5% vs 17.9%;  $p=0.034$ ). Combination therapy was generally well tolerated with a safety profile consistent with the individual treatments. Especially

Peptic ulcer incidence (26 wks)

ASA dose	Esomeprazole 20mg	Esomeprazole 40mg	Placebo
75-325 mg	(n=421) 1.4%(0.2%;2.6%)	(n=435) 0.5%(-0.2%;1.3%)	(n=401) 7.5%(4.8%;10.3%)
75-100 mg	(n=323) 1.1%(-0.1%;2.3%)	(n=332) 0.7%(-0.3%;1.7%)	(n=313) 7.2%(4.2%;10.3%)

no cases of myopathy or rhabdomyolysis were reported.

**Conclusion:** The Fenofibrate 160 mg/Pravastatin 40 mg fixed-dose combination was more effective than Simvastatin 20 mg in achieving lipid targets in type 2 diabetic patients with combined hyperlipidemia in primary prevention

## P2346 : Mesenchymal stem cells from skeletal muscle and adipose tissue improve LV function after myocardial infarction, but do not differentiate into cardiomyocytes

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**Purpose:** Head-to-head comparison of the effects of intramyocardial injection of human skeletal muscle derived mesenchymal stem cells (MD-MSCs), adipose tissue derived mesenchymal stem cells (AT-MSCs), and placebo after acute myocardial infarction in rats.

**Methods:** LAD was ligated in athymic rats to induce acute myocardial infarction. Day 6, echocardiography was performed. Day 7 after ligation, 82 rats were randomized to receive intramyocardial injection of 3 mill. MD-MSCs, 3 mill. AT-MSCs or placebo. Day 35, echocardiography was repeated, animals were euthanized, and hearts were formalin-fixed and paraffin-embedded. On tissue sections, in situ hybridization against the human specific ALU- sequence was performed to identify transplanted cells. Immunofluorescence with anti- SMA, -troponin, -desmin, -Nkx 2.5 and -CD 31 were performed to clarify the MSC phenotype after injection. For statistics, ANOVA with Tukey correction for post-hoc analyses was used.

**Results:** Fractional shortening increased by  $2.8 \pm 3.7\%$  in the MD-MSC group ( $p=0.01$  vs placebo) and  $1.9 \pm 4.0\%$  in the AT-MSC group ( $p=0.06$  vs placebo) compared to a  $-1.2 \pm 4.9\%$  decrease in the placebo group. Ejection fraction (area-length method) increased by  $4.9 \pm 6.8\%$  in the MD-MSC group ( $p<0.001$  vs placebo) and  $2.5 \pm 7.6\%$  in the AT-MSC group ( $p=0.03$  vs placebo) compared to a  $3.9 \pm 7.3\%$  decrease in the placebo group. Change in LVEDDm did not differ significantly between groups. Clusters of transplanted human cells were identified by in situ hybridization after 4 weeks. ALU- positive

cells did not stain positively for SMA, Troponin, Desmin, CD 31 or Nkx 2.5.

**Conclusion:** Both MD-MSCs and AT-MSCs improved LV function compared to placebo, with a trend for better effect of MD-MSCs. Injected cells were identified after 4 weeks, but did not transdifferentiate into cardiomyocytes, endothelial cells or smooth muscle cells, suggesting other mechanisms for the beneficial effect.

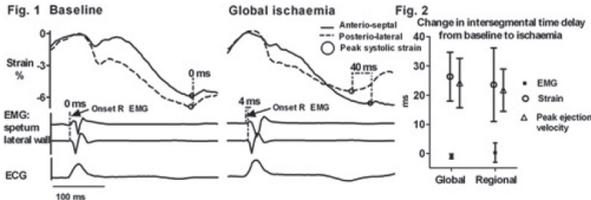
## P2388 : Dyssynchrony in regional and global acute ischemia: mechanical or electrical?

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**Purpose:** The most likely mechanism for response to cardiac resynchronization therapy (CRT) is correction of left ventricular (LV) electrical dyssynchrony. Therefore classifying the observed dyssynchrony as mechanical or electrical is important to accurately select patients. We investigated the mechanism of dyssynchrony observed in acute regional and global ischaemia of the LV.

**Methods:** In 12 anesthetized dogs with LV micromanometers we measured intramyocardial electromyograms (IM-EMG) and myocardial segment lengths by sonomicrometry. The segment lengths were used to measure regional contraction as strain and shortening velocity. Mechanical and electrical dyssynchrony were assessed by peak systolic velocity (S'), peak systolic strain (PS) and onset R in IM-EMG (Fig. 1). Measurements were performed in 6 LV segments at baseline, after 15 minutes of LAD-occlusion ( $n=8$ ) and after global ischaemia induced by intracoronary microsphere injection ( $n=4$ ). Dyssynchrony was assessed as peak intersegmental time delay (ITD) by subtracting the latest from the earliest measurement in each individual.

**Results:** There was no electrical dyssynchrony during ischaemia compared to baseline with minimal changes in EMG during global ( $0.3 \pm 6.7$  ms (mean $\pm$ SD)) and regional ischaemia ( $-1.0 \pm 2.7$ ms). However, mechanical dyssynchrony was observed with an increase in ITD of  $21.6 \pm 14.5$  ms and  $24.0 \pm 23.9$  ms for S' and  $23.5 \pm 25.2$  ms and  $26.3 \pm 23.5$  ms for PS dur-



ing global and regional ischaemia, respectively, compared to baseline (Fig. 2).

**Conclusions:** The dyssynchrony observed in regional and global acute ischaemia in this study was mechanical with no delay in electrical conduction. This suggests that potential benefits from CRT in this patient group must have other mechanisms than resynchronization of electrical activation.

## P2389 : Preejection tug of war between early-activated septum and late-activated lateral wall in left bundle branch block

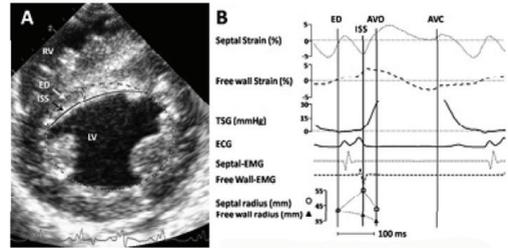
O. Gjesdal (Oslo University Hospital, Dept of Cardiology, and University of Oslo, Oslo / Norway), E.W. Remme (Oslo University Hospital, Institute for Surgical Research, Oslo / Norway), A. Opdahl (Oslo University Hospital, Institute for Surgical Research, Oslo / Norway), H. Skulstad (Oslo University Hospital, Department of Cardiology, Oslo / Norway), K. Russell (Oslo University Hospital, Institute for Surgical Research, Oslo / Norway), E. Kongsgaard (Oslo University Hospital, Department of Cardiology, Oslo / Norway), T. Edvardsen (Oslo University Hospital, Dept of Cardiology, and University of Oslo, Oslo / Norway), O.A. Smiseth (Oslo University Hospital, Dept of Cardiology, and University of Oslo, Oslo / Norway)

**Introduction:** Abnormal septal motion in LBBB has been assumed to represent passive motion related to reversal of the end-diastolic left-to-right transseptal pressure gradient (TSG). Recently, we demonstrated contribution of active septal contraction to this motion during preejection. We now investigate how active septal and LV free wall contractions contribute to septal deformation in LBBB.

**Methods:** In 8 anesthetized dogs with ventricular manometers we measured myocardial deformation (strain) by sonomicrometry and echocardiography and electrical conduction time by intra-myocardial EMG. LBBB was induced by RF-ablation.

**Results:** During LBBB electrical activation of the LV free wall was delayed  $51 \pm 4$  ms ( $\pm$ SEM) relative to septum. The free wall segment was stretched  $2.2 \pm 0.5\%$  between end diastole (ED) and onset of shortening. Preejection sep-

tal deformation was biphasic with  $6.1 \pm 4.5\%$  ( $p < .01$ ) shortening followed by  $3.9 \pm 2.8\%$  ( $p < .01$ ) lengthening which continued into the ejection phase (Fig). The interruption of septal shortening (ISS) coincided with onset of free wall shortening ( $4 \pm 3$  ms after). At ISS the radius of curvature was increased for septum ( $35 \pm 5\%$ ), but reduced for the free wall ( $-6 \pm 2\%$ ,  $p < 0.1$ ), implying higher wall stress in septum.



**Conclusions:** In LBBB, septal preejection deformation is biphasic with active shortening followed by lengthening. The results suggest that the septal wall lengthens due to forces generated in the late-activated free wall. Presystolic stretching increases free-wall force development via the Frank-Starling mechanism, whereas increased septal radius of curvature increases septal wall stress, and both mechanisms contribute to septal lengthening.

## 2691 : Group exercise versus aerobic interval training in myocardial infarction patients. A randomised controlled study with 30 months follow-up

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**Purpose:** Although exercise training, and especially aerobic interval training (AIT), has been found to increase peak oxygen uptake ( $VO_{2peak}$ ) in coronary heart disease patients, the long term effects of organized exercise

programs remains unclear. We aimed to compare the effects of group exercise training offered as usual care by three Norwegian hospitals and treadmill AIT upon VO<sub>2</sub>peak, blood markers of cardiovascular disease, endothelial function, and quality of life in myocardial infarction (MI) patients. We followed them for 30 months after ending the exercise program.

**Methods:** One hundred and seven MI patients (90 men and 17 women, age 56.5±10.1) were randomized to group exercise or treadmill AIT training twice weekly for 12 weeks. The group exercise was offered by the hospitals as usual care while the treadmill AIT was performed as 4x4 minutes intervals at 85-95% of peak heart rate.

**Results:** VO<sub>2</sub>peak increased more (p=0.04) after treadmill AIT (from 31.6±5.8 to 36.2±8.6 mL•kg<sup>-1</sup>•min<sup>-1</sup>, p<0.001) than after group exercise training (from 32.2±6.7 to 34.7±7.9 mL•kg<sup>-1</sup>•min<sup>-1</sup>, p<0.001). The exercise intensity was higher in AIT (90±5% of peak heart rate) versus group exercise (81±8% of peak heart rate) during the most intense part of the exercise sessions. After six and 30 months VO<sub>2</sub>peak decreased in both groups compared to post training, and only the treadmill AIT group still had significantly higher VO<sub>2</sub>peak (33.4±7.0 9 mL•kg<sup>-1</sup>•min<sup>-1</sup>, p=0.013) than at baseline after 30 months. Quality of life increased significantly in both groups (non-significant between-group difference), and the changes were sustained throughout follow-up testing for both groups. Adiponectin increased (from 7.2±3.5 to 8.0±3.4 µg/mL after group exercise and from 6.9±3.0 to 8.0±3.3 µg/mL after AIT, both p<0.05). High-density lipoprotein cholesterol increased significantly only after AIT (from 1.28±0.3 to 1.32±0.3 mmol/L). Flow-mediated dilatation of the brachial artery increased significantly in both groups after the training period (from 7.2±3.6 to 9.1±3.8% after group exercise and from 6.9±2.9 to 10.4±3.3 after treadmill AIT, non-significant between-group difference).

**Conclusion:** Treadmill AIT increased aerobic capacity more than the traditional exercise programs provided to MI patients by the hospitals. Thirty months after ending the program, VO<sub>2</sub>peak was still significantly higher than at baseline only in the AIT group. Our study could have clinical implications regarding organization of exercise training after MI.

## 2708 : NT-proBNP correlates strongly with ejection fraction measured by MRI in patients treated for ST-elevation myocardial infarction

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**Purpose:** Several studies have demonstrated that proBNP obtained in the acute phase of myocardial infarction predicts long-term morbidity and mortality. We aimed to study the relation between NT-proBNP and left ventricular ejection fraction (EF) determined by magnetic resonance imaging (MRI) in the acute phase and during stable conditions after modern treatment of acute ST-elevation myocardial infarction (STEMI).

**Methods:** This was a sub-study of the Norwegian study on District treatment of ST-Elevation Myocardial Infarction (NORDISTEMI), in which patients received thrombolysis and a majority of them also early invasive treatment. NT-proBNP was measured both at 3 days and 3 months after the index infarction, and MRI was performed after 3 months (n=160). The association between NT-proBNP and EF was estimated by linear regression after log transforming NT-proBNP and controlling for confounders, i.e. age, anterior myocardial infarction, body mass index, HbA1c, hypertension, gender and smoking habits.

**Results:** The table shows the relation between NT-proBNP at 3 days and 3 months after STEMI and MRI EF, as well as the relation between the change in NT-proBNP and MRI EF, when controlled for confounders. (Table)

**Conclusion:** Serial measurements of NT-proBNP in STEMI patients showed that NT-proBNP levels at 3 months were closer associated with MRI EF

Table 1

NT-proBNP vs. MRI EF at 3 months (n=160)	β-coefficient	R <sup>2</sup>	p-value
a) Log NT-proBNP at 3 days	-9.21	0.22	<0.0001
b) Log NT-proBNP at 3 months	-13.29	0.42	<0.0001
c) Log ΔNT-proBNP from 3 days to 3 months	-10.95	0.24	<0.0001

after 3 months than NT-pro BNP levels after 3 days, and also closer than the reduction in NT-proBNP. Our data suggest that measurement of NT-proBNP 3 months after myocardial infarction is a better indicator of left ventricular function compared to measurements in the acute phase.

## P2749 : Enhanced RV systolic function but no difference in pulmonary artery pressure in athletes

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**Purpose:** The athlete's heart on the right side is less investigated and understood than on the left side. The right ventricle (RV) with its thinner walls has to deal with the same increased volume load as on the left side. We thus wanted to test in a large-scale study if this would lead to any changes in RV function and systolic pressure in the pulmonary artery (PA) at rest.

**Methods:** 509 male Caucasian elite Norwegian football players and 45 less trained matched Caucasian controls participated in the study as a part of the mandatory heart screening in conjunction with the Union of European Football Associations (UEFA) and Norwegian Football Association (NFF) prior to the 2008 season. Tricuspid annular plane systolic excursion (TAPSE) and peak systolic velocity (RVs) by TVI at the lateral tricuspidal valve attachment was measured as indices of systolic RV function. RV isovolumic relaxation time (RVivrr) at the lateral tricuspidal attachment by TVI was measured. Peak systolic velocity of tricuspid regurgitation (TR) was used as an estimation of PA systolic pressure. End systolic right atrial (RA)- and end diastolic RV areas were measured by two-dimensional echocardiography. Blood pressure was measured, and body mass index (BMI) and body surface area (BSA) were calculated.

**Results:** There was an 22.3% increase in RA and 12.9% increase in RV areas from  $17.6 \pm 3.9$  to  $21.5 \pm 3.9$  cm<sup>2</sup> ( $p < 0.01$ ) and from  $24.3 \pm 4.0$  to  $27.5 \pm 4.9$  cm<sup>2</sup> ( $p < 0.01$ ), respectively. There were no significant differences in age, BMI, BSA or blood pressure between the athletes and the controls. For other results, see table.

**Conclusion:** The present study, to our knowledge the largest on RV in athletes, showed an increase

of RV function at rest in the athletes. The augmented volume load might be one cause for this adjustment in RV function. There was, however, no change in systolic PA pressure in the athletes compared to the controls.

Table 1

	Controls	Football players
TAPSE (cm)	2.6±0.36	2.7±0.37*
RVs (cm/s)	14.5±2.4	15.3±2.3*
RVivrr (ms)	16.3±12.2	15.8±10.2
TRvel (m/s)	2.1±0.2	2.2±0.2

$p < 0.05$  vs. controls.

## 2830 : Prognostic significance of mitral flow derived Doppler indices in a general population with normal systolic function: A prospective population-based cohort study. The Tromso Study 1994-2009

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Mortality is high in heart failure (HF) patients with preserved left ventricular ejection fraction (LVEF). Left ventricular diastolic dysfunction (DD) is often the cause of HF in this group. Pulsed-wave Doppler of mitral flow is widely used to identify patients with DD. It is important to establish the prognostic significance of mitral Doppler indices in a representative, general population to select appropriate populations for prevention- or intervention studies.

In 1994-95 3273 randomly selected participants, aged 25-85 yrs from the municipality of Tromso, Norway, underwent Doppler echocardiography. Our study population consists of 2133 of these participants aged 55-85 years, without atrial fibrillation and LVEF $\geq$ 50%. Previously validated cut-off values for mitral EA-ratio and E-wave deceleration time (EDT) were used to classify the participants into five groups with an assumed

Age- and sex adjusted risk estimates

Groups	n	HR all-cause mortality	HR CV mortality
EA 0.75-1.50 and EDT $\geq$ 140ms	1611	1.0	1.0
EA $\geq$ 1.51 and EDT $\geq$ 140ms	69	1.0 CI (0.6-1.8)	1.1 CI (0.4-2.9)
EA $\leq$ 0.74 and any EDT	394	1.3 CI (1.0-1.5)	1.5 CI (1.0-2.1)
EA 0.75-1.50 and EDT $\leq$ 139ms	30	1.5 CI (0.8-2.9)	1.6 CI (0.5-5.2)
EA $\geq$ 1.51 and EDT $\leq$ 139ms	11	3.5 CI (1.3-9.3)	9.5 CI (3.0-30.1)

increasing degree of DD through group 1 (normal) to 5. Group 1 was defined as EA-ratio 0.75-1.50 and EDT  $\geq$ 140ms, group 2 EA-ratio $\geq$ 1.51 and EDT $\geq$ 140ms, group 3 EA-ratio  $\leq$ 0.74 and any EDT, group 4 EA-ratio 0.75-1.50 and EDT $\leq$ 139ms and group 5 EA-ratio $\geq$ 1.51 and EDT $\leq$ 139ms.

The end-points were all-cause mortality with complete follow-up through 31 Jan 2009 and cardiovascular (CV) mortality with complete follow-up through 31 Dec 2007. There were 521 deaths of all-causes and 164 CV deaths. Age- and sex adjusted Cox regression analysis was used to calculate hazard ratios (HR) with 95%-confidence interval (CI) for all cause- and CV mortality in the different groups. (Table)

There is a significant trend towards increasing HR's for all-cause- and CV mortality through group 1 to 5. We conclude that the combination of EA-ratio and EDT can identify adults 55 yrs and older with preserved LVEF with increased risk of both all-cause- and CV mortality in a general population.

### P3086 : NT-proBNP is a potent prognostic marker in patients with type 2 diabetes hospitalized for acute coronary syndrome - a DIGAMI 2 sub study

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**Purpose:** N-terminal pro-natriuretic peptide (NT-ProBNP) is known to be a predictor of cardiovascular events in both populations with diabetes and in populations with acute coronary syndrome (ACS). Admission blood glucose

(BG) is also a strong predictor of outcome in ACS, but the relation to NT-pro BNP is unclear. We hypothesized that NT-proBNP and admission BG are closely correlated in diabetic patients with ACS as

admission BG may reflect level of cardiac stress. We studied the prognostic value of NT-proBNP and the correlation to admission BG in diabetic patients hospitalized for ACS.

**Methods:** The study was a pre planned sub study to the Diabetes Mellitus Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) 2 trial. The study population comprises all randomized DIGAMI-2 patients with NT-ProBNP measured at admission (N = 389). According to admission NT-ProBNP the study group was divided in tertiles: tertile 1 (NT-ProBNP 0-77 pmol/l), tertile 2 (NT-ProBNP 78-270 pmol/l), tertile 3 (NT-ProBNP 271-15000 pmol/l). Cox proportional hazard models were used to estimate the impact of admission NT-ProBNP on mortality.

**Results:** No major differences in baseline characteristics between DIGAMI 2 patients with (N = 389) and without (N = 864) admission NT-ProBNP were found. Patients in tertile 2 and 3 were significantly older, less often male, had lower body mass index (BMI) and higher serum creatinine compared with patients in tertile 1. However, no differences in admission BG, HbA1c and serum cholesterol were found between the tertiles. Likewise, no correlation between admission BG and NT-ProBNP was found (Pearson correlation coefficient -0.0007, P=0.88). During a mean follow-up of 2.2 years 96 patients (25%) died. With regard to all cause mortality, hazard ratio (HR) for 1 SD increase in log(NT-ProBNP) was 1.6 (95% CI 1.4-1.9, P<.0001). After adjustment for age, sex, smoking, BMI, previous cardiovascular disease, BG, and serum creatinine 1 SD increase in log(NT-ProBNP) still had impact on mortality (HR 1.4, 95% CI 1.2-1.8, P=0.0004). In this model admission BG had no prognostic impact.

**Conclusions:** NT-ProBNP and admission BG are not correlated in diabetic patients with ACS. NT-ProBNP is a very strong predictor of all cause mortality in diabetic patients hospitalized for ACS irrespective of admission BG.

## P3091 : Abnormal glucose regulation and risk of fatal coronary artery disease by gender: long term follow-up in the HUNT 1 study

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**Purpose:** To assess long term mortality from coronary artery disease (CAD) by gender in subjects with impaired glucose regulation (IGR), newly diagnosed diabetes mellitus (NDM) and known diabetes mellitus (KDM) compared to subjects with normal glucose regulation (NGR).

**Methods:** In 1984-86, one of the largest health surveys ever performed (HUNT1) was conducted in the county of Nord-Trøndelag, Norway. 74 977 subjects > 20 years participated. Persons with KDM were identified by self-reporting while IGR and NDM were defined according to guidelines from WHO (1999) by random and fasting glucose measurements and oral glucose tolerance testing. 18 years follow-up mortality of CAD was assessed by linking HUNT1 data to the Cause of Death Registry at Statistics Norway up to 2004. Deaths caused by CAD were defined by ICD codes. Hazard ratio (HR) for CAD mortality was adjusted for age, body mass index, hypertension, previous cardiovascular disease, exercise and smoking. Adjusted HR was compared by gender in subjects with IGR, NDM and KDM using Cox regression analysis. Subjects with NGR were used as reference group.

**Results:** At baseline, 365 subjects with IGR, 429 subjects with NDM, 2100 subjects with KDM and 72064 subjects with NGR were identified. During 18 years of follow-up, adjusted HR of death by CAD in women and men respectively was 1.19 (CI 0.75-1.87) and 1.18 (CI 0.88-1.59) in subjects with IGR, 1.60 (CI 1.15-2.23) and 1.41 (CI 1.07-1.85) in subjects with NDM and 2.44 (CI 2.12-2.81) and 1.88 (CI 1.64-2.16) for subjects with KDM. Using women as the reference category, adjusted HR for CAD mortality in men was 2.17 (CI 2.02-2.33) in subjects with NGR, 1.82 (CI 1.00-3.30) in subjects with IGR, 1.63 (CI 1.01-2.64) in subjects with NDM and 1.33 (CI 1.08-1.64) in subjects with KDM.

**Conclusions:** All levels of abnormal glucose regulation are stronger predictors for fatal CAD

in women than in men and weaken the traditional gender difference in CAD mortality.

## P3133 : Prognostic value of oral glucose tolerance testing in patients with a primary PCI treated STEMI

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**Purpose:** Patients with acute myocardial infarction and newly detected abnormal glucose regulation (AGR) have been shown to have a less favourable prognosis compared to patients with normal glucose regulation. We have previously shown that a very early oral glucose tolerance test (OGTT) after an acute ST elevation myocardial infarction (STEMI) did not provide reliable information about long-term glucometabolic state. The aims of the present study were to relate AGR (classified by an OGTT both early and late after an acute STEMI) to clinical outcome.

**Methods:** Patients (n=224, median age 58 years) with a primary percutaneous coronary intervention (PCI) treated STEMI without previously known diabetes were included and followed for clinical outcome, defined as the sum of all-cause mortality, non-fatal myocardial re-infarction, recurrent ischemia causing hospital admission, and stroke. The patients were classified by a standardised 75 g OGTT at two time points, first, within 24 hours after admission, then at a 3 months follow-up (201 patients, one was dead and 22 were unwilling to repeat the OGTT). Based on the OGTT results, the patients were categorised according to the WHO criteria and the term AGR was defined as the sum of impaired fasting glucose, impaired glucose tolerance and type 2-diabetes.

**Results:** The number of STEMI patients with newly diagnosed AGR in-hospital and three months later were 105 and 50 patients, respectively. During the follow up time of median 33 months, 58 (25.9%) patients experienced a new

clinical event. There were six deaths, 14 non-fatal re-infarctions, 34 recurrent ischemias, and four strokes. By use of Kaplan-Meier analysis the probability of a new clinical event was found similar in patients with abnormal and normal glucose regulation, both when classified in-hospital and re-classified three months later (Log-Rank  $p=0.383$  and  $p=0.264$ , respectively).

**Conclusion:** In a primary PCI treated STEMI population without previously known diabetes, abnormal glucose regulation was not associated with a poor clinical outcome after three years follow-up, regardless of whether they were classified early in-hospital or three months later.

### P3306 : Low circulating eicosatetraenoic acid and high vaccenic acid are associated with disease severity and predict mortality in heart failure

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**Purpose:** Free fatty acids (FFA) are the major energy sources of the heart and fatty acids (FA) are active components of biological membranes. Data indicate that FA and their composition may influence myocardial function and inflammation. This study sought to investigate whether total levels and composition of FA and FFA in plasma are altered in clinical heart failure (HF) and whether any alterations in these parameters are correlated to the severity of HF.

**Methods:** Plasma levels of FFA and total levels and composition of FA in plasma were measured in patients with stable HF (n=183) and compared to healthy controls (n=20) and correlated to functional class, plasma levels of N terminal pro-B-type natriuretic peptide (Nt-proBNP) and high sensitivity C-reactive protein (hsCRP), and cardiac index.

**Results:** (1) Patients with HF had increased levels of FFA in plasma compared to controls, significantly correlated with clinical disease severity.

(2) Patients with HF also had a decreased proportion in plasma of several n-3 polyunsaturated FA, an increased proportion of several monounsaturated FA, and a decreased proportion of several readily oxidized long-chain saturated FA. (3) These changes in FA composition were significantly associated with functional class, impaired cardiac function and enhanced systemic inflammation (i.e., increased hsCRP levels). (4) Low levels of C20:4n-3 (eicosatetraenoic acid) and in particular high levels of C18:1n-7 (vaccenic acid) were significantly associated with total mortality in this HF population.

**Conclusions:** Our data support a link between disturbed FA composition and the progression of HF, and suggest that some of these FA should be further investigated as prognostic markers in this group of patients.

### P3316 : Asynchrony of myocardial deformation in patients with dilative cardiomyopathy: a two-dimensional speckle tracking echocardiography study

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**Background:** Aim of the study was to assess the influence of QRS duration and left ventricular dimensions on the time course of myocardial deformation in patients with dilative cardiomyopathy (DCM).

Table 1

Parameters	Normal group (n=15)	Patient group 1 (n=33)	Patient group 2 (n=35)
QRS (ms)	98±10	113±24*	122±33*
EF (%)	67±11	45±6*	28±9*†
LV mass (g)	236±63	276±63*	360±104*†
LV volume (ml)	123±42	146±40*	228±89*†
Long_S_sd (ms)	33±10	62±23*	77±27*†
Long_SRs_sd (ms)	36±9	47±13*	55±16*†
Long_SRe_sd (ms)	26±8	45±15*	45±19*
Circ_S_sd (ms)	45±9	107±79*	120±42*
Circ_SRs_sd (ms)	40±13	53±24*	53±16*
Circ_SRe_sd (ms)	29±9	43±24	41±19

\* $p<0.05$  vs. normal group/†  $p<0.05$  vs. patient group 1.

**Methods:** Sixty-eight patients with DCM, defined as reduced ejection fraction and normal coronary angiogram, underwent echocardiographic examination. Patients were divided according to ejection fraction (EF) into group 1 (EF = 40–50%) and group 2 (EF < 40%). Fifteen subjects without evidence of heart disease served as control group.

Greyscale cine-loops were obtained from 3 apical and 2 short axis views of the left ventricle (LV). Based on two-dimensional ultrasound speckle tracking echocardiography (2D-STE) the time to peak values of the following parameters were extracted: peak strain (S), systolic (SRs) and diastolic strain rate (SRe). Asynchrony of longitudinal (long) deformation was calculated as standard deviation (sd) of the time-to-peak values in the three apical views. For calculation of circumferential (circ) asynchrony all segments of the 2 short axis views were included.

**Results:** The results are displayed in table 1.

QRS duration correlated with Long\_SRs\_sd ( $r = 0.53$ ,  $p < 0.001$ ). There was only a weak correlation between Long\_SRs\_sd and EF ( $r = -0.31$ ,  $p = 0.017$ ), LV mass ( $r = 0.39$ ,  $p = 0.002$ ) and LV volume ( $r = 0.31$ ,  $p = 0.016$ ). (Table)

**Conclusions:** Asynchrony of myocardial deformation is primarily driven by QRS duration and only secondarily by LV dimensions. In the patient group, LV dilatation had an impact on asynchrony of systolic but not diastolic deformation parameters.

## P3371 : Use of late gadolinium enhancement cardiovascular magnetic resonance images and texture analyses to distinguish patients with high and low risk of arrhythmias after myocardial infarction

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**Purpose:** Late gadolinium enhancement (LGE) examinations provide accurate assessment of the size of non-scarred myocardium, infarct and its core and peri-infarct gray-zone. However,

more comprehensive analysis of LGE images may provide clinically useful information that may improve the diagnostic capability of this method. The purpose of this study was to explore if image processing techniques, like texture analysis and pattern recognition, are able to improve identification of patients with high risk of arrhythmias beyond that of established risk markers such as left ventricular ejection fraction (LVEF).

**Methods:** Two groups of patients with healed myocardial infarction (MI) were compared: 24 consecutive patients with indication for ICD versus 37 patients with no ICD indication. A complete set of LGE images covering the entire LV were analyzed. We used image texture analysis based on estimates of the probability of occurrence of gray level values for two adjacent pixels (co-occurrence) at a specific angle (0°, 45°, 90° or 135°). The resulting co-occurrence matrices can be regarded as estimates of the joint probability density functions (PDF) for the four specified angles. From these estimated PDFs the following image texture features were calculated: "Energy", "Contrast", "Correlation" and "Homogeneity". Using these textural features along with a number of other statistical features, the 2 patient groups were compared by means of pattern classification methods according to Bayes decision theory and ROC analysis.

**Results:** During 1 year follow-up, VT was recorded in 20 of 24 ICD-patients. There was no recorded ventricular arrhythmia, death or resuscitated cardiac arrest in the non-ICD-patients. Median pixel numbers of non-infarcted myocardium, infarct, core and gray zone were significantly ( $p < 0.05$ ) higher in ICD-patients, but they were inferior in comparison with image texture features in their ability to distinguish ICD- and non-ICD-patients. The specificity to discriminate ICD- and non-ICD-patients was calculated at a sensitivity of  $\geq 90\%$  by combining 1, 2 or 3 descriptors: LVEF alone had a specificity of 70% (CI:57-81%). Combining LVEF with an image texture descriptor of the non-scarred myocardium increased specificity to 81% (CI:69-89%). Combining LVEF with 2 image texture descriptors of non-scarred myocardium and infarct at two different angles, further increased specificity to 89% (CI: 78-95%)

**Conclusion:** The addition of myocardial image texture analyses and pattern recognition, improved the ability to identify patients with high risk of serious ventricular arrhythmias.

## 3579 : Comparative efficacy and safety of Fenofibrate/Pravastatin/Ezetimibe therapy and Simvastatin/Ezetimibe therapy in Type 2 Diabetic patients with combined hyperlipidemia and cardiovascular disease

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**Purpose:** Very high risk patients with type 2 diabetes (T2D) and cardiovascular disease often require combination therapy to achieve recommended LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) goals.

This study evaluated the efficacy and safety of Fenofibrate (F) 160 mg/Pravastatin (P) 40 mg fixed dose combination and Ezetimibe (E) 10 mg compared to Simvastatin (S) 20 mg and E10 mg in T2D patients with cardiovascular disease and not at goals on S20 mg.

**Methods:** This randomized, double-blind, parallel group study was conducted at 73 European centers. After a 6-week run-in period on S20 mg, 273 patients with non-HDL-C  $\geq$  100 mg/dL or LDL-C  $\geq$  70 mg/dL and triglycerides (TG) 150-600 mg/dL were randomized (week 0) for a 12-week treatment period to the F160 mg/P40 mg and E10 mg triple therapy or the combination of S20 mg and E10 mg, followed by a 12-week open-label period where all patients received the triple therapy. The primary efficacy comparison was the mean percent (%) changes in non-HDL-C (F/P+E vs S+E). Secondary end-points included LDL-C, HDL-C, TG, ApoB and fibrinogen.

**Results:** No significant differences were observed between the F160/P40+E10 group and the S20+E10 group in reducing non-HDL-C and ApoB. The triple therapy was found more effective than S20+E10 in reducing TG and fibrinogen. The triple therapy was generally well tolerated with a safety profile comparable to the S20+E10 combination therapy. Especially no cases of myopathy or rhabdomyolysis were reported. (Table)

**Conclusion:** The Fenofibrate 160 mg/Pravastatin 40 mg fixed-dose combination associated with Ezetimibe 10 mg was a new alternative to improve the global atherogenic lipid profile in

Percent change from baseline to week 12 in primary and secondary efficacy endpoints (ITT analysis)

Parameters		F160/P40+E10 (n=137)	S20+E10 (n=136)	P value
Non-HDL-C, mg/dl	Week 0 (mean)	145.9	152.8	-
	Week 12 (mean)	115.3	113.0	-
	% change (SE)	-21.2 (1.9)	-24.7 (1.9)	0.09
LDL-C, mg/dL	Week 0 (mean)	109.4	114.2	-
	Week 12 (mean)	87.3	82.8	-
	% change (SE)	-19.8 (2.3)	-25.1 (2.3)	0.05
HDL-C, mg/dL	Week 0 (mean)	44.5	43.3	-
	Week 12 (mean)	45.8	43.4	-
	% change (SE)	3.5 (1.4)	0.5 (1.4)	0.066
TG, mg/dL	Week 0 (mean)	247.6	262.9	-
	Week 12 (mean)	190.4	230.8	-
	% change (SE)	-22.8 (4.7)	-8.2 (4.7)	0.007
ApoB, mg/dL	Week 0 (mean)	94	97	-
	Week 12 (mean)	79	78	-
	% change (SE)	-15.7 (1.7)	-18.1 (1.7)	0.149
Fibrinogen, g/L	Week 0 (mean)	3.80	3.79	-
	Week 12 (mean)	3.30	3.74	-
	% change (SE)	-11.8 (1.4)	0.6 (1.4)	<0.0001

T2D patients with combined hyperlipidemia in secondary prevention.

## P3612 : Peripheral artery disease as a predictor of outcome in high-risk MI patients: pooled analysis from the high risk MI database initiative (pooled data from CAPRICORN, EPEHESUS, OPTIMAAL and VALIANT)

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**Purpose:** Peripheral artery disease (PAD) is associated with poorer prognosis in patients with stable and unstable coronary heart disease but whether PAD is associated with worse outcomes in patients with substantial acute myocardial infarction (MI) is unknown.

**Methods:** We examined the prevalence of PAD and the relationship between PAD and cardiovascular (CV) outcomes (using Cox univariate and multivariable modeling) in an individual-patient meta-analysis of 4 trials (CAPRICORN, EPHE-SUS, OPTIMAAL and VALIANT) which enrolled subjects with left ventricular systolic dysfunction, heart failure or both after acute MI.

**Results:** Of the 28,769 patients randomized, 2,357 (8.2%) had PAD and these patients were older and had more co-morbidity. Over a mean follow-up of 2.7 years, 5,121 (17.8%) patients died and 15,055 (52%) experienced CV death or hospitalization. Patients with PAD have very high absolute rates of adverse outcomes: 44% of patients with PAD experienced CV death, non-fatal MI, non-fatal stroke or heart failure hospitalization over the mean follow-up of 2.7 years (compared to 28% of those without PAD). PAD was an independent predictor of all individual and composite CV outcomes examined (including heart failure), with the exception of stroke. In patients with PAD (compared to those without PAD), the adjusted hazard ratio (HR) for all-cause mortality was 1.25 (95% CI 1.15-1.37;  $p < 0.001$ ) and the HR for CV death, non-fatal MI, non-fatal stroke or heart failure hospitalization was 1.24 (1.16-1.33;  $p < 0.001$ ).

**Conclusion:** PAD is relatively common and is an independent predictor of worse outcomes in patients already at high risk after MI because of left ventricular systolic dysfunction, heart failure or both.

## **P3982 : Esomeprazole 20 mg and 40 mg for 26 weeks reduces the frequency of upper GI symptoms in patients taking low-dose acetylsalicylic acid (ASA) for cardiovascular prevention: the OBERON trial**

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**Purpose:** Patients (pts) with cardiovascular (CV) risk need to take low-dose (75-325mg daily) acetylsalicylic acid (ASA), for CV risk reduction. Pts may experience upper GI symptoms that interrupt low-dose ASA therapy. The effect of 26wks of esomeprazole 20 and 40 mg in reduction of upper GI symptoms in low-dose ASA pts with increased GI risk was a secondary endpoint in the OBERON study (NCT00441727).

**Methods:** Helicobacter pylori-negative pts taking low-dose ASA who fulfilled  $\geq 1$  of these criteria were included; age  $\geq 65y$ ;  $\geq 18y$  with history of peptic ulcer (PU);  $\geq 60y$  with stable coronary artery disease or upper GI symptoms and  $\geq 5$  erosions, or low-dose ASA use begun within 1 month. Pts with reflux esophagitis (Los Angeles grade C or D), previous ulcer complications or PU at baseline endoscopy, or continual use of non-steroidal anti-inflammatory drugs were excluded. Randomisation was to esomeprazole 20 or 40 mg od, or placebo for 26wks. Pt-reported upper GI symptoms were assessed using the Reflux Disease Questionnaire (RDQ), containing 12 items relating to symptom frequency and severity to be answered on a 6-point Likert scale. Dichotomized scores (0 versus  $>0$ ) were obtained for the dyspeptic (burning feeling and pain in the centre of the upper stomach) and GERD (heartburn and regurgitation) dimensions, at baseline and at wk 26 (or last visit).

**Results:** 2303 pts were evaluable. Dyspeptic and GERD symptoms were reported in 259 (34%) and 312 (41%) of 763 placebo pts at wk 26;

		Week 26		
Upper GI Symptoms:	Baseline	Eso 20 mg	Eso 40 mg	Placebo
RDQ Dimension	symptom status	(n=758)	(n=782)	(n=763)
Dyspeptic symptoms	Absent	46/417 (11%)	43/415 (10%)	77/412 (19%)
Present	135/341 (40%)	148/367 (40%)	182/351 (52%)	
GERD symptoms	Absent	50/342 (15%)	47/350 (13%)	73/337 (22%)
Present	171/416 (41%)	181/432 (42%)	239/426 (56%)	

esomeprazole at both 20 and 40mg reduced the incidences of dyspeptic and GERD symptoms to 24% and 29%, respectively. Significantly fewer pts in both groups had dyspeptic and GERD symptoms at wk 26 relative to the placebo group ( $p < .0001$  for all comparisons; test stratified by absence/presence of symptoms at baseline, Table).

**Conclusion:** Esomeprazole 20 mg and 40mg reduce the frequency of upper GI symptoms in pts with increased GI risk taking low-dose ASA for CV prevention.

### **P3992 : High bubble grades after scuba diving at the limits of recreational diving algorithm**

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**Purpose:** Buhlmann's diving algorithm is considered to be very safe due to longer decompression. This procedure has been used by most dive computers for recreational dive. It is well documented that large number of gas bubbles in the right heart after diving entails a considerable risk of decompression sickness (DCS). The objective of this study was to evaluate safety of Buhlmann's diving algorithm.

**Methods:** In the present study, a deep-short dive (54 m/20 min) and shallow-long dive (24 m/70 min) were conducted both in a dry hyperbaric chamber and in-water. The number of gas bubbles in the right heart was post-decompression monitored for two hours by echocardiographic scanning. The dives were performed by fourteen experienced recreational male divers to the limits of the accepted procedures following the Buhlmann algorithm.

**Results:** The mean number of bubbles/cm<sup>2</sup> increased from 0.1 after dry dives to 2.4 after wet dives for deep-short dive (54 m/20 min) and from 0.1 after dry dives to 1.4 after wet dives for shallow-long dive (24 m/70 min). Although the risk of DCS also increased considerably, ranging from 6-9% in the dry dives to 19-28% after the in-water dives, still, no diver reported any signs of DCS.

**Conclusions:** The results suggest that in-water dives at the limits of the Buhlmann's table are associated with unexpectedly very high bubble grade, resulting in considerable DCS risk, even with long decompression time.

### **P4013 : Smoking tobacco versus snuff; impact on endothelial function in a healthy norwegian population**

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**Introduction:** Cigarette smoking is a risk factor for cardiovascular disease. We know little about the effect of snuff on blood vessels. Endothelial dysfunction is an early sign of atherosclerosis. The aim of our study was to explore the effect of snuff vs smoking tobacco on endothelial function.

**Methods:** As part of HUNT3 we tested endothelial function as flow mediated dilation (FMD) in 4737 healthy adults. FMD was tested in the left brachial artery with the cuff placed on the forearm. Baseline recording was performed and arterial occlusion created by cuff inflation to 250 mmHg for 5 minutes. Post diameter was measured 60 sec after cuff deflation. The difference between post and baseline diameters gives FMD of the artery. Smoking habits were self-reported by questionnaires.

**Results:** See Table 1. There were no significant differences in FMD between groups of non-smoking snuff users. There was a significant correlation between age and snuff use ( $R = -0.188$ ,  $p < 0.001$ ), but no correlation between endothelial dysfunction and snuff - use. Smoking and non-smoking women had no significant difference in FMD, but we found a significant difference in prevalence of endothelial dysfunction i.e.  $FMD < 0\%$  (Fisher's exact 0.039). In men FMD in non-smokers was significantly higher than in daily smokers (FMD 4.5% vs 4.1%,  $p = 0.008$ ), and the prevalence of endothelial dysfunction in daily smokers was significantly higher than in non-smokers (Fisher=0.029). Male smokers also

Table 1

		Never used snuff	Former user of snuff	Occasional snuff use	Daily snuff use regard - less use of smoking tobacco	Daily snuff, not using smoke tobacco	Non-smoker not using snuff	Daily smoker not using snuff	Daily smoke and snuff users
Men	n (Prevalens %)	1563 (72)	214 (9.9)	109 (5)	279 (12.9)	100 (4.5)	1014 (45.9)	918 (41.5)	179 (8.1)
	Mean FMD % (SD)	4.29 (3.8)	4.57 (4.2)	4.49 (3.7)	3.98 (3.8)	4.38 (4.2)	4.52 (3.8)	4.13 (3.9)	3.78 (3.6)
	FMD adjusted for age (SD)	4.17 (27.1)	4.48 (30.1)	4.27 (24.4)	3.89 (24.7)	4.37 (25.3)	4.4 (26.1)	4.01 (28.8)	3.66 (24.3)
	Prevalens of FMD <0	17.7	15.4	15.6	16.8	12	16	19.2	19.6
Women	n (Prevalens %)	2377 (96.5)	24 (1)	42 (1.7)	20 (0.8)	6 (0.2)	1238 (49)	1270 (50.2)	14 (0.6)
	Mean FMD % (SD)	5.34 (4.5)	6.89 (6.7)	5.24 (4.4)	4.87 (4.3)	3.09 (5.1)	5.46 (4.9)	5.21 (4.7)	6.63 (3.8)
	FMD adjusted for age (SD)	5.11 (31.6)	6.59 (27.9)	4.87 (23.8)	4.31 (24.9)	2.54 (30.9)	5.19 (29.9)	5.01 (33.0)	5.08 (21.5)
	Prevalens of FMD <0	16	12.5	11.9	15	0.3	14.3	17.7	7.1

had higher resting heart rate (59/min) than non-smoking men (57/min) ( $p < 0.001$ ). (Table)

**Conclusions:** Smoking tobacco had a greater impact on endothelial function than snuff. Adjusting for age revealed a trend towards a larger effect of snuff on FMD in men.

### P4017 : Smokers spend shorter time in hospital than non-smokers following complicated AMI

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**Purpose:** Hospitalizations in patients with reduced left ventricular (LV) function due to ischemic heart disease represent a major burden to health care systems. Smoking is an important contributor to morbidity in this patient population. This study assessed the association between smoking and days spent in hospital following a myocardial infarction (MI) complicated with signs or symptoms of heart failure or LV dysfunction.

**Methods:** This is an observational study based upon data from index hospitalizations from a database generated from three large randomized trials in patients with acute complicated

MI: OPTIMAAL, EPHEBUS and CAPRICORN. Smoking status (current or past smoker versus non-smoker) was recorded in all patients.

**Results:** Data from 12,720 patients were included in this analysis. The mean age was  $65 \pm 11$  years, 9124 patients (72%) were males, and 8056 patients (63%) were current or past smokers. There were significantly ( $p < 0.001$ ) more male smokers (6709/9124 patients, 74%) than female smokers (1347/3596 patients, 38%). The highest proportion of smokers was in the cohort of patients < 60 years of age (3189/4009 patients, 80%). The proportion of smokers decreased with increasing age category (< 60 years, 60-60 years, 70-79 years,  $\geq 80$  years); the lowest proportion of smokers was in patients  $\geq 80$  years of age (435/1060 patients, 41%). Smokers spent significantly shorter time in hospital compared with non-smokers (Table). In a multivariable model that included age, gender, smoking, and gender by smoking interaction terms, smoking remained an independent predictor of hospitalization duration, with effects that appear to vary by gender ( $p < 0.001$ ). Age category had significant ( $p < 0.001$ ) effects on the association between smoking and hospitalization duration.

**Conclusion:** Smokers spent shorter time in hospital than non-smokers following a complicated MI. This association appears to be strongest in women and in patients between 60 and 80 years of age.

*Smoking and duration of hospitalisation*

Gender	Non-smokers (days)	Smokers (days)	p-value
Male	15.4 $\pm$ 9.4	14.3 $\pm$ 10.0	<0.001
Female	18.3 $\pm$ 13.7	13.4 $\pm$ 9.1	<0.001

Gender	Non-smokers (days)	Smokers (days)	p-value
p-value	<0.001	<0.001	

Days are expressed as mean and SD.

## P4080 : Cardiac contractile abnormalities associate with reduced longevity in rats

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We have developed a rat model based on two-way artificial selection for high or low inborn aerobic running capacity (high and low capacity). After 20 generations, those with a low capacity died at a median age of 24.3 months, whereas those with a high capacity died at 34.7 months, representing a 45% (10.7 months) difference. Aerobic capacity (maximal oxygen uptake) differed >70% between the strains, and this gap widened with advanced age. Because cardiac pump function is a major determinant of aerobic capacity, we studied cardiac contractility, intracellular Ca<sup>2+</sup> handling, and morphology in adult (15-20 months) and aged (>25 months; time of death) rats of both high and low capacity strains. Cardiomyocyte contractility was more compromised with aging in the low capacity strain, as cell shortening decreased 50% from adult to aged low capacity rats, whereas it only decreased 26% from adult to aged high capacity rats. These observations were paralleled by intracellular Ca<sup>2+</sup> transient amplitudes, which reduced with aging, but more in low versus high capacity rats. Reduced Ca<sup>2+</sup> transient amplitude can be caused by diastolic sarcoplasmic reticulum Ca<sup>2+</sup> leak. Consistent with this, we observed a higher diastolic Ca<sup>2+</sup> concentration and a higher Ca<sup>2+</sup> spark frequency in cardiomyocytes from low capacity rats relative to high capacity rats. During progression from adult to old age, cardiomyocyte width and length were unchanged in high capacity rats, whereas both width and length, including the width/length ratio, increased in low capacity rats with aging. This remodeling was likely influenced by the higher blood pressures sustained by the low capacity rats. We also found that the relative transverse tubule density was higher in cardiomyocytes from high versus low capacity rats, and that it only declined with aging in low (25%), but not high, capacity rats, suggesting that reduced transverse tubules may have contributed to reduced contractility and Ca<sup>2+</sup> handling. Finally, histopathological lesions such as cardiomyocyte degeneration and necro-

sis were more abundant in aged low capacity rat hearts compared to high capacity rat hearts (84% versus 44% of the hearts), and interstitial edema and fibrosis was only observed in low capacity rat hearts.

In summary, we show that aerobic capacity underlies longevity in rats and that this is coupled to myocardial contractile function, intracellular Ca<sup>2+</sup> handling, and morphology of the cardiomyocyte as well as the myocardium.

## P4136 : Restoration of sinus rhythm improves endothelial function in patients with persistent atrial fibrillation

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**Purpose:** Atrial fibrillation (AF) is associated with endothelial dysfunction. Asymmetric dimethyl arginine (ADMA) is an endogenous inhibitor of nitric oxide synthase which reduces the synthesis of nitric oxide (NO), and may therefore contribute to endothelial dysfunction. We studied levels of ADMA and L-arginine, the substrate for NO, and their relation to maintenance of sinus rhythm after electrical cardioversion for AF, and the effects of angiotensin receptor blockade on these variables.

**Methods:** In a double blind, placebo-controlled study (Candesartan in the Prevention of Relapsing Atrial Fibrillation, CAPRAF), patients with persistent AF were randomised to receive candesartan 8 mg once daily or placebo for 3-6 weeks before and candesartan 16 mg once daily or placebo for 6 months after cardioversion. As part of this study, plasma levels of L-arginine and ADMA were measured at baseline and at the end of the study by use of an HPLC-method. The impact of ADMA and L-arginine levels as well as L-arginine/ADMA ratio on rhythm outcome was analysed using Kaplan Meier analysis of quartiles, whereas analysis of covariance (ANCOVA) was used to analyse the impact of treatment with candesartan and rhythm outcome on these variables.

**Results:** Blood samples were available for analysis of ADMA and L-arginine in 164 patients at baseline and both at baseline and at the end of study in 98 patients. Baseline levels of ADMA, L-arginine and L-arginine/ADMA ratio were not associated with rhythm outcome. Treatment with candesartan had no impact on ADMA levels, L-arginine levels or L-arginine/ADMA ratio. Restoration and maintenance of sinus rhythm for 6 months after cardioversion did not have a

statistically significant impact on L-arginine or ADMA levels ( $p=0.301$  and  $p=0.076$ , respectively). However, an increased L-arginine/ADMA ratio was found in patients who remained in sinus rhythm for 6 months ( $n=37$ ) when compared to patients with AF recurrence ( $n=61$ ) (mean  $+11$  vs.  $-4$ ;  $p=0.006$ ).

**Conclusion:** An increased L-arginine/ADMA ratio was found in patients still in sinus rhythm 6 months after cardioversion for persistent AF. Our findings suggest that sinus rhythm restoration and maintenance is associated with improved nitric oxide synthesis and endothelial function.

## P4179 : Impaired diastolic filling reduces the frequency force reserve during therapeutic hypothermia in an experimental model

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**Background:** Hypothermia, used as neuroprotective treatment after cardiac arrest, also reduces myocardial function. The knowledge of the frequency force reserve of myocardium during hypothermia is limited. We therefore wanted to investigate the ability to maintain or increase cardiac output during increasing heart rate (HR) and to study the impact of left ventricular (LV) relaxation on the frequency force reserve.

**Methods:** Nine anesthetized, open chest pigs were studied. LV pressure (LVP) and left atrial pressure (LAP) were measured from micro-manometer-tipped catheters. Stroke volume (SV) and cardiac output (CO) was measured by thermodilution from a pulmonary artery catheter. The LVP time derivate ( $dP/dt$ ) and the relaxation constant ( $\tau$ ) were calculated, and the left ventricle were considered fully relaxed at 3.5times  $\tau$  after aortic valve closure. LV elastance (E) was calculated as endsystolic pressure ( $0.9 \times \text{peak LVP}$ )/endsystolic volume (by echocardiography). Mild hypothermia ( $33^\circ\text{C}$ ) was performed by intravascular cooling. HR was reduced during hypothermia from  $91 \pm 10$  (mean  $\pm$  SD) to  $80 \pm 11$   $\text{min}^{-1}$  ( $p < 0.01$ ). To compare measurements, atrial

paced HR of 100 and 120 bpm was performed before ( $38^\circ\text{C}$ ) and during hypothermia.

**Results:** At identical frequencies of 100 bpm, hypothermia reduced CO ( $5.2 \pm 0.7$  vs  $4.1 \pm 0.9$  l/min), LVP ( $86 \pm 5$  to  $68 \pm 10$  mmHg),  $dP/dt$  ( $1353 \pm 339$  to  $1039 \pm 293$  mmHg/s) and E ( $2.4 \pm 0.4$  vs  $1.8 \pm 0.2$  mmHg/ml) ( $p < 0.01$  for all).  $\tau$  increased from  $31 \pm 5$  ms to  $54 \pm 8$  ms ( $p < 0.01$ ). At  $38^\circ\text{C}$ , when HR was increased from 100 to 120 bpm, CO, LVP,  $dP/dt$ , E and  $\tau$  was unchanged. In contrast, when HR was increased from 100 to 120 bpm at  $33^\circ\text{C}$ , CO was reduced from  $4.0 \pm 0.9$  vs  $3.5 \pm 1.4$  l/min ( $p < 0.05$ ) and LVP was reduced from  $68 \pm 10$  to  $64 \pm 13$  mmHg ( $p < 0.05$ ). Importantly,  $dP/dt$ ,  $\tau$  and E was unchanged ( $1039 \pm 293$  vs  $1085 \pm 285$  mmHg/s,  $54 \pm 8$  vs  $58 \pm 12$  ms and  $1.8 \pm 0.2$  vs  $1.7 \pm 0.4$  (n.s. for all)). Diastolic duration at  $38^\circ\text{C}$  was  $270 \pm 25$  and  $211 \pm 22$  ms ( $p < 0.01$ ) and at  $33^\circ\text{C}$   $182 \pm 5$  ms vs  $130 \pm 19$  ms ( $p < 0.01$ ) during 100 and 120 bpm, respectively. At  $38^\circ\text{C}$ , LV reached fully relaxation at both frequencies as the fraction of 3.5 times  $\tau$  related to the duration of diastole increased from  $0.42 \pm 0.06$  to  $0.50 \pm 0.10$  ( $p < 0.05$ ). At  $33^\circ\text{C}$ , the time of complete ventricular relaxation reached the duration of diastole at 100 bpm and exceeded the duration of diastole at 120 bpm ( $1.06 \pm 0.13$  vs  $1.63 \pm 0.57$ ,  $p < 0.05$ ) resulting in an incomplete relaxation.

**Conclusion:** The frequency force reserve is reduced during mild hypothermia. This is not caused by reduced contractility, but is as a result of incomplete LV relaxation time.

## P4192 : Preserved left ventricular early diastolic and systolic reserve during supine bicycle exercise in patients with heart transplantation

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**Background:** Patients with orthotopic heart transplantation (HTx) have limited exercise capacity despite normal systolic left ventricular (LV) function. Reduced exercise capacity is often associated with diastolic dysfunction and increased LV filling pressure (LVFP) at rest and during exercise. LVFP can be estimated from the ratio of early transmitral flow (E) to early diastolic annular velocity (E'). We investigated both

systolic and diastolic function, and E/E' ratio during exercise in HTx patients.

**Methods:** Nine patients, 8 men, with age (mean  $\pm$  SD) 56 $\pm$ 11 years with no signs of rejection or cardiac failure were investigated 4.7 $\pm$ 1.8 years after HTx. Colour-tissue Doppler images and transmitral flow were recorded (Vivid 7, GE Vingmed) at rest and during semi-supine bicycle exercise in increments of 25W every 2 minutes exercise. Images were obtained at rest, 50W and submaximal exercise (defined by muscular fatigue and/or marked dyspnea). Systolic (S') and early diastolic (E') mitral annular velocities were averaged from four points in the 4- and 2-chamber views, and displacement from two points in the 4-chamber view.

**Results** (Table 1): Heart rate, E' and S' increased significantly from semi-supine rest to both 50W and submaximal (125 $\pm$ 25 W, Borg 16 $\pm$ 2). E' and S' increased by 84%  $\pm$  39% and 50%  $\pm$  33%, respectively from rest to submaximal. Both E and E' increased significantly during exercise, with their ratio (E/E') maintained unchanged. Displacement increased significantly to 50W, with no further increase to submaximal exercise. (Table)

Table 1

	Supine	Semi-supine		
	Rest	Rest	50W	Submax
HR	87 $\pm$ 7	90 $\pm$ 8	106 $\pm$ 10*	137 $\pm$ 9**†
E'	8.0 $\pm$ 1.4	7.4 $\pm$ 1.6	10.6 $\pm$ 2.0*	13.2 $\pm$ 2.6**†
E/E'	8.0 $\pm$ 2.0	8.7 $\pm$ 1.3	8.7 $\pm$ 2.0	9.2 $\pm$ 2.4
S'	7.3 $\pm$ 1.9	6.3 $\pm$ 1.6	7.6 $\pm$ 2.3*	9.1 $\pm$ 1.6**
Displacement (mm)	10.0 $\pm$ 2.2	8.6 $\pm$ 1.8	11.4 $\pm$ 2.8*	11.7 $\pm$ 1.7**

\* $p$ <0.05 and \*\* $p$ <0.01 vs semi-supine rest. †  $p$ <0.01 vs 50W. All tests Bonferroni corrected.

**Conclusion:** Patients with HTx have a preserved early diastolic and a systolic reserve during exercise. E/E' was unchanged during exercise, indicating that limited exercise capacity in HTx patients is not due to increased LV filling pressure.

## P4222 : Increased left ventricle mass and dimension in adults patients with osteogenesis imperfecta

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**Background:** The aim of this study was to investigate cardiac abnormalities in adults with osteogenesis imperfecta (OI), in particular dimensions of the left ventricle (LV) and aorta.

**Methods and Results:** The clinical and echocardiographic survey included 99 adults with OI divided in three clinical types, I, III and IV, and 52 controls. LV end-diastolic dimensions (LVIDd), mass and four aortic diameters were measured by standard echocardiography and corrected for body surface area (BSA).

Hypertension was registered in 37 individuals (37.4%). The OI group had significantly lower BSA than the control individuals, 1.7 $\pm$ 0.3 vs. 1.9 $\pm$ 0.2 m<sup>2</sup> ( $p$ <0.05). LVIDd and LV mass were significantly larger in the OI group when compared to the controls, 2.98 $\pm$ 0.64 vs. 2.59 $\pm$ 0.26 cm/m<sup>2</sup> ( $p$ <0.05) and 97.3 $\pm$ 30.1 vs. 73.3 $\pm$ 18.0 g/m<sup>2</sup> ( $p$ <0.05), respectively. Type III OI showed significantly enlarged LVIDd as compared to OI type I and IV, 4.33 $\pm$ 1.10 vs. 2.83 $\pm$ 0.33 ( $p$ <0.05), vs. 2.85 $\pm$ 0.37 cm/m<sup>2</sup> ( $p$ <0.05), respectively. All aortic diameters were significantly larger in the OI group than in the control group, as they were in type III compared to type I and IV.

**Conclusion:** We found increased LVIDd and LV mass in adult patients with OI compared to the control group. The changes in LV and dilatation of aorta seemed to be more pronounced in patients with OI type III compared to OI types I and IV.

P4237 : Left ventricular global longitudinal strain is a powerful predictor of one year mortality in heart transplant recipients

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**Background:** Although a significant proportion of heart transplant (HTx) recipients have reduced left ventricular (LV) myocardial strain at the early stages after HTx, no previous study has evaluated the associated risk for mortality. We hypothesised that reduced LV global longitudinal strain (GLS) shortly after HTx is associated with increased one year mortality among HTx recipients.

**Methods:** We included 176 consecutive adult primary single organ orthotopic HTx recipients. Echocardiography was performed 13 $\pm$ 6 days post HTx. Peak systolic longitudinal myocardial strain by two-dimensional speckle tracking echocar-

diography was assessed in 16 LV segments and averaged to GLS - an index of global LV function.

**Results:** Assessment of strain was feasible in 167 (95%) patients. During the first year, 16 (10%) patients died 82±72 days after HTx. GLS was decreased in non-survivors compared to survivors (p<0.01, Table).

Only 4 (3%) patients out of 144 with LV GLS better than -10% (-14.3±2.5%) died the first year after HTx. In contrast, 11 (48%) patients out of 23 with LV GLS worse than -10% (-7.8±1.8%) died during the first year (P<0.05). Importantly, GLS was the only significant predictor of 1 year mortality in a multivariate regression analysis with OR 1.7 (95% CI 1.3-2.1) per 1% decrease in strain.

**Conclusion:** Reduced LV function by GLS early after HTx is related to increased mortality. Early assessment of LV GLS might be a predictor of 1 year mortality in HTx recipients.

*Clinical characteristics*

	Dead (n=16)	Alive (n=151)	p-value
Recipient Age (years)	56±11	53±11	0.25
BPs (mmHg)	128±34	136±19	0.20
BPd (mmHg)	81±14	81±12	0.52
HR (beats per minute)	86±13	87±12	0.17
BMI (kg/m <sup>2</sup> )	25±3	25±4	0.67
Donor age (years)	47±14	39±13	0.03
Transplant ischemia (min)	143±71	155±81	0.54
Global Longitudinal Strain (%)	-8.4±3.2	-13.6±3.1	<0.01

### P4431 : Right ventricular strain reduction in an experimental model of sepsis is closely related to increasing afterload conditions

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**Purpose:** Cardiovascular collapse is a significant cause of mortality in sepsis. The purpose of our study was to detect and describe early signs of failing right ventricular (RV) function in septic circulation. Early detection could allow for early goal-directed therapy.

**Methods:** In an experimental model, 10 anaesthetised open-chest pigs, mean weight 53±2.9 kg, were given an infusion of heat-inactivated *E. coli* (60°C, 60 min) in incremental doses to induce a septic response. RV function was assessed by 2D strain echocardiography in the apical long axis view. Peak systolic RV strain was averaged from the 3 RV lateral segments. Pulmonary artery pressure was measured by a pulmonary artery catheter and cardiac output (CO) calculated by thermodilution to obtain pulmonary vascular resistance (PVR). Recordings were performed at baseline and then every hour through 240 minutes or until cardiovascular collapse. The heart was paced atrially for 5 min at 130 beats/min prior to recordings.

**Results:** After a mean of 204 min (165 to 240 interquartile range) of *E. coli* infusion, cardiovascular collapse was established, and CO (6.8±1.2 vs 4.8±2.2 L/min, p=0.05) had decreased. There was an increase in PVR (141±64 vs 519±266 dynes·sec/cm<sup>5</sup>, p=0.003). Early sepsis induced a marked decrease in RV function (RV strain -21±6 vs -16±8%, p=0.05). Importantly, the decrease in peak systolic RV strain was closely connected to the increase in PVR (r=0.74, p<0.05).

**Conclusions:** Induction of *E. coli* sepsis caused significant deterioration of RV function which was closely related to extensive changes in RV afterload conditions as expressed by PVR.

### P4654 : Heart rate as a predictor of cardiovascular risk in coronary heart disease patients with diabetes

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**Background:** Resting heart rate has been shown to predict cardiovascular events in patients with coronary heart disease (CHD). To determine the effect of heart rate on major cardiovascular events in CHD patients with diabetes we analyzed pooled data from the IDEAL and TNT trials, which were comparisons of moderate to high dose therapy (simvastatin 20-40 mg vs. atorvastatin 80 mg/day in IDEAL and atorvastatin 10 mg vs. 80 mg/day in TNT).

**Methods:** A total of 2411 patients with diabetes (1433 of 10,001 randomized in TNT and 978 of 8888 randomized in IDEAL) with complete data for baseline heart rate and clinical predictors were included in this analysis. The effect of heart rate on major cardiovascular events (CHD death, nonfatal myocardial infarction, resuscitated cardiac arrest, or stroke) was evaluated.

**Results:** Of 2411 patients with diabetes, 34% had a baseline heart rate  $\geq 70$  bpm, and 66% had a heart rate  $< 70$  bpm. The rate of major cardiovascular events was 19.8% in those with baseline heart rate  $\geq 70$  bpm, compared with 15.4% in those with heart rate  $< 70$  bpm (HR 1.30, 95% CI 1.07-1.59,  $p < 0.01$ ). After adjustment for differences in baseline characteristics, baseline heart rate  $\geq 70$  bpm remained a significant independent predictor of major cardiovascular events when compared with heart rates  $< 70$  bpm (HR 1.30, 95% CI 1.06-1.60,  $p = 0.02$ ). A resting heart rate  $\geq 70$  bpm was also associated with increased rates of all-cause mortality (HR 1.65, 95% CI 1.30-2.10,  $p = 0.0001$ ) and hospitalizations for heart failure (HR 2.43, 95% CI 1.80-3.27,  $p < 0.0001$ ) compared with heart rate  $< 70$  bpm in unadjusted analyses. These findings held true after adjustment for differences in baseline clinical characteristics.

**Conclusions:** In CHD patients with diabetes, a baseline heart rate  $\geq 70$  bpm was predictive of major cardiovascular events compared with a resting heart rate  $< 70$  bpm. This increase in risk was only partially explained by baseline differences, and suggests that heart rate should be considered an independent risk factor for cardiovascular events in patients with diabetes.

## P4661: A combination of novel biomarkers for coagulation (XIIaA), vascular inflammation (PTX3) and heart failure (BNP) enhances prognostic information in patients admitted with chest pain

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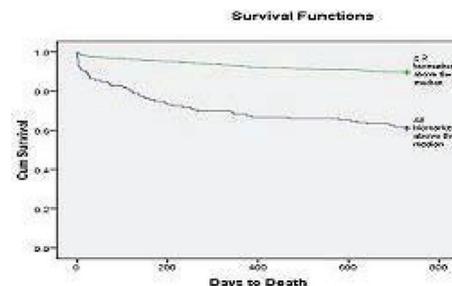
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**Background:** The aim of this analysis was to assess the prognostic value of combining novel biomarkers for coagulation [activated factor XII type A (XIIaA)], vascular inflammation [long Pentraxin 3 (PTX3)] and heart failure [B-type natriuretic peptide (BNP)] in patients admitted with suspected acute coronary syndrome.

**Methods:** Multivariate analysis was performed using a Cox Proportional Hazard Ratio model. Variables included in the model were XIIaA, PTX3, BNP and 18 conventional risk factors for coronary heart disease.

**Results:** 139 of 783 patients had admission levels of all 3 biomarkers above the median. This feature was a significant predictor of all cause mortality (HR 2.36; 95% CI 1.61-3.46, KM survival plot displayed in figure) and of the combined endpoint of death or recurrent TnT positive ( $> 0.05$  ng/mL) event (HR 1.70; 95% CI 1.26-2.29) within 24 months as compared to having only 2 or less biomarkers above the median. Each biomarker added to enhanced C-statistics power with an overall increase from 0.79 to 0.83 (all cause mortality) and 0.76 to 0.77 (combined endpoint). Furthermore, elevation of all 3 biomarkers above the median was a significant predictor in patients with low admission troponin T (TnT  $< 0.05$  ng/mL) (all cause mortality: HR 3.13; 95% CI 1.79-5.49; increase in C-statistics 0.84 to 0.88; combined endpoint: HR 2.42; 95% CI 1.56-3.76; increase in C-statistics 0.79-0.81).

**Conclusion:** A combination of the novel biomarkers XIIaA, PTX3 and BNP improves outcome assessment in unselected patients with suspected ACS.



## P4677 : An analysis of target attainment and safety of pitavastatin in elderly patients

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European Atherosclerosis Society and NCEP target attainment in elderly patients ( $\geq 65$  years) has been reported in a 12-week, double-blind, non-inferiority study ( $n=942$ ) of pitavastatin (PIT) 1, 2, and 4 mg vs. pravastatin (PRA) 10, 20, and 40 mg. The safety of PIT was comparable to these low doses of PRA and did not vary with dose across the dose-range or with age.

Attainment of EAS targets was significantly greater following PIT than PRA: 59.9% and 37.9% for 1 mg data PIT vs. PRA 10 mg, 79.5% and 51.0% for PIT 2 mg vs. PRA 20 mg and 88.1% and 65.7% for PIT 4 mg vs. PRA 40 mg, respectively ( $p < 0.001$  for each comparison); similar, non-significant trends were seen with NCEP criteria. A post-hoc analysis of NCEP target attainment in patients classified as high risk by NCEP criteria showed only 31.3% target attainment at the 1 mg dose, but the majority of patients attained target at 2 mg (58.3%) and the rate was even higher at 4 mg (71.9%).

In the 60-week, open-label extension to this study ( $n=545$ ), 91.0% and 98.7% of the PIT 2 mg group achieved EAS and NCEP targets, respectively. Patients who failed to meet targets on PIT 2 mg ( $n=90$ ) benefitted from up-titration to PIT 4 mg, with 79.2% and 70.1% meeting EAS and NCEP targets, respectively, at Week 60.

The LIVS-01 surveillance study in Japan monitored clinical use of PIT ( $n=19,925$ ) over 2 years. At least 9,614 elderly patients were exposed to PIT, of which 5,136 received PIT 2 mg. In patients receiving any dose of PIT (1 mg, 2 mg or 4 mg), neither dose of PIT nor age were identified as a risk for adverse events (AE) in the rhabdomyolysis/myopathy standard MedDRA Query (R/M SMQ) in a regression analysis when estimated eGFR was included as a factor.

Patients with moderate or severe renal impairment reported significantly more R/M SMQ AEs than patients with normal renal function (moderate vs. normal function, OR=1.663, 95%CI 1.251-2.211,  $p=0.0005$ ; severe vs. normal function, OR=2.968, 95%CI 1.816-4.848,  $p < 0.0001$ ). However, the percentage of patients with an R/M SMQ AE appeared similar across the PIT 1 mg and 2 mg fixed-dose groups, and those taking PIT 4 mg at any time.

In summary, LDL-C lowering with PIT 1-4 mg is superior to PRA 10-40 mg in elderly patients, but patients at moderate to severe risk of cardiovascular events will likely require treatment with 2

or 4 mg doses. Decline in renal function, and not dose of PIT (1-4 mg), or age appears predictive of R/M SMQ events.

## P4702 : Regular alcohol consumption, oral infection status, and the association to myocardial infarction

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**Purpose:** The association of oral infections and cardiovascular disease was studied by exploring the association between alcohol drinking pattern, tooth extraction, and myocardial infarction (MI).

**Methods:** The Oslo II Study 2000 invited 12 764 men, 6 535 of whom gave self reported information on MI, oral health, alcohol, dental status, and other known risk factors for MI. The main oral health issue studied was the reason for tooth extraction grouped in three categories as none, non-infectious, infectious and combined infectious/non-infectious. Results are from cross-sectional study data.

**Results:** No tooth extraction was recorded for 619 men of whom 45 (6%) had a history of MI, non-infectious extractions occurred in 1 587 men of whom 134 (8%) had MI, and 3 626 men had an infectious extraction or a combination of infectious/non-infectious extractions of whom 455 (12%) had a history of MI. Results show that non-infectious extractions were not significantly different compared to no extractions (reference group) (Odds Ratio (OR) =1.14, 95% Confidence Interval (CI): 0.77 - 1.69) in contrast to infectious and a combination of infectious/non-infectious extractions (OR=1.51, 95% CI: 1.05 - 2.16) in logistic regression analysis adjusted for alcohol drinking pattern, age, daily smoking, total cholesterol, systolic blood pressure, level of education, and BMI. Stratified analysis for effect modification by alcohol drinking pattern showed that extraction history was not significant for a regular alcohol drinking pattern of 4-7 times per week but for a less frequent drinking pattern.

**Conclusions:** Infectious tooth extractions are associated with the risk for MI but not non-infectious ones. Regular alcohol drinking (4-7 times per week) modifies the effect of oral infections through tooth extractions on MI indicating a bactericidal effect on the oral microbial flora.

## P4724 : Blood pressure and proximal aortic stiffness is increased in women 3 years after a pre-eclamptic pregnancy

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**Purpose:** Pre-eclampsia is defined by hypertension and proteinuria and occurs in 3-10% of all pregnancies. The pathophysiological adaptation of systemic arterial properties has not been well described.

Thus, we performed a study of systemic arterial properties in women with previous pre-eclamptic pregnancy (PPEP) as compared to women with previous normal pregnancy (PNP).

**Methods:** 35 women (age 37±4 years) with PPEP (3.5±1.0 years) and 65 (age 33±1 years) with PNP (6 months postpartum), were studied. Aortic root pressure and flow were obtained by calibrated right subclavian artery pulse trace, and aortic annular Doppler blood flow recordings. Systemic arterial properties were described by total arterial compliance (C), arterial elastance, (end systolic pressure/stroke volume, Ea) characteristic impedance (parameter of proximal aortic stiffness, ZO), and peripheral arterial

resistance (R). Parameters were estimated both by use of a 4-element Windkessel (WK) model and by Fourier analysis of central aortic pressure and flow data.

**Results:** See Table 1. PPEP had significantly higher blood pressure than PNP. R was not significantly different between the groups, but ZO and Ea was significantly higher, and C trended lower in the PPEP group.

**Conclusion:** Higher blood pressures in women with PEP is not explained by higher peripheral arterial resistance, but is related to a stiffer proximal aorta, and lower arterial compliance. This may relate to the higher risk for later cardiovascular events observed in women with PEP.

## P4812 : N-terminal pro-B-type natriuretic peptide is associated with the incidence of sudden cardiac death in patients with stable coronary artery disease and preserved left ventricular systolic function

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**Purpose:** N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels have been associated with the incidence of sudden cardiac death (SCD) in patients with heart failure of both ischemic and non-ischemic origin. Whether circulating NT-proBNP levels are associated with the incidence of SCD in patients with coronary artery disease (CAD) without heart failure is unknown. Accordingly, we assessed the association between NT-proBNP and the incidence of SCD during long-term follow-up of a large cohort of low risk patients with stable CAD and preserved left ventricular (LV) systolic function.

**Methods:** Circulating concentrations of NT-proBNP at baseline were assessed in 3675 patients with stable

Table 1

	PEP	PNP	P
Mean arterial pressure (mmHg)	102±17	86±8	<0.001
Systolic blood pressure (mmHg)	129±21	110±9	0.002
Heart rate (beats/min)	70±7	66±7	0.011
Cardiac output (L/min)	5.5±1.2	4.9±0.9	0.020
R (mmHg/(ml/s))	1.16±0.31	1.10±0.29	0.295
ZO WK (mmHg/(ml/ms))	87±33	68±23	0.003
ZO FD (mmHg/(ml/ms))	72±30	55±22	0.004
C WK (ml/mmHg)	1.28±0.42	1.40±0.45	0.239
C PPM (ml/mmHg)	1.03±0.33	1.14±0.30	0.104
Ea (mmHg/ml)	1.45±0.39	1.27±0.28	0.004

Mean ± SD.  $p < 0.05$  (unpaired t-test), FD = frequency domain estimate, PPM = pulse pressure method.

NT-proBNP quartiles	Unadjusted HR (95%CI)	p	Adjusted HR (95% CI)	p
women = 15-32 pg/mL	1.00		1.00	
women = 32-61 pg/mL	2.26 (0.70-7.35)	0.174	1.75 (0.52-5.85)	0.367
women = 61-115 pg/mL	2.51 (0.80-8.10)	0.115	1.82 (0.54-6.11)	0.336
women = 115-2427 pg/mL	8.43 (2.98-23.83)	<0.001	4.89 (1.58-15.18)	0.006

CAD and ejection fraction > 40% enrolled in the PEACE trial. SCD was defined as witnessed out-of-hospital cardiac arrest with or without antecedent angina, unwitnessed death without antecedent changes in symptoms, and sudden, unexpected death in-hospital.

**Results:** During follow-up 55 patients died suddenly. After adjustment for treatment assignment only, NT-proBNP levels were strongly associated with the incidence of sudden cardiac death (hazard ratio (95% confidence interval): 2.21 (1.72-2.83) per 1 SD increase in log NT-proBNP). After adjustment for conventional cardiovascular risk markers, NT-proBNP remained a strong predictor of sudden cardiac death (hazard ratio (HR) (95% CI): 2.03 (1.49-2.78);  $p < 0.001$ ). The association between NT-proBNP by sex-specific quartiles and the incidence of SCD is summarized in the Table.

**Conclusion:** In patients with stable CAD and preserved LV systolic function NT-proBNP is associated with the risk of SCD independently of conventional cardiovascular risk factors. In particular, patients with levels in the fourth quartile (i.e. > 98 pg/mL in men and 115 pg/mL in women) seem to be at increased risk.

## P4840 : Beta blockers, statins and recommended doses of ACE-I improve survival in non-randomized patients with heart failure. A propensity score analysis of the Norwegian Heart Failure Registry

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### Norway)

**Purpose:** Randomized controlled trials (RCTs) have shown that ACE-I, ARB and beta blockers improve survival in patients with heart failure (HF). This benefit is difficult to assess in observational studies because of selection bias. Statins, by contrast, have been suggested to have survival benefits that were not reproduced by two large RCTs. This study sought to assess the adherence to HF guidelines for ACE-I, ARB and beta blockers and the possible association of ACE-I or ARB, beta blockers and statins with survival in the large contemporary Norwegian Heart Failure Registry.

**Methods and Results:** This study included 4874 patients newly diagnosed with HF of any etiology (mean LVEF 33%  $\pm$  12) from January 2000 to February 2008 and followed until death or December 2008. On multivariate analysis, baseline characteristics adversely associated with survival were age, s-creatinine, NYHA class III/IV, CHD, diabetes, stroke and intermittent claudication. Weight, hemoglobin, and sodium were independently associated with a better survival. Beta blockers (HR, 0.78; 95% CI, 0.68-0.90;  $P = 0.001$ ) and statins (HR, 0.73; 95% CI, 0.64-0.84;  $P < 0.001$ ) were significantly associated with improved survival. The association between statins and survival was independent from and did not interact with total cholesterol values; higher total cholesterol was associated with improved survival (HR, 0.90; 95% CI 0.85-0.95;  $p < 0.001$ ). In patients without ARB, ACE-I doses  $\geq 50\%$  of the recommended target were associated with improved survival (HR, 0.83; 95% CI, 0.72-0.95;  $P = 0.006$ ). Age and NYHA class III/IV were independent risk factors for being treated with neither ACE-I or ARB nor beta blockers; s-creatinine for not being treated with ACE-I or ARB. A propensity score (PS) was calculated for each drug and used in Cox regression models. Adjusted for PS, ACE-I doses  $\geq 50\%$  of the target (HR, 0.84; 95% CI 0.72-0.99;  $p = 0.04$ ), beta blockers (HR, 0.82; 95% CI 0.70-0.97;  $p = 0.02$ ) and statins (HR, 0.73; 95% CI, 0.62-0.85;  $p < 0.001$ ) were associated with better survival.

**Conclusion:** Multivariate and propensity score analyses both showed survival benefits with beta blockers, statins and ACE-I doses  $\geq 50\%$  of target in this contemporary heart failure cohort. Old age and NYHA class III/IV were risk factors for not being treated with guidelines indicated drugs. This study raises again the possible protective

effect of statins in heart failure, but more importantly, stresses the importance of guidelines adherence, particularly the use of beta blockers. Moreover, respecting the recommended target doses of ACE-I appears to have a crucial role in survival improvement.

## P4892 : Athletes do not exhibit enhanced LV systolic and diastolic function at rest by standard echo and tissue velocity imaging

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**Background:** Resting LV stroke volume is increased in athletes compared to controls. The changes in resting LV systolic- and diastolic function in athletes evaluated by tissue velocity imaging (TVI), have been contradictory. Noteworthy, the sample sizes of these studies have been small. The aim of the present study was therefore to investigate this issue in a study with a larger number of athletes.

**Methods:** As part of the mandatory cardiac screening of elite Norwegian male football players prior to the 2008 season, the following TVI indices were measured in 594 players and 46 matched controls: S (average of peak systolic velocity at septal and lateral LV basal walls) as an index of LV systolic function, E' (average of early diastolic peak velocity at the septal and lateral part of the mitral valve), and early (E) and atrial (A) transmitral peak filling velocities by standard Doppler echo. From these measurements the E/E' and E/A ratios were calculated as indices of LV diastolic function. LV end-diastolic (LVEDV) and systolic volume (LVESV) were analysed by standard 2D echo, and LVmass by M-mode according to the formula:  $0.8 \times (1.04[(LVlDd + PWTd + SWTd)^3 - (LVlDd)^3]) +$

$0.6g$ , where PWTd and SWTd are posterior- and septal wall thickness, and LVlDd, LV interventricular diameter at end-diastole, respectively. All echo measurements were performed blinded. Blood pressure was measured, and body mass index (BMI) and body surface area (BSA) were calculated.

**Results:** There were no significant differences in age, BMI, BSA or blood pressure between the groups. For other results, see Table 1.

**Conclusion:** The present large scale study has demonstrated, as expected, that the athletes have increased LV volumes and mass. There was, however, no difference in LV systolic or diastolic function by standard echocardiography or novel TVI between the football players and the controls at rest.

## P4893 : Peak systolic acceleration: a new marker of long axis contractility

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**Background:** Myocardial and endomyocardial accelerations have been shown to relate to contractility in adults and children. This study was designed to assess and validate myocardial acceleration of the left ventricular lateral mitral valve annulus by tissue Doppler in neonatal pigs by comparison with invasive hemodynamic data.

**Methods:** Ten newborn pigs were studied under general anesthesia. Modulation of inotropy (dobutamine, esmolol), preload and afterload was done. Heart rate was increased by atrial pacing at each stage of inotropy. Tissue Doppler velocities were measured at each stage of inotropy and

again with increased heart rate. Invasive measurements consisted of high fidelity pressures (Millar catheters)

Table 1

	LVSV (ml)	LVEF (%)	LVEDV (ml)	LVESV (ml)	LVmass (g)	S (cm/s)	E' (cm/s)	E/A	E/E'
Football players (n=594)	82.3*	56.3	145.9*	63.6*	181.5*	7.2	13.2	2.1	6.3
	±17.3	±3.7	±28.0	±12.7	±35.2	±1.1	±2.2	±0.5	±1.2
Controls (n=46)	69.3	55.5	124.8	55.5	149.7	7.2	12.9	1.9	6.6
	±14.1	±3.6	±23.9	±3.6	±35.6	±1.1	±2.4	±0.5	±1.7

\*p<0.001 vs. controls.

in the left ventricle (LV) and aorta, and volume (conductance) in the LV. Velocity was derived into acceleration, and pressures and volume into  $dP/dt$  and Flow respectively. All data were integrated in a computer and analyzed on a beat to beat fashion. ESPVR, Emax, PRSW was extracted for each stage of inotropy. We used mixed linear models for statistical modelling. Statistical models included unique hemodynamic determinants and assessed their effect on systolic acceleration. Peak systolic acceleration (pSac) was measured after the onset of left ventricular pressure rise. The parameter estimate (beta) indicates the magnitude and directional change in the tissue Doppler parameter for a 1-unit increase in the corresponding variable.

**Results:** Maximum  $dP/dt$  was found to be the strongest determinant of pSac (beta=0.9±0.1; P<0.001) during inotropy modulation. Log pSac was related to logarithmic transformed ESPVR, Emax and PRSW (beta= 0.35±0.11; P= 0.005, beta= 0.53±0.14; P= 0.001 and beta= 0.9±0.14; P< 0.001 respectively). During preload reduction pSac determined log  $dP/dt_{max}$  (beta= 1.33±0.37; P< 0.001), while during afterload increase log ET (beta= -0.76±0.33; P< 0.032) and log SW (beta= 0.26±0.10; P< 0.026) were the strongest determinants of pSac. Log pSac increased by 0.10±0.03 cm/s<sup>2</sup> (P=0.03) with pacing at a higher rate. Accelerations occurring before and during the isovolumic period were not associated with inotropic parameters.

**Conclusion:** A stable and constant relation towards maximum  $dP/dt$  and preload independent parameters could be established in this study. pSac is a marker of long axis contractility, and this study provides evidence that pSac should be viewed upon as the long axis contribution to maximum  $dP/dt$ .

## P4903 : Determinants of mitral annulus peak systolic velocity - a study in piglets

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**Background:** Systolic long axis myocardial dysfunction is an important determinant for mortality in adults. This study aimed at defining hemodynamic determinants of tissue Doppler derived, long-axis function, parameters in the newborn.

**Methods:** Ten newborn pigs were studied under general anesthesia. Modulation of inotropy (dobutamine, esmolol), preload and afterload was done. Heart rate was increased by atrial pacing at each stage of inotropy. Tissue Doppler velocities in the mitral valve annulus were measured at each stage. Invasive measurements included high fidelity pressures (Millar catheters) in the left ventricle (LV) and aorta, and volume (conductance) in the LV. Velocity was integrated into displacement, and stroke volume and pressure was derived into flow and  $dP/dt$  respectively. All data were integrated in a computer and analyzed on a beat to beat fashion. For statistical modelling we used linear mixed models. Statistical models included unique hemodynamic determinants (stroke volume, flow, heart rate, ejection time and maximum  $dP/dt$ , effective arterial elastance) to assess their effect on peak systolic velocity (S') and displacement (D). The parameter estimate (beta) indicates the magnitude and directional change in the tissue Doppler parameter for a 1-unit increase in the corresponding variable.

**Results:** During inotropy modulation with dobutamine S' increased, while (D) did not change. There was no change in S' with pacing at a higher rate, while D decreased with pacing. The strongest determinants of S' included both peak systolic flow (PSF, beta= 0.09 cm/mL; P<0.001) and end-systolic pressure (ESP, beta= -0.07 cm/mL; P=0.003). At the same time a strong association was found between stroke volume (SV) and D (D, beta= 0.05cm/mL; P<0.001). Hemodynamic changes were evident during modulation of pre- and afterload. Ejection time, stroke volume, end-systolic pressure, maximum  $dP/dt$  and PSF were all found to influence S' and D during preload and afterload modulation. The ratio PSF/S' and SV/D were found to be stable under the different hemodynamic modulations.

**Conclusion:** First, this study provides feasibility of tissue Doppler assessment of the lateral mitral valve annulus long axis velocity in the neonate, even at higher heart rates. Secondly it provides validity to the assumption that systolic mitral valve annulus displacement is the long axis contribution to stroke volume, and peak systolic mitral valve annulus velocity is the long axis contribution to peak systolic flow.

## 4936 : Evaluation of left ventricular electrical dyssynchrony by onset of myocardial shortening: rate of LV pressure rise is an important confounder

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**Background:** Onset of myocardial shortening (OS) has been proposed as a marker of LV dyssynchrony. There is, however, limited insight into the mechanisms which determine OS. We investigate the hypothesis that timing of OS is determined not only by electrical conduction and electromechanical activation, but also by rate of change of LV pressure (dP/dt) at the time of regional electrical activation.

**Methods:** In 7 anaesthetised dogs with left bundle branch block (LBBB) and LV micromanometers we measured intramyocardial electromyograms (EMG) and myocardial segment lengths by sonomicrometry during changes in load. As reference method for timing of electrical activation we used EMG and for mechanical activation onset of active force generation by pressure-segment length loop analysis. Time to onset OS was calculated from onset R in intramyocardial EMG. Measurements were done in the septum and LV lateral wall (Fig 1).

**Results:** Timing of electrical activation and mechanical activation remained unchanged during changes in load. There was no significant correlation between time to OS and LV pressure at time of electrical activation. There was, however,

a strong correlation between time to OS and LV dP/dt at time of electrical activation ( $r=0.88$ , Fig 2). Therefore, changes in timing of OS were not caused by changes in electromechanical activation, but were attributed to changes in LV dP/dt.

**Conclusions:** Timing of OS is highly dependent on rate of LV pressure rise. We suggest that the underlying mechanism is that a segment does not shorten until it generates active stress at a rate which is faster than the rate of increase in LV pressure. In late activated segments which contract at higher LV dP/dt, this mechanism may cause additional delay in onset of shortening, and thus aggravates mechanical dyssynchrony.

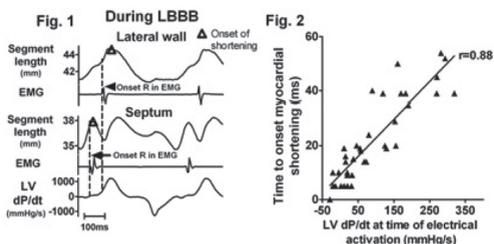
## 4965 : Troponin-T, but not CK-MB, predicts mortality after coronary artery bypass graft surgery

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**Purpose:** The prognostic value of elevated cardiac biomarkers after coronary artery bypass graft (CABG) surgery is not clear. We aimed to test the hypothesis that the biomarkers CK-MB and troponin-T are predictors of mortality, i.e. intermediate-term survival after CABG surgery.

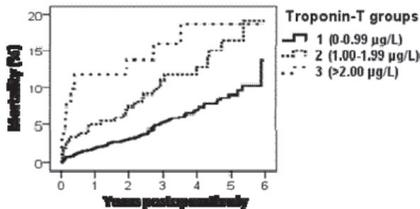
**Methods:** 1351 consecutive patients undergoing elective isolated on-pump CABG surgery were prospectively included. The median follow-up time was 3.7 years. Survival status on all patients was ascertained through the Norwegian National Registry. CK-MB and troponin-T were measured at 7, 20 and 44 hours postoperatively and the maximal value for each patient was analyzed further using Kaplan-Meier plots and Cox regression models. As there is no clear consensus in the literature regarding the level of CK-MB and troponin-T that should be considered as cut-off for per- or postoperative myocardial infarction, we stratified the patients into groups using cut-off values based on a pilot study (n=100).

**Results:** Troponin-T was divided into three groups: 0-0.99  $\mu\text{g/L}$  (n=1072), 1-1.99  $\mu\text{g/L}$  (n=210) and >1.99  $\mu\text{g/L}$  (n=51). CK-MB was divided into four groups: 0-24.9  $\mu\text{g/L}$  (n=545), 25-49.9  $\mu\text{g/L}$  (n=582), 50-74.9  $\mu\text{g/L}$  (n=109) and >75  $\mu\text{g/L}$  (n=88). Comparing the three groups for troponin-T (figure), both group 2 and group 3 had significantly higher Hazard Ratio



(HR) for mortality compared to group 1 (HR 1.97, CI 1.27-3.06, p=0.003 for group 2 and HR 2.65, CI 1.33-5.28, p=0.006 for group 3). There were no significant changes in mortality between the CK-MB groups.

**Conclusions:** Increased postoperative levels of troponin-T, but not CK-MB, were rather strongly associated with increased mortality after CABG surgery. Our data suggest that postoperative troponin-T is a marker of survival after CABG surgery.



Kaplan-Meier plot for troponin-T groups

## 4985 : Risk factors for unexpected sudden death in patients with non-symptomatic aortic stenosis (the SEAS study)

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**Purpose:** Sudden death (SD) is a rare, but feared complication in aortic stenosis (AS). Risk in true asymptomatic patients is reported to be <1%/year, based on small studies with few events. Characteristics of and risks for SD have not been studied prospectively in a large trial.

**Methods:** In prospective SEAS study, including 1,873 patients with asymptomatic AS (Vmax 2.5 to 4.0 m/s), followed for 52.2 months, 40 patients experienced SD as classified by a blinded Endpoint Committee according to a pre-defined protocol. Cox regression analyses were performed, including all n=40 with available biochemical and clinical data, of these n=35 with available baseline echocardiographic data, and of these n=24 without previous endpoint events of either aortic valve- or ischemic-related nature.

**Results:** Biochemical or clinical variables at baseline did not significantly predict SD. Consistently through any grouping of patients, the strongest predictors of SD were Left ventricular mass (LVM) and LVM index (LVMI) at baseline and last echocardiographic examination before death, posterior wall thickness (PW) and mean transaortic gradient at baseline. Omitting patients with previous events before SD, baseline LVMI, LVM and PW remained strong predictors (Table 1).

**Conclusions:** LVM, LVMI and PW are strong predictors of SD in asymptomatic to moderate AS.

Table 1. HR per 1 SD change for sudden death with 95% CI of selected baseline variables

Variable	Unit	HR	95% CI	p-value
N=40*				
Heart rate	b/min	1.27	0.95-1.70	0.107
Body Mass Index	kg/m <sup>2</sup>	0.76	0.53-1.09	0.137
N=35 with baseline echocardiography*				
Aortic jet velocity	m/sec	1.33	0.97-1.82	0.073
Aortic valve area	cm <sup>2</sup>	0.77	0.51-1.16	0.214
Max aortic gradient	mmHg	1.36	0.98-1.88	0.061
Mean aortic gradient	mmHg	1.37	1.01-1.87	0.049
Posterior wall thickness	mm	1.55	1.14-2.11	0.006
Left ventricular mass	g	1.61	1.23-2.10	< 0.001
LV mass index	g/m <sup>2</sup>	1.65	1.29-2.11	<0.001
N=24 with complete data and no other CVD event**				
Posterior wall thickness	mm	1.63	1.14-2.32	0.007
Left ventricular mass	g	1.72	1.32-2.25	<0.001
LV mass index	g/m <sup>2</sup>	1.87	1.46-2.39	<0.001

\*Adjusted for age and sex. \*\*Adjusted for age.

## 4986 : Left ventricular mass, an independent predictor of morbidity and mortality in aortic valve stenosis

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Table 1

	MCE	AVE	ICE
LV mass index (31 g/m <sup>2</sup> , 1 SD)	1.18(1.09-1.28)*	1.15(1.06-1.24)*	1.28(1.15-1.42)*
Aortic jet velocity (0.54 m/sec, 1 SD)	1.93(1.77-2.09)*	2.07(1.90-2.25)*	1.41(1.26-1.58)*
Simvastatin/Ezetimibe treatment	0.95(0.81-1.11)	0.95(0.80-1.12)	0.77(0.61-0.97)†
Female gender	1.01 (0.85-1.20)	1.02(0.85-1.22)	0.75(0.59-0.97)†
Age (9.6 years, 1 SD)	1.09 (1.01-1.18) †	1.06(0.97-1.15)	1.62(1.43-1.85) *

Predictors of cardiovascular events in Cox regression analysis. Results presented as Hazard ratio (95% confidence intervals); \* $p < 0.01$ ; †  $p < 0.05$ .

**Purpose:** Higher left ventricular (LV) mass is associated with increased morbidity and mortality in general and hypertensive populations. It is unknown if LV mass is a prognosticator in aortic stenosis (AS).

**Methods:** Cox regression analysis was used to assess the impact of baseline left ventricular (LV) mass on rate of major cardiovascular events (MCE, the primary endpoint, combined aortic valve and cardiovascular death and morbid events) and aortic valve events (AVE) and ischemic cardiovascular events (ICE, both secondary endpoints) in 1730 patients (39% women) with asymptomatic AS participating in the Simvastatin Ezetimibe in Aortic Stenosis (SEAS) study. Patients were follow-up during 4.3 years of randomized placebo controlled treatment with combined simvastatin 40 mg and ezetimibe 10 mg. LV mass was calculated by Devereux's equation and indexed for body surface area.

**Results:** At baseline, mean age was 67 years, average LV mass index  $102 \pm 31$  g/m<sup>2</sup> and peak aortic jet velocity  $3.09 \pm 0.54$  m/sec, respectively. During follow up, 606 MCE, 560 AVE and 296 ICE occurred. In Cox regression analysis, 1 standard deviation (31 g/m<sup>2</sup>) higher LV mass index predicted 15-28% increased rate of cardiovascular events ( $p < 0.01$ ), independent of AS severity, age, gender and randomized study treatment. (Table)

**Conclusion:** Higher LV mass index predicts increased cardiovascular morbidity and mortality in AS independent of severity of AS.

## 5010 : Exercise-induced ventricular arrhythmias in CPVT patients occur at lower heart rate on beta-blocker therapy

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**Purpose:** Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited cardiac disease which predisposes to exercise-induced life-threatening arrhythmias. The current therapeutic recommendations are beta-blocker therapy and ICD implantation. We aimed to determine the effect of beta-blocker treatment on exercise-induced arrhythmias in CPVT patients.

**Methods:** A total of 36 CPVT patients were followed for 24 (8-288) months. Of these, 6 were index patients and 30 were mutation positive family members diagnosed by cascade genetic screening. Clinical evaluation including exercise test was performed at inclusion and repeated 3 months after initiation of beta-blocker therapy in maximum tolerable doses. Heart rate and workload at occurrence of ventricular premature beats (VPB), couplets and non-sustained VT (nsVT) were recorded.

**Results:** Exercise-induced arrhythmias were observed in 27 patients (75%) before treatment. Resting and maximum heart rate during exercise test were reduced by beta-blocker treatment ( $p < 0.001$ ) (Table). VPBs and most severe arrhythmias on beta-blocker therapy appeared at 14% and 15% lower heart rate, respectively (both  $p = 0.01$ ), but at a similar workload as without beta-blocker therapy (Table). Beta-blocker therapy suppressed nsVT in 4 of 6 mutation carriers. Less serious arrhythmias were not affected.

**Conclusion:** Exercise-induced arrhythmias in CPVT patients occurred at lower heart rates on beta-blocker treatment. Beta-blocker therapy appeared to suppress nsVT, while less severe arrhythmias were unchanged. These findings suggest that the protective effects of beta-blocker therapy in CPVT patients are not only due to negative chronotropy.

### Results of exercise test

	Before beta-blocker	On beta-blocker	p-value
Heart rate at rest (bpm)	70±17	55±14	<0.001
Maximum heart rate during exercise test (bpm)	173±24	139±22	<0.001
Heart rate for debut of VPB (bpm)	132±37	114±22	0.01
Workload for debut of VPB (Watt)	121±43	123±44	0.78
Heart rate at most severe arrhythmia (bpm)	144±30	123±20	0.01
Non-sustained VT (n)	6	2	0.08

Mean ± standard deviation. P-value from paired Student t-test and Wilcoxon rank test. Bpm: beats per minute, VPB: ventricular premature beat.

## 5087 : Prognostic value of osteoprotegerin in chronic heart failure: the GISSI-HF trial

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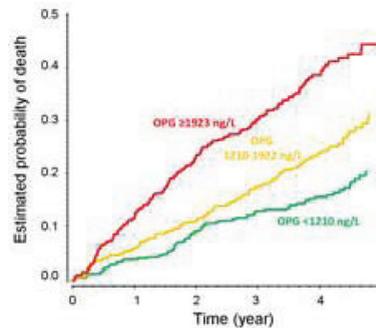
**Purpose:** Osteoprotegerin (OPG), a member of the tumor necrosis factor receptor superfamily, is a strong prognostic indicator of mortality and heart failure in patients with acute coronary syndromes. The association between OPG levels and outcome in patients with chronic heart failure (CHF) is unknown. Accordingly, we assessed the association between OPG at baseline and the incidence of mortality from all causes in a large cohort of patients with chronic heart failure.

**Methods:** Circulating concentrations of OPG at baseline were assessed in 1229 patients with CHF recruited from 51 clinical centres and included in the GISSI-HF trial. Patients were randomized to n-3 PUFA (1 g/d) or rosuvastatin (10 mg/d) vs. placebo. OPG was analyzed by ELISA.

The association between OPG and outcome was assessed by Cox proportional hazards regression.

**Results:** During a median follow-up time of 3.9 years 332 patients died. By univariate analysis, baseline OPG levels were strongly associated with the incidence of death (hazard ratio (95% confidence interval): 1.53 (1.40-1.67) per 1 SD increase in log OPG. After adjustment for conventional risk markers, including age, LVEF, history of COPD, diabetes, atrial fibrillation, prescription of digitalis, beta blockers and diuretics, OPG remained a significant predictor of death (HR (95% CI): 1.20 (1.06-1.35); p<0.001). The figure shows the cumulative mortality rate by tertiles of OPG (p<0.0001).

**Conclusion:** In patients with CHF OPG is associated with the incidence of death independently of conventional cardiovascular risk factors.



OPG\_GISSI\_HF\_figure

## 5089 : No impact of atrial fibrillation on mortality risk in optimally treated heart failure patients

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**Purpose:** The aim of this study was to investigate the impact of atrial fibrillation (AF) on mortality in a large registry on heart failure (HF) patients treated at specialized HF outpatient clinics in Norway.

**Methods:** Patients referred to Norwegian HF outpatient clinics were enrolled between October

2000 and February 2006. Patients with other heart rhythm than AF or sinus rhythm (SR) were excluded. Mortality data were obtained from the National Statistics Bureau, Statistics Norway with the last update February 2008. Univariate Cox regression analysis was used to investigate the impact of AF and other variables on survival. Multivariate analysis was performed using Cox regression models including variables related to both AF and risk of death with a p-value of <0.1.

**Results:** 4048 patients were included. AF was present at baseline in 1391 patients (34.4%), whereas 2657 were in SR. Adherence to guidelines regarding medical treatment was high; 88.4% received angiotensin converting enzyme inhibitors and/or angiotensin receptor blockers, whereas 82.8% received beta blockers. Median follow-up was 28 months. AF patients were older than patients in SR (74±10 vs. 68±13 years, p<0.001). In univariate analysis, AF patients had a higher risk of death than patients in SR (hazard ratio (HR) 1.18 (95% confidence interval (CI) 1.04-1.34); p=0.008). However, after adjusting for confounding factors (age, NYHA class, coronary artery disease as the main cause of HF, use of any loop diuretic, hemoglobin level and serum-creatinine), AF was no longer associated with increased risk of death (HR 1.04 (95% CI 0.90-1.19); p=0.619).

**Conclusion:** In this cohort of 4048 HF patients receiving optimal medical treatment at specialized HF clinics, AF was not associated with increased risk of death after adjusting for confounding factors.

## 5117 : Hypoperfusion by contrast echocardiography predicts coronary artery disease severity in non-ST elevation myocardial infarction

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**Background:** Thrombolysis In Myocardial Infarction (TIMI) score used for risk prediction in non-ST elevation myocardial infarction (NSTEMI)

may underscore angiographic coronary artery disease (CAD) severity.

**Methods:** We evaluated hypoperfusion diagnosed by contrast echocardiography in relation to TIMI score and quantitative coronary angiography (QCA) in 110 patients (age 67 years, 31% women) with NSTEMI scheduled for coronary angiography. Segmental myocardial wall motion and perfusion was visually scored using a 17 segment left ventricular model. CAD was assessed by QCA.

**Results:** In the total study population 29% had ST-depression, 35% prior CAD, 45% hypertension, 19% diabetes, 40% a family history of CAD, 50% hypercholesterolemia, and 28% were current smokers. All patients had elevated troponin T (mean 0.68±1.2 µg/l), and mean TIMI risk score was 3.1±1.5. By QCA 15% of patients had normal angiography, while 1-, 2- and 3-vessel disease (VD) was present in 35%, 27% and 23%, respectively. Angiographically severe CAD (left main stem stenosis, proximal LAD stenosis or 3-VD) was found in 42%. TIMI risk score as well as the number of left ventricular segments with hypoperfusion or wall motion abnormality by echocardiography increased with number of stenotic vessels by QCA (Table 1). However, in multiple logistic regression hypoperfusion by contrast echocardiography predicted presence of angiographically severe CAD (OR 1.39 [1.19-1.64], p<0.01) independent of TIMI risk score (OR 1.24 [0.91-1.69], p=0.170) and wall motion score (OR 1.01 [0.87-1.16], p=0.929). Receiver Operating Curve analysis confirmed hypoperfusion by contrast echocardiography as the superior identifier of angiographically severe CAD (AUC 0.78 [0.69-0.87], p<0.01). (Table)

**Conclusion:** Detection of hypoperfusion by contrast echocardiography in acute NSTEMI can identify patients with severe CAD independent of TIMI score and wall motion score.

## 5160 : Long- term symptomatic and hemodynamic results of percutaneous transluminal septal myocardial ablation (PTSMA). Results from Scandinavian HOCM database

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Table 1

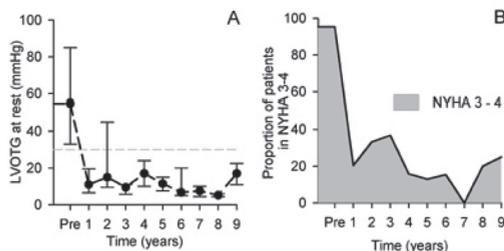
	0-VD (n=16)	1-VD (n=39)	2-VD (n=30)	3-VD (n=25)
Hypoperfusion (segments)	3.8±2.2	5.8±2.4	7.9±3.5**	10.5±2.7**
Wall motion abnormality (segments)	2.1±3.2	3.0±2.6	3.9±3.4	5.4±4.8*
TIMI risk score	2.3±0.9	3.3±1.4	3.5±1.6*	3.7±1.4*

\*p<0.05;\*\*p<0.01 vs. 0-VD group.

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**Background:** PTSMA is performed at low volume in heart centres world wide, without solid evidence of the safety and long-term efficiency. Scandinavian HOCM Database (HOCM - Hypertrophic obstructive cardiomyopathy) was established to analyse long term results of PTSMA performed at low volume in centres performing percutaneous coronary intervention (PCI) at high volume.

**Methods and results:** Four Scandinavian tertiary heart centres with an annual PTSMA volume of < 25 procedures per year retrospectively analyzed results of 233 patients treated with 255 PTSMA procedures from 1999 to 2009. The PTSMA procedures were performed by highly experienced PCI operators (>1000 PCI procedures per operator). Patients were 60±14 years of age and 49% were female. Left ventricular outflow tract gradient (LVOTG) at rest decreased from 55 (33-85) mmHg (median (inter quartile range)) at baseline to 11 (7-20) mmHg at one year follow up (p<0.001; Fig. A). LVOTG during Valsalva manoeuvre decreased from 97 (70-140) mmHg at baseline to 15 (9-34) mmHg at one year follow up (p<0.001). The LVOTG at rest and during Valsalva manoeuvre remained low during 9 years of follow up. At one year the prevalence of NYHA 3-4 decreased from 95% at baseline to 20% (p<0.001) (Fig. B), syncope decreased from 17% to 1.4% (p<0.01), and CCS 3-4 decreased from 14% to 4% (p<0.01). This symptomatic improvement was sustained during 9 years follow up.



Long term results of PTSMA

**Conclusion:** HOCM patients with severe symptoms due to high degree of LVOTG can be managed by PTSMA performed at low volume in highly experienced PCI centres. The hemodynamic and symptomatic improvements after PTSMA are sustained at long-term.

## P5337 : The influence of cyp 2c19\*2 polymorphism on functional platelet testing in clopidogrel users

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Different platelet function tests can be used to evaluate the degree of achieved platelet inhibition in patients treated with clopidogrel. The presence of CYP 2C19\*2 polymorphism can reduce the formation of the active metabolite of clopidogrel in the liver, resulting in less platelet inhibition.

**Aims and Methods:** Patients with symptomatic, coronary artery disease (78% male, mean age 62 years), all on chronic single aspirin treatment (160 mg/d) were randomized to continue on aspirin or change to clopidogrel 75 mg/d in the ASCET study. In 225 randomly selected patients blood samples for platelet function tests and genotyping were drawn in fasting condition 24 hours after the last intake of medication, after 1 month on clopidogrel. VASP was determined by use of flowcytometry (PLT VASP/P2Y12, Biocytex, France) and expressed as Platelet Reactivity Index (VASP-PR). The platelet reaction unit (PRU) was determined by use of VerifyNow P2Y12 (Accumetrics, US). We defined the cut-off for clopidogrel response as measured by VASP and VerifyNow, as the lower 5 percentile of patients on chronic aspirin treatment (n=105), giving VASP-PR ≥55% and PRU ≥170 respectively, to be resistant. The 2C19\*2 G/A polymorphism (rs 4244285) was determined by the Applied Biosystems 7900HT Fast Real-time PCR system.

**Results:** The total frequency of clopidogrel resistance was 20.8% by VASP-PR and 31.1% by PRU. The concordance (agreement) between clopidogrel resistance determined by the two methods was 74.7% (kappa 0.389, p<0.001). The number

of patients being hetero- and homozygote combined for the CYP 2C19\*2 polymorphism (GA/AA), was 64 (28%).

Platelet reactivity was significantly higher in clopidogrel-treated patients with the polymorphism compared to wild-type patients (GG). VASP-PRI was 50.9% (SD19) in patients having the polymorphism compared to 38.3% (SD21) in patients with the GG genotype ( $p=0.001$ ). Correspondingly, the mean PRU was 165 (SD67) compared to 124 (SD69) ( $p<0.001$ ). The frequency of clopidogrel resistance in patients with the polymorphism was 32% compared to 16% in wild-type patients when defined by VASP-PRI ( $p=0.006$ ). When defined by VerifyNow (PRU), the corresponding frequencies were 53% and 22% ( $p<0.001$ ).

**Conclusions:** Clopidogrel treated patients with the CYP 2C19\*2 polymorphism have significantly increased platelet reactivity compared to patients with wild-type, evaluated with the VASP determination, and even more pronounced with the VerifyNow P2Y12 method. The consequences for clinical outcome are under investigation.

## **P5509 : Circulating PAI-1 activity and t-PA antigen are associated with newly diagnosed abnormal glucose regulation in patients with acute STEMI**

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**Purpose:** Increased risk of coronary artery disease in patients with abnormal glucose regulation (AGR) is not fully explained by traditional risk factors. Impaired haemostasis with enhanced thrombotic risk in patients with AGR may be mediated by impaired fibrinolysis. Tissue plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1) have been shown to be elevated both in patients with coronary artery disease and glucose abnormalities and may indi-

cate long-standing vascular damage associated with insulin resistance.

The aims of the present study were to elucidate possible associations between the levels of circulating PAI-1 activity and t-PA antigen measured in-hospital and AGR classified by an oral glucose tolerance test (OGTT) three months later, in patients with acute ST-elevation myocardial infarction (STEMI) without previously known diabetes.

**Methods:** PAI-1 activity and t-PA antigen were measured in fasting blood samples from 199 patients (35 women) within 24 hours after a primary percutaneous coronary intervention (PCI). A standardised OGTT was performed three months later. The patients were categorised according to the WHO criteria and the term AGR ( $n=49$ ) was defined as the sum of impaired fasting glucose, impaired glucose tolerance, and type 2-diabetes. Continuous variables were categorised into quartiles. A trend analysis across the quartiles identified the cut off point used. The Mantel-Haenszel method was used to highlight potential effect modification and to quantify potential confounders. Adjustment for confounders (scTroponinT, age, and gender) was performed using a logistic regression model.

**Results:** The median (25th, 75th percentiles) levels of PAI-1 activity and t-PA antigen measured in-hospital were 16.7 (10.2, 24.2) U/ml and 12.5 (10.1, 16.2) ng/ml, respectively. The median levels of PAI-1 activity and t-PA antigen measured in-hospital were higher in patients with abnormal compared to normal glucose regulation classified at three months ( $p=0.008$  and  $p=0.003$ , respectively). High levels of PAI-1 activity ( $\geq 75$  percentile) measured in-hospital were associated with AGR with an adjusted OR 2.2 (1.05, 4.40). Gender was an effect modifier on the association between high levels of t-PA antigen ( $\geq 75$  percentile) and AGR and the adjusted OR for the association in men was 2.78 (1.19, 6.51).

**Conclusion:** High levels of circulating PAI-1 activity and t-PA antigen measured within 24 hours after an acute STEMI were associated with AGR classified three months later. The association between high levels of t-PA antigen and AGR was, however, present only in men.

## **P5556 : Tumor Necrosis Factor-alpha antagonists reduce intima media progression rate and improve aortic stiffness in patients with inflammatory arthropathies: a one year controlled study**

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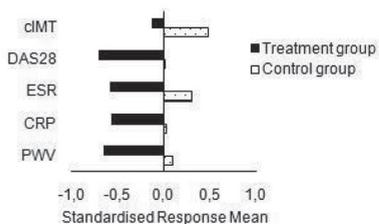
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**Purpose:** Patients with inflammatory arthropathies such as rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) have increased cardiovascular morbidity and mortality. The aim of this study was to examine the effect of one year treatment with TNF- $\alpha$  antagonists on carotid intima media thickness (cIMT) and aortic stiffness in patients with inflammatory arthropathies.

**Methods:** Fifty-five patients with active RA, AS or PsA and clinical indication for anti-TNF- $\alpha$  therapy were included. 36 patients started with anti-TNF- $\alpha$  therapy and were compared with a non-treatment group of 19 patients. cIMT was measured at baseline, 6 and 12 months with the Art.Lab system. Aortic stiffness was assessed as carotid-femoral pulse wave velocity (PWV) with the Sphygmocor device at baseline, 3, 6, 9 and 12 months. Furthermore, clinical and biochemical inflammatory markers were measured at each visit.

**Results:** Mean (SD) age in the treatment/control group was 47.2 (12.2)/51.2.0 (14.1) years ( $P=0.53$ ) and 42.9/50.0% ( $P=0.63$ ) were females. After 12 months, cIMT was reduced in the treatment group compared to control group (-5 (45)  $\mu\text{m}$  versus 23 (48)  $\mu\text{m}$ , respectively;  $P=0.01$ ), and PWV was improved in the treatment group, but not in the control group (-0.52 (0.80) m/s versus 0.04 (0.48) m/s, respectively;  $P=0.001$ ). CRP and the Disease Activity Score (DAS28) were significantly reduced in the treatment group after 12 months (-8.2 (19.2) mg/L  $P<0.001$  and -0.82 (1.18)  $P=0.004$ ).

**Conclusion:** These findings indicate that anti-TNF- $\alpha$  therapy improves cIMT and aortic stiffness in patients with inflammatory arthropathies concurrent with reduction in inflammatory markers.



Change from baseline to 12 months

## P5703 : Circumferential strain by echocardiography identifies acute occlusions in non ST-elevation acute coronary syndromes

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**Background and purpose:** Patients with non ST-segment elevation acute coronary syndrome (NSTEMI-ACS) due to acute coronary occlusion may risk substantial myocardial damage and might benefit from urgent revascularisation. The purpose of this study was to evaluate the ability of global and territorial circumferential strain by speckle tracking echocardiography to identify acute coronary occlusions.

**Methods:** In 105 patients with suspected NSTEMI-ACS, echocardiography was performed median 1 hour (interquartile range 0.5, 4) after admittance and coronary angiography after 28 $\pm$ 19 hours. Peak systolic strain was assessed in a 16 segments left ventricular model, based on 3 short axis planes. Global strain was defined as the average of all segmental values. Territorial strain was the average of all values within the perfusion areas of the 3 major coronary arteries. The lowest absolute territorial strain value was chosen. The ability to detect acute coronary occlusions was calculated by ROC analyses.

**Results:** An acute coronary occlusion was found in 21 patients. Global and territorial circumferential strain was reduced in patients with occlusion compared to those without (19.9 $\pm$ 4.7% vs. 16.6 $\pm$ 3.6%,  $p<0.01$  and 14.7 $\pm$ 5.2% vs 5.6 $\pm$ 4.0%,  $p<0.01$ , respectively). Both global and territorial circumferential strains were able to identify acute occlusion, but the accuracy of territorial strain was significantly better ( $p<0.001$ ) (Table 1).

Table 1

Parameter	Cut-off	Sensitivity	Specificity	Area under the curve
Territorial circumferential strain	-10.0	0.91	0.87	0.93*
Global circumferential strain	-18.4	0.81	0.64	0.73

ROC analyses for the ability to identify acute coronary occlusions. \* $p<0.001$  vs. global circumferential strain.

**Conclusion:** Territorial circumferential strain by echocardiography enables accurate identification of acute coronary occlusions in patients with suspected NSTEMI-ACS, and should be obtained early in the evaluation of these patients.

## **P5707 : Lower left ventricular peak systolic twist rate, but enhanced and earlier peak diastolic untwist rate in elite football players**

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**Purpose:** Left ventricular (LV) torsional function contributes to increased systolic and diastolic function during exercise, and depends on heart size, morphology, and inotropic state. This study aimed to systematically assess LV torsional function at rest in a large cohort of highly trained athletes.

**Methods:** 103 consecutive male elite Norwegian football players undergoing mandatory pre-participation echocardiographic screening in conjunction with the Union of European Football Associations (UEFA) prior to the 2008 season were compared with 46 age-matched healthy controls. LV rotation was obtained from 2D basal and apical short axis views using speckle-tracking imaging (STI) by an experienced investigator who was blinded to the study groups. LV torsion was defined as the net difference between apical and basal LV rotation, while rotational rates and twisting rates were derived from integrating rotation or torsion over time. Time-to-peak (TTP) data were normalized to systole duration (i.e. the time from QRS onset to aortic valve closure =100%).

**Results:** LV ejection fraction, body mass index, body surface area, and blood pressure were similar in both groups, but players had lower heart rates ( $50 \pm 1$  vs  $63 \pm 2$  bpm), greater computed LV mass ( $173 \pm 3$  vs  $150 \pm 5$  g) and LV enddiastolic volumes (LVEDV,  $158 \pm 3$  vs  $125 \pm 4$  mL); all  $P < 0.001$  vs controls. Peak basal and apical rotation were not different between groups. Peak systolic torsion occurred at similar time points (TTP,  $93.5 \pm 0.8$  vs  $94.4 \pm 1.4\%$ ) and was not different between players and controls ( $14.3 \pm 0.5$  vs  $15.2 \pm 0.9$  deg), but was significantly lower in players when indexed to LVEDV ( $P < 0.01$ ). Moreover,

peak basal rotational rate was lower ( $-55.9 \pm 2.1$  vs  $-65.1 \pm 3.7$  deg/s,  $P < 0.02$ ) and occurred earlier in players (TTP,  $57.5 \pm 1.0$  vs  $62.1 \pm 2.2\%$ ,  $P < 0.05$ ), while magnitude and timing of apical rotational rate was similar in both groups. Peak systolic twisting rate was significantly lower in players ( $86.4 \pm 2.8$  vs  $101.9 \pm 5.2$  deg/s,  $P < 0.01$ ) with unaltered timing. Peak diastolic untwisting rate occurred significantly earlier (TTP,  $112.7 \pm 0.8$  vs  $117.4 \pm 2.4\%$ ,  $P < 0.02$ ) in players and was augmented ( $-124.5 \pm 4.2$  vs  $-106.9 \pm 6.7$  deg/s,  $P < 0.05$ ).

**Conclusion:** The present study robustly demonstrated lower resting LV peak systolic twisting rate in elite football players. LV torsion was similar to controls. However, normalized for LVEDV, lower torsion values suggest considering LV size when comparing torsional function between different cohorts. Diastolic untwisting rate was augmented and may contribute to enhanced LV early diastolic function in athletes.

## **P5708 : Consistent impairment of left ventricular function in patients with arrhythmogenic right ventricular cardiomyopathy**

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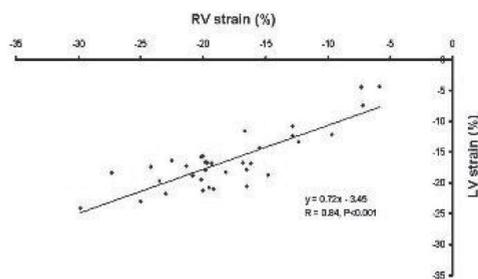
**Purpose:** Recent reports indicate that left ventricular (LV) involvement is more frequent in ARVC patients than earlier suggested. Myocardial strain by echocardiography is a sensitive tool for assessing cardiac function. The purpose of this study was to investigate how frequently LV function is reduced in patients with established ARVC.

**Methods:** We included 36 patients with an ARVC diagnosis according to current guidelines. 20 healthy individuals served as control group. Strain measurements were assessed by speckle tracking echocardiography. RV strain was calculated in a 6 RV segment model and LV strain in a 16 LV segment model.

**Results:** All ARVC patients had documented ventricular arrhythmias. ARVC patients had significantly reduced strain in RV ( $-19.3 \pm 6.6\%$  vs.  $-27.3 \pm 5.7\%$ ,  $p < 0.001$ ) and LV ( $-16.4 \pm 4.7\%$

vs.  $-22.4 \pm 2.6\%$ ,  $p=0.001$ ) compared to healthy individuals. ARVC patients had lower LV ejection fraction ( $56 \pm 14\%$  vs.  $65 \pm 5\%$ ,  $p=0.02$ ). LV strain was significantly correlated to RV strain in ARVC patients ( $R=0.84$ ,  $p<0.001$ ). Figure shows correlation of RV and LV function by strain in ARVC patients. Reduced LV strain ( $<-20\%$ ) was found in 30 patients (83%), and 30 patients (83%) had reduced RV strain ( $<-25\%$ ). Reduced LV strain was present in 4 patients (11%) despite normal RV strain and 4 patients (11%) had reduced RV strain with normal LV strain.

**Conclusion:** Systolic function was reduced in both ventricles, indicating that ARVC is a biventricular disease. In some cases, however, there was isolated reduction in LV function. These findings suggest that RV and LV strain may serve as means to identify patients with ARVC and that ARVC diagnosis should be considered even in patients with merely LV dysfunction and ventricular arrhythmias.



Right and left ventricular strain

## P5734 : A simplified 6 segments model of circumferential strain by echocardiography reflects LV infarct size in NSTEMI

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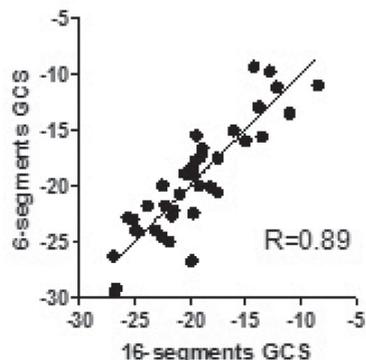
**Purpose:** Circumferential strain by speckle tracking echocardiography predicts infarct size in acute myocardial infarction. However, measurement of global circumferential strain (GCS) from three short axis planes is time consuming. Our

aim was to investigate whether circumferential strain from one short axis plane is sufficient for prediction of infarct size.

**Methods:** 40 patients with non-ST-elevation myocardial infarction (NSTEMI) were studied. Echocardiographic measurements were performed  $22 \pm 6$  hours after percutaneous coronary intervention. All patients were examined by contrast-enhanced MRI,  $8 \pm 4$  months after revascularization. GCS was assessed in a 16-segments model (GCS-16) as the average segmental strain in three short-axis planes, and in a 6-segments model (GCS-6) based on the papillary muscle plane.

**Results:** Mean infarct size was 7% (range 0-28%). There was a very good correlation between GCS-16 and GCS-6 (figure). Both GCS-16 and GCS-6 correlated well with infarct size ( $R=0.78$  and  $R=0.70$ , respectively) and demonstrated excellent ability to identify infarct size  $>10\%$  (table) in ROC analyses.

**Conclusions:** In patients with NSTEMI, a simplified 6-segments model of circumferential global strain correlates to the 16-segments model and yields comparable diagnostic precision for identification of medium and large myocardial infarctions.



Identification of infarct size  $>10\%$

Variable	Area under the curve	Sensitivity	Specificity	Cut-off
16-segments global circumferential strain	0.98	0.90	0.97	-16.8%
6-segments global circumferential strain	0.98	0.90	0.93	-16.2%