NORSKE ABSTRAKTER I ROMA

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P4362. The systolic paradox in hypertrophic cardiomyopathy, normal ejection fraction and decreased longitudinal function

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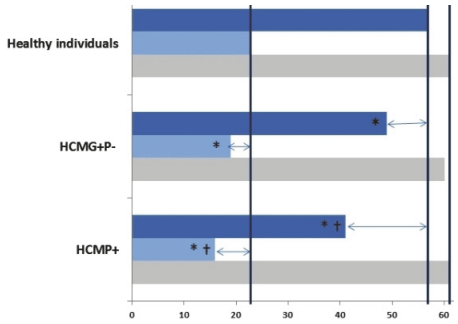
Background: Patients with hypertrophic cardiomyopathy (HCM) typically have normal ejection fraction (EF), despite a decreased longitudinal function.

Purpose: We explored HCM related changes in cardiac volumes and the effects on systolic function in 180 phenotype positive HCM patients (HCMP+), 100 genotype positive, phenotype negative family members (HCMG+P-) and 80 healthy individuals.

Methods: End-diastolic (EDVI) and end-systolic (ESVI) volume index, EF and maximum wall thickness (MWT) were measured by echocardiography. Left ventricular (LV) global longitudinal strain (GLS) was assessed from 16 LV segments by speckle tracking echocardiography.

Results: EDVI and ESVI were smaller in HCMP+ compared to HCMG+P- (41±14 ml/m^2 vs. 49±13 ml/m^2 and 16±7 ml/m^2 vs. 19±6 ml/m^2, both p<0.001) and compared to healthy (57±14 ml/m^2 and 23±9 ml/m^2, both p<0.001) (Figure). EF was similar (61±7% vs. 60±8% vs. 61±6%, p=0.43) in all groups, despite significantly worse GLS in the HCMP+ compared to HCMG+P- and healthy (-16.4±3.7% vs. -21.3±2.4% vs. -22.3±3.7%, p<0.001). In the total HCM population, the decrease in ESVI was closely correlated to EF (R^2=0.19, p<0.001) as expected, but not to GLS (R^2=0.01, p=0.08). Worse GLS correlated significantly with increased MWT (R^2=0.56, p<0.001), but with no correlation observed between EF and MWT (R^2<0.01, p=0.24).

Conclusion: HCMP+ patients with normal EF and reduced GLS had small cardiac volumes compensating the EF equation. Greater MWT correlated with worse GLS, but not with EF. Our results demonstrate that HCM result in loss of longitudinal function and that smaller volumes normalize EF.



P2855, High osteoprotegerin levels measured in the very early stage of acute myocardial infarction are related to heparin administration

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Background: Elevated levels of osteoprotegerin (OPG) have been reported in ST-elevation myocardial infarction (STEMI) patients. Such analyses however, may potentially be influenced by adjunctive medication. In vitro studies have demonstrated rapid release of OPG from smooth muscle cells after heparin administration. In a study of 272 STEMI patients treated with primary PCI, we found significantly higher levels of OPG before and after reperfusion compared to levels on day 1 after admission. The early measured high levels of OPG were not associated with peak troponin levels, infarct size, myocardial salvage, or left ventricular remodelling measured by CMR after 4 months follow-up.

Purpose: We hypothesized that the high levels of OPG measured early during a STEMI were related to heparin administration. The main objective was therefore to elucidate the influence of heparin administration during coronary angiography and PCI on OPG levels.

Methods: We included 20 elective patients referred to coronary angiography. Exclusion criteria were acute coronary syndromes, anticoagulant treatment, and absence of written informed consent. Blood samples for OPG were drawn prior to the angiography procedure (venous sample), from the arterial cannula before administration of unfractionated heparin (5000 IU and additional bolus if PCI was performed) and at the end of the angiography procedure. OPG levels were quantified by commercially available enzyme immunoassay.

Results: There was no difference between OPG levels measured in the venous samples compared to the arterial samples before heparin administration. However, there was a substantial increase in OPG levels following heparin administration with a median increase of 77% ($p<0.0001$, Figure). There was no significant difference in OPG levels between patients treated with PCI compared to patients with coronary angiography only, despite differences in time from heparin administration to blood sampling and total dosage of heparin in the two groups.

Conclusion: OPG levels appear to be profoundly affected by heparin administration, possibly by release from the vessel wall. Our results in stable patients undergoing coronary angiography indicate that OPG levels obtained during PCI in STEMI patients may be confounded by simultaneous heparin administration.

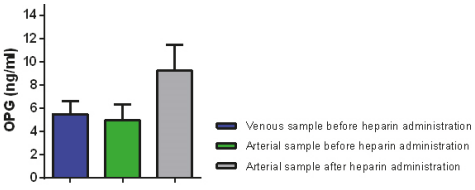

Figure Serum OPG levels in relation to heparin administration. Values presented as median (top of boxes) with upper interquartile range (whiskers).

P3578. Surprisingly frequent findings of subclinical dysfunctional left ventricle in COPD without pulmonary hypertension

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Background: There is little and contradicting knowledge on how chronic obstructive pulmonary disease (COPD) affect left ventricular (LV) function.

Table 1. LVMPI and longitudinal strain by tissue Doppler imaging at LV basal septum and lateral wall in controls, COPD-PH (pulmonary hypertension) and COPD-non-PH

Variables	Controls (n=34)	COPD-non-PH (n=74)	COPD-PH (n=26)
3D LVEF %	61 (57, 64)	57 (54, 60)*	57 (54, 61)*
Septal strain	−21.7 (−23.1, −20.4)	−15.5 (−16.9, −14.2)*	−13.7 (−15.0, −12,5)*#
Lateral strain	−22.3 (−24.0, −20.7)	−15.3 (−16.8, −14.2)*	−14.1 (−16.2, −12.9)*
Septal LVMPI	0.35 (0.29, 0.43)	0.54 (0.46, 0.61)*	0.62 (0.53, 0.70)*#
Lateral LVMPI	0.36 (0.32, 0.39)	0.53 (0.48, 0.63)*	0.62 (0.53, 0.67)*

Aim: The present study therefore aimed to elucidate the prevalence of dysfunctional LV in a cohort of stable COPD where left sided heart disease had been thoroughly excluded.

Methods: 112 COPD outpatients in GOLD stages I-IV and 34 controls were prospectively included. Patients were divided by invasive mean pulmonary artery pressure (mPAP) ≥ or <25 mmHg in COPD-PH (pulmonary hypertension) and COPD-non-PH, respectively. LV myocardial performance index (LVMPI) and longitudinal strain at basal septum and lateral wall by tissue Doppler imaging, as well as 3 dimensional LVEF, were acquired. Descriptive data are given as median (25%, 75%). A composite score value based on combined normalized LVMPI (septal + lateral) and strain values (septal+lateral) were calculated. Abnormal values were defined as values below average -2 SD for controls (<82.4% = dysfunctional LV).

Results: Prevalence of subclinical LV dysfunction based on combined score was 2.9%, 94.6%, and 100% in controls, COPD-non-PH and COPD-PH, respectively. LV strain and MPI show concordant findings, with the most abnormal values at septal site, with significant difference between COPD-non-PH and PH (#), however, significantly ($p<0.001$) reduced at lateral segment also compared to controls (*).

Conclusion: Subclinical dysfunction is frequent present in COPD-non PH as in COPD-PH. LVMPI was increased and LV strain reduced surprisingly equally both at the lateral and septal wall. Pressure load from the right side and inter-ventricular interdependency might explain the septal findings; however additional mechanism must be present to explain the dysfunctional lateral wall, in particular in the non-PH group.

P1779. Influence of lifetime exposure to physical exercise on ventricular arrhythmias in patients with hypertrophic cardiomyopathy

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Introduction: Competitive sports are discouraged in patients with hypertrophic cardiomyopathy (HCM), as the risk of ventricular arrhythmias (VAs) may increase during physical exercise (PE). It is not known how lifetime exposure to PE influences risk of VAs.

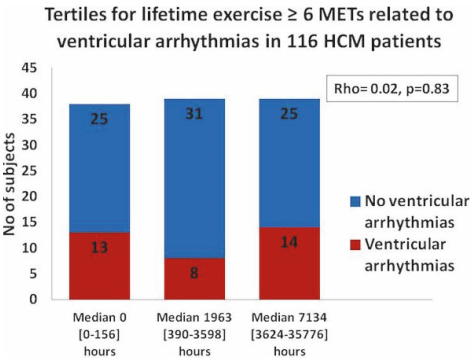
Purpose: We studied the relation between accumulation of vigorous PE and VAs in HCM patients. We hypothesized that a greater lifetime exposure to vigorous PE was associated with increased occurrence of VAs.

Methods: Consecutive HCM patients were invited to answer a questionnaire on history of PE. PE intensity ≥6 metabolic equivalents (METs) was defined as vigorous. We recorded lifetime accumulated hours of vigorous PE and divided patients into tertiles. VAs were defined as aborted cardiac arrest, sustained or non-sustained ventricular tachycardia. All patients underwent standard 2D echocardiography.

Results: Of 180 HCM patients, 116 (66%) (age 55±13yrs, 40% female) answered the PE questionnaire and were included in the study. VAs occurred in 35 (30%) patients. Patients with VAs had greater maximum wall thickness (MWT) (21±4mm vs 18±4mm, p<0.01), but there were no differences in age (52±15yrs vs 55±12yrs, p=0.21) or mean left ventricular outflow tract (LVOT) gradient (24±27mmHg vs 32±36mmHg, p=0.22).

Median lifetime vigorous PE was 1983 (0–35776) hours and 37 patients (32%) reported no vigorous PE. Patients with and without VAs had similar lifetime exposure to vigorous PE (2137 (0–17701) hours vs 1736 (0–35770) hours, p=0.93).

The proportion of patients with VAs was similar in all PE tertiles (34%, 21% and 36%, p=0.28) (Figure), and there was no correlation between PE tertiles and VAs (rho=0.02, p=0.86). Patients without vigorous PE (tertile 1) had higher LVOT gradients compared to those with the most PE (tertile 3) (42±39mmHg vs 20±27mmHg, p=0.02), but there were no differences in age



Exercise tertiles and VAs in HCM

(p=0.83), MWT (p=0.71), nor LVEF (p=0.16) between tertiles of vigorous PE.

Conclusions: In 116 HCM patients, 30% had ventricular arrhythmias. MWT was the only echocardiographic marker of VAs. High lifetime exposure to vigorous PE did not increase risk of VAs in our HCM patients.

P808. Circulating miR-106a and miR-424 predict future fatal myocardial infarction in healthy individuals

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On behalf: CERG

Background: Coronary heart disease (CHD) is currently the most common cause of death globally, and the number of individuals at risk is increasing. To manage this pandemic, improved tool for risk prediction, including more sensitive biomarkers is needed. Circulating microRNAs (miRs) have emerged as promising biomarkers for diagnosis of cardiovascular diseases in health and disease.

Objectives: To explore the potential of circulating miRs to predict future fatal myocardial infarction (MI) in healthy participants.

Methods: We performed a prospective nested case-control study with a 10-year observation period with fatal MI as endpoint. In total, 179 circulating miRs were quantified by real-time quantitative polymerase chain reaction in serum of 112 healthy men and women (40–70 years) from the HUNT2 study that either (1) suffered from fatal MI within 10 years [n=56], or (2) remained healthy [n=56, risk factor-matched controls]. Candidate miRs were validated in a separate cohort of healthy individuals (n=100, 44% women). Conditional logistic regression was used to determine the combination of miRs with the best potential for risk prediction.

Results: We found 12 miRs significantly regulated between cases and controls in the exploration cohort. Among these, 10 miRs were also regulated between cases and controls in the validation cohort (p<0.05). Using a more conserved p-value of 0.01, the circulating levels of miR-106a-5p, miR-151a-5p, let-7g-5p and miR-26a-5p were lower in cases compared to controls. In addition, miR-424-5p was significantly higher in male cases versus controls. The best miR-based risk-prediction model for future MI consisted of a combination of miR-424-5p and miR-106a-5p providing an overall 68% correct classification for both genders, and a 66% and 73% and

overall correct classification for women and men, respectively.

Conclusion: miR-424–5p and miR-106a-5p represent promising new risk markers of MI, especially in men.

P769. Combining peak mitral inflow and annular velocities with left atrial strain improves estimation of left ventricular filling pressure

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Introduction: Classification of left ventricular (LV) filling pressure as normal or high using E/e' below 8 or above 15, respectively, results in a large number of unclassified patients in the intermediate range. Peak left atrial (LA) strain during left ventricular (LV) systole has been shown to correlate with LV filling pressure.

Purpose: We tested if combining E/e' and LA strain would improve estimation of LV filling pressure.

Method: In 58 patients we recorded pulmonary capillary wedge pressure, an indirect estimate of LV filling pressure, while simultaneously acquiring echocardiographic images. LA strain was assessed by speckle tracking echocardiography. Patients were first classified using E/e' alone (average of septal and lateral e') (Fig. 1a). Optimal cut-off-value for LA strain to classify normal or increased LV filling pressure, was found by ROC-analysis (Fig. 1b). Patients were subsequently classified combining E/e' and LA strain as shown in the algorithm in Fig. 2.

Results: The number of wrongly classified patients using E/e' alone, was very small (2%), but came at a price of a large proportion of unclassified patients (40%), (Fig.3.). Combining E/e' with LA strain, correctly classified 88% of the patients, reduced the number of unclassified to 3, while 9% were wrongly classified (Fig. 3).

Conclusion: Combining E/e' and LA strain in the evaluation of LV filling pressure, significantly improved the ability to correctly classify patients, while there was a modest increase in the number of wrongly classified patients. Our results suggest that LA strain should become part of the echocardiographic evaluation of patients with suspected heart failure.

P750. Load sensitivity in left bundle branch block: septal contribution to left ventricular stroke work is abolished with elevated afterload

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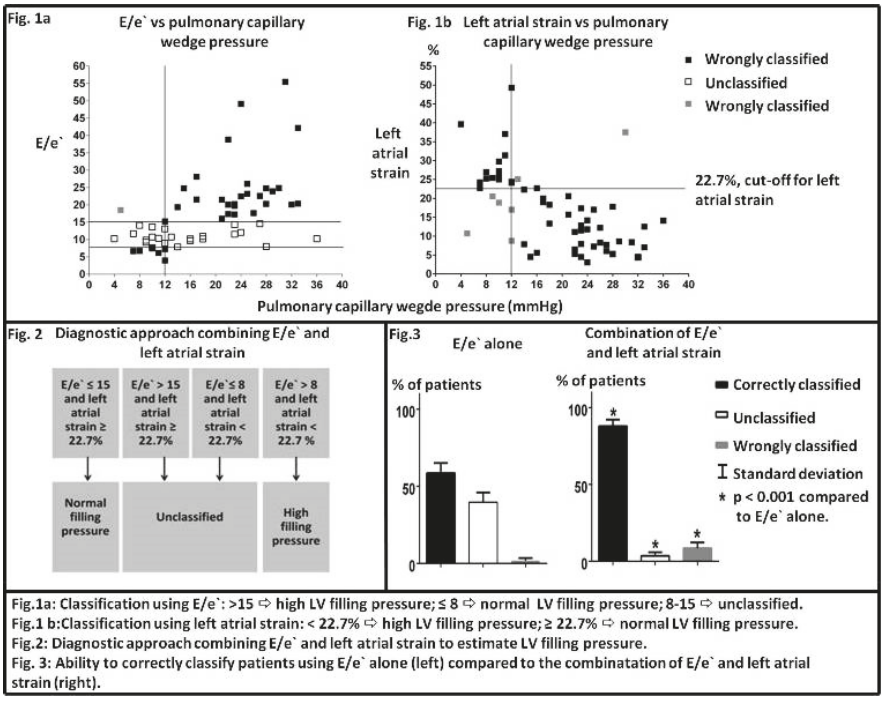

Fig.1a: Classification using E/e`: >15 ⇨ high LV filling pressure; ≤ 8 ⇨ normal LV filling pressure; 8-15 ⇨ unclassified.
Fig.1 b:Classification using left atrial strain: < 22.7% ⇨ high LV filling pressure; ≥ 22.7% ⇨ normal LV filling pressure.
Fig.2: Diagnostic approach combining E/e` and left atrial strain to estimate LV filling pressure.
Fig. 3: Ability to correctly classify patients using E/e` alone (left) compared to the combinatation of E/e` and left atrial strain (right).

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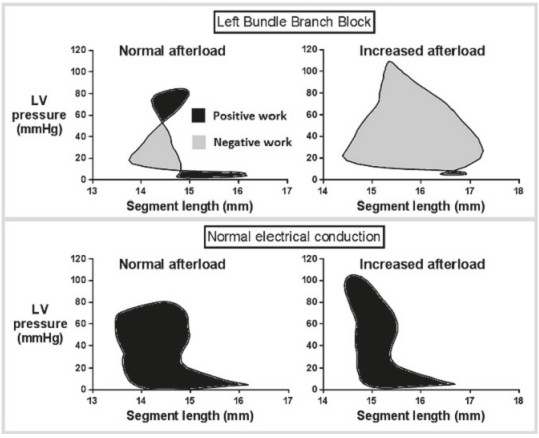
Introduction: In patients with left bundle branch block (LBBB) a dyssynchronous contraction pattern reduces septal contribution to left ventricular (LV) function. It is not known how this is affected by increased afterload.

Purpose: To assess the effect of increased afterload on regional LV function during LBBB to test the hypothesis that increased afterload further deteriorates septal performance.

Methods: In eight anaesthetized dogs, septal and LV lateral wall circumferential segment lengths (SL) by sonomicrometry and LV pressure by micromanometer were measured during baseline and LBBB induced by radiofrequency ablation. Afterload was increased by aortic constriction. Segmental work was calculated by pressure-segment length analysis. Since segments which shorten in systole perform positive work, whereas segments which lengthen do negative work, we calculated net work as the sum of positive and negative work.

Results: During LBBB, aortic constriction increased LV pressure from 94±10 (mean±SD) to 118±16 mmHg (P<0.01). Net septal work decreased from 43±194 to -227±168 mmHg*mm (P<0.01), which means that the septum made no net contribution to LV work and instead absorbed energy from work done in the LV lateral wall (figure). In the LV lateral wall there was no significant change in net work (685±157 to 666±300 mmHg*mm). Prior to induction of LBBB, aortic constriction caused no significant change in septal net work, but a small decrease (P<0.05) in net work in the LV lateral wall.

Representative septal segment



Conclusions: Elevation of afterload during LBBB resulted in a complete loss of septal contribution to LV stroke work. Instead the septum absorbed energy from work performed by the LV lateral wall. These findings indicate that ventricles with LBBB are highly sensitive to changes in afterload. Future studies should investigate if a similar afterload dependency is present in patients with LBBB.

P754. Septal motion in left bundle branch block: more wobbling with high afterload

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Background: In patients with left bundle branch block (LBBB) there is "wobbling" of the interventricular septum and deformation analysis shows typically three phases of contraction, (1) preejection shortening, (2) ejection shortening, and (3) postsystolic shortening (Figure).

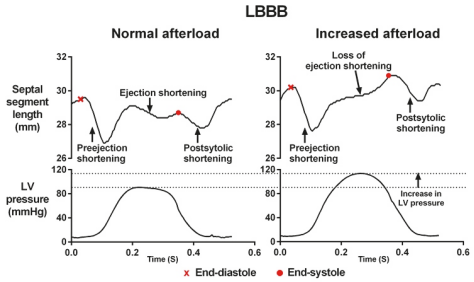
Purpose: To investigate if increased afterload modifies septal contraction pattern in LBBB.

Methods: LBBB was induced by radiofrequency ablation in 6 anaesthetised dogs. Measurements were done at baseline and during increased afterload by aortic constriction. Septal circumferential segment length was measured by sonomicrometry and left ventricular (LV) pressure by micromanometer.

Results: Peak LV pressure increased from 91±9 to116±11 mmHg with aortic constriction (P<0.05). At baseline, septal preejection shortening was -7±4% and remained unchanged at -7±4% with aortic constriction. Shortening during LV ejection, however, was abolished and there was instead net lengthening from end-diastole to end-systole (1±2% with aortic constriction vs -4±3% without aortic constriction, P<0.05). Postsystolic shortening increased from -1±2 to -3±2% (P<0.05) with aortic constriction. The figure shows a representative experiment.

Conclusions: Elevation of afterload during LBBB converted septal shortening to net lengthening during systole, indicating aggravation of septal dysfunction. This load dependency also implies that care should be

exerted when using time delay between septal and LV lateral wall shortening as a marker of electrical dyssynchrony.



Septal response to increased afterload

P6511. Hyperemesis gravidarum and all-cause mortality: no increase in cardiovascular mortality, but reduced cancer mortality

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Background: Pregnancy is considered a physiological stress test, especially for the cardiovascular system. Pregnancy-complications, such as hypertension, preeclampsia and placental abruption, are associated with increased risk of cardiovascular disease (CVD) later in life. Hyperemesis gravidarum, characterized by extreme nausea and vomiting in early pregnancy, is associated with all aforementioned conditions. Although hyperemesis gravidarum is the most common reason for hospitalization during first trimester, little is known about the long-term consequences of this condition, including mortality. In particular the cardiovascular risk after hyperemesis exposure may be of interest.

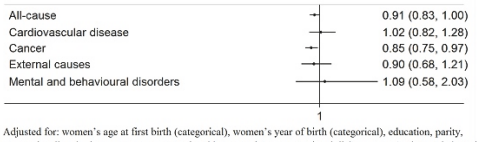
Purpose: To investigate if exposure to hyperemesis gravidarum is associated with increased maternal long-term mortality.

Methods: Population-based cohort study. Data from the Medical Birth Registry of Norway were linked to the Norwegian Cause of Death Registry, and mortality among women with singleton births between 1967 and 2002 was studied. Women were followed until the end of 2009 or death, whatever occurred first. Associations between hyperemesis gravidarum and all-cause mortality were assessed by hazard ratios (HRs) estimated by Cox regression. In addition, cause-specific mortality was investigated (CVD-mortality, deaths due to cancer, external causes and mental and behavioural disorders). In order to further explore any associations between hyperemesis gravidarum and CVD-mortality, a subanalysis differentiating between ischaemic heart disease, cerebrovascular disease and other cardiovascular diseases as causes of death, was performed.

Results: Among the 999 161 women (median age 25 years) included in the study, 13 397 (1.3%) experienced hyperemesis gravidarum in at least one pregnancy. During a median follow-up time of 26 (range 0.5 - 42) years (25 902 036 person-years), a total of 43 470 women died (4.35%); 7 197 (0.72%) died due to CVD. An inverse association between hyperemesis gravidarum and over-all mortality was observed (HR 0.82, 95% CI 0.75–0.90); after adjustment for possible confounders, the mortality reduction in women exposed to hyperemesis gravidarum was only borderline significant [HR 0.91 (0.83–1.00)] (figure 1). Adjusted HR for cardiovascular death was 1.02 (0.82–1.28). An inverse association between hyperemesis gravidarum and cancer mortality was observed, and remained significant also after adjustment [adjusted HR 0.85 (0.75–0.97)]. The adjusted mortality-rates from ischaemic heart disease, cerebrovascular disease and other CVD were similar in women exposed to hyperemesis gravidarum compared to controls.

Conclusion: In this large cohort study, hyperemesis gravidarum was not associated with an increased risk of long-term all-cause mortality, and there was no increase in mortality due to CVD. There was however an inverse association between hyperemesis gravidarum and death from cancer.

Figure 1. Risk of death during study period in women exposed to hyperemesis gravidarum vs women not exposed to hyperemesis gravidarum



* Adjusted for: women's age at first birth (categorical), women's year of birth (categorical), education, parity, hypertensive disorder in pregnancy, pregestational hypertension, pregestational diabetes type 1, placental abruption.

P5250. One-year outcomes of a randomized study in renal denervation: results for Oslo-RDN study

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On behalf: Oslo-RDN study group

Background: The blood pressure (BP) lowering effect of renal sympathetic denervation (RDN) in treatment resistant hypertension (TRH) shows variation among the few randomized studies. The duration of antihypertensive effect and long-

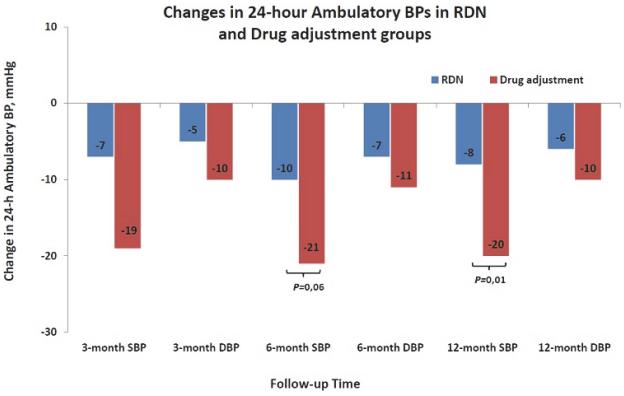
term effect and safety of RDN requires further follow-up.

Purpose: We aimed to report the office and ambulatory blood pressure (BP) changes as well as long-term safety at 12-month follow-up in our Oslo-RDN study.

Methods: Patients with apparent TRH (n=65) were referred specifically for RDN and those with secondary and spurious hypertension (n=26) were excluded. TRH was defined as office systolic BP>140 mmHg despite maximally tolerated doses of at least 3 antihypertensive drugs including a diuretic. Additionally, ambulatory daytime systolic BP>135 mmHg following witnessed intake of antihypertensive drugs was required, after which 20 patients had normalized BP, indicating poor drug adherence. Patients with true TRH were randomized and underwent RDN with Symplicity catheter (n=9) versus adjusted drug treatment (n=10).

Results: 24-hour ambulatory systolic and diastolic BPs in the drug adjustment group changed from 151±13/84±7 mmHg (±SD) at baseline to 131±12/75±5 mmHg at 12 months (p<0.0005 for all), and in the RDN group from 149±9/89±7 to 141±11/83±5 mmHg (p=0.07 and p=0.04, respectively). The absolute difference in change between groups in systolic BP was significantly higher in favor of the drug adjustment group (p=0.01). Office, daytime and nighttime ambulatory BPs changed in parallel to the 24-hour ambulatory BPs. There were no significant changes in renal arteries assessed by MRI or CT scans after 12 months follow-up. No deterioration of renal function assessed by s-creatinine and p-cystatin.

Conclusions: Our 12 months outcome suggest that RDN has inferior lowering effects compared to adjusted drug treatment in patients with true treatment resistant hypertension after excluding patients with confounding poor drug adherence. However RDN is a safe procedure that allows future research to improve the procedure and identify characteristics of patients who might respond to RDN.



P2185. Impact of smoking on circulating troponin I concentrations and cardiovascular events in the general population: The HUNT Study

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Background: Both smoking and circulating cardiac troponin levels are strongly associated with the risk of myocardial infarction and cardiovascular death. However, the prognostic relationship and interaction between the two remain unclear.

Purpose: Assess the predictive properties of high-sensitivity cardiac troponin I (hs-cTnI) levels on myocardial infarction and cardiovascular death in current smokers and non-smokers.

Methods: Using the ARCHITECT STAT High-Sensitive Troponin assay, we measured hs-cTnI in 2 550 current smokers and 6 165 non-smokers (previous smokers and non-smokers clustered) participating in the prospective observational Nord-Trøndelag Health Study. All subjects were free from known cardiovascular disease and diabetes mellitus at baseline. Cox survival models were generated with time to a composite endpoint of admission for myocardial infarction or cardiovascular death. ROC curves for the ability of hs-cTnI to discriminate between participants with and without events were generated for both groups.

Results: The age of the participants were 19–94 years, 55.5% were women. After a median follow-up time of 5 140 days, 574 events were registered. We observed an association between increasing concentrations of hs-cTnI and events in the total study cohort. After adjustment for sex, age, total and HDL cholesterol, hypertension, estimated glomerular filtration rate and C-reactive protein, this association was attenuated for current smokers, but remained for non-smokers (see Table). The ROC areas under the curve of hs-cTnI were 0.70 (0.65–0.74) for current smokers and 0.77 (0.74–0.79) for non-smokers (p=0.006, see Figure).

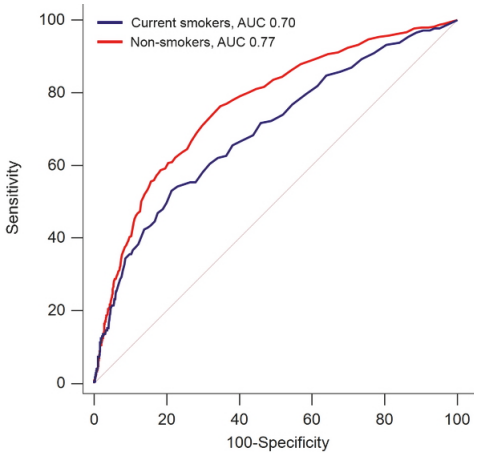
Conclusion: The association between hs-cTnI levels and myocardial infarction and cardiovascular

death is stronger in non-smokers than in current smokers. The detrimental cardiovascular impact of smoking may be mediated via mechanisms other than those involving cardiac troponins.

Table 1. Associations between hs-cTnI concentrations and outcomes

	Hazard ratio per 1 SD in log hs-cTnI (95% CI)	
	Unadjusted	Adjusted*
Total cohort	2.09 (1.97–2.21)	1.27 (1.14–1.41)
Current smokers	1.85 (1.66–2.06)	1.11 (0.92–1.35)
Non-smoker	2.30 (2.13–2.94)	1.40 (1.24–1.58)

**Adjusted for sex and age, total and HDL cholesterol, hypertension, estimated glomerular filtration rate, and C-reactive protein.*



P2485. Long-term survival in cardiac surgery patients compared to the general population; associations with smoking status, intervention and age above 80 years

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On behalf: Cardiac Surgery Outcome Study

Background/Introduction: During the 1980–90s, cardiac surgery underwent major technological advances.

Purpose: The aim was to provide an update on long-term survival in patients undergoing cardiac surgery. We assessed observed and relative long-term survival associated with smoking status, different surgical interventions and age ≥80 years.

Methods: The study was based on 8,564 adult patients undergoing cardiac surgery in Trondheim, Norway, from 2000 through 2014. Patients were followed until 31.12.2014; median follow-up time was 6.6 years. Expected mortality due to other causes was estimated based on data from the Norwegian population matched on gender, age and calendar year. We compared observed and relative (observed/expected) long-term survival (1) in smokers vs. non-smokers, (2) across different surgical interventions (coronary artery bypass grafting - CABG - vs. aortic valve replacement - AVR - vs. combined CABG+AVR, as well as across EuroScore 2's weighted categories) and (3) in octogenarians vs. patients <80 years. Excess mortality associated with cardiac surgery was derived by subtracting the expected mortality from the observed. Relative mortality was calculated as the ratio between the observed and expected number of deaths. Multivariate analyses of observed and excess mortality were performed.

Results: Smoking was associated with higher observed and relative mortality. The prevalence of smoking increased with decreasing age ($p<0.001$), and the effect on both observed and excess mortality was dependent on age (significant interaction terms, $p<0.001$ and $p=0.02$, respectively). Given survival the first 30 days postoperatively, relative survival was similar for all surgical interventions the first seven years of follow-up. Subsequently, there was a reduction in relative survival for procedures other than isolated CABG. When adjusting for different age and gender distribution amongst the surgical procedures, isolated CABG and AVR showed no significant difference in long-term excess mortality. Patients undergoing combined CABG and AVR had a poorer long-term prognosis. The proportion of octogenarians undergoing cardiac surgery increased during the study period ($p=0.01$). Despite undergoing more complicated procedures with longer operation times, this age group showed excellent results with a relative survival >100% throughout the follow-up period.

Conclusion: Smoking was associated with reduced long-term survival following cardiac surgery, with highest negative prognostic impact in younger age groups. Patients undergoing CABG, AVR and concomitant CABG and AVR all showed similar relative survival the first seven years postoperatively. Subsequently, there was a modest reduction in relative survival, which increased parallel with increasing surgical complexity. The excellent long-term results in octogenarians underlines that the decision for surgery should be based on preoperative function and comorbidities, not chronological age as such.

P5635. Characteristics of patients with obstructive coronary artery disease referred to acute angiography with unstable angina

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Background: The yield of obstructive coronary artery disease (CAD) in patients with non-ST elevation acute coronary syndrome (ACS) is above 80%. As the yield in patients with unstable angina is low, a pre-angiography score with high diagnostic accuracy for obstructive CAD is warranted. ESC guidelines recommend that all ACS patients with intermediate GRACE score or relevant comorbidity or positive stress testing should have a coronary angiography within 72 hours. In stable CAD, only revascularisation of obstructive CAD in the main stem or proximal left anterior descending artery or three-vessel disease has been shown to be of prognostic significance.

Purpose: Validate GRACE risk score against other clinical variables as predictors of obstructive CAD in patients with unstable angina referred to acute angiography.

Methods: From 2005–2012, all coronary angiographies performed by the sole provider for a regional population of 479,000 inhabitants were registered in a clinical registry. This PCI-hospital was the primary hospital for 1,063 admissions of unstable angina (troponin<15 nmol/L), enabling retrospective collection from patient hospital records of further consecutive information from admission to discharge. Obstructive CAD was defined as >50% obstruction of a coronary vessel. Characteristics were analysed by logistic regression analyses and all reported differences had p-values <0.05. A score was developed based on odds ratios from significant factors in a multivariable logistic regression model.

Results: The overall rate of obstructive CAD in patients with unstable angina was 53% (n=568), falling from 64% (n=91) in 2005 to 36% (n=41) in 2012. Patients with and without obstructive CAD had an average age of 65 and 59 years, respectively. In 50% of the admissions the patient already had CAD. These patients had 71% obstructive CAD versus 37% in those without known CAD. Age and known CAD had a combined area under the curve (AUC) of 0.72 (95% CI 0.69–0.75). GRACE score had an AUC of 0.63 (95% CI 0.60–0.67). Comorbidities, positive stress testing, smoking history, gender, typical angina symptoms, class of angina severity (Canadian Cardiovascular Society) and history of recent variable threshold for angina were independent predictors and increased the AUC to 0.78 (95% CI 0.73–0.79). A score derived from this model had a negative predictive value (NPV) of 94% in 42% of the patients under 55 years (n=105) with an AUC of 0.86 (95% CI 0.81–0.91). 23% of the obstructive CAD were indicative of prognostic importance. The derived score had a NPV of 99% for prognostic obstruction in the patients under 55 years, identifying 64% (n=162) possibly without need of angiography. Similarly, 29% patients (n=313) in the total sample had a NPV of 96%.

Conclusion: Improving pre-test selection to angiography of patients with unstable angina beyond GRACE score is possible based on symptoms and clinical information either to rule out or delay angiography in 29% of patients.

P5487. Insomnia and the closing sound from mechanical heart valves

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On behalf: PROCARD Research Group

Background: The closing sound of mechanical heart valve prostheses is quite often clearly audible. Annoyance by the valve sound has shown to negatively influence the patient's quality of life. Little is known on how the valve sound affects the patient's sleep.

Purpose: The aim of the study was to describe patients' perception of the closing sound from the valve and the association between subjective valve sound perceptions and insomnia.

Methods: Patients (N=1045) that had undergone aortic valve replacement (AVR) at a university hospital in 2000–2011 were invited to participate in the study. Data were collected by self-report in a postal survey during April 2013, and 245 of 908 patients that responded had a mechanical valve implant and were included in this analysis. Seven items assessed the audibility of the valve, how much stress the valve sound put on the patient in daily life, and if they wanted to replace the valve with a soundless valve if possible. The Minimal Insomnia Symptom Scale (MISS) was used to document sleep (score range: 0–12).

Results: Mean (SD) age was 60 (11) years, and 186 (76%) were men. Mean (max-min) time since surgery was 7 (1–13) years. One-hundred and ninety-four (79%) reported that they

sometimes or often could hear the valve sound, 174 (71%) that the sound was audible to other people, 42 (17%) felt worried because of the valve sound, 27 (11%) were disturbed by the sound during day time and 64 (26%) were disturbed by the sound during their sleep. Eighty-five (35%) often or sometimes wanted to replace their prosthetic valve with a soundless type. The insomnia sum score indicated that 123 (53%) had no insomnia, 42 (31%) had subclinical insomnia, 27 (12%) had moderate insomnia and 11 (5%) had severe insomnia. The association between annoyance of the valve sound (scale 1–10) and insomnia was moderate (Pearson's r = 0.35, p<0.001). A strong association was found between annoyance of the valve sound and desire for a replacement with a soundless prosthetic valve (Pearson's r = 0.61, p<0.001). A linear regression analysis revealed that annoyance by the valve sound decreased by age (b = - 0.029, p=0.043) and time since surgery (b = - 0.104, p=0.020), while gender or living alone did not affect the results.

Conclusions: For most patients with mechanical valves the closing sound of the valve is audible. Almost half of the patients had some degree of insomnia. There is an association between annoyance by the closing sound and insomnia. Annoyance by the valve sound decreases by age and when time goes by.

P5524. Lower trans-aortic flow rate is associated with increased cardiovascular and all-cause mortality in aortic valve stenosis

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On behalf: SEAS study group

Background: Low trans-aortic flow may complicate severity assessment of aortic valve stenosis (AS). However, whether trans-aortic flow rate (FR) itself is associated with outcome in AS has not been tested in a large clinic study.

Purpose: We aimed to assess the association of FR with cardiovascular and all-cause mortality in AS patients participating in the Simvastatin Ezetimibe in Aortic Stenosis (SEAS) study.

Methods: FR was calculated from Doppler-derived stroke volume in 1742 patients with initially mild-to-moderate asymptomatic AS. Low FR was defined as <200 ml/sec. The association of FR with mortality during a median of 4.3 years follow-up was tested in time-varying Cox regression models and reported as odds ratio (OR) and 95% confidence interval (CI).

Results: Low FR was found in 21% of patients at baseline, and associated with older age, female sex, lower body size, aortic annulus diameter and LV ejection fraction, and presence of LV hypertrophy (all p<0.05) (Table 1). Although the group with low FR had lower peak aortic jet velocity and mean gradient, the aortic valve area was significantly smaller, also when pressure recovery in the aortic root was taken into account (all p<0.01) (Table 1). In time-dependent Cox regression analyses, one standard deviation lower FR was associated with higher cardiovascular mortality (OR 1.39 [95% CI 1.05–1.84], p=0.02) and all-cause mortality (OR 1.22 [95% CI 1.01–1.48], p=0.04) independent of well-known prognosticators in AS including sex, AS severity, LV hypertrophy and older age.

Conclusion: In AS patients participating in the SEAS study, lower FR was more common among older women with more severe AS, and associated with higher cardiovascular and all-cause mortality, independent of well-known prognosticators.

Table 1. Patient characteristics

Variables	Flow rate <200 ml/sec	Flow rate >200 ml/sec	P-value
Age, year	69.6±9.4	66.8±9.6	<0.001
Female, %	66	34	<0.001
BMI, kg/m^2	26.1±4.5	27.1±4.3	<0.001
Aortic annulus diameter, cm	1.96±0.19	2.26±0.25	<0.001
LV hypertrophy, %	83	17	<0.01
LV ejection fraction, %	66±7	67±7	<0.05
Peak aortic jet velocity, m/sec	3.0±0.5	3.1±0.6	<0.01
Mean trans-aortic gradient, mmHg	22±9	23±9	<0.05
Aortic valve area, cm^2	0.84±0.20	1.40±0.45	<0.001
Energy loss index, cm^2/m^2	0.58±0.26	0.99±0.47	<0.001

P4340. Pro-coagulant activity during exercise testing in patients with coronary artery disease

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Background: Strenuous exercise may trigger myocardial infarction through increased pro-co-

agulant activity. We intended to investigate whether patients referred for exercise testing, who were found to have angiographically verified coronary artery disease (CAD), have a more hypercoagulable profile during exercise testing compared to those without CAD.

Materials and methods: 106 patients (62 males, mean age 62±10 years) with symptoms suggestive of stable CAD were examined with exercise electrocardiography on bicycle ergometer. Venous blood samples were taken at rest and within 5 minutes after end of exercise. The following haemostatic variables were analysed: tissue factor pathway inhibitor (TFPI) activity and antigen, prothrombin fragment 1+2 (F1+2), D-dimer and endogenous thrombin potential (ETP). The latter was measured by the calibrated automated thrombogram (CAT) assay and the others with ELISAs. All participants underwent conventional coronary angiography. CAD was defined as having any degree of atherosclerosis.

Results: Out of 106 patients enrolled, 70 were found to have angiografically verified CAD. Mean exercise duration was 10:06±4:11 min and mean metabolic equivalent (MET) 6.7±1.8, with non-significant differences between the two groups. A significant increase from baseline to after exercise testing was observed in all measured markers in the total population ($p \leq 0.002$ for all). The increase remained significant in all markers except for D-dimer ($p=0.071$) when adjusting for change in hematocrit. In patients with angiographically verified CAD, total TFPI was significantly lower at baseline compared to patients without CAD (median value 67.4 and 76.6 ng/ml respectively, $p=0.027$). However, no significant differences in changes of the measured markers during exercise were observed between the two groups.

Conclusion: Pro-coagulant activity increased during exercise testing in patients with symptoms suggestive of CAD, but the hypercoagulable state observed after undergoing strenuous exercise, was not more pronounced in patients with CAD than in patients without CAD.

P4512. Secretoneurin, a novel endogenous CaMKIId inhibitor, inhibits Ca^{2+}-dependent arrhythmogenesis

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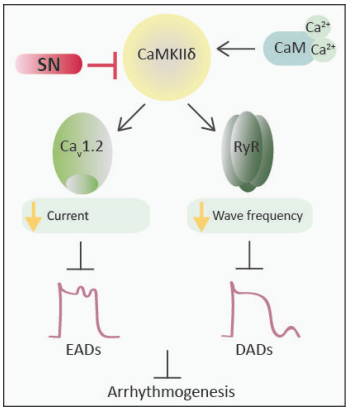
Background: Secretoneurin (SN) levels are increased in heart failure patients and patients with ventricular arrhythmia-induced cardiac arrest, and are predictive of clinical outcomes. SN has been shown to alter Ca^{2+} homeostasis in cardiomyocytes by inhibition of Ca^{2+}/calmodulin (CaM)-dependent protein kinase II δ (CaMKIIδ) activity.

Purpose: Examine the role of SN in arrhythmogenic Ca^{2+} regulation.

Methods and results: In Langendorff-perfused mouse hearts, SN reduced isoproterenol-induced autophosphorylation of CaMKIIδ, and inhibited CaMKIIδ-dependent RyR phosphorylation. In line with CaMKIIδ and RyR inhibition, SN treatment decreased the frequency and dimensions of Ca^{2+} sparks in cardiomyocytes during isoproterenol challenge. Ca^{2+} wave frequency was also reduced, which corresponded to a lower incidence of delayed after-depolarizations and fewer spontaneous action potentials in patch-clamped cardiomyocytes. Furthermore, SN treatment reduced the incidence of early after-depolarizations induced by isoproterenol; an effect paralleled by reduced magnitude of L-type Ca^{2+} current.

Conclusions: SN treatment reduces CaMKIIδ activity, which inhibits arrhythmogensis by 1) reducing RyR activity, Ca^{2+} waves, and delayed after-depolarizations, and 2) inhibiting L-type Ca^{2+} current and early after-depolarizations. These findings suggest that increased SN levels are protective in patients with ventricular arrhythmia, and that further elevating SN levels may be therapeutic.



P1194. Long term survival in patients with acute myocardial infarction and out of hospital cardiac arrest, a prospective cohort study from South Eastern Norway

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Background: Studies are limited on long-term prognosis in patients with acute myocardial infarction (AMI) complicated by out-of-hospital cardiac arrest (OHCA).

Purpose: To study long-term survival in unselected AMI patients with and without OHCA, and to identify prognostic factors in the AMI+OHCA cohort.

Methods: Single-centre prospective cohort study. Consecutive AMI patients admitted to our university hospital during 2005–2011 were registered into a local AMI registry. All-cause mortality during follow-up was obtained by linkage to the Norwegian Cause of Death registry, with censoring date 31.12.2013. The Kaplan-Meier method was used to estimate long-term survival in patients with AMI+OHCA (OHCA), ST-elevation myocardial infarction without OHCA (STEMI) and Non-STEMI without OHCA (NSTEMI), and Cox regression to identify independent prognostic factors in the OHCA cohort.

Results: We identified 404 patients with OHCA (20% women), 4527 with STEMI (25% women) and 4903 with NSTEMI (35% women). OHCA- and STEMI patients were younger than NSTEMI patients (median 63 vs 71 years). Most OHCA patients were treated with immediate percutaneous coronary intervention (PCI) (Table). Survival to discharge was 68% (52% with good neurologic outcome) in OHCA, 96% in STEMI and 96% in NSTEMI patients. Median follow-up was 4.0 years (25th-75th percentile: 2.4–5.8 years). Among OHCA patients, a total of 195 patients died and survival during follow-up was 52%. This was significantly lower compared to STEMI and NSTEMI patients without OHCA, mainly due to high early mortality (Figure). Initial ventricular fibrillation (VF) (Hazard ratio (HR) 0.58 [95% CI 0.37–0.91]) and systolic blood pressure (SBP) on admission (HR pr. increase in mmHg 0.99 [95% CI 0.98–0.99]), were factors associated with better outcome in OHCA patients. Increasing age, previous AMI, coma on admission and high heart rate on admission were associated with decreased survival during follow-up.

Conclusions: Long-term survival in patients with AMI and OHCA was excellent, with about half of the patients alive after eight years follow-up. Increased mortality compared to AMI patients without cardiac arrest was mainly due to higher early mortality. Initial VF and higher SBP were factors associated with better prognosis. More data are needed on initial management of OHCA patients to further improve long-term survival.

Table 1. Invasive management in-hospital

	AMI with OHCA	STEMI without OHCA	NSTEMI without OHCA
	n=404	n=4527	n=4903
Coronary angiography, %	87	97	80
One- or multiple vessel disease, %	82	94	69
PCI, % of total	68	84	41

PCI: percutaneous coronary intervention.Kaplan-Meier survival estimates

P1681. Change in physical activity and cardiovascular risk factors over 16 years

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Background and purpose: Physical activity is considered a major factor in prevention of cardiovascular disease, but most studies conducted have only measured physical activity once. The main purpose of this study was to examine associations between changes in physical activity and cardiovascular risk factors over 16 years in a cohort of 3671 Norwegian men and women. A secondary objective was to study ethnic differences in physical activity and associations with cardiovascular risk factors over time.

Methods: This is a prospective cohort study of 1129 Sami and 2542 non-Sami men and women with a mean baseline age of 45 years. Data were collected from two population-based health studies in Northern Norway conducted in 1987 (baseline) and 2003–2004 (follow-up). Leisure time physical activity was assessed with a similar, validated questionnaire at baseline and follow-up, and change in physical activity was defined as shown in Table 1. Cardiovascular risk factors (body mass index (BMI), resting heart rate, triglycerides, cholesterol, systolic and diastolic blood pressure) were examined using standard procedures at both surveys.

Results: Change in physical activity was in general not associated with change in risk factors over 16 years, with a few exceptions (Table 1). In the non-Sami population, those who were active at both surveys had a larger reduction in BMI than those who were inactive at both surveys (−0.4 kg/m^2, P<0.05). A larger proportion of the Sami population was inactive at baseline (31.5%) and follow-up (27.5%) compared with the non-Sami (26.1% and 23.3%, respectively) (P<0.05), but this difference in physical activity levels was not reflected in the risk factors.

Conclusion: In this cohort study over 16 years, those who were persistently active had similar or clinically insignificant changes in cardiovascular risk factors compared with those who were persistently inactive. Moreover, increasing

Table 1

	Sami				Non-Sami			
	Inactive in both	Active to inactive	Inactive to active	Active in both	Inactive in both	Active to inactive	Inactive to active	Active in both
	(reference)	β (95% CI)	β (95% CI)	β (95% CI)	(reference)	β (95% CI)	β (95% CI)	β (95% CI)
BMI (kg/m²)	0.0 (reference)	0.0 (−0.6, 0.6)	−0.4 (−1.0, 0.1)	−0.2 (−0.7, 0.3)	0.0 (reference)	−0.0 (−0.4, 0.4)	−0.1 (−0.5, 0.3)	−0.4 (−0.7, −0.0)
Resting heart rate (bpm)	0.0 (reference)	1.3 (−1.1, 3.7)	0.3 (−2.0, 2.5)	0.4 (−1.6, 2.3)	0.0 (reference)	−0.5 (−2.2, 1.3)	−1.0 (−2.7, 0.6)	−0.6 (−2.0, 0.7)
Triglycerides (mmol/L)	0.0 (reference)	−0.06 (−0.26, 0.14)	−0.10 (−0.29, 0.10)	−0.10 (−0.26, 0.10)	0.0 (reference)	0.13 (−0.01, 0.28)	−0.07 (−0.21, 0.07)	−0.03 (−0.15, 0.09)
Cholesterol (mmol/L)	0.0 (reference)	−0.01 (−0.25, 0.25)	−0.06 (−0.29, 0.18)	−0.02 (−0.23, 0.19)	0.0 (reference)	0.20 (0.03, 0.37)	0.07 (−0.09, 0.24)	0.26 (0.13, 0.40)
Diastolic blood pressure (mm Hg)	0.0 (reference)	1.5 (−0.6, 3.5)	1.4 (−0.6, 3.3)	2.7 (1.0, 4.3)	0.0 (reference)	0.2 (−1.2, 1.7)	0.2 (−1.1, 1.6)	0.4 (−0.7, 1.6)
Systolic blood pressure (mm Hg)	0.0 (reference)	0.5 (−3.5, 4.4)	0.2 (−3.6, 3.9)	0.9 (−2.4, 4.2)	0.0 (reference)	−0.9 (−3.8, 2.0)	−1.3 (−4.1, 1.4)	−1.5 (−3.8, 0.8)

Values are adjusted for age, sex, smoking habits, and respective baseline values.

or decreasing physical activity level was not followed by respective changes in cardiovascular risk factors.

P1681. Change in physical activity and cardiovascular risk factors over 16 years

R. Hermansen[1], A.R. Broderstad[2], B.K. Jacobsen[1], M. Mahonen[3], T. Wilsgaard[1], B. Morseth[4], [1]University of Tromso, Faculty of Health Sciences, Department of Community Medicine - Tromso - Norway, [2]UiT The Arctic University of Norway, Centre for Sami Health Research - Tromso - Norway, [3]University of Oulu - Oulu - Finland, [4]University of Tromso, Department of Sport Sciences - Tromso - Norway,

Background and purpose: Physical activity is considered a major factor in prevention of cardiovascular disease, but most studies conducted have only measured physical activity once. The main purpose of this study was to examine associations between changes in physical activity and cardiovascular risk factors over 16 years in a cohort of 3671 Norwegian men and women. A secondary objective was to study ethnic differences in physical activity and associations with cardiovascular risk factors over time.

Methods: This is a prospective cohort study of 1129 Sami and 2542 non-Sami men and women with a mean baseline age of 45 years. Data were collected from two population-based health studies in Northern Norway conducted in 1987 (baseline) and 2003–2004 (follow-up). Leisure time physical activity was assessed with a similar, validated questionnaire at baseline and follow-up, and change in physical activity was defined as shown in Table 1. Cardiovascular risk factors (body mass index (BMI), resting heart rate, triglycerides, cholesterol, systolic and diastolic blood pressure) were examined using standard procedures at both surveys.

Results: Change in physical activity was in general not associated with change in risk factors over 16 years, with a few exceptions (Table 1). In the non-Sami population, those who were active at both surveys had a larger reduction in BMI

Table 1

	Sami				Non-Sami			
	Inactive in both	Active to inactive	Inactive to active	Active in both	Inactive in both	Active to inactive	Inactive to active	Active in both
	(reference)	β (95% CI)	β (95% CI)	β (95% CI)	(reference)	β (95% CI)	β (95% CI)	β (95% CI)
BMI (kg/m²)	0.0 (reference)	0.0 (−0.6, 0.6)	−0.4 (−1.0, 0.1)	−0.2 (−0.7, 0.3)	0.0 (reference)	−0.0 (−0.4, 0.4)	−0.1 (−0.5, 0.3)	−0.4 (−0.7, −0.0)
Resting heart rate (bpm)	0.0 (reference)	1.3 (−1.1, 3.7)	0.3 (−2.0, 2.5)	0.4 (−1.6, 2.3)	0.0 (reference)	−0.5 (−2.2, 1.3)	−1.0 (−2.7, 0.6)	−0.6 (−2.0, 0.7)
Triglycerides (mmol/L)	0.0 (reference)	−0.06 (−0.26, 0.14)	−0.10 (−0.29, 0.10)	−0.10 (−0.26, 0.10)	0.0 (reference)	0.13 (−0.01, 0.28)	−0.07 (−0.21, 0.07)	−0.03 (−0.15, 0.09)
Cholesterol (mmol/L)	0.0 (reference)	−0.01 (−0.25, 0.25)	−0.06 (−0.29, 0.18)	−0.02 (−0.23, 0.19)	0.0 (reference)	0.20 (0.03, 0.37)	0.07 (−0.09, 0.24)	0.26 (0.13, 0.40)
Diastolic blood pressure (mm Hg)	0.0 (reference)	1.5 (−0.6, 3.5)	1.4 (−0.6, 3.3)	2.7 (1.0, 4.3)	0.0 (reference)	0.2 (−1.2, 1.7)	0.2 (−1.1, 1.6)	0.4 (−0.7, 1.6)
Systolic blood pressure (mm Hg)	0.0 (reference)	0.5 (−3.5, 4.4)	0.2 (−3.6, 3.9)	0.9 (−2.4, 4.2)	0.0 (reference)	−0.9 (−3.8, 2.0)	−1.3 (−4.1, 1.4)	−1.5 (−3.8, 0.8)

Values are adjusted for age, sex, smoking habits, and respective baseline values.

than those who were inactive at both surveys (−0.4 kg/m^2, P<0.05). A larger proportion of the Sami population was inactive at baseline (31.5%) and follow-up (27.5%) compared with the non-Sami (26.1% and 23.3%, respectively) (P<0.05), but this difference in physical activity levels was not reflected in the risk factors.

Conclusion: In this cohort study over 16 years, those who were persistently active had similar or clinically insignificant changes in cardiovascular risk factors compared with those who were persistently inactive. Moreover, increasing or decreasing physical activity level was not followed by respective changes in cardiovascular risk factors.

P6402. Unrecognized myocardial infarction does not improve risk prediction for future myocardial infarction or all-cause death beyond traditional cardiovascular risk factors: a population-based cohort study

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On behalf: Epidemiology of chronic diseases, the Tromso Study

Background: A substantial proportion of patients with myocardial infarctions (MIs) are unrecognized, often because they have little or no symptoms. Previous studies have found that unrecognized MI is associated with similar risk of death as recognized MI, however these studies were not fully adjusted for cardiovascular risk factors and were done before the age of widespread angiography and statin therapy. The benefit of unrecognized MI in cardiovascular risk prediction in the general population is therefore uncertain.

Purpose: To investigate if presence of unrecognized MI on the ECG improved prediction of MI and all-cause death in a general population without recognized MI.

Methods: We included 5,705 participants (38–87 years) without prior recognized MI from a population-based cohort study in 2007–2008. Participants with unrecognized MI were classified on ECG using the Third Universal Definition of MI. They were followed through 31st December 2012 for MI and all-cause death, each event was reviewed and manually validated by persons with medical expertise. We used Cox proportional hazard model to examine the association between unrecognized MI on the ECG and future MI and all-cause death, using the population without MI as reference group. Hazard ratios (HRs) were calculated with 95% confidence intervals (CI), unadjusted and adjusted for traditional cardiovascular risk factors. We compared receiver operating characteristic area under the curve (AUC) to examine whether addition of unrecognized MI on ECG to the Systematic COronary Risk Evaluation (SCORE) improved prediction of future MI during the follow-up period.

Results: Unrecognized MI was present in 469 (8.2%) participants at baseline. We identified 120 MIs and 179 all-cause deaths during 25,580 person-years follow up. Unrecognized MI was associated with an increased risk of MI (HR 2.00, 95% CI 1.21–3.30) and all-cause death (HR 1.73, 95% CI 1.13–2.67) in the unadjusted analyses. After adjustment for sex, age, hypertension, diabetes, daily smoking, HDL and LDL cholesterols, total serum cholesterol, use of statins, and family history of premature MI, there was no significant association between unrecognized MI and future recognized MI (HR 1.30, 95% CI: 0.76–2.22) or all-cause death (HR 1.33, 95% CI: 0.86–2.08). Addition of unrecognized MI on the ECG to the European SCORE did not improve risk prediction for MI (area under the curves 0.72 vs 0.73, p=0.92).

Conclusion: Unrecognized MI was associated with future risk of MI and all-cause death, but did not improve prediction of future MI or death beyond traditional cardiovascular risk factors.

P4117 Personal activity index (PAI) for promotion of physical activity and prevention of CVD

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Background: Low levels of physical activity (PA) has reached pandemic proportions, contributing to >5 million deaths each year worldwide, and making it 1 of the 10 leading causes of death and disability. The major challenge in activity counseling and promotion of PA is to provide clear feedback to individuals with personalized and meaningful information about their activity behaviour. Implicitly, PA behaviors are highly heterogeneous and multi-dimensional in nature, and just one aspect may lead discrepancies in terms of PA status. Although, several methods exist to assess minute-by-minute PA energy expenditure, there is no single outcome measure available that captures all relevant information in a single metric. If such a metric was available, it could potentially be included in wearable devices and provide the user with real-time feedback on

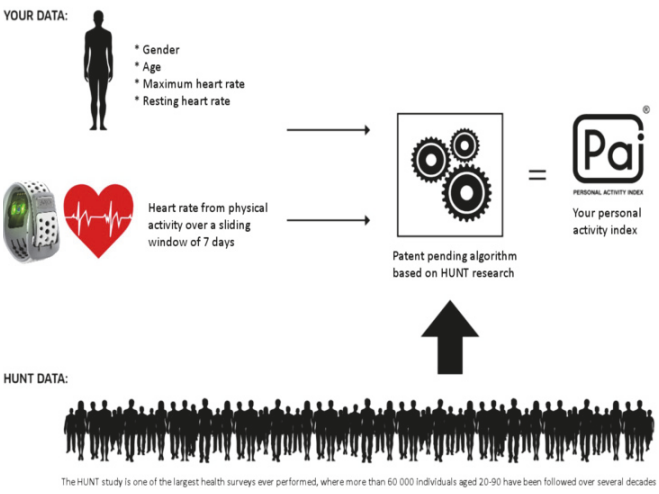
whether they are doing enough PA to promote health and reduce the risk of chronic disease.

Purpose: The aim of the current study was to derive and validate an algorithm that incorporates the different components of PA needed to increase cardiorespiratory fitness and substantially reduce the long-term risk of cardiovascular mortality.

Methods: Using HUNT Fitness Study (n=4637), we derived an algorithm (Personalized Activity Index: PAI) based on PA questions relating to frequency, duration and intensity of exercise where relative intensities of low, medium and high corresponds to 44%, 73% and 83% of heart rate reserve. The validation cohort consists of general healthy HUNT population (n=39,298; f 20,029: m 19,269), and PAI was divided into 3 groups (≤50, 51–99, and ≥100), and inactive (0 PAI) were used as reference.

Results: After a median follow-up of 28.7 years, there were 10,062 deaths, including 3867 deaths (2207 men and 1660 women) from CVD. Men and women with a PAI-level ≥100 had 17% (95% CI, 7–27%) and 23% (95% CI, 4–38%) reduced risk of CVD mortality compared to the inactive groups, respectively, after multiple adjustment for confounders. The corresponding risk reduction for all-cause mortality was 13% (95% CI, 6–20%) and 17% (95% CI, 6–26%) for men and women, respectively. The relative risk reductions were dose dependent over groups ranging from inactive, ≤50 PAI, 51–99 PAI to the recommended level of ≥100 PAI (all p-trends <0.001). Participants with presence of known risk factors such as smokers, hypertension, overweight/obese, and in different age strata showed similar risk reductions by obtaining ≥100 PAI compared to the inactive groups.

Conclusion: Personal Activity Index (PAI) predicted long-term all-cause and CVD disease mortality. The PAI algorithm/wearable devices could be used as a motivational tool for behaviour changes in PA, as the approach firmly focuses on the individual at the center as a user of information in control of his or her personal physical activity.



PAI scheme

P784 Cardiorespiratory fitness in women with previous preeclampsia

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Background: Preeclampsia (PE) increases the risk of future cardiovascular disease (CVD) in premenopausal age of women. Poor cardiorespiratory fitness (CRF) is a prognostic factor for development of CVD.

Purpose: To investigate CRF on long-term follow-up of women after severe PE.

Method: Sixty women, age 41±4 (mean±SD) with previous severe PE and 25 healthy controls (age 38±4) performed a cardiopulmonary exercise test on a treadmill to exhaustion for measurement of maximal oxygen uptake (VO2max). In addition, pulmonary function, and blood pressure were measured.

Results (Table 1): Sixty women fulfilled test criteria for VO2max (respiratory exchange ratio ≥1.15 or a Borg score ≥17). VO2max was 9% lower in the PE-group compared to the controls (p<0.01). Systolic and diastolic blood pressure at rest and at maximal exercise were significantly higher in the PE-group compared to controls. There were no differences in pulmonary function and ventilatory efficiency (VE/VCO2)between the groups.

Conclusion: Our study demonstrates that women with previous severe preeclampsia have a clinically lower cardiorespiratory fitness compared to healthy controls. This important finding indicates a poorer health status and increased CVD risk. Women with a history of preeclampsia need a proper CVD risk assessment and counselling.

Variables at rest and exercise

Variables	PE group (n=60)	Control group (n=25)	p-value
Body mass index, kg/m^2	25.5±5.5	22.8±2.9	0.03
Functional vital capacity, L	3.74±0.47	4.08±0.44	0.04
Forced expiratory volume in 1 sec, L	3.11±0.40	3.16±0.72	ns
Resting systolic BP, mmHg	133±17	114±12	<0.01
Resting diastolic BP, mmHg	87±11	73±10	<0.01
Max. oxygen uptake (VO2max), mL kg^{-1} min^{-1}	34.3±7.7	37.7±7.4	0.01
Maximal heart rate (HRmax), beat min^{-1}	178±11	184±11	0.04
Oxygen pulse, mL beat^{-1}	13.1±2	13.5±1.9	ns
Max systolic BP, mmHg	185±21	165±19	<0.01
Max diastolic BP, mmHg	87±17	74±11	<0.01
Minute ventilation (VE), L min^{-1}	89.4±11.9	91.1±14.4	ns
SpO2max, %	92±4	94±4	ns
VECO2slope	25.1±3.9	24.4±1.6	ns
VEO2slope	24.6±8.3	22.0±5.0	ns
Blood lactate, mmol L^{-1}	10.1±3.0	9.9±2.5	ns

Data presented as mean (± SD).

P4521. Incidence and mortality risk of QT prolongation in a community hospital cohort. A review of more than 200.000 ECGs

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Introduction: Computer based acquisition analysis and storage of ECG enables diagnostics of corrected QT time prolongation. Sykehuset Telemark Norway, serving 138 000 inhabitants has used such a system from 2004 to date.

Methods: During the years 2004 through 2014, 225 117 ECG, was acquired from 63 286 unique patients. 2709 ECG's, sampled from 1855 patients, were identified through logic computer search for corrected QT interval (QTc) more than 500 ms. ECG's with QRS >120 ms, atrial fibrillation or atrial flutter was excluded. Manual reexamination exposed computer reading error in ECGs from 321 patients and those patients was excluded from the cohort. Historical and current clinical data were collected from the patients' medical record. All surviving patients was invited to a follow-up visit and given the option of a genetic test for known LQT genes. 62% of the 842 survivors came to the study follow –up.

Results: The average age of the 1534 LQT patients was 71 years (median 73years), 906 (59%)female, 628 (41%) male. The QT prolongation was transient in 1010 patients, and regression of the QT interval to less than 500 ms was seen after median 81 days. Described risk factors for development of QT prolongation, electrolyte disturbances, QT-prolonging medication, sepsis and trauma were seen in 850 patients. In 185 patients the condition of QT prolongation was recognised and documented in the patient records, whereas the condition in the remaining 1349 patients (92%) was unnoted. Comparison of life expectancy with matched control patients shall be performed.

Conclusion: Computer calculation of corrected QT time enables increased quality in ECG reading, and we find in our database an incidence of severe QT prolongation on approximately 24/1000 patients. Most cases of severe QT-prolongation are acquired and reflect severe clinical conditions requiring revision of medication, electrolytes and underlying disease.

1122. The cost-effectiveness of sacubitril/valsartan (LCZ696) in the treatment of patients with heart failure with reduced ejection fraction in Norway

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Objective: To evaluate the cost-effectiveness of sacubitril/valsartan (LCZ696) in the treatment of patients with heart failure with reduced ejection fraction (HFREF) in Norway.

Design: A decision analytic model was utilised to analyse lifelong health outcomes, quality adjusted life-years (QALYs), costs and the incremental cost-effectiveness ratio (ICER) of sacubitril/valsartan compared to generic enalapril. The model combines clinical trial data from the PARADIGM-HF trial with Norwegian baseline patient characteristics and unit costs. Costs (reported in Euro [€] 2015) and outcomes were analysed over a lifetime time horizon and were both discounted at 4%.

Results: The long-term cost of sacubitril/valsartan increased by €10,603, compared to enalapril. Most of the increase is caused by the increase in medication costs, while hospitalisation costs were, on the other hand, reduced by €1,310, compared to enalapril. Life-years increased by 0.56 with sacubitril/valsartan, while QALYs increased by 0.46. The ICER of sacubitril/valsartan compared with enalapril was €18,836 per life-year gained and €23,277 per QALY gained. Sensitivity analysis demonstrated that the result is highly robust to changes to the analysis assumptions and the input data.

Conclusion: The cost per QALY of treating HFREF-patients with sacubitril/valsartan compared with enalapril is below conventional willingness-to-pay thresholds in Norway. Sacubitril/valsartan is therefore considered to be a highly cost-effective treatment option.

P755 Septal beaking in left bundle branch block induces right ventricular dysfunction

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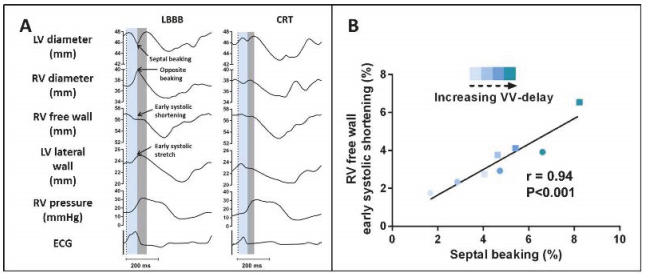
Background: We have previously demonstrated that left bundle branch block (LBBB) reduces right ventricular (RV) long axis function due to abnormal early systolic shortening in the RV free wall, and this contraction pattern is restored by cardiac resynchronisation therapy (CRT) (Figure A). We hypothesised that abnormal RV early systolic shortening in LBBB is a result of preejection leftward motion of the interventricular septum, named septal beaking or flash.

Purpose: To explore the mechanism of reduced RV work during LBBB.

Methods: Eight anaesthetised dogs with LBBB induced by RF-ablation received CRT. Pressures by micromanometer and dimensions by sonomicrometry were used to calculate myocardial shortening and work. In two additional dogs, measurements were also obtained during progressive interventricular (VV) conduction delay (4–16–32ms) and ultimately LBBB (44ms).

Results: In the eight dogs CRT improved RV function by reducing early systolic shortening in the RV free wall from 4±1 to 2±2% (P<0.01) (Figure A), however, total systolic shortening was unchanged at 8±3 vs 8±3%. Therefore, regional RV free wall work increased from 24±16 to 36±17 mmHg*mm (P<0.01). Septal work increased correspondingly from 8±60 to 91±50 mmHg*mm (P<0.01). With increasing VV-delay there was progressive increase of septal beaking and reduction of septal work (r=-0.95, P<0.001). Similarly, in the RV free wall, regional work was progressively reduced as RV early systolic shortening increased (r=-0.77, P<0.05). There was a significant correlation between the septal beaking and RV free wall early systolic shortening (Figure B). Furthermore, the magnitude of septal beaking correlated with the reduction of regional work in the RV free wall (r=-0.79, P<0.05).

Conclusion: The extent of early systolic shortening and reduced regional work in the RV free wall correlated with septal beaking in LBBB. This suggests that reduced RV free wall function in LBBB is a direct mechanical effect of septal beaking.



P6278 Cardiac resynchronisation therapy improves systolic function during left bund branch block by an upward shift of the end-systolic pressure-volume relation

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Background: Left bund branch block (LBBB) leads to electrical and mechanical dyssynchrony in the left ventricle (LV), and therefore a heterogeneous distribution of myocardial work. Cardiac resynchronisation therapy (CRT) improves systolic function in LBBB, however, it is not fully understood how this relates to an improvement in contractility.

Purpose: To determine the effect of CRT on contractility during LBBB by assessing changes in the peak LV systolic elastance (Emax) and the end-systolic pressure-volume relation (ESPVR).

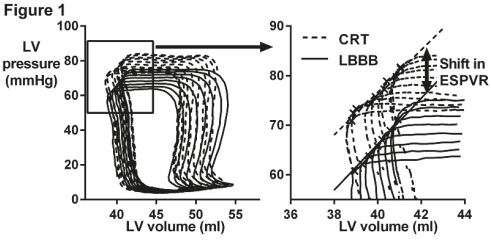
Methods: In seven anaesthetised dogs, we measured pressures by micromanometers and LV volume by sonomicrometry. Stroke work (SW) was calculated from pressure-volume loops. LBBB was induced by radio frequency ablation. Transient caval constrictions were performed to obtain a range of LV volumes. Slopes and positions of the ESPVR were calculated using linear regression analysis before and during CRT (Figure 1). Data were compared at similar preloads (end-diastolic volumes).

Results: CRT increased SW from 651±222 mmHg*ml (mean±SD) to 848±183 mmHg*ml (p<0.05). There was no significant change in Emax during CRT compared to LBBB with CRT off (4.1±1.7 vs 3.9±1.2 ml/mmHg, ns). There was,

however, a significant parallel upward-shift in the ESPVR from 74±36 to 89±37 mmHg ($p<0.05$) when CRT was turned on (Figure 1). This implies that the LV generated higher systolic pressure at any given end-diastolic volume when CRT was on.

Conclusions: CRT improved global systolic function acutely by shifting the ESPVR upwards with no change in Emax. The improvement in systolic function was pre-load independent. This finding is important in the understanding of how CRT improves cardiac systolic function and suggests that the shift of the ESPVR rather than Emax should be used to measure improvement of LV contractility in the dyssynchronous heart.

Figure 1



P5624 Infusion of TRO40303 in patients with ST-elevation myocardial infarction prior to primary percutaneous coronary intervention did not alter levels of inflammatory biomarkers in the MITOCARE study

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Background: In the MITOCARE study there was no statistically significant effect in the prevention of reperfusion injury after administration of the mitochondrial permeability transition pore inhibitor TRO40303 in patients with ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PPCI). The effects of TRO40303 on pro-inflammatory cytokines and acute phase proteins have not previously been assessed in this population.

Median values of biomarkers at 0, 12 ,72h

	Time	IL 1b	IL 6	IL 10	TNF	Pentraxin-3	CRP
	(hours)	(pg/ml)	(pg/ml)	(pg/ml)	(pg/ml)	(ng/ml)	(mg/L)
TRO40303	0	0.0263	1.842	0.795	6.25	0.77	2.92
	12	0.0235	3.113	0.170	6.96	1.63	6.49
	72	0.0389	1.925	0.160	8.17	1.10	24.42
Placebo	0	0.0222	1.210	1.188	6.34	0.70	2.46
	12	0.0284	3.600	0.145	6.99	1.14	6.75
	72	0.0259	1.890	0.153	7.67	0.90	16.65

IL 1b (Interleukin 1b), IL 6 (Interleukin 6), IL 10 (Interleukin 10) ,TNF (tumor necrosis factor), and CRP (C-reactive protein).

Methods: STEMI patients (n=163, mean age 61.9) with chest pain within 6 hours before admission for PPCI were randomized to i.v bolus of TRO40303 (n=83) or placebo (n=80) prior to reperfusion in the MITOCARE study. To test whether the groups differed in levels of Interleukin 1b, Interleukin 6, Interleukin 10, tumor necrosis factor, Pentraxin-3 and C-reactive protein at time points 0, 12, and 72 hours, Mann-Whitney U tests were performed. Further, Mann-Whitney was repeated to find differences between groups in the change of biomarker levels between 0–72, 0–12 and 12–72 hours respectively. A significance level of $\alpha=0.05$ was chosen for all tests.

Results: There were no statistically significant differences between the two groups, neither in levels of pro-inflammatory cytokines nor in levels of acute phase proteins at any time point (median values, Table 1). Moreover, there were no statistically significant differences in the changes of the biomarkers from 0–72 hours, 0–12 hours and 12–72 hours between groups.

Conclusion: Infusion of TRO40303 prior to reperfusion does not alter the pharmacokinetics of pro-inflammatory cytokines or acute phase proteins during the first 72 hours post PPCI.

P4587 Atrio-ventricular plane excursion is impaired after ten weeks of anthracycline treatment in breast cancer patients: Data from the PRADA study

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Background: Anthracyclines are well known for their dose-dependent cardiotoxic effect. The effect of low to moderate doses of the anthracycline epirubicin on left ventricular (LV) systolic function in otherwise healthy women remains unclear.

Purpose: To assess changes in various echocardiographic indices of LV systolic function in the early phase of anthracycline therapy in breast cancer patients.

Methods: 126 women without heart disease and other serious co-morbidities scheduled for anthracycline-containing adjuvant treatment with epirubicin, were randomized in a placebo-controlled double blind clinical trial with candesartan and metoprolol (PRADA (NCT01434134)). Human epidermal growth factor receptor 2 (HER2)-positive patients received 4 cycles of epirubicin 100 mg/m^2 (moderate dose), while HER2-negative patients received 4–6 cycles of 60 mg/m^2 (low dose). Mean treatment time was 10 weeks (±2). For this analysis we report the echocardiography data obtained at baseline and after completion of anthracycline therapy in the whole population. The following echocardiographic indices were used: Two-dimensional (2D) strain, 2D and 3D left ventricular ejection fraction (LVEF), tissue Doppler systolic S' and mitral annular plane systolic excursion (MAPSE). Measurements for MAPSE and S' were performed at the base of the LV septum and lateral wall and averaged.

Results: MAPSE and S' were significantly reduced after completion of moderate doses of the anthracycline epirubicin (HER2-positive group), whereas no such effect was observed in patients receiving low-dose (HER2-negative group) (Table 1). Only MAPSE showed a significant difference between HER2-positive and -negative patients (p=0.035).

Conclusion: Moderate dose of epirubicin was associated with a significant reduction in MAPSE and S' but not 2D strain, 2D or 3D LVEF. This suggests that LV longitudinal function is impaired already after 10 weeks of anthracycline treatment in breast cancer patients without prior cardiac disease.

	n	Mean (SD) value at baseline	Mean (SD) value after anthracycline	Within group p-value
MAPSE, mm				
HER2-negative	91	14.4 (2.2)	14.0 (2.1)	0.11
HER2-positive	26	14.9 (2.2)	13.5 (2.1)	0.001
Tissue Doppler systolic S', cm/s				
HER2-negative	92	9.1 (1.5)	9.0 (1.5)	0.326
HER2-positive	27	9.3 (1.6)	8.6 (1.3)	0.011

MAPSE, mitral annular systolic excursion; HER, human epidermal growth factor receptor; SD, standard deviation.

4914 Physical activity, body mass index and mortality among subjects with coronary heart disease

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Background: The association between body mass index (BMI) and mortality in subjects with coronary heart disease (CHD) remains uncertain. An "obesity paradox" is suggested, with lower mortality in subjects who are overweight or obese. The role of physical activity in the BMI-survival relationship is unclear.

Purpose: Our objective was to examine the isolated and combined associations between BMI and physical activity, and mortality in subjects with CHD.

Methods: This was a prospective population-based cohort study. We studied 5385 subjects with angina pectoris and/or myocardial infarction who participated in one or more of the Nord-Trøndelag Health studies in Norway, with examinations in 1986, 1996, or 2007, followed until the end of 2014. Cox proportionate hazard regression models were used to estimate hazard ratios (HR) for all-cause and CVD mortality, adjusted for age, smoking, diabetes, and alcohol. To reduce the chance of reversed causality, we removed the first three years of follow-up in separate analyses.

Results: There were 3 848 deaths during 30 (median 15.1) years of follow up, out of which 2 390 were due to CVD. Compared to BMI (in weight in kilograms divided by the square of height in meters.) 18.5–22.4, we found that BMI categories (25.0- 27.4, 27.5–29.9, and 30.0–34.9) had reduced all-cause mortality risk (HR, 0.80 [95% confidence interval (CI), 0.71–0.89]; 0.81 [95% CI, 0.72–0.91]; 0.85 [0.75–0.97]), respectively (Figure 1, Panel A). BMI categories 25.0–27.4 and 27.5–29.9 had reduced CVD mortality risk (HR, 0.81 [95% CI, 0.70–0.93)]; 0.84 [95% CI, 0.72–0.98)]), respectively. There was not increased all-cause or CVD mortality risk among those with BMI ≥35.0. Compared to physically inactive, all levels of PA (low, recommended, and high) had reduced all-cause mortality risk (HR, 0.89 [95% CI, 0.77–0.90)]; 0.75 [95% CI, 0.67–0.84]; 0.75 [95% CI, 0.65–0.87]), respectively, with similar estimates for CVD mortality. In inactive, all BMI categories above 25.0 had reduced all-cause mortality risk (HRs across BMI categories: 0.87, 0.75, 0.79, 0.80, 0.75, Figure 1, Panel B), whereas in active subjects, only those with low activity

level and BMI 22.5–27.4 had reduced risk (Figure 1, Panel C-D). When early deaths (subjects who died within the first three years of follow-up) were excluded, the results were essentially the same.

Conclusion: We found lower mortality risk in subjects with CHD who were overweight and obese. In physically active subjects, however, BMI did not have a significant role for predicting survival. These results suggest that PA is important to improve prognosis in subjects with CHD, and that body weight is of minor importance in secondary CHD prevention as long as the subjects are physically active.

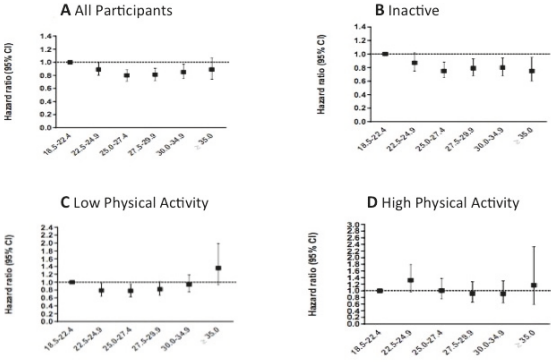

Figure 1. Hazard ratios for all-cause mortality, according to physical activity level.

P3795 High osteoprotegerin levels are associated with adverse left ventricular remodelling in patients with ST-elevation myocardial infarction

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Background: Elevated levels of osteoprotegerin (OPG) have been reported in patients with ST-elevation myocardial infarction (STEMI) compared to patients with non-STEMI, unstable angina, and stable coronary artery disease (CAD). Recent studies have shown that OPG levels are associated with infarct size in STEMI patients, although the results have been somewhat inconsistent.

Purpose: The main aims of the present study were to elucidate the potential role of OPG in ischemia-reperfusion (IR) injury in STEMI patients. Associations between OPG and left ventricular (LV) remodelling, myocardial salvage index, final infarct size and microvascular obstruction (MVO), were assessed by cardiac magnetic resonance imaging (CMR).

Methods: The Postconditioning in ST-Elevation Myocardial Infarction (POSTEMI) trial was a prospective, randomised clinical trial investigating ischemic postconditioning (iPost) as cardioprotective strategy in STEMI patients. The effect of iPost on the primary endpoint of the study, final infarct size measured by CMR after 4 months, was neutral. The study population consisted of 272 patients with first-time STEMI, treated with primary percutaneous coronary intervention (PCI). Blood samples for serum OPG were drawn before and immediately after the PCI procedure, during in-hospital follow-up 8–20 hours (median 14.7) and 20–32 hours (median 23.8) after admission, and at 4-month follow-up. LV remodelling was defined as change in LV end-diastolic volume (delta EDV). CMR was performed both in the acute phase (median 2 days after the index event) and after 4 months, allowing assessment of final infarct size, LV ejection fraction (LVEF), myocardial salvage index, MVO and change in EDV. OPG levels were quantified by commercially available enzyme immunoassay.

Results: Patients with high OPG levels (above median, 4.46 ng/ml) measured in the time frame 20–32 hours after primary PCI had significantly larger increase in EDV (median 13.0 vs 1.0 ml, p=0.009, Figure), in addition to lower myocardial salvage (41.8 vs 68.0%, p=0.0001), larger final infarct size (17.0 vs 8.2% of LV, p<0.0001), lower LVEF (52.0 vs 60.5%, p=0.002) and higher frequency of MVO (60.9 vs 32.6%, p=0.012), compared to patients with low OPG levels. OPG remained significantly associated with delta EDV and final infarct size after adjustments in multi-

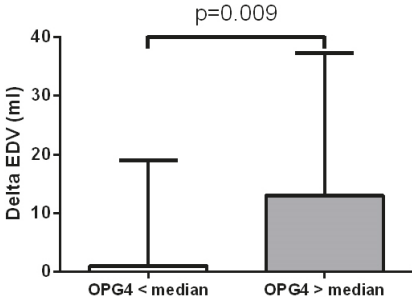

Figure Change in end-diastolic volume (EDV) from the acute phase to 4 months, as assessed by CMR. Values presented as median (top of boxes) with interquartile range (whiskers).

variate linear regression analyses including peak troponin values.

Conclusion: High levels of OPG are associated with impaired recovery of LV function and adverse left ventricular remodelling in STEMI patients.

385 Referance values for cardiopulmonary function in older men and women: the generation 100 study

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On behalf: CERG (cardiac exercise research group)

Background: Reference values on cardiopulmonary function at rest and during exercise in elderly are limited, and derived from relatively small studies. In addition, previous studies exclusively exclude people with cardiovascular diseases. The aim of this study was to establish reference values for cardiopulmonary function and objectively measured fitness in a general older population.

Methods: All men and women born in the years 1936 to 1942 (n=6966) who were residents in our city, were invited to participate. In total 1567 (790 women) fulfilled the inclusion criteria for the study. Clinical examinations and cardiopulmonary exercise tests (CPET) were performed.

Results: Data from the CPET test show that there were a significantly gender difference in peak oxygen uptake (26.2±5.0 and 31.3±6.7 mL/min/kg for women and men, respectively), peak CO2 production (2.9±0.2 and 1.9±0.1 L/min for women and men, respectively), peak ventilation 61.1±21.6 and 96.2±21.7 L/min for women and men, respectively), and peak breathing frequency 39.7±7.1 and 41.8±8.0 breath/min for women and men, respectively). Anaerobic threshold was achieved at 87.7±7.8 and 86.9±7.9% of VO2peak for women and men, respectively. Peak oxygen uptake was 19.5% lower for women with cardiovascular disease compared to those who report to use no medication (p<0.01). Men with cardiovascular disease had a 19.5% lower peak oxygen uptake compared to men reporting to use no medication (p<0.01). Peak heart rate was significantly lower for both women and men with cardiovascular disease compared to those who report no use of medication (−5 and −9 beats per minutes for women and men, respectively).

Conclusion: Our study represents the largest reference material on objectively measured fitness and cardiopulmonary function in elderly men and women. This study is the first to included older adults with cardiovascular diseases in the material.

P1494 CHA2DS2-VASC score, left atrial size and atrial fibrillation as stroke risk factors in the Tromso Study

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Background: Ischemic stroke is the most devastating complication resulting from atrial fibrillation (AF). The CHA2DS2-VASc score estimates stroke risk in non-anticoagulated patients with AF. It combines common risk factors for stroke such as congestive heart failure, hypertension, age, diabetes, previous stroke/TIA, vascular disease and sex. CHA2DS2-VASc score, left atrial (LA) size and AF have individually been associated with stroke risk. How to combine these factors to identify stroke risk has been unclear, as most of the studies have assessed the association with stroke risk for each factor separately.

Purpose: We investigated the predictive ability of combinations of CHA2DS2-VASc score, LA size and AF for the odds of incident stroke in a population-based cohort study.

Methods: We followed 2844 participants from the Tromso Study from 1994 through 2012. Information on CHA2DS2-VASc score (age, sex, congestive heart failure, hypertension, vascular disease and diabetes) and LA size were obtained at baseline. AF status was recorded from medical records. The outcome measure was all strokes. The association between co-variates and stroke was investigated by means of multivariable logistic regression analysis.

Results: A total of 325 subjects (45% women, mean age at baseline 59.3 years) had a stroke. Incidence rates for stroke were 6.4 in women and 8.4 in men per 1000 person-years. Subjects with CHA2DS2-VASc score >0 and LA size <2.8 had approximately 4 times (95% CI, 2.6–5.3) increased odds of stroke, whereas subjects with CHA2DS2-VASc score >0 and LA size >2.8 had approximately 9 times (95% CI, 5.3–16.4) increased odds of stroke, compared to subjects with CHA2DS2-VASc score 0, irrespective of AF status. For those with CHA2DS2-VASc score >0, LA size >2.8 and no AF, adjustment for significant covariates increased the odds from 12.1 (95% CI, 6.3–23.2) to 12.5 (95% CI, 6.4–24.3).

Conclusion: Combining CHA2DS2-VASc score >0 and enlarged LA size identifies subjects with high odds of stroke regardless of AF status. The risk factors that increase the CHA2DS2-VASc score as well as AF risk factors should be monitored and managed properly.

4261 Peak left atrial strain is determined by left ventricular systolic function and filling pressure

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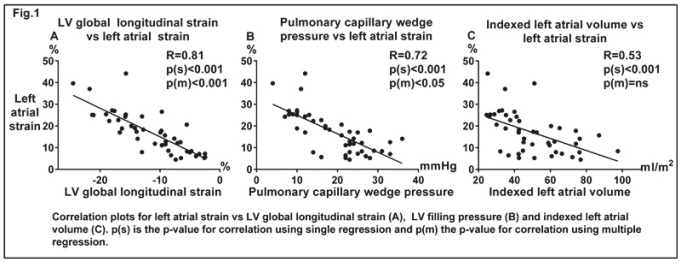
Introduction: Peak left atrial (LA) strain during left ventricular (LV) systole has been proposed as an index of LV filling pressure. Since LA filling is determined mainly by the suction effect that results from systolic descent of the atrioventricular plane, we hypothesized that LV longitudinal shortening is a determinant of LA strain. Potentially, LA volume may also influence LA strain, as a large cavity is associated with relatively reduced deformation.

Purpose: To explore determinants of LA strain.

Method: In 45 patients we performed simultaneous echocardiography and measurement of pulmonary capillary wedge pressure, which is an indirect measure of LV filling pressure. LA strain and LV global longitudinal strain (GLS) were assessed by speckle tracking echocardiography. We used GLS as a measure of LV longitudinal shortening. LA volume was measured by echocardiography. We analyzed the relationship between LA strain and each of the three putative predictors: LV GLS, LV filling pressure and LA volume.

Results: Using single regression analysis, we found that LA strain correlated significantly with each of the three predictor variables (Fig.1 a-c), but the strongest correlation was with LV GLS. When using multiple regression analysis, only the correlations to LV GLS and LV filling pressure remained significant (Fig. 1 a–c).

Conclusion: LV GLS and LV filling pressure were strong determinants of LA strain. This implies that LA strain is determined by LV systolic as well as diastolic function. Therefore, the ability of LA strain to predict LV filling pressure is confounded by interaction with LV systolic function.



Correlation plots for left atrial strain vs LV global longitudinal strain (A), LV filling pressure (B) and indexed left atrial volume (C). p(s) is the p-value for correlation using single regression and p(m) the p-value for correlation using multiple regression.

P3143 Markers of thrombin generation in patients with ST-elevation myocardial infarction are associated with long term clinical outcome

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Introduction: Thrombin generation and fibrin formation, in addition to platelet activation, play important roles in intracoronary thrombus formation, which may lead to acute myocardial infarction (AMI). Whether increased pro-coagulant activity during AMI is associated with clinical outcome is not clarified.

Aim: To investigate whether levels of the pro-thrombotic markers pro-thrombin fragment 1+2 (F1+2) and D-dimer measured in the acute phase of ST-elevation myocardial infarction (STEMI) are associated with later clinical outcome.

Material/Methods: Patients (n=971) with STEMI were included. Warfarin users were excluded for this purpose. Blood samples were drawn at a median time of 24 hours after onset of symptoms and 18 hours after percutaneous coronary intervention (PCI). The primary outcome was a composite of all-cause mortality, re-infarction, stroke, unscheduled revascularization or re-hospitalization for heart failure; secondary outcome was total mortality. The median follow up time was 4.6 years, recorded by telephone call and cross-checked with hospital records. Associations were calculated by trend analyses through quartiles and multivariate analyses were performed by logistic regression, with the variables dichotomized at median levels.

Results: The number of composite endpoints and total mortality was 195 (20.1%) and 79 (8.1%). Significantly higher levels of D-dimer were observed in patients both with combined endpoints and total mortality compared to those without events (both p=≤0.01), whereas F1+2 was higher with respect to total mortality (p=0.001).

There were significant trends for increased numbers of both events through quartiles of both markers. When dichotomizing levels at median values (F1+2 265 pmol/L, D-dimer 519 ng/mL) significantly increased risk of events was observed in univariate analyses (composite endpoint p=0.013 and 0.015 respectively, total mortality p<0.001, both). When adjusting for relevant covariates (age, gender, admission glucose,

NT-proBNP and peak Troponin T) no significant associations were found with regard to the composite endpoint, whereas D-dimer was significantly associated with total mortality (OR 2.04, 95% CI 1.07–3.86, p=0.03) and F1+2 borderline significant (OR 1.67, 95% CI 0.93–2.98, p=0.08).

Summary/Conclusion: The hypercoagulable state in the acute phase of an AMI seems to be of significant importance for future clinical outcome, especially for mortality. Thus, anticoagulant treatment after AMI might still be discussed.

P1141 Left ventricular mechanical dispersion predicts outcome in conservatively treated patients with aortic stenosis

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Introduction: Surgical aortic valve replacement (AVR) provides excellent survival benefit in patients with aortic stenosis (AS). However, some patients are not eligible for AVR due to absence of symptoms or severe comorbidities. Markers of prognosis in these patients are sparse.

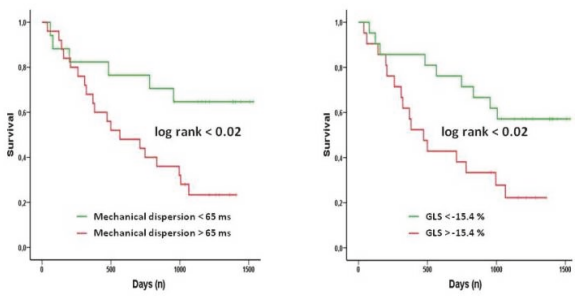
Purpose: We aimed to investigate if parameters from strain echocardiography are markers of prognosis in conservatively treated AS-patients.

Methods: We included 42 patients (50% women, age 79±7 years) with AS. We performed a standard 2D echocardiography including speckle tracking strain. Global longitudinal strain (GLS) was calculated as the average of peak longitudinal shortening from a 16 left ventricular (LV) segments model. Mechanical dispersion was defined as standard deviation of time from onset of Q/R on ECG to peak longitudinal strain in 16 segments.

Results: Average aortic valve (AV) area was 0.8±0.3 cm^2. Patients had LV septal hypertrophy (12±2 mm) and preserved LV ejection fraction (EF) (56±14%). During 27±16 months follow-up, 25 (60%) patients died. Number of patients not eligible for surgical AVR due to comorbidity (n=19) or sparse symptoms (n=23) was similarly distributed between survivors and non-survivors (p=0.09). Mechanical dispersion was lower and GLS better in survivors compared to non-survivors (60±16 ms vs. 80±23 ms, p<0.01, and −17.2±3.7% vs −13.9±4.9%, p=0.04, respectively), while LVEF was similar (60±11% vs 53±15%, p=0.10). C-statistics for mechanical dispersion and GLS showed an AUC of 0.76 (0.61–0.91) and 0.71 (0.55–0.87) respectively. Mechanical dispersion >65 ms (Figure) and GLS >−15.4% were associated with mortality (both log rank <0.02). Mechanical dispersion predicted mortality independently of AV mean pressure gradient and gender [HR=1.25 (1.05, 1.49), p=0.01, per 10ms increase].

Conclusion: Annual mortality was 30% in patients with severe AS not treated with AVR. Increased mechanical dispersion and worse GLS may be used as additional risk factors and strengthen the indication for interventional treatment in patients with severe AS and preserved LVEF not eligible for AVR when using traditional criteria.

Survival in 42 AS-patients without AVR by mechanical dispersion and GLS



No. at risk

Mech. disp. < 65 ms	17	12	9	1	GLS < 15.4 %	21	16	12	6
Mech. disp. > 65 ms	25	13	7	0	GLS > 15. 4 %	21	10	4	0

174 Anti hypertrophic effects of LCZ696 in chronic cardiac pressure overload

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Background/Introduction: LCZ696 is a newly approved drug for treatment of Heart failure with reduced ejection fraction (HFrEF). It combines the effects of angiotensin receptor blockade and neprilysin inhibition, and was in a large clinical trial shown to yield a major reduction in mortality when compared to current standard therapy for HFrEF. The mechanisms mediating this beneficial effect remain largely unknown. Furthermore, better understanding of this new molecule's

mechanisms of action can potentially open up for other clinical applications.

Purpose: To investigate the effects of LCZ696 on cardiac function and remodeling in a chronic model of increased afterload.

Methods: Thirty male Sprague Dawley rats were randomly assigned to three different groups: vehicle treated sham operated (Sham, n=5); vehicle treated transverse aortic banding (TAC) (vehAB, n=12); LCZ696 treated transverse aortic banding (LCZAB, n=13). Oral gavage was performed once daily in all groups for six weeks. Echocardiography and MRI were performed at six weeks, organ weights were assessed, and tissues were examined using PCR and HPLC. * indicates $p<0.05$ for vehAB vs. LCZAB.

Results: Both LCZAB and vehAB had similar trans-stenosis gradients as assessed by echocardiography at randomization. MRI demonstrated increased left ventricular mass in TAC animals, with LCZ reducing the observed change (Sham; LCZAB; vehAB: 197±8,5; 213±8.46; 248±13.24 mm^3*). Echocardiography indicated a trend towards better diastolic function in LCZ treated animals. MRI showed a trend towards decreased EF in TAC animals, with LCZ yielding improvement (73.8±2.44; 71.42±1.5; 66.55±2.25%). At six weeks, LCZAB had a 11,5% lower left ventricular weight than vehAB (0.85±0.02; 1.0±0.045; 1.1±0.057 g *). Lung weight was lower in LCZAB than vehAB (1.5±0.049; 1.6±0.020; 1.72±0.07 g *), indicating improved cardiac function. There was a trend towards an increase in Myh-7 in TAC, with lower levels in LCZAB than in vehAB, indicating possible favorable effects on cardiac remodeling. At six weeks TAC did not show increased collagen on HPLC for hydroxyproline. Similarly, there were no increases of Col1. There was a trend towards vehAB showing the highest expression of Col3 and lowest expression of MMP9.

Conclusion(s): LCZ696 treatment reduces cardiac hypertrophy in this model of sustained pressure overload, and showed a favorable trend for improved diastolic and systolic function. Our findings support that the beneficial effects observed in recent clinical studies could reflect favorable anti cardiac remodeling properties and that the clinical utility of this novel compound might be extended to patients with diastolic dysfunction secondary to pressure overload. There was no observed fibrosis in this study. Further studies are warranted to investigate the underlying mechanisms responsible for the observed beneficial effect and the possible utility of LCZ696 in other disease states involving cardiac pressure overload.

P6542 Platelet- and monocyte-derived circulating microparticles and microparticles carrying tissue factor are related to acute myocardial infarction severity in an elderly population

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Background: Circulating microparticles (cMPs) are phospholipid-rich vesicles released from cells when activated or injured. cMPs are increased in patients with acute coronary syndromes and may contribute to the formation of intracoronary thrombi, with subsequent acute myocardial infarction (AMI). Tissue factor (TF, CD142) is the main trigger of fibrin formation and cMPs carrying TF are considered the most procoagulant cMPs. Similar types of atherosclerotic lesions may lead to different types of AMI, ST-elevation myocardial infarction (STEMI) or non-STEMI. The mechanisms behind are still unresolved, but important because of its clinical implications.

Purpose: To investigate the phenotype of cMPs found in plasma that may potentially influence AMI severity.

Methods: Two hundred patients aged 75±4 years were included in the study 2–8 weeks after suffering an AMI. At inclusion, Annexin V positive (+)-cMPs derived from cells of the vascular compartment were measured in citrated plasma by flow cytometry. Concentrations of peak troponin T (TnT, measured in the acute phase) and pro B-type natriuretic peptide (NT-proBNP, measured at inclusion) were quantified by standardized methods, and clinical data was recorded. One-way ANOVA was used to assess the differences in cMPs according to the type and severity of AMI. Correlation analyses were performed with Pearson's correlation coefficient.

Results: STEMI patients (n=75) showed higher levels of platelet-derived cMPs [CD61+, CD31+ (platelet/endothelial cell adhesion molecule 1), CD42b+ (von Willebrand factor receptor) and CD31+/CD42b+, p=0.048, 0.038, 0.009 and 0.006, respectively], in addition to higher levels of peak TnT and NT-proBNP ($p<0.0001$, both) compared to NSTEMI patients (n=125). Patients who suffered a heart failure during AMI (n=17) had increased levels of platelet (CD61+)- and monocyte (CD14+)-derived cMPs carrying TF (CD142+), $p<0.0001$ and 0.004, for CD61+/CD142+ and CD14+/CD142+, respectively, as well as increased levels of peak TnT (p=0.038) and NT-proBNP (p=0.005). Additionally, patients at NYHA functional classification class III (n=23) also showed higher levels of CD142+,

CD14+ and CD14+/CD142+ cMPs compared to patients in class I and II (p=0.001, 0.015 and 0.014, respectively). Finally, no correlations were found between any cMP and TnT or NT-proBNP concentrations.

Conclusions: cMPs from platelets and monocytes and cMPs carrying TF are related to AMI severity, without any correlation to peak TnT or NT-proBNP levels in elderly patients 2–8 weeks after the event. Our results indicate that these cMPs provide information of ongoing processes during AMI different from TnT and NT-proBNP pathways. Therefore, TF-carrying, platelet and monocyte cMPs may be alternative and sensitive markers of AMI severity.

P4992 Effect of secondary prevention care: Total blood cholesterol and lipid-lowering drug use after first-ever myocardial infarction by sex and age. The Tromso Study 1994-2008

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Background: Positive lifestyle changes after acute myocardial infarction (MI) are associated with improved prognosis and lower mortality. However, the European survey of cardiovascular disease prevention and diabetes (EUROASPIRE) showed that secondary prevention care is inadequate, and that the majority of MI patients do not achieve cardiovascular risk profile goals. In Norway, one of four acute MI hospitalizations are recurrent events, despite high reported prevalence of medical treatment at hospital discharge. Close up to 100% of all Norwegian MI patients receive medical treatment like lipid-lowering drugs at discharge, in accordance with European guidelines. Lipid-lowering drug treatment is efficient and is associated with lower mortality in MI patients, but the treatment adherence and effect in the Norwegian population is unknown.

Purpose: We investigated the change in total blood cholesterol levels after MI among participants in a Norwegian prospective cohort study.

Methods: A total of 10,326 participants attending the population-based Tromso Study in 1994–95 were followed for first-ever MI up to the second screening in 2007–08. Non-fasting blood samples were collected and analyzed with standard methods. Information on lipid-lowering drug use was collected via questionnaires. We used linear regression models to investigate sex and age differences in total cholesterol change between baseline (pre-MI) and second screening (post-MI).

Results: A total of 395 participants (32% women) had a first-ever MI during follow-up (>3 months before the second screening) and valid cholesterol measurements at both screenings. Mean age at first MI was 67 years in women and 63 years in men. Mean cholesterol was 7.33 and 6.88 mmol/L at baseline and 5.00 and 4.54 at second screening, in women and men, respectively. Virtually none used lipid lowering drugs at baseline, and lipid-lowering drug use prevalence at second screening was 86% in women and 92% in men. Mean decrease in cholesterol was -2.34 mmol/L (SD 1.14), with no sex or age differences (p=0.9 for sex and p=0.7 for age).

Conclusion: Both women and men achieved treatment goals for total cholesterol, and no age or sex differences in cholesterol change after first MI was found in this population. There is a need for further research on the effect of secondary prevention care after MI, as improvement in patient care will increase cardiovascular health and quality of life, and reduce society costs.

P5527 Higher left ventricular mass-stress-heart rate product is associated with increased cardiovascular morbidity and mortality in aortic valve stenosis

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Background: The association of increased myocardial oxygen demand with impaired prognosis was recently demonstrated in hypertensive patients.

Purpose: We postulated that increased myocardial oxygen demand could help explain the association of left ventricular (LV) hypertrophy with impaired prognosis in patients with aortic valve stenosis (AS).

Methods: Myocardial oxygen demand was calculated as LV mass-stress-heart rate product by echocardiography in 1432 patients with initially

asymptomatic mostly moderate AS participating in the Simvastatin Ezetimibe in AS (SEAS) study. The association of LV mass-stress-heart rate product with major cardiovascular events, a composite of aortic valve and ischemic cardiovascular events, and with total mortality and combined cardiovascular death and hospitalization for heart failure during a median of 4.3 years follow-up were tested in time-varying Cox regression models. High LV mass-stress-heart rate product was identified as > upper 95% confidence interval limit in normal subjects.

Results: High LV mass-stress-heart rate product was found in 19.3% at baseline, and associated male sex, concomitant hypertension and obesity, and more severe AS. Adjusting for these confounders and presence of LV hypertrophy at study baseline in time-varying Cox regression analysis, 1 standard deviation higher LV mass-stress-heart rate product was associated with higher hazard rate (HR) of major cardiovascular events (HR 1.34 [95% confidence interval {CI}1.23–1.46]), total mortality (HR 1.47 [95% CI 1.28–1.68]) and combined cardiovascular death and hospitalization for heart failure (HR 1.59 [95% CI 1.33–1.89]) (all p<0.0001).

Conclusion: In patients with AS participating in the SEAS study, higher LV mass-stress-heart rate product was independently associated higher cardiovascular event-rate, suggesting unmet myocardial oxygen demand to contribute to the impaired prognosis reported in asymptomatic AS patients with LV hypertrophy.

P4349 Strain echocardiography demonstrates alterations in left ventricular deformation in preadolescents with previous fetal growth restriction

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Background: Fetal growth restriction (FGR) affects about 5 to 10% of newborns and is associated with increased cardiovascular mortality in adulthood. FGR might induce primary cardiac alterations, explaining susceptibility for cardiovascular disease later in life.

Purpose: Our goal was to assess LV deformation by 2D speckle-tracking strain echocardiography in preadolescence with previous FGR.

Methods: Within a cohort of fetuses with FGR identified in fetal life and followed-up into preadolescence, echocardiography was performed in 58 preadolescents with FGR (defined as birthweight below 10th centile) and 94 preadolescents with normal birthweight centile. Peak systolic longitudinal strain was assessed in 18 LV segments and peak systolic circumferential and radial strain were assessed in 6 LV segments and were averaged to global longitudinal strain (GLS), global circumferential strain (GCS) and global radial strain (GRS), respectively. The presence of post systolic shortening, a marker of increased afterload, was also investigated in the LV segments.

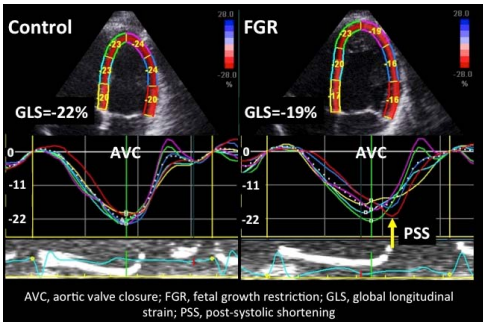
Results: GLS was significantly decreased (Figure) while GCS and GRS were increased in FGR as compared to controls. FGR cases also showed a higher prevalence of post-systolic shortening. Ejection fraction and cardiac index were similar (Table).

Conclusions: Our results suggest that primary cardiac alterations are present in preadolescence with previous FGR. Although, longitudinal LV function was reduced, global LV function was preserved due to increase in circumferential and radial deformation. Nevertheless, these subclinical alterations may explain the increased predisposition to cardiovascular disease in adulthood.

Left ventricular echocardiographic data

	Controls (n=94)	FGR (n=58)	p-value
LV ejection fraction, %	58 (56–60)	58 (57–62)	0.53
LV cardiac index, L/min/kg	2.9 (2.5–3.4)	3.1 (2.6–3.4)	0.55
LV global longitudinal strain, %	-22.4±1.37	-21.5±1.16	<0.001
LV global circumferential strain, %	-22.6±2.65	-24.2±2.55	0.001
LV global radial strain, %	46.4±12.6	54.7±16.7	<0.001
Presence of post-systolic shortening*, n (%)	20 (21)	19 (33)	0.04

*Data expressed as mean ± SD, median (interquartile range) and n (%). Right column shows P-values for Student's t, non-parametric and Chi-square tests. FGR, fetal growth restriction; LV, left ventricular. *Presence of post-systolic shortening by M-mode.LV deformation in FGR*



AVC, aortic valve closure; FGR, fetal growth restriction; GLS, global longitudinal strain; PSS, post-systolic shortening

P2186 Secretoneurin levels provide prognostic information after cardiac surgery

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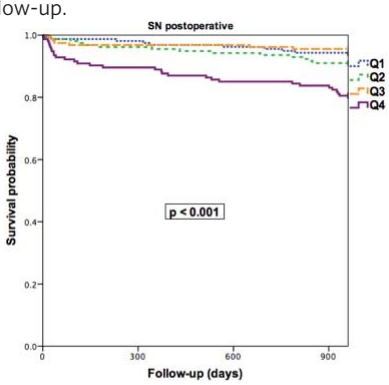
Background: Circulating levels of secretoneurin (SN) provide incremental prognostic information to established risk indices in patients with acute cardiovascular events, but whether SN may also provide additional prognostic information after cardiac surgery is not known.

Methods: 648 patients from the FINNAKI-Heart Study hospitalised due to cardiac surgery had preoperative and 625 had postoperative blood samples available. We adjusted for clinical risk factors and N-terminal pro-B-type natriuretic peptide (NT-proBNP) and high-sensitivity troponin T (hs-TnT) in multivariate Cox regression analysis.

Results: Sixty patients (9.6%) died during a maximal follow-up of 961 days. SN levels measured on day 1 after cardiac surgery were higher in non-survivors compared to survivors: 178 (Q1–3 129–218) vs. 144 (111–175) pmol/L, p<0.001. Postoperative NT-proBNP levels (2975 [Q1–3 1267–9223] vs. 1284 [663–2550] ng/L, p<0.001), but not hs-TnT were also higher in non-survivors than in survivors. The area under the curve (AUC) by receiver-operating statistics for postoperative SN, NT-proBNP, and hs-TnT levels to predict time to death were 0.65 (95% CI 0.57–0.73), 0.71 (0.64–0.78), and 0.57 (0.49–0.65), respectively. When stratifying patients according to postoperative SN levels, patients with SN levels in the 4th quartile had increased mortality compared to the other patients (Figure). After cardiac surgery, SN correlated only weakly with NT-proBNP (rho=0.15; p<0.001) and hs-TnT levels (rho=0.08; p=0.05), while hs-TnT and NT-proBNP levels were more closely correlated (rho=0.42, p<0.001). In univariate Cox regression models, postoperative SN levels were associated with time to death: HR (per 1 SD in lnSN) 4.06 (95% CI 2.15–7.65) p<0.001. Adjusting for clinical risk factors and established cardiac biomarkers, postoperative SN levels were still associated with mortality during follow-up: HR 3.74 (1.80–7.81); p<0.001.

Conclusions: SN levels after cardiac surgery are independently associated with mortality during follow-up.



Kaplan-Meier plot

P734 Circulating chromogranin B levels and outcome in patients with cardiovascular related-acute respiratory failure

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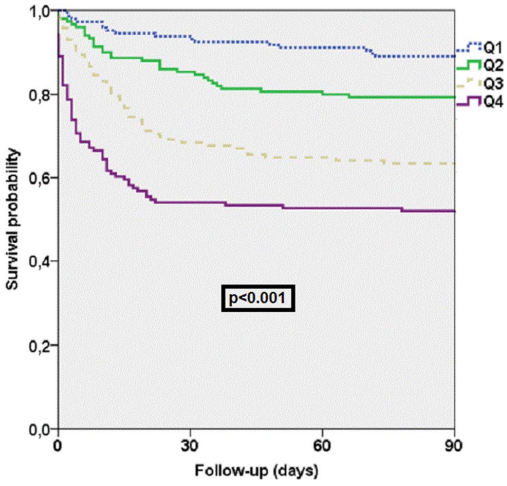
Background: Circulating chromogranin B (CgB) levels are elevated in conditions characterized by systemic and myocardial stress, but whether CgB provides incremental prognostic information to established risk indices in patients with acute respiratory failure (ARF) is unknown.

Methods: We included 584 patients with ARF, defined as ventilatory support >6 h, and with blood samples available on ICU admission. CgB levels were measured by radioimmunoassay on study inclusion and after 48 h, follow-up was 90 days, and the patients were categorized as either cardiovascular (CV)-related ARF (n=209) or non-CV-related ARF (n=375).

Results: CgB levels were similar in patients with CV- and non-CV-related ARF on ICU admission: 1.00 (95% CI 0.79–1.41) vs. 0.99 (0.79–1.32) nmol/L, p=0.47. Admission CgB levels were higher in 90 day non-survivors than in survivors, both for patients with CV-related ARF (median 1.32 [Q1–3 1.05–1.81] vs. 0.88 [0.76–1.13] nmol/L, p<0.001) and non-CV-related ARF

(1.18 [0.96–1.65] vs. 0.93 [0.74–1.25] nmol/L, p<0.001). Stratifying patients according to CgB quartiles on ICU admission, CgB levels provided prognostic information across the spectrum of ARF (Figure). In multivariate Cox regression analyses, admission CgB levels (logarithmically transformed) provided incremental prognostic information to clinical and biochemical risk markers both regarding CV-related (HR 2.17 [95% CI 1.25–3.76], p=0.006) and non-CV-related ARF (HR 3.56 [2.20–5.77], p<0.001). The correlation coefficient between CgB and NT-proBNP levels on study inclusion was 0.34, p<0.001 and the AUC of admission CgB and NT-proBNP levels to predict 90 day mortality was 0.72 (95% CI 0.67–0.76) for both. CgB levels on ICU admission also provided incremental prognostic information to SAPS II and SOFA scores, which both were based on data recorded 24 h after admission. CgB levels after 48 h also provided additional prognostic information to established risk indices in CV-related ARF (HR 6.34 [95% CI 2.39–16.79]), while CgB levels after 48 h did not improve risk prediction in patients with non-CV-related ARF.

Conclusions: CgB levels measured on ICU admission provided prognostic information independently of conventional risk markers across the spectrum of patients with ARF, while CgB levels after 48 h only improved risk stratification in patients with CV-related ARF.



Survival according to CgB quartiles

P801 Preoperative NT-proBNP levels, but not hs-TnT levels, provide independent prognostic information after cardiac surgery

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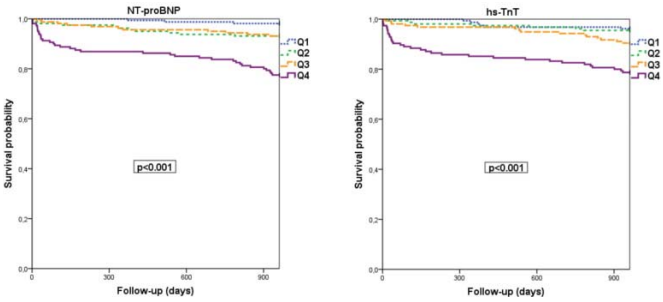
Background: N-terminal pro-B-type natriuretic peptide (NT-proBNP) and high-sensitivity troponin T (hs-TnT) are established cardiac biomarkers, but whether preoperative NT-proBNP or hs-TnT levels individually or in combination improve risk prediction in cardiac surgical patients is not known.

Methods: We included 640 consecutive patients from FINNAKI-Heart Study that were hospitalised for cardiac surgery and had preoperative blood samples available. Maximum follow-up was 961 days.

Results: In total, 61 patients (9.5%) died during follow-up with no perioperative deaths. Median preoperative levels of both NT-proBNP and hs-TnT were higher in non-survivors compared to survivors (2032 [Q1–3 476–5389] vs. 374 [136–1352] ng/L; and 39 [16–191] vs. 13 [8–32] ng/L, respectively, p<0.001 for both). Stratifying patients according to preoperative biomarker levels demonstrated highest risk in the patients with NT-proBNP and hs-TnT levels in the 4th quartile (Figure). The area under the curve (AUC) by receiver-operating statistics for preoperative NT-proBNP levels to predict time to death was 0.73 (95% CI 0.67–0.80) and the AUC for preoperative hs-TnT to predict time to death was 0.70 (0.63–0.77). A significant correlation between preoperative levels of NT-proBNP and hs-TnT existed (r=0.58; p<0.001). In univariate Cox regression models, both NT-proBNP and hs-TnT were associated with mortality (p<0.001). In a multivariate Cox regression model that included clinical risk factors and both cardiac biomarkers, preoperative NT-proBNP levels, but not preoperative hs-TnT levels, were associated with mortality during follow-up: HR (per 1 SD in lnNT-proBNP) 1.43 (95% CI 1.18–1.74); p<0.001. Moreover, in separate multivariate Cox regression models for NT-proBNP and hs-TnT levels, only preoperative NT-proBNP levels were associated with mortality when adjusting for clinical risk factors: HR 1.44 (1.18–1.75); p<0.001.

Conclusion: Preoperative NT-proBNP levels, but not preoperative hs-TnT levels, provided incremental prognostic information to established risk indices in patients hospitalised for cardiac surgery.



Kaplan-Meier plot

P636 NT-proBNP levels after 24 hours provide independent prognostic information in patients with ventricular arrhythmia-induced out-of-hospital cardiac arrest

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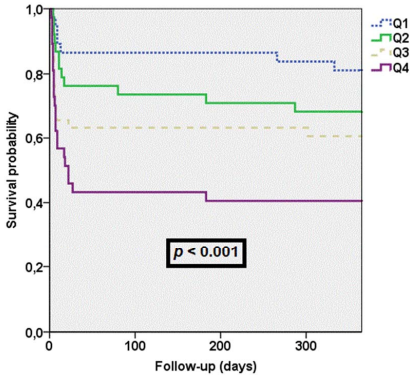
Background: Patients with out-of-hospital cardiac arrest due to ventricular tachycardia or fibrillation (OHCA-VT/VF) have a poor prognosis, but whether N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels improve risk prediction in in OHCA-VT/VF is not known.

Methods: We measured NT-proBNP levels in 155 patients with OHCA-VT/VF enrolled into a prospective multicenter observational study in 21 ICUs in Finland (FINNRESUSCI Study). Blood samples were drawn <6 h of OHCA-VT/VF and later after 24 h, 48 h, and 96 h. The co-primary end-points were mortality and neurological outcome classified according to Cerebral Performance Category (CPC) after one year. NT-proBNP levels were compared to high-sensitivity troponin T (hs-TnT) levels and established risk scores.

Results: NT-proBNP levels were higher in non-survivors compared to survivors on study inclusion (median 1003 [quartile 1-3 502–2457] vs. 527 [179–1284] ng/L, p=0.001) and after 24 h (1913 [1012–4573] vs. 1080 [519–2210] ng/L, p<0.001). NT-proBNP levels increased from baseline to 96 h after ICU admission (p<0.001) and NT-proBNP levels were significantly correlated to hs-TnT levels after 24 h (rho=0.27, p=0.001), but not to hs-TnT levels on study inclusion (rho=0.05, p=0.67). NT-proBNP levels at all time points were associated with clinical outcomes, including when stratifying patients according to quartiles of NT-proBNP (Figure; NT-proBNP quartiles after 24 h). Still, only NT-proBNP levels after 24 h predicted mortality and poor neurological outcome in models that also adjusted for SAPS II and SOFA scores. hs-TnT levels did not add prognostic information to the information obtained by measuring NT-proBNP alone.

Conclusion: NT-proBNP levels at 24 hours improved risk assessment for mortality and neurological outcome after one year on top of established risk models in OHCA-VT/VF, while hs-TnT measurements did not further add to risk prediction.



NT-proBNP quartiles after 24h

5802 Cardiovascular outcomes according to LDL cholesterol levels in EMPA-REG OUTCOME

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On behalf: The EMPA-REG OUTCOME Investigators

Background: Evidence suggests a dose-dependency between LDL cholesterol (LDL-C) levels and cardiovascular (CV) risk. We analysed the effects of empagliflozin (empa) compared to placebo on CV outcomes according to different LDL-C levels.

Methods: In EMPA-REG OUTCOME, patients with T2DM and high CV risk received empa 10 mg or 25 mg or placebo in addition to standard of care. All CV outcomes were independently adjudicated. We investigated the time to (first) 3P-MACE, CV death, hospitalisation for heart failure (HHF) and total mortality for empa vs placebo between baseline LDL-C categories: <70, 70-<85, 85-<100, 100–115, and >115 mg/dL by a Cox regression including the interaction of baseline LDL-C category and treatment.

Results: Of the 7020 patients randomised and treated, 81.0% of patients received lipid lowering therapy (77.0% statins) and the mean (SD) LDL-C was 85.6 (35.7) mg/dL. Baseline characteristics by categories of LDL-C, indicated differences in statin use, diabetes duration, blood pressure, use of antihypertensives, and proportion with albuminuria. The CV incidence rates varied according to LDL-C levels, however, the impact of empagliflozin on these CV outcomes were consistent with the overall trial results (interaction p-values: 0.278 3P-MACE, 0.0852 CV death, 0.5005 HHF and 0.1563 total mortality) (table).

Conclusions: The modulating effects of empa on CV outcomes did not differ between the categories of baseline LDL-C levels.

Table 1

	n	Statin use	Mean (SD)	3P-MACE HR (95% CI)/	CV death HR (95% CI)/	HHF HR (95% CI)/	Total mortality HR (95% CI)/
			LDL-C (mg/dL)	incidence rate EMPA/PBO per 1,000 yrs at risk	incidence rate EMPA/PBO per 1,000 yrs at risk	incidence rate EMPA/PBO per 1,000 yrs at risk	incidence rate EMPA/PBO per 1,000 yrs at risk
Overall population	7020	77.0%	85.6 (35.7)	0.86 (0.74, 0.99)/	0.62 (0.49, 0.77)/	0.65 (0.50, 0.85)/	0.68 (0.57, 0.82)/
				37.4/43.9	12.4/20.2	9.4/14.5	19.4/28.6
LDL-C <70 mg/dL	2669	91.1%	53.8 (11.9)	0.74 (0.58, 0.94)/	0.48 (0.33, 0.71)/	0.52 (0.34, 0.80)/	0.66 (0.48, 0.91)/
				33.5/44.6	9.7/19.9	8.2/15.3	16.2/24.4
LDL-C 70-<85 mg/dL	1294	87.9%	77.4 (4.0)	0.94 (0.66, 1.35)/	0.69 (0.39, 1.21)/	0.57 (0.31, 1.06)/	0.77 (0.49, 1.20)/
				34.3/37.8	11.2/16.9	8.2/15.9	18.8/25.4
LDL-C 85-<100 mg/dL	986	83.9%	91.9 (4.4)	1.25 (0.82, 1.91)/	1.42 (0.71, 2.83)/	0.88 (0.42, 1.86)/	1.04 (0.61, 1.77)/
				40.4/32.7	15.9/11.4	10.0/11.7	21.6/20.8
LDL-C 100–115 mg/dL	736	75.1%	107.0 (4.2)	0.82 (0.53, 1.27)/	0.52 (0.26, 1.02)/	1.06 (0.47, 2.40)/	0.41 (0.24, 0.69)/
				42.1/50.8	12.6/23.9	14.5/13.2	18.5/44.6
LDL-C >115 mg/dL	1247	73.5%	144.3 (27.8)	0.77 (0.56, 1.07)/	0.51 (0.32, 0.80)/	0.71 (0.36, 1.39)/	0.61 (0.41, 0.89)/
				42.4/54.9	15.6/30.3	9.3/12.9	25.1/41.0
p-value for interaction (treatment by baseline LDL-C cat.)	N/A	N/A	N/A	0.2785	0.0852	0.5005	0.1563

105 Reduction of body weight promotes regression of left ventricular hypertrophy in obese hypertensive outpatients: a real-world analysis from the campania salute network

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Background: Reduction of left ventricular (LV) mass index (LVMi) during antihypertensive treatment is difficult to achieve in obese subjects, despite optimal blood pressure (BP) control. Our analysis investigates probability of reduction of LVMi in treated obese hypertensive patients related to changes of body weight.

Methods: From the Campania Salute Network (CSN) registry, we identified 1754 patients (53±11 years, 46% women) with body mass index (BMI) ≥30 kg/m^2 and ≥12-month follow-up. Echocardiographic LVMi was assessed at baseline and at the last available visit. LV hypertrophy (LVH) was defined as LVMi ≥47 g/m$^{2.7}$ in women or ≥50 g/m$^{2.7}$ in men. We adjudicated significant reduction of LVMi when achieving normal values or reducing LVMi ≥10% of baseline value. Weight reduction was considered as ≥5% reduction in body weight.

Results: LVH was initially present in 1061 patients (46% women, 15% diabetic). At the end of follow-up (median: 49 months, 30–92), LVMi was reduced in 98 patients (6%, RED); 1137 patients had LVH (PERS) and 519 maintained LVMi under the threshold for LVH (NOR). At baseline, RED were younger, less likely to be diabetic and had lower baseline BMI, LVMi and average systolic BP during follow-up, while glomerular filtration rate (GFR, by CKD-EPI) was higher than in PERS (all p<0.05). Significant reduction of LVMi occurred

more frequently (8.3% vs 4.6%, p<0.009) in patients losing weight (n=481 or 27%) than in those maintaining initial weight (n=1273). In multinomial logistic regression analysis, comparing RED, PERS and NOR (used as reference), weight reduction increased the chance of LVMi reduction by near 2-fold (Table), independently of age, female sex, average follow-up systolic BP, and baseline GFR, diabetes and LVMi.

Table 1. Independent predictors of reduction of LV Mass index during follow-up

	Reduction of LV mass index		LVH at the end of follow-up	
	OR (95% CI)	p≤	OR (95% CI)	p≤
Age	0.98 (0.95–1.01)	0.15	1.02 (0.99–1.04)	0.15
Female sex	2.63 (1.54–4.50)	0.001	4.57 (3.06–6.84)	0.001
Average follow-up SBP	0.98 (0.96–1.01)	0.17	1.01 (0.99–1.03)	0.17
GFR	1.00 (0.99–1.02)	0.67	1.00 (0.99–1.01)	0.87
Diabetes	0.91 (0.37–2.21)	0.83	1.53 (0.85–2.78)	0.16
LV mass index	1.55 (1.44–1.66)	0.001	1.74 (1.63–1.85)	0.001
≥5% weight loss	1.89 (1.11–3.22)	0.02	0.92 (0.60–1.39)	0.68)

Conclusion: In treated obese hypertensive patients, weight reduction during follow-up promotes significant reduction of LVMi, independent of baseline characteristics and BP control.

P5184. NADPH oxidase-4 regulates a novel adaptive switch from cardiac glucose to fatty acid oxidation

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Background: NADPH oxidase-4 (Nox4) is a specialised enzyme generating reactive oxygen species (ROS) involved in intracellular signalling. Previous studies show that Nox4 promotes adaptive remodelling during pressure-overload cardiac hypertrophy.

Purpose: To investigate the mechanisms underlying Nox4-mediated beneficial effects during cardiac hypertrophy.

Methods and results: Unbiased proteomic analyses in cardiac-specific Nox4 transgenic (TG) and wild-type (WT) mouse hearts indicated metabolic pathways as a key Nox4-dependent change. Similar effects were not observed in Nox2 transgenic hearts. In ex-vivo working heart studies, TG had higher rates of palmitate oxidation than WT both in the unstressed and pressure-overloaded heart (3.6 fold increase; n=6/group; p=0.01) whereas glucose oxidation was reduced. Consistent with better contractile function in TG mice after aortic constriction, cardiac energetics assessed by 31P-NMR spectroscopy also showed better PCr/ATP ratio in TG cf. WT after acute stress (1.6 fold improvement; n=6/group; p=0.01). Using metabolite profiling by NMR and mass spectrometry, we identified an increase in flux through the hexosamine biosynthetic pathway (HBP, a branch pathway of glycolysis) in TG hearts. The secondary O-GlcNAc modification of cardiac proteins by N-acetylglucosamine, the end-product of HBP, was significantly increased in TG cf. WT (2.4 fold; n=4/group; p=0.02). We also identified that increased O-GlcNAcylation of the fatty acid uptake protein CD36 may be involved in the Nox4-dependent upregulation of fatty acid oxidation.

Conclusion(s): Nox4 drives a metabolic reprogramming from glucose oxidation to fatty acid oxidation which appears to better adapt the heart to both acute and chronic stress (pressure-overload). The underlying mechanism may involve an HBP-mediated post-translational modification (O-GlcNAcylation) of CD36. These results identify a novel redox mechanism that reprograms cardiac metabolism to facilitate adaptation to chronic pressure overload.

P3115 Circadian rhythm in heart rate is due to an intrinsic circadian clock in the sinus node

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On behalf: Institute of Cardiovascular Research Group

Introduction and purpose: There is a circadian rhythm in heart rate (HR), which slows at night. On the basis of heart rate variability (HRV), this is attributed to a circadian rhythm in vagal tone, but we have recently challenged the use of HRV to measure autonomic tone. Here we tested the alternative hypothesis that it is the result of an intrinsic circadian rhythm in the pacemaker of the heart, the sinus node.

Methods and results: In conscious C57BL6/J mice (n=9) maintained during a strict 12 h light-12 h dark cycle, there was a circadian rhythm in HR measured using telemetry – the HR was 61 beats/min slower at the start of sleep period, Zeitgeber time 0 (ZT0), compared to the start of awake period, ZT12 (P<0.05). Hearts were isolated (and denervated) at the two time points and Langendorff-perfused (n=8/9) – the intrinsic HR was 97 beats/min slower at ZT0 compared to ZT12 (P<0.01). Therefore, the circadian rhythm

in HR is intrinsic to the heart. To study the underlying mechanism, patch clamp experiments were conducted on sinus node myocytes isolated at the two time points. A key pacemaker current is the funny current (If) and this was measured during 5 s hyperpolarizing pulses from a holding potential of -35 mV. There was a circadian rhythm in If. For example, If (measured at -125 mV) at ZT2 was 17.8±2.8 pA/pF (n=10), whereas at ZT14 it was doubled at 35.0±6.3 pA/pF (n=6; P<0.05). This circadian rhythm in If could explain the circadian rhythm in HR. The principal ion channel responsible for If is HCN4. Sinus node biopsies were collected at ZT0 and ZT12 and the expression level of clock genes and HCN4 was measured at the mRNA level by quantitative PCR; in addition, expression of HCN4 protein was measured by Western blot. Clock genes (e.g. CLOCK and BMAL1) were expressed and varied in a circadian manner (n=8/8; P<0.05). HCN4 mRNA was 89% higher at ZT0 compared to ZT12 (n=7/9; P<0.05), whereas HCN4 protein was 49% lower at ZT0 compared to ZT12 (n=7/7; P<0.05); a time lag of hours is expected between mRNA, protein and ionic current. In silico analysis of 10 kb of the HCN4 promoter revealed 7 conserved consensus (EBOX) binding sites for the BMAL1:CLOCK heterodimer. Chromatin immunoprecipitation enrichment of these sites was observed by overexpressing BMAL1 in vitro.

Conclusion: We have shown circadian rhythms in CLOCK, BMAL1, HCN4 mRNA, HCN4 protein, If, the intrinsic HR in vitro and the normal HR in vivo. It is concluded that the well known circadian rhythm in HR is not the result of vagal tone and instead could be the result of a circadian rhythm in transcription of the HCN4 gene driven by a circadian clock in the sinus node.

P2580 Ratio of TEE usage in the era of NOACS: TALENT multicenter European Registry

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On behalf: TALENT Cardioversion Registry Group

Introduction: Anticoagulant (AC) treatment timing for elective cardioversion (CV) is recommended by the guidelines. Transesophageal echocardiography (TEE) is not an obligatory measure before CV if the patient is pretreated by AC for at least 3 weeks before CV, though there are some centers which perform the TEE in the AC-pretreated cases also. In 5-15 of patients with AF, TEE before planned cardioversion revealed an LA or LAA thrombus. If there is longer than 48 hrs of Afib without any AC treatment it is reasonable to perform TEE to avoid thrombembolism according to the guidelines. TEE guidance is an alternative to 3 weeks of anticoagulation before cardioversion

Aim of our registry was to set up a cardioversion prospective+retrospective registry, particularly focusing on AC and TEE strategies in the participating European countries.

Methods: Patient records were collected between Sept 2014 to Oct 2015 in 7 European hospitals (Hungary and Italy 2 sites each, France, Spain and Lithuania). All the data of patients were collected consecutively who undewent CVs due to AF. Since it was unclear in the participating centers what is the ratio of TEE usage in AC-pretreated patients awaiting for CV, even whether NOAC treatment has any influence on the usage of TEE, our registry has recorded the duration of OAC usage before and after CV, which has been measured on a five category scale before CV (0, <3 weeks, ≥3 weeks, overlap with heparin, same day only).

Results: A total of 1101 patients (retrospective/prospective: 679/422, mean age: 67.3 years ± 11.2) were registered. 97% of the cardioversions were electrical ones. TEE-guided CV was performed in 584 cases, vs nonTEE guided in 517 cases. The TEE-guided group was treated by apixaban in 3.5%, by dabigatran and rivaroxanban in 11% each, and by VKA in 75% of the cases (p<0.001). Ratio of OAC usage before cardioversion more than 3 weeks was found to be significant concerning of pretreatment in each AC groups in comparison to the other time-plans: apixaban 91%, dabigatran and rivaroxaban 81% each, warfarin in 79% of the cases (p=0.008). Over time non-TEE usage has increased in the apixaban (p<0.001) and rivaroxaban treated groups (p=0.015), but no change was observed in the dabigatran group, and decrease of VKA usage was found in the non-TEE group (p0.033).

Conclusion: In conclusion, TEE usage is not obligatory in routine elective cardioversion. Our results show that the usage of NOACs decrease the high number of TEEs performed though it is not recommended to be used routinely.

1359 Changes of oral anticoagulation in elective cardioversion - results from a European cardioversion registry

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Introduction: In patients with atrial fibrillation (AF) pharmacological or electrical cardioversion may be performed to restore sinus rhythm. The procedure is associated with an increased risk of thromboembolic events, which can be significantly reduced by adequate anticoagulation (AC).

Aim: Our aim was to create a partly prospective, partly retrospective cardioversion registry, particularly focusing on AC strategies in different European countries, and on emerging choice of AC over time.

Methods: From September 2014 to October 2015 the cardioversions due to AF performed in six European city hospitals in five European countries (Budapest – Hungary (two sites), Bari and Pisa – Italy, Amiens – France, Madrid – Spain, Kaunas – Lithuania) were recorded in the registry.

Results: A total of 1101 patients (retrospective/prospective: 679/422, male/female: 742/359, mean age: 67.3 years ± 11.2) were registered. Most of the cardioversions were electrical (97%). Oral anticoagulants were administered in 87% of the patient, the usage of novel oral anticoagulants (NOACs) vs K-vitamin antagonists (VKA) was 31.5% vs 68.5%. 77% of the patients were given oral anticoagulants more than 3 weeks before the procedure, and 86% more than 4 weeks after the procedure. When using VKA, INR at cardioversion was above 2.0 in 76% of the cases. A decline in VKA usage (p=0.033) in elective cardioversion over approximately one year was observed (Fig. 1a). During the observation period an increase in apixaban (p<0.001), a slight increase in rivaroxaban (p=0.028) and no changes in dabigatran (p=0.34) usage for elective cardioversion was noticed (Fig. 1b). There were differences in use of AC between the countries: Spain used most VKA (89%), while France used least VKA (39%, p<0.001).

Conclusions: According to current AF guidelines NOACs are adequate alternatives to VKA for thrombembolic prevention in AF patients undergoing elective cardioversion. Our results show a significant decrease in VKA usage over time, while NOAC usage displays a gradual increase.

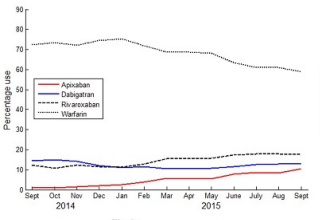

Fig. 1a

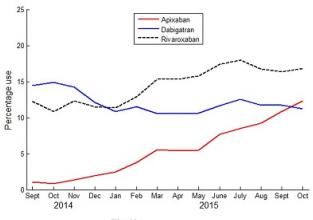

Fig. 1b

5970 Impact of diabetes mellitus and chronic kidney disease on cardiovascular outcomes and platelet P2Y12 receptor antagonist effects in patients with acute coronary syndromes:insights from the PLATO trial

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University, Department of Medical Sciences, Cardiology, and Uppsala Clinical Research Center - Uppsala - Sweden,

On behalf: PLATO Investigators

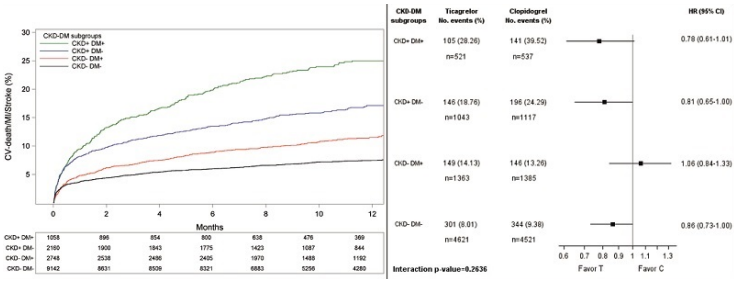
Background: Patients with diabetes mellitus (DM) are at increased risk of atherothrombotic events. Importantly, DM is a key risk factor for the development of chronic kidney disease (CKD), which further enhances the atherothrombotic risk. To date there are limited data from large cohorts specifically assessing cardiovascular outcomes in patients with DM and CKD. The ever growing prevalence of CKD in patients with DM underscores the need to define effective platelet inhibition strategies in these high-risk patients.

Purpose: To assess clinical outcomes in patients enrolled in the PLATO trial according to the presence or absence of DM and CKD, as well as the differential effects of P2Y12 receptor antagonists (ticagrelor vs. clopidogrel) in these subgroups.

Methods: Patients with acute coronary syndrome (ACS) enrolled in PLATO with available CKD and DM status at baseline (n=15108) were included in the analysis. CKD was defined as a creatinine clearance <60 mL/min. Diabetic status was assessed by the investigators at the time of randomisation. Patients were classified into four groups: no-CKD/no-DM (n=9142), CKD/no-DM (n=2160), no-CKD/DM (n=2748), and CKD/DM (n=1058). The primary efficacy endpoint was a composite of vascular death, myocardial infarction, and stroke. The primary safety endpoint was all major bleeding defined according to PLATO definition.

Results: Patients with CKD/DM had a more than 3-fold higher incidence of the primary endpoint at 12 months compared with no-CKD/no-DM patients (23.3% vs. 7.1%, adjusted HR: 2.22; 95% CI: 1.88–2.63; p<0.001). Patients with CKD/no-DM (adjusted HR: 1.60; 95% CI: 1.37–1.86) and no-CKD/DM (adjusted HR: 1.34; 95% CI: 1.16–1.55) had an intermediate risk profile (See Kaplan-Meier plot). The same trend was shown for the individual components of the primary endpoint, including vascular death, and for major bleeding. As compared with clopidogrel, ticagrelor significantly reduced the incidence of the primary endpoint consistently across subgroups (p interaction=0.264). The absolute risk reduction with ticagrelor vs. clopidogrel was considerably higher in CKD/DM patients (11.26%), as compared with no-CKD/no-DM (1.37%) with an adjusted HR of 0.78; 95% CI: (0.61–1.01) (See Forest plot). Although the effects on major bleeding were consistent across subgroups (p interaction=0.288), there was no increased risk of major bleeding with ticagrelor vs. clopidogrel in the subgroup of patients with CKD/DM (27.4% vs. 26.9%; HR: 1.02; 95% CI: 0.75–1.40).

Conclusions: ACS patients with DM and CKD are at markedly increased risk for long-term atherothrombotic events compared with patients without DM and CKD, as well as with those with only one of these risk factors. Although the ischemic benefit of ticagrelor vs. clopidogrel was consistent in all patient subgroups, the magnitude of benefit was enhanced according to the patient risk profile, without signals of increased risk of major bleeding.



5867 Diabetes mellitus and insulin resistance associate with left ventricular remodeling and function by cardiac magnetic resonance imaging from the Multi-Ethnic Study of Atherosclerosis

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On behalf: Multi-Ethnic Study of Atherosclerosis

Background: Although diabetes mellitus (DM) and insulin resistance are related to adverse cardiovascular outcomes, the mechanisms of adaptation that alter the cardiovascular system in subjects with glucose metabolism disorders remain largely unknown.

Purpose: The aim of study was to evaluate how left ventricular (LV) indices are associated with DM or insulin resistance among participants free of clinical cardiovascular disease.

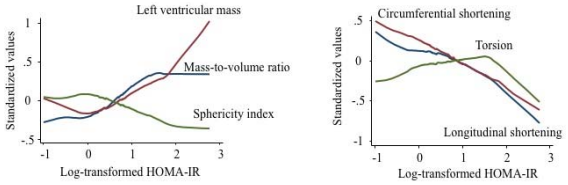
Methods: We studied 1,476 participants who

were free of clinical cardiovascular disease at baseline and who underwent tagged cardiac magnetic resonance (CMR) in the Multi-Ethnic Study of Atherosclerosis (MESA). LV volumes, shape, and longitudinal myocardial shortening and torsion were assessed by CMR.

Untreated DM was defined as fasting glucose ≥126 mg/dl without any use of hypoglycemic medication or insulin. Treated DM was defined as use of hypoglycemic medication or insulin. Impaired fasting glucose (IFG) was defined as fasting glucose levels between 100 mg/dl and 125 mg/dl. All other participants were defined as having normal fasting glucose (NFG). Participants with DM were excluded from the HOMA-IR calculation. Multivariable linear regression was used to evaluate the associations of DM or homeostasis model assessment-estimated insulin resistance (HOMA-IR) index with CMR indices.

Results: Of the total 1,476 participants population, 210 (14%) had DM and 262 (18%) had IFG. The median LV ejection fraction was 70% interquartile range (64%, 74%) in the whole study population, and did not differ among DM fasting glucose criteria. In multiple linear regression, longitudinal shortening was lower in impaired fasting glucose than NFG (0.36% lower vs. NFG, P<0.05); torsion was greater in treated DM (0.24 °/cm greater vs. NFG, P<0.05) after full adjustments. Among participants without DM (n=1266), greater log-HOMA-IR was correlated with greater LV mass (3.92 g/index, P<0.05) and LV mass-to-volume ratio (0.05 /index, P<0.01), and lower sphericity index (−1.26/index, P<0.01). Torsion was positively correlated with log-HOMA-IR until 1.5 of log-HOMA-IR (0.16 °/cm/index, P=0.030), and tended to fall above 1.5 of log-HOMA-IR (−0.50 °/cm/index, P=0.203).

Conclusions: Glucose metabolism disorders associate with LV concentric remodeling, conical LV shape, and altered systolic myocardial shortening in the general population. Increased torsion may be a key compensation mechanism to maintain ejection fraction despite impaired myocardial contractile function due to compromised glucose metabolism.



- A higher sphericity index represents a more spherical shape of the ventricle and a lower conicity shape.
- Positive numbers of shortening represent more contraction.
- Locally weighted smoothing curve using unadjusted standardized values are displayed (n=1266).
- HOMA-IR indicates homeostasis model assessment-estimated insulin resistance.

Figure. Associations of HOMA-IR with left ventricular indices by cardiac magnetic resonance

P6096 The evaluation of cardiac performance by pressure-strain loops: a useful tool for the identification of responders to cardiac resynchronization theraphy

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Background: Cardiac resynchronization therapy (CRT) in heart failure is limited by still too many non-responders. Aim of the present study is to evaluate if the estimation of cardiac performance by pressure-strain loops (PSLs) is useful for the selection of CRT candidates.

Methods and results: 2D echocardiography and speckle tracking echocardiography (STE) were performed in 97 (age: 65±10 years) CRT candidates before CRT implantation. Conventional dyssynchrony parameters were estimated and left ventricular (LV) global longitudinal strain (GLS) by STE was used to calculate PSLs and estimate LV positive work (posW), negative work (negW), and work efficiency (WE). After a median 6-month follow-up, the positive response to CRT (CRT+) was defined as ≥15% reduction in LV end-systolic volume and was observed in 63 (65%) patients.

Table 1 shows the main predictors of CRT + at univariable logistic regression analysis.

The best cut-off value of PosW and NegW for the prediction of CRT+ were: 1057 (AUC 72%, p<0.0001) and of -384 (AUC 0.67, p<0.005) respectively. At multivariable logistic regression analysis including the indicated PosW and NegW cut-off, septal flash (OR 7.42, CI 95%: 1.90–28.97, p=0.004), PW>1057 mmHg/% (OR 8.26, CI 95%: 2.03–33.57, p=0.003), and NegW>- 384 mmHg/% (OR 13.26 CI 1.95–90.43) emerged as the only predictors of CRT+.

Conclusions: The estimation cardiac performance by PSL curves appears to be a novel and very promising tool to identify CRT responders, even when compared with traditional indexes of cardiac dyssynchrony. Further studies on larger series should be designed to confirm these results.

Table 1

	OR (95% CI)	p-value
LV end-diastolic diameter, per mm	0.93 (0.88–0.98)	0.01
LV end-systolic diameter, per mm	0.93-(0.89–0.99)	0.001
Ischemic etiology	0.27 (0.11–0.65)	0.004
LBBB	2.20 (0.77–6.26)	0.14
Atrio-ventricular dyssynchrony	1.79 (0.67–4.81)	0.25
Interventricular dyssynchrony	3.47 (1.45–8.30)	0.005
Intra-ventricular dyssynchrony	0.51 (0.15–1.72)	0.45
Septal flash, n (%)	7.29 (2.82–18.83)	0.0001
Positive work, per mmHg/%	1.00 (1.00–1.01)	0.03
Negative work, per mmHg/%	0.99 (0.98–1.00)	0.004
Work efficiency, per %	0.09 (0.45–1.03)	0.69

P3096 Obesity and female sex are associated with development of left ventricular hypertrophy in treated hypertensive outpatiens: the campania salute network

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Background: The aim of this study was to evaluate incident left ventricular (LV) hypertrophy (LVH) in a treated hypertensive population.

Methods: From the Campania Salute Network registry, we identified 4290 hypertensives (age 50.3±11.1 years, 40% women) without LVH at baseline. LVH was censored at the first yearly echocardiographic control exhibiting LV mass index (LVMi) above the threshold for LVH (≥47 g/m$^{2.7}$ in women and ≥50 g/m$^{2.7}$ in men).

Results: After a follow-up (FU) of 47.4 months (interquartile range 26.5–85.1), 915 patients (21.3%) exhibited LVH. These patients were older, more frequently females, obese (both p<0.0001) and diabetic (p<0.03). At baseline, patients developing LVH during FU presented with lower heart rate and glomerular filtration rate (GFREPI both p<0.0001), higher fasting glucose, body mass index (BMI), longer history of hypertension and shorter duration of FU (all p<0.001). During FU average systolic BP was higher and heart rate lower in patients developing LVH (both p<0.0001). At baseline patients developing LVH exhibited higher LVMi, intimal medial thickness, and LV stroke work (all p<0.0001), without significant difference in relative wall thickness. During FU patients with LVH were prescribed more medications, in particular Ca^{2+}-channel blockers and diuretics (all p<0.02). In Cox regression analysis, using a repeated contrast for obesity-sex (i.e. comparing each category, except the first one, to the category that precedes it), incident LVH was associated with obesity and female sex (figure), independent of significant effect of older age, higher average systolic BP during FU and greater baseline LVMi.

Conclusions: Despite more aggressive antihypertensive therapy, 21.3% of patients develop LVH. After adjusting for confounders, risk of incident LVH was associated with obesity and female sex.

1352 Patients with atrial fibrillation and history of falls are at high risk for bleeding but have less bleeding with apixaban than warfarin: results from the ARISTOTLE trial

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Background: History of falls is a common reason for withholding anticoagulation in patients with atrial fibrillation (AF). Little is known about the associated risk of bleeding and stroke among patients on anticoagulants with history of falls, and whether the benefits of apixaban vs. warfarin are consistent in this population.

Methods: We included 16,491 patients in ARISTOTLE with information available about history of falls. We compared baseline characteristics and outcomes according to history of falls, and assessed the efficacy and safety of apixaban vs. warfarin on stroke/SE and on bleeding. HRs were derived from Cox proportional hazards models.

Results: At baseline, 753 (4.6%) patients had a history of falls in the past year. Compared with those without history of falls, patients with a falls were older (median 75 vs. 70 years), more likely to be female, to have dementia, depression, osteoporosis, fractures, prior bleeding of most types, higher CHADS2 (mean 2.53 vs. 2.14) and HAS-BLED scores (mean 2.40 vs. 1.77), and higher rates of study drug discontinuation. They had similar adjusted rates of stroke and of hemorrhagic stroke as those without a history of falls;

Table 1

Event	Fall(s) within 1 year			No fall(s) within 1 year			p-value interaction
	Apixaban	Warfarin	HR (95% CI)	Apixaban	Warfarin	HR (95% CI)	
	Rate (Events)	Rate (Events)		Rate (Events)	Rate (Events)		
Death from any cause	6.41 (45)	6.74 (45)	0.96 (0.63–1.44)	3.17 (469)	3.71 (546)	0.86 (0.76–0.97)	0.63
Hemorrhagic stroke	0.14 (1)	0.45 (3)	0.32 (0.03–3.09)	0.23 (33)	0.47 (68)	0.48 (0.32–0.73)	0.73
Stroke/SE	1.76 (12)	1.99 (13)	0.88 (0.40–1.93)	1.23 (177)	1.63 (234)	0.75 (0.62–0.91)	0.70
ISTH major bleeding	4.35 (26)	5.38 (31)	0.81 (0.48–1.36)	2.07 (274)	3.00 (389)	0.69 (0.59–0.81)	0.57
Major or CR Non-major bleeding	8.81 (50)	9.15 (51)	0.96 (0.65–1.41)	3.88 (506)	5.98 (756)	0.65 (0.58–0.73)	0.06
Any bleeding	28.86 (135)	45.72 (181)	0.65 (0.52–0.81)	17.85 (2014)	25.64 (2638)	0.71 (0.67–0.75)	0.46
Stroke/SE/Major bleeding/Death	11.41 (75)	11.98 (76)	0.95 (0.69–1.31)	5.75 (817)	6.96 (979)	0.83 (0.75–0.91)	0.40

Cumulative Hazard for incident LVH

however, they had higher rates of major bleeding (HR 1.39, 95% CI 1.05–1.85) and mortality (HR 1.70, 95% CI 1.36–2.14). The benefits of apixaban, compared with warfarin, on stroke/SE, bleeding, MI, and death were preserved, irrespective of falls.

Conclusion: Patients with AF treated with anticoagulation and a history of falls were at high risk for bleeding and death compared with those without prior falls. The net clinical benefit of apixaban over warfarin in reducing stroke and causing less bleeding was preserved in patients with history of falls. Our findings support the use of apixaban for patients with a history of falls when anticoagulation therapy is indicated.

P1173 Changes in BNP prior to major cardiovascular events in patients with type 2 diabetes and a recent coronary event

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Background: Patients with type 2 diabetes and a recent coronary event are at high risk of subsequent cardiovascular (CV) events. B-type natriuretic peptide (BNP) has been shown to be a predictor of future CV morbidity and mortality in patients with a recent coronary event. We utilised serial sampling of BNP to assess whether changes in BNP preceded major clinical CV events.

Methods: Patients with type 2 diabetes and a recent coronary event (n=6068) were prospectively enrolled in the Evaluation of Lixisenatide in Acute Coronary Syndrome trial (ELIXA, NCT01147250). Blood samples were collected at baseline and at wks 24, 76, 108 after randomisation and analysed for BNP concentrations by a core laboratory. The last sample obtained prior to the occurrence of major CV events ("Before event") was compared to baseline for each of the following outcomes; death, CV death, myocardial infarction (MI), hospitalization for heart failure (HF) and stroke. Due to right-skewness, BNP concentrations are summarised as geometric mean±95% CI. Changes between Baseline and Before event are shown as percent change from baseline ±95% CI.

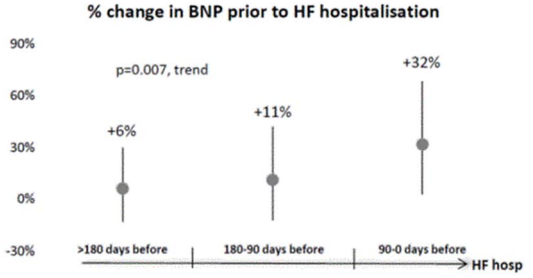
Results: Those experiencing death, CV death, MI, HF, or stroke during the trial had higher baseline BNP values than those without CV events. For death, CV death, MI, and stroke, no significant further increases in BNP occurred prior to the event. However, prior to HF hospitalisation, BNP increased 16% (1–33%, p=0.038) in samples collected on average 146 days before admission for HF. Moreover, BNP samples obtained closer to HF hospitalisation showed greater increases from baseline than earlier samples (test for trend, p=0.007), see figure.

Conclusion: In patients with type 2 diabetes and a recent coronary event, a further BNP increase occurred prior to HF hospitalisation and not preceding death, CV death, MI or stroke. The magnitude of increase in BNP was greater more proximal to the HF hospitalisation. The BNP increase may indicate early subclinical deterioration prior to overt HF in high risk patients with type 2 diabetes.

Table 1. BNP changes and major CV outcomes

Outcome	Baseline (pg/ml)	Before event (pg/ml)	Before Δ (% change)	Sample time Before event (days)
Death (n=288)	265 (236-299)	270 (236-308)	2% (−8 to 13%), p=0.66	198 [101 310]
CV death (n=209)	294 (258-337)	302 (258-353)	3% (−9 to 16%), p=0.67	183 [92 304]
Myocardial infarction (n=309)	135 (119-153)	120 (105-137)	−11% (−29 to −2%), p=0.01	131 [69 228]
Heart failure (n=150)	238 (201-279)	274 (230-326)	+16% (1 to 33%), p=0.038	146 [63 251]
Stroke (n=94)	210 (170-260)	198 (160-247)	−5% (−20 to 12%), p=0.52	172 [77 290]
No events (n=4960)	95 (93-98)	N/A	N/A	N/A

Concentrations are summarised as geometric mean ± 95% CI. Sample time summarised as median [IQR].



Changes from *Baseline* to *Before event*, grouped according to timing of sample in relation to HF hospitalisation. Average percent changes are diplayed. Bars represent 95% CI.

P1420 Interest of a combinatory approach based on traditional LV dyssynchrony parameters and cardiac work estimated by pressure-strain loop curves for the prediction of CRT response

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Background: Cardiac resynchronization therapy (CRT) in heart failure is limited by still too many non-responders. Aim of the present study is to evaluate if the use of an approach combining traditional dyssynchrony parameters and the estimation of LV performance by pressure-strain loops (PSLs) can be useful for the prediction of CRT response (CRT +).

Methods and results: 2D echocardiography and speckle tracking echocardiography (STE) were performed in 97 (age 65±10 years) CRT candidates before CRT implantation. Conventional dyssynchrony parameters were estimated and left ventricular (LV) global longitudinal strain (GLS) by STE was used to calculate PSLs and estimate LV positive work (posW), negative work (negW), and work efficiency (WE). After a median 6-month follow-up, positive response to CRT (CRT+) was defined as ≥15% reduction in LV end-systolic volume and was observed in 63 (65%) patients.

The main cut-off value able to predict CRT+ was 1057 for PosW (AUC 72%, p<0.0001) and -384 (AUC 0.67, p<0.005) for NegW. As shown in Table 1, the use of a combinatory approach including the concomitant presence of atrio-ventricular dyssynchrony (AV), interventricular dyssynchrony (IV), septal flash (SF), posW>1057 mmHg/%, and negW>-384 mmHg/% showed the great accuracy (97%), sensibility (98%), and positive predictive value (98%) for the prediction of CRT+.

Conclusions: The estimation of cardiac performance by PSL curves in combination with more conventional parameters of LV dyssynchrony might provide a valuable tool for the identification of CRT responders. Further studies on larger series should be designed to confirm these results.

Table 1. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy in a monoparametric and multiparametric approach to predict CRT+

	Sensibility	Specificity	PPV	NPV	Accuracy
AV	0.32	0.79	0.37	0.75	0.66
IV	0.68	0.62	0.71	0.59	0.66
SF	0.81	0.35	0.69	0.51	0.64
PosW >1057 mmHg/%	0.55	0.85	0.72	0.73	0.73
NegW >−338 mmHg/%	0.40	0.94	0.72	0.80	0.79
AV+IV+SF+ PosW >1057+ NegW >−384	0.98	0.27	0.98	0.22	0.97

P207 Prognostic value of left ventricular remodeling, renal function and 24-h ECG recordings in elderly asymptomatic hypertensive patients

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Backgroun: Predictors of cardiovascular outcome in elderly hypertensive patients have been so far scarcely investigated.

Purpose: We assessed the impact of left ventricular geometry, renal function and 24 hour-Holter electrocardiogram (ECG) recordings and outcome in elderly hypertensive patients.

Methods: We enrolled 251 asymptomatic hypertensive elderly patients (>65 year-old). Left ventricular remodeling was evaluated by 2-D echocardiogram. Kidney function was assessed by serum creatinine and estimated glomerular filtration rate (eGFR) calculated according to the CKD-EPI formula. Lown's class, mean QTc and standard deviation of all normal R-R intervals (SDNN) were assessed by 24-hour Holter-ECG recordings. Data on all-cause and cardiovascular mortality were collected for 2 years.

Results: Mean age was 76.2±11.4 years; 46.6% were male and 32.3% were diabetic. Normal cardiac geometry was found in 14 patients (5.6%), concentric remodeling in 45 patients (17.9%), concentric hypertrophy in 135 patients (53.8%), and eccentric hypertrophy in 57 patients (22.7%). High Lown's classes (> class2) were more frequently observed in the presence of eccentric hypertrophy (66.7%) as compared to other patterns [concentric hypertrophy (53.3%), concentric remodeling (24.4%), normal (21.4%)]. Mean QTc was 444.8±34.8 ms and resulted directly correlated with indexed left ventricular mass (r=0.228; p=0.001). According to renal function, chronic kidney disease (CKD) was observed in 44.6% of patients and was associated with high classes of Lown (57.4% vs. 42.7%; p=0.014).Patients with CKD showed lower SDNN as compared with those with preserved renal function (92.02±36.11 ms vs. 103.84±33.96 ms, respectively; p=0.017); and SDNN was directly correlated with eGFR (r=0.168; p=0.015). At 2 years, all-cause and cardiovascular mortality rates were 38.0% and 21.1%, respectively. Diabetes mellitus (HR: 2.40; 95% C.I.1.16 to 4.99; p=0.019), CKD (HR: 2.22; 95% C.I.1.10 to 4.52; p=0.028), prolonged QTc (HR: 2.18; 95% C.I.1.07 to 4.41; p=0.030) and SDNN<96 ms (HR: 1.98; 95% C.I.1.03 to 4.13; p=0.048) were independent predictors of cardiovascular death at 2 year follow-up.

Conclusions: In elderly hypertensive patients, even in absence of symptoms, an assessment of renal function and LV geometry in addition to a 24-hr Holter ECG (including QTc and SDNN measurements) might represent simple and reproducible tools for the clinicians, able to both categorize the risk of elderly hypertensive patients and predict their outcome.

1885 Cardiac rehabilitation after percutaneous coronary intervention in Norway

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Background: Cardiac rehabilitation (CR) is one of the core components in contemporary care of patients with established coronary heart disease (CHD). Previous research has shown that less than half of the eligible patients participate in CR in most of the European countries. The participation rate in Norway is unknown.

Purpose: To estimate the proportion of Norwegian CHD patients participating in CR programs after percutaneous coronary interventions (PCI), and to explore regional differences.

Methods: This is a sub-study of the Norwegian Coronary Stent Trial (ClinicalTrials.gov Identifier: NCT00811772), which included 70% (N=9013) of all patients undergoing first time PCI in Norway during September 2008–February 2011. Data were collected at baseline and every year during a period of five years. Patient-reported CR participation was assessed after three years of follow-up. A total of 7052 patients (78%) responded to the survey. All reported differences were significant at p<0.05.

Results: In the entire cohort (n=9013) the mean age was 63 years (SD 11) and 75% were male. A total of 1878 patients (27% of those who responded to the survey) reported that they had participated in CR initiatives. Compared to the non-participants, the CR participants were younger (60 yr vs. 64 ys) and a higher proportion smoked (40% vs. 32%). CR participants were more likely than non-participants to have myocardial infarction as indication for PCI (75% vs 51%). CR participation rate differed among the four regional health authorities in Norway, varying from 20% in the north to 34% in south/east.

Conclusion: This is the first study to provide nationwide estimates of the proportion of Norwegian CHD patients undergoing cardiac rehabilitation after PCI. Despite that the majority of the patients in this study suffered from myocardial infarction and would benefit from cardiac rehabilitation, the estimated participation rate in cardiac rehabilitation was low. These results also demonstrate regional differences in in cardiac rehabilitation in Norway.