NORSKE ABSTRAKTER PRESENTERT PÅ ESC 2019

P1749 Mortality in ST segment elevation myocardial infarction treated with primary percutaneous intervention in Norway A report from the Norwegian registry of invasive cardiology (NORIC)

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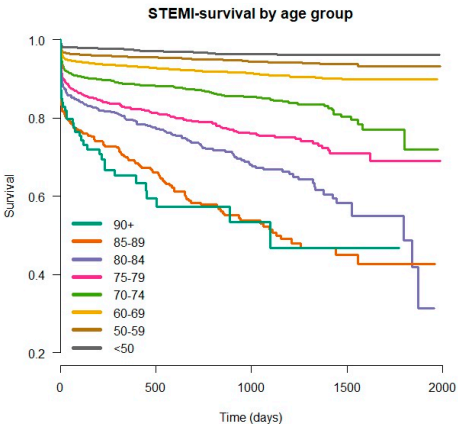
Introduction: Limitations of the current reports on prognosis in ST elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI), are that they are based on selected samples from hospitals voluntary registries, trials and surveys and thereby lack full population coverage. In contrast to most developed countries, Sweden and the UK were for a long term, the only two countries worldwide that had continuous national clinical registries for acute coronary syndrome with mandated participation for all hospitals. This is now also the case in Norway. Of all STEMIs admitted to hospital in Norway, 77 % is treated with PCI (2016). Since 2013 invasive coronary procedures is registered in The Norwegian registry for invasive cardiology (NORIC).

Purpose: The purpose of the current report from NORIC was to assess the mortality rates in patients treated with PCI for STEMI in Norway. Moreover we sought to assess the relationship between mortality and age at admission in this population.

Methods: NORIC, which is a part of the Norwegian Cardiovascular Disease Registry (NCDR), is a national person-identifiable health registry that does not require consent from the registered individual. Data were registered from 1st of January 2013 to 13th of June 2018.

Results: During this period 10524 patients were registered with a STEMI. The incidence is calculated for the years of 2015-2017 when the registry had full national coverage. The incidence of STEMI treated with PCI in Norway was (53 in 2015, 50 in 2016 and 52 in 2017 per 100 000). For patients younger than 80 years at admission, the mortality rates were 4.9 %, 6.8 % and 8.0 % at 30 days, 365 days and 730 days respectively. For patients older than 80 years at admission the mortality rates were 8.3 %, 15.6 % and 19.0 % at 30 days, 365 days and 730 days respectively. The mortality rates stratified by age are illustrated in figure 1.

Conclusions: Mortality in STEMI patients offered primary PCI in Norway is equal or even lower than the mortality reported from well-established national registries from UK and Sweden. This indicates a well functioning treatment strategy despite challenging geography. Age is an important determinant of mortality.



STEMI survival stratified by age

P6563 Time trends in incidence rates of atrial fibrillation in Norway 2004-2014. A CVDNOR project

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ment of Public Health and Nursing - Trondheim - Norway, [7]Norwegian Institute of Public Health, Department of Health Registries - Bergen - Norway,

Background: The reported incidence and prevalence of atrial fibrillation (AF) has been inconsistent among studies.

Purpose: We aimed to study time trends in incidence (first time) of AF hospitalizations or AF deaths in Norway in the period 2004-2014 by age and sex.

Methods: Nationwide hospital discharge diagnoses in the Cardiovascular Disease in Norway (CVDNOR) database and in the National Patient Registry were linked to the National Cause of Death Registry. All hospitalizations with AF as primary or secondary diagnosis and out-of-hospital deaths with AF as underlying cause (ICD-9: 427.3 or ICD 10: I48; AF or atrial flutter) in individuals = 18 years were obtained during 1994-2014. Incident AF was defined as first hospitalization or out-of-hospital death due to AF with no previous hospitalization for AF the past 10 years. Age-standardized incidence rates with 95% confidence intervals (CIs) were calculated using direct standardization to the age-distribution in the Norwegian population per Jan 1st 2004. Age-adjusted average yearly incidence rate ratios (IRR) with 95% CIs were estimated by Poisson regression analyses. Accumulated prevalence during 1994-2014 was assessed in Norwegian residents 18 years and older per Dec 31st 2014.

Results: During 39,865,498 person years of follow up from 2004 to 2014 we identified 175,979 incident AF cases of which 30% were registered with AF as primary diagnosis, 69 % as secondary diagnosis and 1% as out-of-hospital cause of death. The age-standardized incidence rate of AF hospitalization or out-of-hospital death per 100,000 person years was stable at 433 (426-440) in 2004 and 440 (433-447) in 2014. IRR were stable or declining across age groups of both sexes, except for the youngest age group 18-44 years, where incidence rates of AF hospitalization or out-of-hospital death increased by 2% per year, IRR 1.02 (1.01, 1.03). By 2014, the prevalence of AF assessed from hospital or death records was 2.9% in the adult population 18 years and older.

Conclusion: We found overall stable incidence rates of AF from 2004 to 2014 in the adult Norwegian population. Increased incidence rates of AF in the population 18-44 years are worrying and need further investigation.

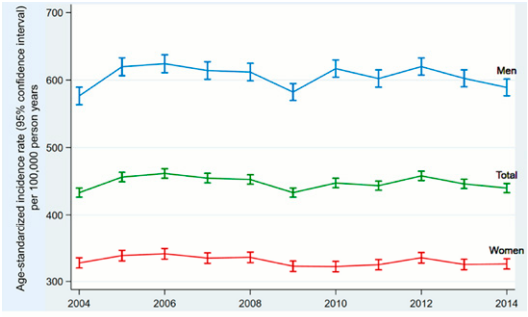

Figure. Age-standardized incidence rates of hospitalization or death from atrial fibrillation from 2004 to 2014 in Norway by year and sex

P818 Incidence of coronary heart disease in patients with familiar hypercholesterolemia compared to age- and sex- matched controls

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Background: Familial hypercholesterolemia (FH) is caused by mutations leading to high levels of low-density lipoprotein cholesterol (LDL-C) in the blood. The primary aim was to describe mutations in a large sample of individuals with FH, and compare risk of first-time hospitalization for coronary heart disease (CHD) and acute myocardial infarction (AMI) between FH mutation carriers and healthy controls. The secondary aim was to compare risk of death and re-hospitalization among FH mutation carriers and controls with a first event of CHD and AMI.

Methods: This study is a prospective matched cohort study comprising a sample of 5691 persons with FH and 119 511 age- and sex- matched controls randomly selected from the general Norwegian population. Information on CHD and AMI were obtained from Norwegian Patient Registry, the Cardiovascular Disease in Norway project and the Norwegian Cause of Death Registry. Endpoints are defined according to the International Classification of Diseases, version 9 (ICD9) or version 10 (ICD10). Risk among persons with FH will be compared to healthy controls in terms of hazard ratios (HR) from Cox regression with follow-up time calculated from time of FH-diagnosis for the person with FH in each matched set.

Results: In total 51.8 % (n=61866) of the combined sample were women with mean age 49.0±20.3 years, whereas 48.2 % (n=57645)

were men with mean age 46.8±19.6 years. There were 236 different FH mutations registered among the FH mutation carriers. The most frequent mutation was 313+1g>A, that accounted for 20.7 % (n=1178) of the total, followed by C210G with 12.1 % (n=690). Results for incidence of CHD, AMI, and mortality after CHD and AMI and readmission rates are not yet available but will be presented at the conference.

P1480 Left atrial strain improves estimation of left ventricular filling pressure

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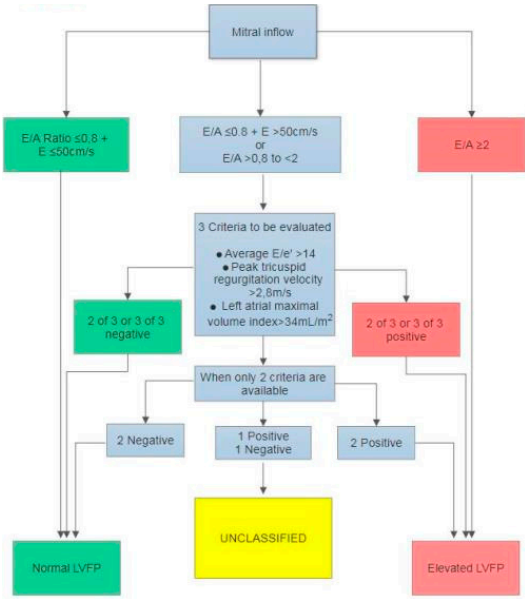
Background: The current algorithm in the 2016 recommendations for echocardiographic estimation of left ventricular filling pressure (LVFP) as normal or elevated, combines traditional indices of mitral inflow velocities, tissue Doppler, left atrial volume and tricuspid regurgitation velocity (figure A). Some of the patients remain unclassified by this algorithm. Left atrial (LA) strain is a novel index that correlates well with LVFP and may improve estimation of LVFP in these patients.

Purpose: We tested if LA strain can improve estimation of LVFP for the patients that are unclassified by the 2016 algorithm.

Methods: We analyzed data from 100 patients who were referred to right heart catheterization due to unexplained dyspnea or suspected heart failure. Echocardiography was performed simultaneously with or within 24 hours of right heart catheterization. Pulmonary capillary wedge pressure (PCWP) was used as an estimate for LVFP and defined as elevated if above 12 mmHg. Elevated LVFP was first estimated using the 2016 algorithm. In patients who were unclassified by the algorithm due to conflicting indices or unattainable indices, LA strain was subsequently used to detect elevated LVFP using a cut-off found from ROC analysis of the whole cohort.



Results: Six patients were unclassified by the 2016 algorithm. The ROC analysis of all 100 patients showed that at an LA strain cut-off of above or below 16.2%, LVFP was correctly classified as normal or elevated, respectively, with a sensitivity of 83% and specificity of 88%. All 6 unclassified patients by the 2016 algorithm were correctly classified using the LA strain cut-off, effectively increasing the accuracy of the algorithm by 6 percentage points.

Conclusions: LA strain may have a role in non-invasive estimation of LVFP, particularly in patients who remain unclassified when using the conventional echocardiographic indices.

P826 Peri-procedural treatment with high dose Rosuvastatin reduces soluble TNF receptor 1 in patients treated with primary percutaneous coronary intervention for ST elevation myocardial infarction

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Background: The extent of cardiac injury in ST elevation myocardial infarction (STEMI) depends on the level of inflammation and subsequent immune cell recruitment. An inflammatory phase that is disproportionately prolonged, of excessive magnitude, or insufficiently suppressed, can lead to sustained tissue damage and improper healing, promoting infarct expansion, adverse remodelling and chamber dilatation. Soluble TNF receptor 1 (sTNFR-1) is believed to mirror systemic pan-inflammatory status more closely than a single cytokine antigenic level. sTNFR-1 levels might give prognostic information, independent from and, at the same time, additive with some

well-recognized outcome predictors such as left ventricular ejection fraction.

Purpose: We hypothesised that sTNFR-1 and other inflammatory markers could be modulated by statins.

Methods: Plasma levels of inflammatory markers were measured at baseline, 2 days, 7 days and 2 months in consecutive patients with first time STEMI with single vessel disease. Twenty-five patients (treatment group (TG)) were treated with 80 mg Rosuvastatin daily with first dose before primary percutaneous coronary intervention (PCI) whereas the control group (CG) consisted of 34 patients in whom treatment with 20 mg simvastatin daily were initiated the day after PPCI.

Results: sTNFR1 increased during the first 48 hours following PCI and this increase was larger in the CG compared with the TG (0.22±0.30 ng/mL vs 0.08±0.19 ng/nmL, p=0.025). The difference in increase during one week was only borderline statistically significant (0.21±0.30 ng/mL vs 0.08±0.26 ng/mL, p=0.081). These differences in the kinetics of sTNRF-1 were mirrored by changes in Pentraxin 3 (PTX3) between groups from baseline to 1 week, CG vs TG. (0.28±0.70 µmol/l vs 0.10 ±0.05 ng/mL, p=0.014) and at 2 months (-0.42 ±0.56 ng/mL vs 0.08±0.60 µmol/l, p=0.032)

Conclusion: High dose Rosuvastatin therapy initiated peri-procedural during PPCI for STEMI reduces pan inflammation as reflected by sTNFR1 and is associated with a less abrupt fall in PTX3 at 1 week and 2 months supporting recent research suggesting that PTX3 plays a cardiovascular protective effect in cardiovascular disease and healing.

P4398 Potentially modifiable clinical and psychosocial factors associated with recurrent cardiovascular events in an outpatient coronary population

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Background: Regular assessment and management of lifestyle, biological and psychosocial factors are recommended in coronary patients. The relative importance of these factors on risk of recurrent cardiovascular (CV) events in the outpatient coronary population is not well known.

Purpose: To estimate the relative effect of potentially modifiable risk factors on recurrent CV events in coronary patients from routine clinical practice.

Methods: A prospective cohort multicenter study from Norway included 1127 (21% women, 83% participation rate) consecutive patients aged 18-80 years 2-36 (mean 16) months after myocardial infarction and/or a coronary revascularization procedure. Thirty percent had at least one coronary event prior to the index event. The primary composite endpoint of recurrent major adverse CV events (MACE): myocardial infarction, revascularization, stroke, heart failure or cardiovascular death was obtained from the hospital records. Cox proportional hazard models stratified for 1 vs. 2+ previous coronary events were performed with model 1 adjusting for age and model 2 with add-on for coronary risk factors and CV comorbidity.

Results: At baseline 99% used platelet inhibition, 93% were taking antihypertensive agents and statins, and 45% had participated in cardiac rehabilitation (CR). During follow-up of mean 4.2 (SD 0.3) years, a total of 355 MACE occurred in 240 patients corresponding to a MACE risk of 31.5%. In model 1, smoking, insufficient physical activity, diabetes, not taking statin therapy, no participation in CR, peripheral artery disease (PAD), previous stroke, kidney failure and higher anxiety and depression scores were significantly associated with recurrent MACE (Table). In model 2, smoking, no physical activity, not taking statin, PAD, kidney failure, anxiety and depression remained significant.

Conclusions: Coronary patients in routine clinical practice were at significant risk of recurrent MACE, particularly in the presence of CV comorbidity. Not taking statin therapy, insufficient physical activity, smoking, anxiety and depression were the major potentially modifiable factors contributing to CV risk. Preventive efforts that target these factors are required to further reduce CV risk in the coronary population.

P4425 The exercise-induced troponin I elevation is highly correlated with power output during exercise in recreational cyclists with coronary atherosclerosis

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On behalf: ***NEEDED study group***

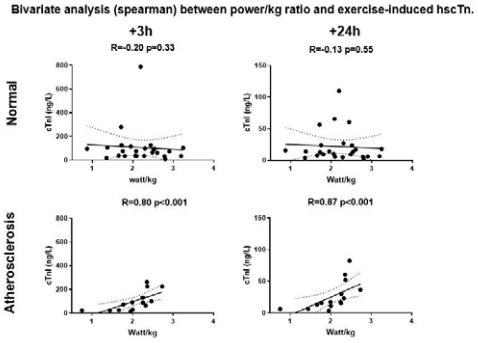
Background: Following strenuous exercise there is an increase cardiac Troponins (cTn) elevation considered being a physiological response. During prolonged strenuous physical activity, high work-loads may induce demand myocardial ischemia due to an oxygen demand/supply mismatch in susceptible subjects, causing an excessive cTn elevation.

Purpose: This study aimed to assess the relationship between exercise-induced cTnI elevation and direct measurement of work performed during prolonged strenuous exercise in subjects with and without atherosclerotic CAD.

Methods: Work during a 91 km mountain bike race was quantified by Stages™ power meters. Power (Watt) and heart rate data were stored in Garmin™ Forerunner 935 monitors. Coronary computed tomography angiography was performed after the race. Blood pressure was measured 4 times during the race. Blood samples (hs-cTnI from Abbot Diagnostics) were obtained one day prior to the race and at 3 and 24 h after the race. Data are presented as mean±SD or median (25th and 75th percentile).

Results: 40 subjects (10 women) were included in the final analysis. 15 Participants (4 women) had atherosclerosis, none had obstructive CAD. These participants were significantly older (55±8 years vs. 46±8 years p=0.007) and had higher training volumes (METS: 69(64-102) hrs/week) compared with normal subjects (METS: 51(33-88) hrs/week) (p=0.03). Baseline cTnI was higher (p=0.04) in the atherosclerotic group (4.5(3.4-8.8) ng/L) compared with normals (2.6(1.6-4.8) ng/L). There were no differences in baseline blood pressure, peak VO2 max, heart rate or BMI. There was no significant difference in race duration between normals (3.9(3.5-4.5) hrs) and subjects with atherosclerosis (4.1(3.6-4.5) hrs). During the race there were no differences in peak power or peak Watt/kg. cTnI increased after the race in all participants, but there were no differences between groups: 3h: atherosclerosis: 89(27-131) ng/L vs. normal 77(36-104) ng/L, 24h: atherosclerosis: 13(6.3-23.7) ng/L vs. normal: 17(12-37) ng/L. There were no significant difference between the groups in average power during the race: atherosclerosis: 167±50 Watt vs. 174(±50) Watt or ratio: 2.0±0.49 Watt/kg vs 2.2±0.58 Watt/kg during the race. Maximal systolic and diastolic blood pressures during the race were higher (p=0.002) in the atherosclerotic group: SBP: 241±14 mmHg vs. 219±26 mmHg, DBP: 107±8 vs 95±8 mmHg. In atherosclerotic subjects cTnI both at 3h and 24 h were highly correlated (p<0.001) with Watt/kg ratio during the race in contrast to no correlations in the normal group (Figure).

Conclusions: Our findings suggest that the presence of coronary atherosclerosis, even in the absences of significant stenosis, alters the relationship between workload and the troponin response. This indicates different release kinetics in exercise-induced cTn in participants with and without CAD, with prolonged elevation in cTnI in CAD subjects exceeding the highest work-intensities.



P3528 Circulating microRNA-210 concentrations are increased in patients with acute heart failure and provide prognostic information

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Background: MicroRNA(miR)-210 is induced by cellular hypoxia and circulating miR-210 concentrations are associated with clinical outcome in

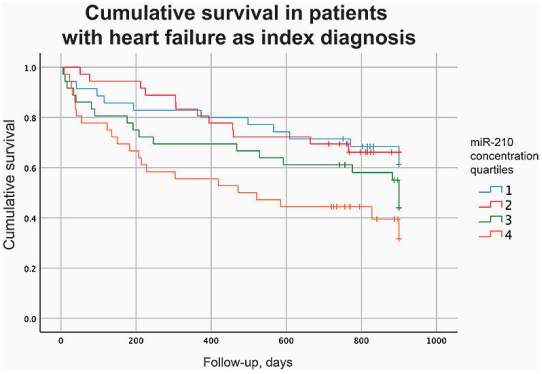
patients with myocardial infarction and aortic stenosis. Whether circulating miR-210 concentrations provide diagnostic and prognostic information in unselected patients with dyspnea is not known.

Purpose: To assess the diagnostic and prognostic value of circulating miR-210 concentrations in patients hospitalised due to acute dyspnea.

Methods: We extracted microRNA from plasma samples obtained on admission from 314 patients hospitalised for acute dyspnea and 10 healthy control subjects. miR-210 concentrations were measured by quantitative polymerase chain reaction and we used miR-425 for normalisation. The merit of circulating miR-210 concentrations to diagnose and provide prognostic information in patients with acute heart failure (HF) was compared to the merit of N-terminal pro-B-type natriuretic peptide (NT-proBNP).

Results: In total, 143 patients (46%) were adjudicated as hospitalised due to acute heart failure (HF) and 84 patients (27%) due to acute exacerbation of chronic obstructive lung disease (AECOPD). All patients and control subjects had miR-210 concentrations within the range of detection (Cq 26-32) and analytical variation was low. miR-210 concentrations correlated with age, NT-proBNP and cardiac troponin T concentrations in the total cohort. Circulating miR-210 concentrations were increased in patients with HF (4.7±3.3 fold increase, p<0.0001) and AECOPD (3.4±1.7 fold increase, p<0.0001) compared to control subjects. Circulating miR-210 concentrations were not different between patient groups and receiver operating characteristics area under the curve (AUC) for miR-210 to diagnose acute HF was 0.50 (95% CI 0.43-0.57) compared to AUC 0.85 (0.81-0.89) for NT-proBNP. During a median 817 days of follow-up, 66 patients (46%) with acute HF died and 35 patients (42%) with AECOPD died. Circulating miR-210 concentrations separated acute HF patients with a poor and favourable outcome (figure 1; p by the log rank test =0.017). Circulating miR-210 concentrations were also associated with mortality during follow-up in Cox regression model: hazard ratio (HR) for lnRQ of miR-210 was 2.11 (95% CI 1.27-2.50), p=0.004. The association between circulating miR-210 concentrations and outcome was attenuated and no longer significant after adjusting for NT-proBNP concentrations. Circulating miR-210 concentrations did not predict outcome in patients with AECOPD: HR 1.38 (0.65-2.93); p=0.4.

Conclusions: Circulating miR-210 concentrations are increased in patients with acute HF, and provide prognostic information during follow-up. Still, circulating miR-210 concentrations did not diagnose acute HF among unselected patients with dyspnea and the association with outcome was attenuated by NT-proBNP.



3298 Prehospital assessment of the one-hour rule-in/rule-out algorithm using a high-sensitivity cardiac troponin t assay in a low-prevalence population for acute coronary syndrome (OUT-ACS)

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Background: The majority of patients with chest pain in Norway initially present to the primary health care system, which serves to triage them to the specialist health care services including hospitals. In some emergency primary care institutions, patients who are not hospitalised directly undergo further diagnostic testing to rule out acute myocardial infarction (AMI).

Purpose: Several studies have shown the advantage of using high-sensitivity assays for fast interpretation of cardiac troponins. The majority of these studies included patient populations from hospital emergency departments. In contrast, we aimed to investigate whether the 1-hour algorithm for high-sensitivity cardiac troponin T (hs-cTnT) is safe and useful for implementation in a primary care emergency setting where the patients have a much lower pre-test probability for an acute coronary syndrome.

Methods: In this prospective cohort study, we included 1672 patients with acute non-specific chest pain from November 2016 to October 2018

at a primary care emergency outpatient clinic in Norway. Serial hs-cTnT samples were analysed after 0, 1 and 4 hours on the Cobas 8000 e602 analyzer. We divided the results into one of three groups (rule-out, rule-in, or further observation), according to the 0/1-hour algorithm for hs-cTn from the current ESC guidelines on non-ST-elevation myocardial infarction. In the rule-out group, the 0/1-hour results were compared to the standard 4-hour hs-cTnT. Final hospital diagnoses were collected as a gold standard for the patients in the rule-in group.

Results: A total of 44 (2.6%) of 1672 patients were diagnosed with AMI. By applying the algorithm, 1274 (76.2%) patients were assigned to the rule-out group. One of the rule-out patients had a significant increase in hs-cTnT in the 4-hour sample. This results in a sensitivity for AMI of 97.7% (95% confidence interval [CI] 88.0-99.9) and negative predictive value of 99.9% (95% CI 99.6-100.0). There were 50 (3.0%) patients in the rule-in group, amongst whom 35 had a verified AMI. This gives a specificity for AMI of 99.1% (95% CI 98.5-99.5) and a positive predictive value at 70.0% (95% CI 55.4-82.1). Among the 348 (20.8%) patients assigned to further observation, eight patients had an AMI. The 15 rule-in patients who did not have an AMI, had other acute illnesses that required further diagnostic work-up at the hospital.

Conclusions: With a negative predictive value at 99.9 %, the 1-hour algorithm for hs-cTnT seems safe and applicable for a faster assessment of patients with non-specific chest pain in a primary care emergency setting. Prehospital implementation of this algorithm may reduce the need for hospitalisation of these patients and hence may probably lower the costs.

ClinicalTrial.gov identifier: NCT0298312

Table 1. Probability of recurrent cardiovascular events in an outpatient coronary population, estimated by Cox proportional hazard models

	Model 1*		Model 2 *	
	Relative risk (95% CI)	p-value	Relative risk (95% CI)	p-value
Male sex	0.86 (0.63-1.15)	0.299		
Never smoking	1.00 (reference)		1.00 (reference)	
Smoking prior to interview	1.53 (1.08-2.18)	0.017	1.45 (1.01-2.08)	0.042
Smoking at interview	1.51 (0.99-2.28)	0.054	1.14 (0.73-1.77)	0.571
LDL cholesterol per mmol/l increase	1.17 (0.99-1.37)	0.059	1.14 (0.97-1.35)	0.121
Adequate physical activity**	1.00 (reference)		1.00 (reference)	
Low physical activity	1.36 (1.01-1.87)	0.049	1.33 (0.96-1.84)	0.085
No physical activity	1.85 (1.30-2.63)	0.001	1.73 (1.19-2.53)	0.004
Diabetes	1.69 (1.22-2.19)	0.001	1.34 (0.98-1.83)	0.062
Systolic blood pressure per 10 mmHg increase	1.05 (0.99-1.13)	0.124	1.06 (0.99-1.14)	0.096
Body Mass Index per kg/m^2 increase	1.02 (0.99-1.05)	0.190		
C-reactive protein per mg/L increase	1.00 (0.99-1.01)	0.462		
Not participating in cardiac rehabilitation	1.42 (1.09-1.86)	0.010	1.28 (0.97-1.70)	0.077
Not taking statin	2.08 (1.42-3.03)	<0.001	2.14 (1.36-3.36)	0.001
Heart failure	1.21 (0.86-1.69)	0.281		
Atrial fibrillation	1.21 (0.82-1.80)	0.340		
Peripheral artery disease	1.96 (1.39-2.75)	<0.001	1.74 (1.21-2.49)	0.003
Stroke or transient ischemic attack	1.43 (0.94-2.16)	0.091	1.12 (0.72-1.74)	0.617
Estimated GFR<60 mL/min/1.73m^2	1.88 (1.35-2.61)	<0.001	1.58 (1.13-2.22)	0.008
HADS Anxiety sum per unit increase	1.05 (1.01-1.08)	0.012	1.04 (1.00-1.08)	0.040
HADS Depression sum per unit increase	1.07 (1.03-1.11)	0.001	1.05 (1.01-1.09)	0.018

*Model 1 is adjusted for age and stratified for 1 vs. 2+ previous coronary event, Model 2 is also adjusted for coronary risk factors and CV comorbidity with p-value <0.10 in bivariate associations
**Adequate physical activity: ≥ moderate intensity of 30 min ≥2-3 times/week, Low physical activity: < moderate intensity of 30 min ≥2-3 times/week, No physical activity: < 1 time/week

4101 Identification of genetic variants associated with the cardiovascular disease risk factor, low aerobic fitness - The HUNT study

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Abstract: Background: Low maximal oxygen uptake (VO2max) is a strong and independent risk factor for all-cause and cardiovascular disease (CVD) mortality. Although physical activity is a major determinant of VO2maxlevel, genetics contribution is estimated to be ~50 %.

Methods: We performed a genetic association study on 123.545 single-nucleotide polymorphisms (SNPs) and directly measured VO2max in 3470 individuals (exploration cohort). The candidate SNPs were subsequently analyzed in a separate cohort of 718 individuals (validation cohort), in addition to 7 wild-card SNPs previously associated with VO2max, but not included on the chip used in the exploration cohort. Sub-analyses were performed for each gender. In silico analysis and genotype-phenotype databases were used to predict physiological function of the SNPs.

Results: In the exploration cohort, 42 SNPs were associated with VO2max (p<5.0*10-4). Six of the candidate SNPs were also found to be associated with VO2max in the validation cohort (p<0.05, either in men, women or both), in addition to three wild-card SNPs. By using these nine SNPs we created a genetic score for inborn VO2max-level. Together, these nine SNPs explained ~8% of the variation in VO2max, and discriminate individuals with inborn high versus low VO2max based on simultaneous carriage of multiple favorable alleles. The cumulative number of favorable SNPs correlated negatively with the presence of several CVDrisk factors, e.g. waist-circumference, visceral fat, fat %, cholesterol levels and BMI. In silico analysis indicated that several of the SNPs influence gene expression across multiple organs, including adipose tissue, skeletal muscle and heart.

Conclusion: We identified six novel genetic variants associated with VO2max, and validated three SNPs previously associated with fitness related traits.

2232 Circulating levels of ST2 are associated with myocardial injury, left ventricular function and future adverse clinical events in patients with ST-elevation myocardial infarction

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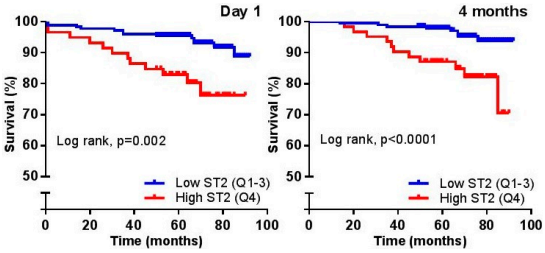
Background: Soluble ST2, a member of the IL-1 receptor family, seems to be associated with adverse outcome in acute myocardial infarction and heart failure (HF), and is suggested to be involved in left ventricular (LV) remodelling.

Purpose: To elucidate a possible role of ST2 in LV injury, remodelling and prognosis in ST-elevation myocardial infarction (STEMI) patients. The main objectives of the study were to investigate whether circulating ST2 levels were associated with infarct size, LV function, adverse remodeling and clinical outcome in a cohort of patients with STEMI.

Methods: 270 patients with clinically stable first-time STEMI treated with primary percutaneous coronary intervention (PCI) were included. Blood samples were drawn before and immediately after the PCI procedure, at day 1 (median 18.3 hours after PCI) and after 4 months. Cardiac magnetic resonance (CMR) was performed in the acute phase and after 4 months. Clinical events and all-cause mortality were registered during 12 months' and 70 months' follow-up, respectively. A composite endpoint was defined as death, MI, unscheduled revascularisation >3 months after the index infarction, rehospitalisation for HF or stroke. Associations between ST2 and CMR parameters and clinical events were evaluated with linear regression and logistic regression, respectively.

Results: There was a significant increase in ST2 levels from the PCI procedure to day 1 with a subsequent decline from day 1 to 4 months in the POSTEMI cohort. Patients with high ST2 levels (>median) at all sampling points during hospitalisation had significantly larger infarct size, lower myocardial salvage, lower LVEF, larger increase in EDV and higher frequency of MVO. After adjustment for relevant clinical variables, peak CRP and peak troponin T, ST2 measured at day 1 remained associated with infarct size (ß 2.0 per SD of ST2, p<0.001) and LVEF (ß -1.8 per SD of ST2, p=0.02) at 4 months. High levels of ST2 measured at day 1 (>75th percentile) were associated with increased risk of having an adverse clinical event during the first year and with long-term all-cause mortality (figure). High levels of ST2 measured in a stable phase 4 months after STEMI were also associated with an increased risk of all-cause mortality (figure).

Conclusions: High levels of ST2 in STEMI patients were associated with large infarct size, impaired recovery of LV function, and adverse clinical outcome in patients with STEMI. ST2 measured 4 months after STEMI remained associated with all-cause mortality.



P6373 Serum amyloid A and left ventricular mass in psoriasis patients treated with infliximab

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Background: Serum amyloid A (SAA) is an acute phase reactant associated with amyloid tissue deposition. Chronic skin inflammation in psoriasis could cause increased production of SAA in the liver and subsequent deposition in cardiac tissue.

Purpose: To assess if higher SAA is associated with higher left ventricular (LV) mass in psoriasis patients treated with infliximab

Methods: Data from 47 psoriasis patients treated with the tumour necrosis factor-a blocker infliximab (mean age 47±14 years, 66% men) was compared to 106 age and sex-matched control subjects (mean age 47±11 years, 70% men). LV mass was assessed by echocardiography and index to height m^2.7. SAA was analysed by Matrix-Assisted Laser Desorption/Ionization Time-Of-Flight mass spectrometry.

Results: Psoriasis patients were more likely to be smokers than controls (38% vs. 16%, p=0.005), while other cardiovascular risk factors and SAA levels were similar. Psoriasis patients had lower LV mass index than controls (35.6±9.6 g/m^2.7 vs. 40.3±9.8 g/m^2.7, p=0.008). In the total

study population, higher SAA level (ß=0.23, p=0.003) was associated with higher LV mass index independent of presence of psoriasis (Table). In psoriasis patients, higher SAA level (ß=0.48, p<0.001) was associated with higher LV mass index after adjustment for age and body mass index in multivariable analysis (Table). No association between SAA and LV mass index was found in controls.

Conclusion: In psoriasis patients on infliximab treatment, higher SAA level was associated with greater LV mass index, pointing to a potential role of chronic inflammation and SAA production in the development of subclinical cardiac disease in psoriasis.

	Total study population		Psoriasis	
	LV mass index R^2 0.33, p<0.001		LV mass index R^2 0.43, p<0.001	
	β	P	β	P
Psoriasis	-0.21	0.006	na	na
SAA, µg/ml	0.23	0.003	0.48	<0.001
BMI, kg/m²	0.39	<0.001	0.50	<0.001
Age, years	0.18	0.03	0.11	0.35
Female gender	-0.11	0.15	--	--
Hypertension	0.08	0.35	--	--
Smoking	0.03	0.75	--	--

Multivariable associations of LV mass index in the total study population and in psoriasis patients. BMI, body mass index; LV, left ventricular; SAA, serum amyloid A; na, not applicable

P2452 Application of left atrial strain for differentiation between pre- and post-capillary pulmonary hypertension

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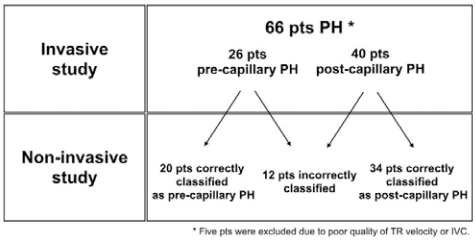
Background: Pulmonary hypertension (PH) is classified as pre- or post-capillary PH, and pulmonary capillary wedge pressure (PCWP) > 15 mmHg is used as criterion for post-capillary PH. Elevated left atrial (LA) pressure is associated with reduced LA reservoir strain. Thus, LA strain may potentially serve to differentiate between these diagnoses.

Objectives: This study tested the hypothesis that LA strain can be used as a noninvasive parameter to differentiate between pre- and post-capillary PH.

Methods: We analyzed 103 patients (mean age: 58 years, 51 female) referred to right heart catheterization due to unexplained dyspnea or suspected heart failure. Echocardiography was performed within 24 hours of the invasive procedure. Mean pulmonary artery pressure (PAP) was noninvasively estimated from tricuspid regurgitation (TR) velocity and inferior vena cava (IVC) diameter and collapsibility. LA reservoir strain was calculated from apical four-chamber view by speckle tracking echocardiography, and was feasible in 101 patients.

Results: Twenty-eight patients were invasively confirmed with pre-capillary PH and 43 patients with post-capillary PH. The remaining 32 patients had no PH. LA reservoir strain was significantly lower in patients with post-capillary PH than patients with pre-capillary PH (9.9 ± 5.5% vs. 24.6 ± 8.2%, p< 0.01). At a cut-off value of 15.4%, LA reservoir strain could predict elevated PCWP > 15 mmHg with AUC=0.88, sensitivity=84.8% and specificity=81.8%. As shown in the figure, echocardiography with LA reservoir strain correctly differentiated 82% of patients into pre- and post-capillary PH.

Conclusions: These results suggest that LA reservoir strain can be used to predict elevated PCWP, thus allowing discrimination between pre- and post-capillary PH.



P4368 Estimation of pulmonary artery pressure from right atrial strain and tricuspid regurgitation velocity

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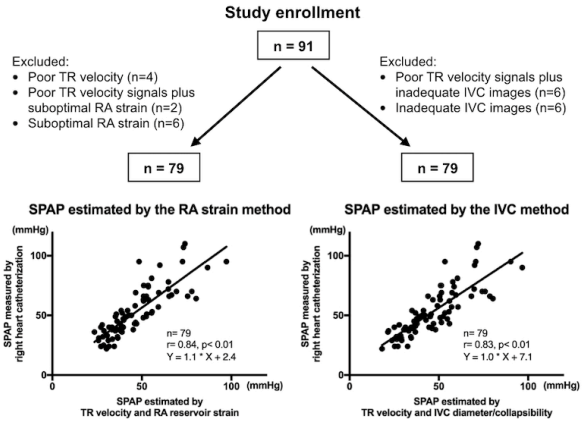
Background: Systolic pulmonary artery pressure (SPAP) can be estimated non-invasively as the sum of indices for right atrial (RA) pressure and tricuspid regurgitation (TR) pressure gradient. Although echocardiographic evaluation of inferior vena cava diameter and collapsibility is currently being used to estimate RA pressure (IVC method), RA strain may be an alternative since atrial strain is related to atrial pressure.

Objective: We tested if RA strain by speckle tracking echocardiography can be used as a surrogate of mean RA pressure (RA strain method), and by adding the TR pressure gradient, be used to estimate SPAP.

Methods: We retrospectively analyzed 91 patients (mean age, 58 years) referred to right heart



catheterization due to unexplained dyspnea or suspected pulmonary hypertension. Echocardiography was performed within 24 hours of the invasive procedure. RA reservoir strain was calculated from apical four-chamber view. SPAP was calculated as the sum of peak TR pressure gradient and estimated RA pressure by the IVC or RA strain methods.

Results: Right heart catheterization showed SPAP and mean RA pressures of 51 ± 20 mmHg and 9 ± 6 mmHg, respectively. RA reservoir strain was inversely correlated with mean RA pressure (r= -0.61, p< 0.01). Thus, we set mean RA pressure as 5, 10 and 15 mmHg depending on high (=25%), middle (10-25%) and low (=10%) values of RA reservoir strain. As shown in the figure, both the RA strain and IVC methods when combined with peak TR velocity, provided good estimates of invasively measured SPAP.

Conclusions: RA strain provides a semiquantitative measure of RA pressure, which can be used in combination with peak TR velocity to estimate SPAP. This approach can be used as an alternative when the IVC method is not available in cases with poor subcostal window.

P627 Patterns of physical activity over 22 years and mortality: the HUNT Study, Norway

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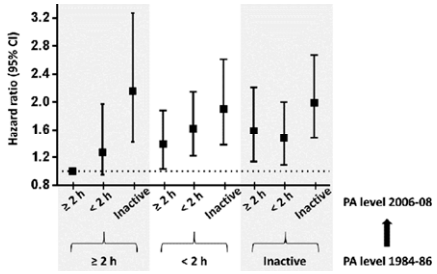
Background: The majority of studies relating physical activity (PA) to mortality have assessed PA using one baseline measure. Important questions in a preventive perspective are whether you can compensate for prior physical inactivity by taking up PA at a later stage in life and whether being physically active earlier in life can confer benefits even if you become inactive later. We investigated how patterns of PA over 22 years associated with all-cause and cardiovascular disease (CVD) mortality.

Methods: We used data from the prospective population-based HUNT Study in Norway, including 10,491 men and 12,655 women aged = 20 years who participated at HUNT in 1984-86 and 2006-08. PA was categorised into inactive, < 2 h/week or = 2 h/week, making nine categories of patterns of PA over 22 years. All-cause and CVD mortality were assessed from the national Cause of Death Registry, with follow-up until the end of 2013. We used Cox regression to estimate adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for all-cause and CVD mortality within categories of PA patterns, compared to the reference category of individuals who reported = 2 h/week at both examinations. Estimates were adjusted for baseline age, sex, body mass index, smoking, education level and blood pressure.

Results: Individuals who were inactive in both 1984-86 and in 2006-08 had increased risk of all-cause mortality (HR 1.99, 95% CI 1.48-2.67) and CVD mortality (HR 2.68, 95% 1.47-4.86) compared to those who were physically active = 2 h/week at both examination. The HRs for all-cause and CVD mortality were 1.60 (1.22-2.15) and 1.90 (1.06-3.42), respectively, for those who reported PA of < 2h/week at both examinations. Individuals who went from being physically active in 1984-86 to inactive in 2006-08, had a comparable risk of all-cause and CVD mortality as those who were inactive at both examinations. Overall, the mortality risk was still increased in those who took up PA between the two examinations, compared to the reference category.

Discussion: Individuals who remained physically inactive or who decreased their PA over 22 years had substantially increased all-cause and CVD mortality risk. Taking up PA only attenuated the risk but a high level of sustained PA was associated with the lowest risk.



P1544 Circulating secretoneurin concentrations provide incremental prognostic information to established risk indices in patients with moderate to severe aortic stenosis

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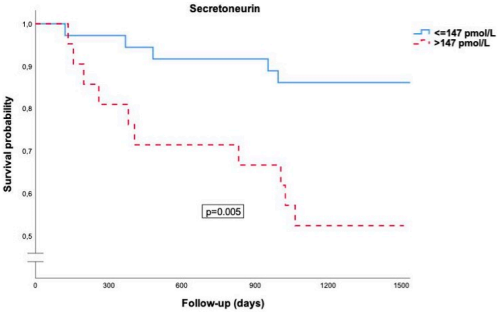
Background: Secretoneurin (SN) concentrations provide important prognostic information in patients with myocardial dysfunction. Whether preoperative SN concentrations improve risk assessment in patients with moderate to severe aortic stenosis (AS) is unknown.

Methods: We included 57 patients with moderate to severe AS referred for presurgical evaluation and recorded all-cause mortality during follow-up. All patients were examined with comprehensive echocardiography, electrocardiogram (ECG), and high-sensitivity cardiac troponin T (hs-TnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) measurements.

Results: Median (quartile 1-3) SN concentration in the AS patients was 141 (121-163) pmol/L. Lower estimated creatinine clearance and use of diuretics, but not standard ECG or echocardiographic indices and cardiac biomarkers, were associated with increasing SN concentrations. In total, 15 patients (26%) died during 3.5 years median follow-up. SN concentrations were higher in non-survivors than survivors: 156 (133-209) vs. 140 (116-155) pmol/L, p=0.007. The optimal cut-off concentration for SN in discriminating long-term mortality was 147 pmol/L (sensitivity 67% [95% CI 38-88%], specificity 74% [58-86%]) and patients with SN concentrations above the optimal cut-off had worse prognosis than patients below the cut-off (figure; p=0.005 with the log-rank test). Higher SN concentrations were associated with increased risk of mortality after adjustment for clinical risk factors, echocardiographic and ECG variables, hs-TnT and NT-proBNP concentrations, and whether patients were subjected to aortic valvular surgery (n=34): hazard ratio per lnSN 15.13 (95% CI 1.05-219.00); p=0.046. Receiver operating characteristics area under the curve for SN to predict mortality was 0.74 (95% CI 0.60-0.88) compared to 0.73 (0.59-0.87) for hs-TnT and 0.67 (0.51-0.82) for NT-proBNP.

Conclusions: SN concentrations seem to reflect additional pathophysiology to established risk indices and improve risk assessment in patients with moderate to severe AS.



P4661 Increased levels of sST2 in patients with mitral annulus disjunction and ventricular arrhythmias

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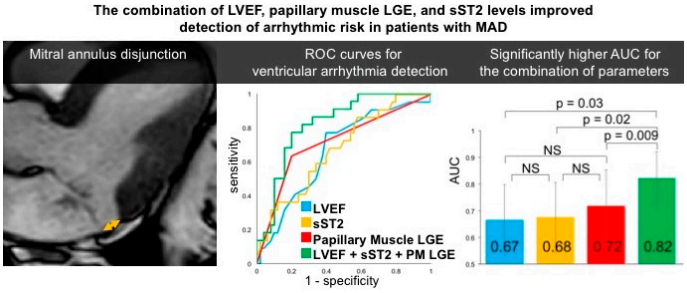
Background: Mitral annulus disjunction (MAD), a basal displacement of the mitral valve annulus, is described as a possible aetiology of sudden cardiac death. Stretch-induced fibrosis in the sub-valvular apparatus has been suggested as the substrate of arrhythmias.

Purpose: We hypothesized that the stretch related biomarker soluble Suppression of Tumorigenicity-2 (sST2) is a marker of ventricular arrhythmias in patients with MAD.

Methods: We included patients with =1 mm MAD on cardiac magnetic resonance imaging, and recorded left ventricular ejection fraction (LVEF) and late gadolinium enhancement (LGE) suggesting papillary muscle fibrosis. Circulating levels of sST2 were assessed by blood sampling. The occurrence of ventricular arrhythmias, defined as aborted cardiac arrest, sustained or non-sustained ventricular tachycardia, was assessed retrospectively.

Results: We included 72 patients with MAD [55 (35-62) years old, 48 (67%) female], of which 22 (31%) had ventricular arrhythmias. Patients with ventricular arrhythmias had lower LVEF (60 ± 6 % vs. 63 ± 6 %, p=0.04), more prevalent



papillary muscle fibrosis [14 (64%) vs. 10 (20%), p < 0.001] and higher sST2 levels [31.6 ± 10.1 ng/mL vs. 25.3 ± 9.2 ng/mL, p=0.01] compared to those without. Combining sST2-level, LVEF and papillary muscle fibrosis optimally detected individuals with arrhythmias (area under the curve 0.82, 95%CI 0.73-0.92) and improved the risk model (p < 0.05) compared to individual parameters (figure right panel).

Conclusion: Circulating sST2 levels were higher in patients with MAD and ventricular arrhythmias compared to patients without arrhythmias. Combining sST2, LVEF and LGE may improve risk stratification in patients with MAD.

P6527 Patients discharged on the same day following elective PCI report equal satisfaction using health related quality of life instruments as compared to usual care: results from a randomized trial

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Background: Earlier observations in the era of femoral procedures using warfarin as the anticoagulant agent have shown safety following same day discharge after elective percutaneous coronary intervention (PCI) for stable coronary artery disease (CAD). Procedures have evolved with most European centres adopting radial procedures with corresponding improvement in technique and equipment. Adoption of "radial lounges" has improved and simplified the observation routines with early ambulation. Antiplatelet therapy has also become more efficacious. The safety of same day discharge has been demonstrated. The economic benefit of such a strategy is significant with reported cost reductions of approximately 50%. Patient reported satisfaction is also shown to be comparable to standard care.

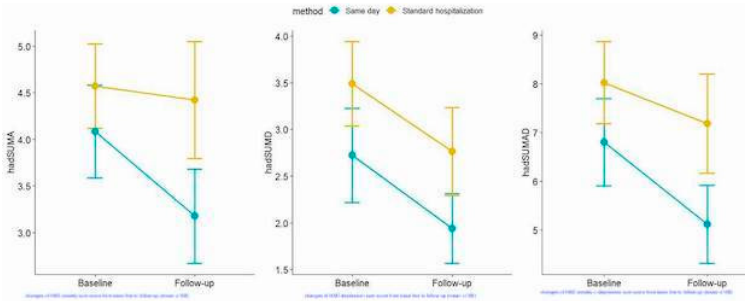
The current bed availability in health care facilities has made it a necessity to explore measures to reduce bed occupancy rates. Reduction in bed occupancy can further permit health personell to focus on other duties and obligations in wards with patients requiring hospitalization. Early discharge may cause anxiety and dissatisfaction among patients.

Purpose:The aim of our study was to evaluate safety and patient satisfaction of same discharge following uncomplicated elective radial access PCI.

Methods:Randomized controlled single center study. Eligible patients scheduled for elective PCI with radial access were prescreened following predefined inclusion and exclusion criteria. Health related quality of life instruments (HRQOL), Seattle Angina Questionnaire (SAQ), Short form 36 (SF-36) and Hospital Anxiety and Depression Scale (HADS) were completed by the patients and received at base line and at 30 days post-procedure. All same day discharged patients were contacted by phone by a specialized study nurse the day after the procedure.

Results:517 patients were screened between November 2015 and November 2018 and 82 patients with mean age of 65 years were block randomized post-procedure. 38 patients were randomized to same day discharge after 6 hours of observation and 44 patients to standard care group which necessitated an overnight hospitalization. 11 female patients and 71 male patients were included.

No adverse events were registered in either group. No significant difference between groups were observed in the SAQ (treatment satisfaction score p = 0.48, angina frequency scale p =0.58), SF-36 (SF vitality p = 0.93) or HADS (HADS anxiety + depression p =0.15).



Conclusions: discharge on the same day following uncomplicated PCI for stable angina is safe and patient health related quality of life instruments confirm that patients are equally satisfied with this new care strategy when compared to usual care.

P1547 Circulating lipoprotein subfractions as new non-invasive biomarkers of coronary atherosclerosis

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Objectives: Coronary artery disease (CAD) is the most common cause of death globally. In the next decade, the number of people at risk is expected to increase, due to obesity, inactivity and diabetes. Therefore, precise risk-prediction models will be increasingly important for the healthcare system, to be able to initiate cost-efficient prevention strategies. One of the first steps in CAD-development is sub-clinical atherosclerosis. Biomarkers that could reflect the presence of coronary atherosclerosis would be extremely valuable for risk prediction of myocardial infarction (MI). Serum cholesterol levels are key variables in risk prediction; however, there is growing interest for exploring the potential of other lipid subclasses. The aim of this study is to identify specific lipoprotein subfractions that are associated with the extent of coronary atherosclerosis.

Methods: 60 patients with suspected CAD were enrolled. Blood samples were collected before the partiens underwent coronary angiography. The extent of coronary atherosclerosis were quantified using the Gensini score. The partients were classified into three groups based on their Gensini score (<20.5: normal, 20.6-30: non-significant CAD and >30.1: significant CAD). The blood samples were analyzed by nucelar magnetic resonance (NMR) lipidomics. Univariate and multivariate statistical tests were used to determine whether lipoprotein subfractions were associated with the extent of coronary atherosclerosis.

Results and discussion: Of the 117 lipoprotein subfractions quantified, 10 were different in patients with significant CAD compared to patients with normal vessels in non-statin users (p=0.005). Despite no difference in total cholesterol, LDL and HDL cholesterol between the three Gensini groups, NMR lipidomics revealed that patients with significant CAD had twice as many circulating LDL-5 and LDL-6 particles as patients with normal vessels. Furthermore, three types of small LDL-subfractions, called LDL-5-TG, LDL-5-ApoB and LDL-6-ApoB, were significantly increased in patients with significant CAD. Interestingly, previous studies have suggested that small LDL particles are more atherogenic than larger particles. In addition, patients with significant CAD had low levels of ApoA1 containing HDL particles, and high levels of two different small VLDL particles. Previous studies have indicated that small VLDLs are more atherogenic than larger VLDLs, and does to a greater extent penetrate the vessel intima.

Conclusions: This study reveals strong associations between serum lipoprotein subfractions and the degree of coronary atherosclerosis quantified by Gensini score. Especially, the high levels of certain types of small LDL-particles in patients with CAD, indicates that measuring lipoprotein subfractions may provide added value to risk prediction models for MI. However, these findings needs to be further explored and validated in large cohort studies.

3051 Effectiveness and safety of apixaban, dabigatran and warfarin compared to rivaroxaban in non-valvular atrial fibrillation; a Norwegian nationwide cohort study

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Introduction: Non-vitamin K oral anticoagulants (NOACs) are increasingly used for stroke prevention in patients with non-valvular atrial fibrillation (NVAF). Although proven effective and safe, there is limited knowledge of the comparative effectiveness and safety of the different NOACs in real life. Norway has nationwide registries of good quality, being suitable for doing such a comparison.

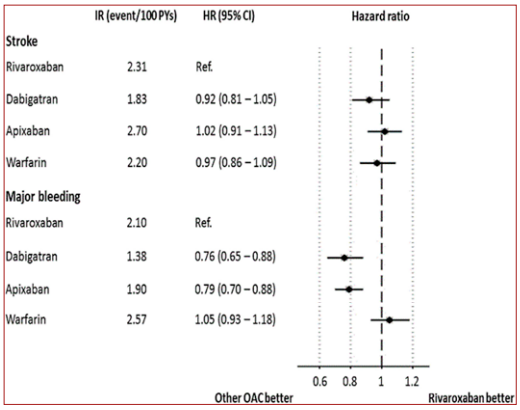
Purpose: The aim of this nationwide cohort study was to compare the risk of stroke/systemic embolism (SE) and major bleeding in patients with NVAF treated with dabigatran, apixaban and warfarin compared with patients treated with rivaroxaban.

Methods: By merging nationwide registries (the Norwegian Patient Registry and the Norwegian Prescription Database), a cohort was created including all oral anticoagulant (OAC)-naïve adult NVAF patients initiating OAC in the study period 1 Jan 2013 to 31 Dec 2017. The patients were followed until switching of OAC type, discontinuation, death, or end of study-period.

Cox proportional-hazards regression was used to estimate adjusted hazard ratios (HRs) for the risk of stroke/SE or bleeding in patients using dabigatran, apixaban and warfarin compared to rivaroxaban.

Results: A total of 65 563 new users of OAC were included; 10 413 initiated dabigatran, 28 363 apixaban, 13 087 warfarin and 13 700 rivaroxaban. The median age was 71 yrs for dabigatran, 74 yrs for apixaban, 75 yrs for warfarin, and 73 yrs for rivaroxaban; 58.3% were men. Dabigatran-users were younger and had less comorbidities than all other OAC-users; the greatest difference was in the proportion with chronic kidney disease (2.4% in the dabigatran-group versus 7.0%, 12.5%, and 4.6% in the apixaban, warfarin and rivaroxaban groups, respectively). During a median follow-up time of 14.7 months (IQR 4.9 – 30.6), 2 361 (3.6%) patients suffered a stroke/SE, 2 051 (3.1%) had a major bleeding, and 4 250 (6.5%) died. Adjusted HRs for stroke/SE and major bleeding are presented in the figure. When the risk of stroke/SE and major bleeding was assessed solely in patients that received the standard dose of OAC (73% of NOAC users), the results were similar to the results for the entire population.

Conclusion: In this nationwide cohort study of patients with NVAF being new users of OAC, we found no significant differences in risk of stroke/SE between different OACs and rivaroxaban, whereas dabigatran and apixaban were associated with significantly lower risk of major bleeding.



P2545 Long-term use of anabolic-androgenic steroids in male weightlifters is associated with left ventricular systolic dysfunction

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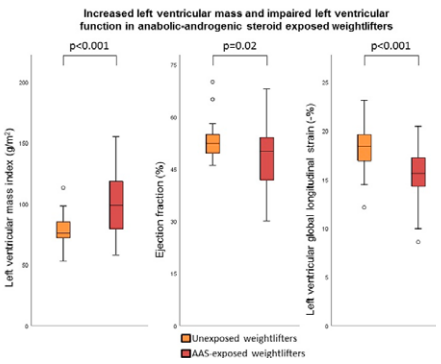
Background: Illicit use of anabolic-androgenic steroids (AAS) is widespread and has adverse psychological and cardiovascular effects. Few well-powered studies have explored the effect of long-term AAS-use on left ventricular systolic function.

Purpose: To explore the relationship between long-term use of AAS and left ventricular mass and systolic function.

Methods: We included male weightlifters with a history of >1 year of cumulative AAS-use and male weightlifters unexposed to AAS. We performed echocardiography in all and assessed left ventricular mass using 2D echocardiographic linear measurements and Cube formula, left ventricular ejection fraction (EF) ad modum Simpson, and left ventricular global longitudinal strain (GLS) by speckle-tracking echocardiography.

Results: We recruited 100 male weightlifters, 58 of whom were previous or current AAS-users with mean±SD AAS-use of 10.4±7.0 years, and 42 unexposed weightlifters. There were no difference in age (35.5±9.2 vs. 35.3±7.5 years, p=0.8) nor body mass index (BMI) (BMI 31.4±5.0 vs.30.1±3.5, p=0.6) between AAS-exposed and unexposed weightlifters. Compared with unexposed weightlifters, AAS-exposed weightlifters demonstrated thicker interventricular septum (11.2±2.4 vs. 9.2±1.3 mm, p<0.001), thicker left ventricular posterior wall dimension (10.1±2.1 vs. 8.9±1.3 mm, p<0.001), and higher left ventricular mass index (99.7±25.4 vs. 78.4±12.1 g/



m2, p<0.001). Both left ventricular EF and left ventricular GLS were decreased in AAS-exposed weightlifters compared with unexposed weightlifters (49±9 vs. 53±6%, p=0.02, and -15.6±2.6 vs. -18.3±2.1%, p<0.001) (figure).

Conclusion: AAS use in male weightlifters was associated with increased left ventricular mass and impaired left ventricular systolic function. Our results suggest considerable adverse cardiac effects of AAS use, but the results need confirmation in prospective observational trials.

P3719 Myocardial injury during TAVI with self-expanding prosthesis is not associated with patient-prosthesis features, hemodynamics or clinical outcome

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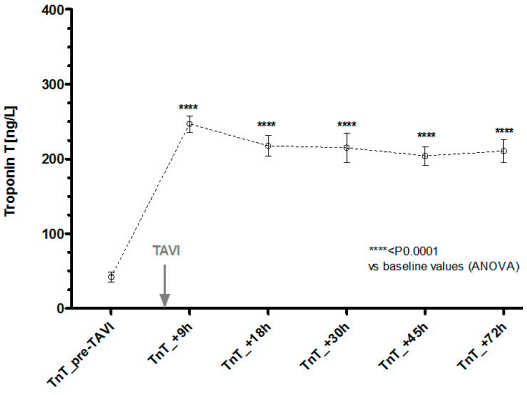
Background: Transcatheter aortic valve implantation (TAVI) has been associated with increases in markers of myocardial injury but underlying mechanisms as well as relevance for prosthesis hemodynamics, cardiac function and clinical outcome remain unclear.

Purpose: To study the trajectory of high-sensitivity troponin T (hs-TnT) during TAVI and elucidate putative associations with demographics, anatomical and procedural features, as well as clinical and echocardiographic outcome.

Methods: This prospective real-world registry study included all patients (n=275) undergoing transfemoral TAVI using a self-expanding or balloon-mounted system at a large tertiary university hospital over the most recent three-year period. Plasma levels of hs-TnT (reference level 0-14 ng/l) at 24 hours (h) before TAVI and at 9h, 18h, 30h, 42h and 72h after TAVI were analyzed. Patients with ongoing myocardial ischemia and acute coronary syndrome were excluded. We studied the association between hs-TnT values and patient characteristics, echocardiographic and CT findings at baseline as well as procedural features including the use of pre- and postdilatation. Moreover, we studied the association between hs-TnT and and echocardiography and clinical outcome at 1 year after TAVI.

Results: In this real-world TAVI cohort (median age 83.2±0.2 years; 48.7% women; 5.2±0.2 comorbidities; eGFR 58.0±6.0 ml/min/1.73m^2; mean±standard error), 100% of patients exhibited significant elevations of hs-TnT at approximately 9-fold (207.0±11.0) compared to baseline (23±0.2 ng/L, median±SE). Peak



hs-TnT values were reached at 9 h post-TAVI (207±11 ng/L) with subsequent gradual decline (FIGURe). Myocardial injury was confirmed by elevated creatin kinase (CK) and CKMB isozyme. No significant association was found between peak hs-TnT, delta hs-TnT (peak minus baseline values) or area under the curve (AUC) of hs-TnT on the one hand, and patient demographics including renal dysfunction, comorbidity, age and gender on the other side. Moreover, no significant association between hs-TnT and anatomical features, prosthesis sizing, or use of pre- and postdilatation was found. No association between hs-TnT during TAVI and NYHA functional class, transvalvular pressure gradient, cardiac function or survival at 1 year was found. In subjects with at least one year of follow-up after TAVI (n=138), NYHA functional class (1.7 vs 2.7) and NT-proBNP plasma levels (1126±316 vs 1581±563 ng/L) were significantly lower compared to pre-TAVI.

Conclusions: Modest transient elevations of hs-TnT occur in all patients undergoing TAVI and are consistent with subtle myocardial injury. The lack of significant association between the extent of myocardial injury during TAVI and clinical and hemodynamic outcome as well as all-cause mortality is reassuring for current real-world practice.

P3516 Sex differences in cardiac function and muscular dystrophy in lamin A/C genotype positive family members

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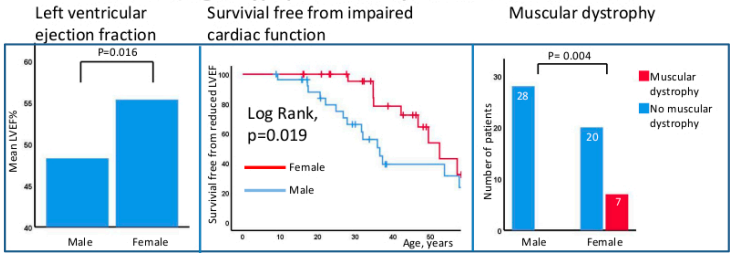
Background: Lamin A/C dilated cardiomyopathy is a highly penetrant inheritable cardiomyopathy with some patients developing muscluar

55 lamin A/C genotype positive family members´ sex differences.



dystrophy. Studies have indicated higher morbidity and mortality in men compared to women with lamin A/C.

Purpose: To explore sex differences in cardiac function, arrhythmias and muscular dystrophy in lamin A/C genotype positive family members of lamin A/C probands.

Methods: We included consecutive lamin A/C genotype positive family members recruited for cardiological evalutation based on the identification of lamin A/C genotype by cascade genetic screening. Cardiac function was assessed by echocardiography. Impaired cardiac function was defined according to guidelines as left ventricular ejection fraction (LVEF) < 52% in men, <54% in women. Presence of AV-block, atrial fibrillation and ventricular arrhythmias were evaluated by12-lead ECG, Holter monitoring, and interrogation of cardiac implantable electronic devices. Presence of muscular dystrophy was assessed retrospectively from medical records, and defined as present or not based on description of typical symptoms and/or findings on neurological exam.

Results: We included 55 lamin A/C genotype positive family members (age 35±15 years, 49% female). Men were younger at time of evaluation (31±15years vs. 40±14 years, p=0.047). Despite lower age, men had significantly lower LVEF (48±12% vs. 55±9%, p=0.016) (figure left panel), and showed worse survival free from impaired cardiac function compared to women (log rank p=0.019) (figure, mid panel). Male sex was a marker for impaired cardiac function when adjusted for age (adjusted OR 5.3[95%CI;1.5-18.8]) . Women had higher prevalence of muscular dystrophy compared to men (35% vs. 0%, p=0.004) (figure right panel). We observed no sex related differences for AV-block, atrial fibrillation, nor ventricular arrhythmias.

Conclusions: Male lamin A/C genotype family members had earlier penetrance and more frequently impaired cardiac function compared to women. AV-block and arrhythmic disease did not differ. Muscular dystrophy was more frequent in women. These findings indicate sex differences in the phenotypical expression of lamin A/C disease.

P860 Adding clinical risk scores to troponin-based rule-out algorithms improves identification of patients at high risk for coronary revascularization within 6 weeks: the WESTCOR study

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Background: The ESC 0/3-h and High-STEACS study algorithms using high-sensitive troponin assays have proven effective in ruling out NSTEMI, but the safety of out-of-hospital follow-up of ruled out patients is disputable. Clinical risk scores may help to identify patients who develop major adverse cardiac events (MACE) defined as NSTEMI, death or coronary lesions in need of acute or elective revascularization within six weeks after admittance.

Purpose: Assess the ability of the ESC and High-STEACS study algorithms alone and in combination with clinical risk scores to identify MACE in unselected patients presenting with chest pain.

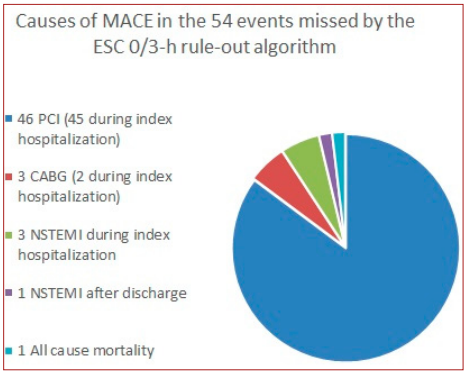
Methods: 985 patients (mean 63 years, 61% male) with suspected NSTE-ACS were consecutively included from Sept. 2015 to Feb. 2017. Serum samples were collected at 0, 3 and 8-12 hours and hs-cTnT and hs-cTnI were measured. The final diagnosis was adjudicated by two independent cardiologists. The troponin-based algorithms where compared to nine clinical risk

		True pos.	True neg.	False pos.	False neg.	NPV	PPV	Sens.	Spes.	Prop. low-risk	AUC
Troponin-based algorithms, end-point NSTEMI	ESC 0/3h TnT	118	628	196	3	99.5	37.6	97.5	76.2	66.8	0.87
	High-STEACS TnI	118	715	109	3	99.6	52.0	97.5	86.8	76.0	0.92
Troponin-based algorithms, end-point MACE	ESC 0/3h TnT	143	577	171	54	91.4	45.5	72.6	77.1	66.8	0.75
	High-STEACS TnI	130	651	97	67	90.7	57.3	66.0	87.0	76.0	0.77
Troponin-based algorithms combined with HEART score, endpoint MACE	ESC 0/3h HEART 3	185	414	334	12	97.2	35.7	94.1	55.4	44.6	0.85
	High-STEACS HEART 3	186	411	337	11	97.4	35.6	94.7	55.0	44.7	0.85

scores, HEART, CARE, GRACE, T-MACS, TIMI, EDACS, sEDACS, Goldman and Geleijnse.

Results: The prevalence of NSTEMI during index hospitalization was 13%. The ESC 0/3-h and High-STEACS algorithms missed 3 events of NSTEMI with excellent NPV of 99.5 and 99.6. Rule-out patients with normal ECGs, GRACE score <140 and no residual pain had a prevalence of MACE within 6 weeks of 9% using both algorithms. The most frequent event was non-acute revascularization due to unstable angina pectoris. Three of ten clinical risk scores had higher accuracy than the ESC 0/3-h algorithm for identification of MACE: HEART (AUC 0.84), CARE (AUC 0.79) and T-MACS (AUC 0.76). Combining the ESC 0/3-h rule-out algorithm and HEART=3 had the best AUC of 0.85, missing only 12 (3%) MACE.

Conclusion: The ESC 0/3-h and High-STEACS algorithms identify almost all patients with low risk of NSTEMI, who are candidates for none or out-of-hospital follow-up. However, 9% of ruled out patients have MACE within 6 weeks. The combination of ESC algorithm and clinical risk scores markedly reduce the number of ruled out patients with MACE.



P2562 Changes in the electrocardiographic / mechanical relation may explain the low risk of arrhythmia during moderate hypothermia

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Introduction: Hypothermia is therapeutically used after cardiac arrest. The moderate hypothermia alters cardiac function, with reduced heart rate (HR), prolonged systolic duration and increased QT interval. The risk of arrhythmia increases with prolonged QT-interval, but clinical studies have not been able to demonstrate an increase of arrhythmic events during moderate hypothermia. The mechanism of this is not thoroughly described, but the concurrent increase in mechanical systolic duration may play a part of the explanation.

Purpose: QT prolongation and increased electromechanical window (EMW) negativity; the duration of left ventricle mechanical systole relatively to the duration of the electrical systole, are associated with arrhythmia. We hypothesized that moderate hypothermia would increase ECG intervals and systolic duration without an increase in EMW negativity.

Methods: In an open-chest porcine model (n=10), 2D echocardiography measurements and Doppler recordings were performed with concurrent 3-lead ECG registrations during normothermia (38°C) and moderate hypothermia (33°C) at spontaneous HR. Diastolic and systolic durations were assessed by valve opening to valve closure and Doppler assessed ejection time (ET). Isovolumetric contraction time (IVCT) and EMW, were measured. Systolic function was assessed by ejection fraction (EF), stroke volume (SV) and systolic velocity (s'). Results are presented as means ± SD. Two-sided T-test was used for comparison and P-value < 0.05 was considered significant.

Results: Moderate hypothermia reduced HR from 91±9 to 82±7 beats/min (p<0.0001) and increased QT and QT-corrected (QTc) intervals, the latter from 484±52 to 555±50 ms (p <0.0001). Systolic duration increased as ET was prolonged from 293±15 to 397±39 ms (p<0.0001). There was a reduction in systolic velocity (s') (p=0.003) but a non-significant reduction in EF and SV. EMW changed from a negative to a positive value, -49±57 to 9±53 ms (p=0.017) during moderate hypothermia.

Conclusion: Moderate hypothermia increased the QTc-interval but the mechanical systolic duration was even more prolongated. The EMW became positive demonstrating that the mechanical systole outlasted the electrical systole. As less EMW negativity is considered to be protective regarding arrhythmia, these findings may explain why arrhythmia is not frequently occurring during moderate hypothermia.

P1531 The association between plasma choline and acute myocardial infarction is modified by potential markers of endogenous PPAR activation

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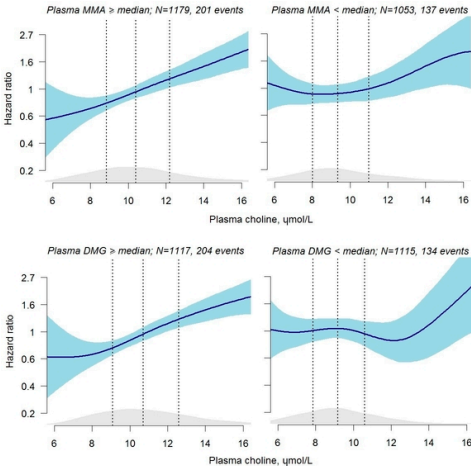

Background: Choline is related to lipid handling and higher plasma concentrations have been associated with an adverse cardiovascular risk profile. However, previous studies have suggested that the relationship between plasma free choline and later cardiovascular events may differ according to patient phenotypes.

Purpose: To explore the risk association between plasma choline and later acute myocardial infarction (AMI) according to plasma methylmalonic acid (MMA) or dimethylglycine (DMG). The latter two metabolites are suggested markers of endogenous activation of perixosome proliferator-activated receptors (PPARs), which are nuclear receptor proteins involved in lipid metabolism.

Methods: Risk relationships were explored by Cox regression among 2232 patients evaluated for suspected stable angina pectoris in the overall population and according to median plasma MMA and DMG.

Results: Baseline plasma choline was related to several cardiovascular risk factors (Table 1). After median follow-up of 7.3 years, 338 patients were reported with at least one incident AMI. In the overall population, the age and gender adjusted HR (95% CI) for each increment of 1 SD log-transformed plasma choline and AMI was 1.21 (1.08-1.35), P=0.001, and the association persisted in multivariate analyses.

In patients with plasma MMA or DMG=median, the HRs (95% CIs) were 1.33 (1.16-1.54) and 1.38 (1.20-1.58), respectively, both P<0.0001; however no significant relationships were observed between plasma choline and later AMI among patients with either plasma MMA or DMG < median (P interaction <0.008) (figure 1).

	Quartile 1	Quartile 4	P for trend
Age, years	58 (52-66)	66 (58-73)	<0.0001
Smoking, n (%)	212 (37.9)	153 (27.9)	<0.0001
Diabetes, n (%)	61 (10.9)	85 (15.5)	0.12
Previous acute myocardial infarction, n (%)	200 (35.7)	238 (43.4)	<0.0001
Estimated glomerular filtration rate, mL/min/1.73m2	96 (87-104)	79 (63-92)	<0.0001
Serum hs-troponin T, ng/L	4 (3-8)	9 (4-17)	0.0002
Serum triglycerides, mmol/L	1.35 (1.00-2.03)	1.60 (1.16-2.25)	<0.0001
Serum apolipoprotein A1, mg/L	1.29 (1.12-1.51)	1.32 (1.17-1.53)	0.01
Statin therapy, n (%)	384 (68.6)	435 (79.4)	0.01

Baseline characteristics according to plasma choline quartiles.

Conclusion: Among patients with stable angina, plasma choline was related to increased long-term AMI risk among patients with higher plasma MMA or DMG only. This finding potentially reflects increased risk conferred by choline during concomitant endogenous PPAR activation.

P2647 Impact of hypertension on extent of non-obstructive coronary artery disease (The NORIC registry)

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Background: In non-obstructive coronary artery disease (CAD), increasing extent of disease is associated with a worse prognosis. Statin therapy has been suggested to improve the prognosis. Whether hypertension, a modifiable CV risk factor, affects the extent of non-obstructive CAD in patients with stable angina is less explored.

Purpose: To assess the association between hypertension and extent of non-obstructive coronary artery disease.

Methods: We identified 1117 patients (mean age 62±10 years, 48% women) from the Norwegian Registry for Invasive Coronary angiography (NORIC). All subjects had stable angina and non-obstructive CAD defined as 1-49% stenosis in any coronary artery segment by coronary computed tomography angiography (CCTA). The extent of non-obstructive CAD was assessed as coronary artery segment involvement score (SIS) on CCTA. Extensive non-obstructive CAD was defined as SIS=4.

Results: Hypertension was present in 44% and patients with hypertension were older with a higher prevalence of diabetes, obesity, smoking and statin therapy (all p<0.05). Coronary artery SIS and calcium score were higher in patients with hypertension compared to those without hypertension, (3.1±2.0 vs. 2.6±1.7, p<0.001 and 41(116) vs. 32(91) HU, p<0.05), respectively. There was no significant sex difference in the prevalence of hypertension. In univariable analysis, hypertension, age, calcium score and statin treatment were significantly associated with extensive non-obstructive CAD (Table). Hypertension remained a strong, independent predictor of extensive non-obstructive CAD after adjusting for other known covariables (Table).

	Univariable analysis			Multivariable analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Hypertension	1.57	1.21-2.04	0.001	1.47	1.03-2.10	0.035
Age	1.06	1.05-1.08	<0.001	1.04	1.01-1.06	0.001
Calcium score	1.02	1.01-1.02	<0.001	1.01	1.01-1.02	<0.001
Statin treatment	1.34	1.03-1.75	0.029	1.20	0.83-1.70	0.341
Smoking	1.33	1.00-1.77	0.052	1.24	0.86-1.78	0.251
Diabetes mellitus	1.34	0.86-2.12	0.191	1.10	0.57-2.09	0.781
Obesity	1.03	0.76-1.41	0.839	1.19	0.79-1.80	0.425

Covariables of extensive non-obstructive CAD in univariable and multivariable logistic regression analysis.

Conclusions: Hypertension is associated with extensive non-obstructive CAD in patients with stable angina, suggesting that early and aggressive antihypertensive treatment may impact disease progression.

P769 Quality of life in outpatients with heart failure in relation to mortality and admissions for heart failure

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Studies report relation between quality of life and outcome. However, less is known about how various aspects of quality of life relates to mortality and admissions for heart failure.

Method: Mortality was examined in 7001 patients with completed Minnesota Living with Heart Failure Questionnaire (MLWHFQ) at the first visit to specialised hospital outpatient clinics included in our registry. A subset of 4264 patients with a second MLWHFQ at a late follow-up visit was assessed for the number of admissions and days in hospital for reason of heart failure during a six months period prior to the late visit.

Results: In multivariate Cox proportional hazard regression model for time to death after the first visit with a median 19 months follow-up and 1001 deaths, the MLWHFQ score for the subset of the "physical domain" (question 2 to 9) was a significant independent predictor for mortality (P=0.002) adjusted for gender, NYHA-class, blood pressure, s-sodium, stroke, obstructive lung disease, eGFR, anemia, age, daily dose diuretic, and ischemic cause for heart failure. The total MLWHFQ score and the Minnesota "emotional domain" (question 17-21) were not significant variables when the MLWHFQ "physical domain" was entered in the analysis.

The number of admissions for heart failure and the number of days in hospital for these admissions in a six months period prior to the late visit were analysed by linear regression for related variables. The total MLWHFQ score at the late visit was highly significant for the number of admissions in the six months period (p<0.001) adjusted for the daily

dose diuretic, NYHA functional class and proBNP. The MLWHFQ "physical domain" and the MLWHFQ "emotional domain" were not significant variables when the total score was entered. The number of days in hospital was related to the daily dose diuretic, NYHA functional class, proBNP, and in addition anaemia at the late visit again with the MLWHFQ total score being a significant predictor (=0.001)

Conclusions: Disease specific quality of life measured with MLWHFQ "physical domain" was a highly significant predictor for mortality after the first visit. The late total MLWHFQ score was a better predictor for heart failure related admissions and days in hospital than the subset domains in multivariate analysis.

	Model 1	Model 2	Model 3
		B (95% CI)	
GLS (n=2395)	0.17 (-0.07 to 0.42)	-0.04 (-0.28 to 0.20)	-0.44 (-0.70 to -0.18)
LVEF (n=2383)	0.01 (-0.52 to 0.54)	0.21 (-0.31 to 0.73)	0.72 (0.14 to 1.29)
LVMI (n=2371)	2.00 (0.32 to 3.68)	-0.37 (-1.98 to 1.24)	-0.42 (-2.16 to 1.33)
		OR (95% CI)	
GLS (n=2395)	1.35 (0.98 to 1.87)	1.28 (0.92 to 1.78)	0.81 (0.56 to 1.17)
LVEF (n=2383)	1.04 (0.75 to 1.44)	0.88 (0.62 to 1.24)	0.73 (0.50 to 1.07)
LVMI (n=2371)	1.27 (0.91 to 1.76)	1.12 (0.79 to 1.57)	1.11 (0.75 to 1.64)

Linear regression models constructed on continuous levels of GLS, LVMI and LVEF. Logistic regression models constructed on the upper sex specific deciles of GLS and LVMI, and on the lower sex specific decile of LVEF. GDF-15, hs-cTnT and NT-proBNP were all transformed by the natural logarithm. Model 1, unadjusted. Model 2, adjusted for sex, age and study site. Model 3, adjusted for sex, age, study site, BMI, eGFR, total and HDL cholesterol, CRP, higher education, hypertension, diabetes mellitus, statin use, current smoking, alcohol consumption, hs-cTnT and NT-proBNP.

Associations between GDF-15 and indices of left ventricular structure and function

P3433 Growth differentiation factor 15 predicts subclinical left ventricular dysfunction: Data from the Akershus Cardiac Examination 1950 Study

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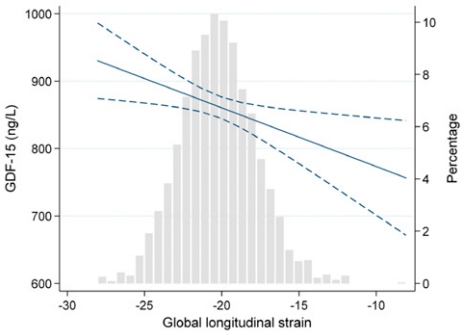
Background: Growth differentiation factor 15 (GDF-15) is upregulated in response to both acute and chronic cardiac injury, and concentrations of GDF-15 are increased in acute myocardial infarction and acute heart failure. Associations between GDF-15, left ventricular structure and preclinical stages of left ventricular dysfunction in the general population remain unclear.

Methods: We measured GDF-15 in 1237 women and 1158 men participating in the prospective observational Akershus Cardiac Examination (ACE) 1950 Study, which included community dwellers aged 63-65 residing in Akershus county, Norway. All study participants were free from known coronary heart disease and underwent extensive cardiovascular phenotyping at baseline, including detailed echocardiography. Regression models were constructed on global longitudinal strain (GLS), left ventricular mass index (LVMI), and left ventricular ejection fraction (LVEF), and adjusted for demographics, established cardiovascular risk factors, hs-cTnT and NT-proBNP.

Results: Concentrations of GDF-15 were measurable in 98.1% of study participants, and were positively associated with male sex, age, BMI, current smoking, diabetes mellitus, as well as concentrations C-reactive protein, hs-cTnT and NT-proBNP. Higher education, alcohol consumption, eGFR and concentrations of total cholesterol were all associated with lower concentrations of GDF-15. Concentrations of lnGDF-15 were significantly associated with GLS (B -0.44 [95% CI -0.70 to -0.18]; Figure) and LVEF (B 0.72 [95% CI 0.14-1.29]), but not LVMI (Table).

Conclusion: Concentrations of GDF-15 are inversely associated with GLS, a highly sensitive index of subclinical myocardial dysfunction. In healthy subjects free from known cardiovascular disease, GDF-15 appears protective and promotes beneficial cardiac function.



P6367 Predictors and covariables of incident hypertension in mid-life: the Hordaland Health Study

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Background: Different blood pressure (BP) development in midlife have been described in women and men. Less is known about factors associated with incident hypertension in this age group.

Purpose: To identify predictors and covariables of incident hypertension in women and men in their forties.

Methods: 2936 women (60%) and men born 1950-51 who participated in the community-based Hordaland Health Study both in 1992-93 (baseline, mean age 42±0.7 years) and in 1997-99 and were normotensive at baseline were included. Hypertension was defined as use of antihypertensive medication and/or systolic BP = 140 mmHg and/or diastolic BP = 90 mmHg. High-normal BP was defined as systolic BP 130-139 mmHg and/or diastolic BP 85-89 mmHg following European guidelines. Predictors and covariables of incident hypertension were identified in logistic regression analyses and reported as odds ratio (OR) and 95% confidence intervals (CI).

Results: 348 (12%) subjects developed hypertension during an average of 5.9 years follow-up. Incident hypertension was more common among men than women (14 % vs. 10%, p=0.005). In univariate analyses, incident hypertension was positively associated with high normal BP and higher body mass index (BMI), serum total cholesterol and serum triglycerides at baseline, as well as with larger increase in BMI and serum triglycerides during follow-up (all p<0.05). In multivariable analysis, incident hypertension was associated with high-normal BP and higher serum triglycerides at baseline, and larger increase in BMI during follow-up, while the association with sex became non-significant (Table).

	Multivariable analysis	
Variable	OR (95 % CI)	P-value
High-normal BP	4.87 (3.82-6.20)	<0.001
Δ BMI at follow up (kg/m^2)	1.33 (1.24-1.42)	<0.001
Ln serum triglycerides (mmol/L)	1.41 (1.14-1.75)	0.002

Conclusion: In the community-based Hordaland Health Study, a larger proportion of men than women developed hypertension in midlife. However, this sex difference in incidence was explained by differences in prevalence of high-normal BP at baseline and metabolic factors.

P6180 Septal negative work correlates inversely with septal scar in patients referred for cardiac resynchronization therapy

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Background: Myocardial scar is frequently present in patients with heart failure and left bundle branch block (LBBB), and associated with reduced response to cardiac resynchronization therapy (CRT). Furthermore, LBBB may be associated with markedly reduced strain, work, metabolism and perfusion in septum, even without septal ischemia. Therefore, it may be challenging to identify scar by functional imaging methods.

Purpose: To investigate the ability of advanced echocardiographic and nuclear imaging techniques to detect septal and left ventricular (LV) lateral wall scar in patients referred for CRT, compared to late gadolinium enhancement (LGE) cardiac magnetic resonance.

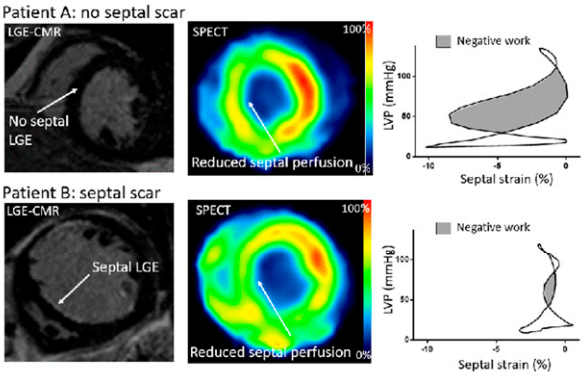
Methods: Scar was quantified as percentage LGE in five septal and five LV lateral wall segments of 131 patients (age 66±10, 66% male, QRS-width 164±17ms) referred for CRT, 92% with LBBB. Longitudinal strain was assessed by speckle tracking echocardiography in 130 patients (652 septal and 631 LV lateral wall segments). Myocardial work was calculated by LV pressure-strain analysis. Systolic shortening defined positive work, while systolic lengthening defined negative work. Glucose metabolism was assessed by 18F-fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) in 52 patients (260 septal and 260 LV lateral wall segments). Perfusion was assessed in 46 patients (230 septal and 230 LV lateral wall segments) by either 13N-ammonia

PET (n=32) or Single Photon Emission Computed Tomography (SPECT) (n=14). Metabolism and perfusion were reported as percentages of the segment with maximum tracer uptake. We evaluated parameter relationship to scar with Spearman correlation (rs) and regression analysis.

Results: LGE was present in 198 septal (30%) and 136 LV lateral wall (21%) segments. In a multivariate regression model with negative work, metabolism, perfusion and peak strain, only the first three parameters showed a significant association with LGE percent in septum ($p<0.001$, $p=0.022$ and $p<0.001$, respectively), while peak strain did not ($p=0.270$). Negative work in septum correlated inversely with percentage septal LGE-uptake ($rs=-0.33$): increasing amount of scar was associated with less negative work (figure).

In the LV lateral wall, however, negative work did not shown a significant association with percentage LGE in univariate regression analysis ($p=0.109$). In a multivariate regression model positive work, metabolism and perfusion correlated with percentage LGE ($p=0.049$, $p=0.008$ and $p<0.001$), while peak strain did not ($p=0.607$).

Conclusions: Septal negative work correlates inversely with septal scar in patients referred for CRT. This finding is probably linked to LBBB, and may be explained by increased stiffness of scar tissue. Myocardial work, but not peak strain, reflects scar in the LV lateral wall. Future studies should explore the assessment of scar in the complete LV and how this relates to CRT response.



P5288 Slice position vulnerability in the basal and apical parts for right ventricular circumferential strain measurement with feature tracking cardiac magnetic resonance

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Background: Strain is a more sensitive and precise parameter than ejection fraction (EF) for detection and characterization of subclinical left ventricular (LV) dysfunction and remodeling. Similar relationship is expected for right ventricle (RV); however, RV functional parameters are less validated. Feature tracking strain analysis based on standard cardiac magnetic resonance (CMR) cine imaging is available for both ventricles. We experience a large slice-to-slice variation for RV global circumferential strain (GCS), possibly making the parameter vulnerable to minute position changes.

Purpose: To evaluate slice-to-slice differences in RV GCS for identification of the least variation region in a patient group without regional RV disease, in order to achieve a robust method for measurement.

Hypothesis: The slice-to-slice difference in peak GCS is lower in the mid-ventricular part of the RV than in the basal and apical parts.

Methods: 50 patients 6-72 months after pulmonary embolism without other major cardiopulmonary disease were included; mean age 60 years (range: 18-75 years); 68% men.

Standard 2D cine CMR was obtained in longitudinal planes and in 10-12 consecutive 10 mm short axis planes for complete coverage of the RV. RV free wall and the inner contour of the septum were manually segmented on every end-diastolic and end-systolic slice from the pulmonary valve to the apex for feature tracking strain analysis.

Peak RV GCS for every short axis slice and GCS difference (absolute percentage points) between adjacent slices were calculated. RV EF and peak RV GLS from the 4-chamber image were measured for correlation to RV GCS. Wilcoxon signed rank test and Pearson correlation were performed. Confidence intervals of means are based on 1000 bootstrap samples.

Results: RV EF was 46.6% (95%CI: 44.3; 48.8), RV peak GLS was -17.6% (95%CI: -18.6; -16.6). RV mid-ventricular GCS was -10.9% (95%CI: -12.0; -9.9). RV peak GCS slice-to-slice difference

was 6.8 absolute percentage points (95%CI: 6.0; 7.6) in the basal part, 2.7 (95%CI: 2.4; 3.0) in the mid-ventricular part and 4.6 (95%CI: 3.9; 5.3) apically. Difference was significantly lower in mid-ventricular ($p<0.001$) compared to both basal and apical.

RV EF correlated to RV peak GLS (r: -0.397, $p=0.004$) and mid-ventricular peak GCS (r: -0.356, $p=0.01$) but not to basal or apical peak GCS. RV peak GLS correlated to basal and mid-ventricular peak GCS (r: 0.313, $p=0.03$ and r: 0.301, $p=0.03$ respectively) but not to apical peak GCS.

Conclusion: Slice-to-slice difference in RV peak GCS was significantly lower in the mid-ventricular region. Large differences in the basal and apical parts indicate that measurements largely depend on slice positioning.

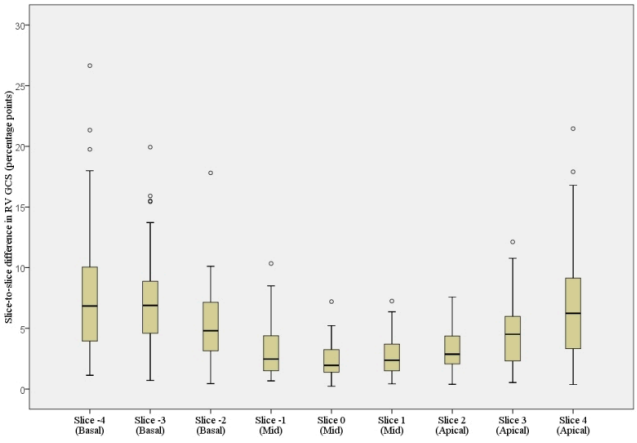

Figure 1 shows slice-to-slice difference (expressed in absolute percentage points) in right ventricular peak GCS.

P4487 Inhibition of aortic valve calcification by SNF472 in vitro

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Background: Calcific aortic valve disease is the 2nd most frequent cause of open heart surgery. The valve interstitial cells (VIC) are crucial for calcification. SNF472 (a derivative of phytic acid) is a calcification inhibitor currently in clinical development for the treatment of cardiovascular calcification (Phase 2 CaLIPSO trial, EudraCT 2016-002834-59). SNF472 has been shown to inhibit vascular calcification in several preclinical models.

Purpose: 1. Establish a new model of calcification in cultured human VIC; 2. Investigate whether SNF472 would inhibit calcification in this model, and 3. Study if SNF472 might inhibit ongoing calcification processes.

Methods: Healthy and calcified aortic valves were obtained from heart transplant recipients and patients undergoing aortic valve replacement due to calcific valve disease, respectively. VIC were isolated and seeded in basic growth medium, osteogenic differentiation medium (Osteodiff) alone, and with addition of different concentrations of SNF472. The following series of studies were performed: 1. VIC from healthy and calcified valves were cultured for three weeks with Osteodiff; 2. VIC from calcified valves were cultured for 3 weeks in Osteodiff media with 0, 1, 3, 10, 30, or 100 µM SNF472; 3. VIC from calcified valves were cultured for 3 weeks in Osteodiff media in total, but after 1 or 2 weeks 30 or 100 µM SNF472 was added to the cultures (n=8). Calcification was visualized by Alzarin Red staining and quantified by spectrophotometry. Statistics analysis was performed nonparametric One-Way ANOVA (Friedman and Kruskal–Wallis tests) with Dunn's post-test.

Results: Calcification was found to be 30% stronger in cultures of VIC from calcified valves as compared to cultured VIC from healthy valves ($p=0.03$). SNF472 successfully inhibited VIC calcification in a dose-dependent manner. SNF472 concentrations of 1, and 3 µM inhibited calcification by 7 % (not significant) and 66 % ($p=0.08$) respectively. Concentrations of 10, 30, and 100 µM completely inhibited calcification. 30 and 100 µM of SNF472 added after 1 week reduced ongoing calcification by 84% ($p<0.01$) and 100% ($p<0.01$) respectively. When given after 2 weeks of ongoing calcification non-significant inhibition was still observed (21 and 30%, respectively).

Conclusions: VIC from calcified valves have a more pro-calcification phenotype than VIC from healthy valves. SNF472 is able to inhibit the development VIC calcification in vitro. By early intervention SNF472 is also able to stop the progression of ongoing calcification. SNF472 shows to be a promising therapy to treat heart valve calcification.

P602 Septal function and viability determine response to cardiac resynchronization therapy

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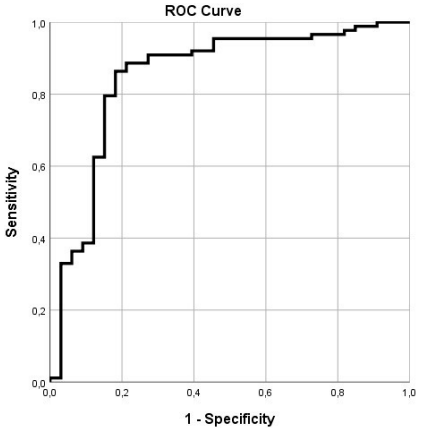
Introduction: Cardiac resynchronization therapy (CRT) has evolved as an important treatment in patients with symptomatic heart failure, reduced left ventricular (LV) ejection fraction and wide QRS. However, as one third of patients do not benefit from the therapy, there is need for better selection criteria. Previous studies have shown an association between recovery of septal function and response to CRT.

Purpose: To test the hypothesis that septal dysfunction in the absence of scar predicts response to CRT.

Methods: In 121 patients undergoing CRT implantation according to current European Society of Cardiology guidelines, we performed speckle-tracking echocardiography and estimated LV pressure non-invasively based on a method recently innovated in our lab. Pressure-strain analysis was used to calculate myocardial work. Septal dysfunction with asymmetric LV workload was calculated as the difference between LV lateral wall and septal work. Late gadolinium enhancement cardiac magnetic resonance imaging (LGE-CMR) was performed to assess septal scar. CRT response was defined as =15% reduction of LV end systolic volume by echocardiography at 6 months follow-up.

Results: Eighty-eight patients (73%) responded to CRT at 6 months follow-up. Multivariate logistic regression analysis including lateral-to-septal work difference, septal scar, QRS duration and QRS morphology found that only lateral-to-septal work difference and septal scar were significant predictors of CRT response (both $p<0.005$). Using logistic regression and receiver operating characteristic (ROC) curve analysis, we found that the combined approach of these two parameters identified CRT responders with a sensitivity of 86% and a specificity of 82%. The area under the curve (AUC) for CRT response prediction was 0.85 (95% CI: 0.76-0.94) (FIGURe). In comparison, the AUC value for QRS duration was 0.63 (95% CI: 0.52-0.75). Furthermore, for the subgroup of patients with QRS duration 120-150 ms (n=27), the AUC value for lateral-to-septal work difference in combination with septal scar was 0.90 (95% CI: 0.78-1.00).

Conclusions: A multimodality approach with strain echocardiography and LGE-CMR was able to detect CRT responders with high accuracy, also in the subset of patients with intermediate QRS duration. A dysfunctional but viable septum appears to be an ideal target for CRT.



P1224 Statin treatment in children with familial hypercholesterolemia in Scandinavia

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Introduction: New European guidelines recommend that patients with familial hypercholesterolemia (FH) should initiate treatment with statins at age 8-10 years. The number of children using statins has not yet been investigated. The aim of the present study was to describe the number of statin users <19 years of age in the Scandinavian countries: Sweden, Denmark and Norway.

Methods: In the Scandinavian countries, statins are only available by prescription, and there are national registries for the use of perscriptional drugs. In the present study, we assumed that the number of children using statins is equivalent to a positive FH diagnosis in these countries. Using the estimated frequency of FH of 1:250, we calculated the number of expected children with FH per year. Next, the percentage of all FH chil-

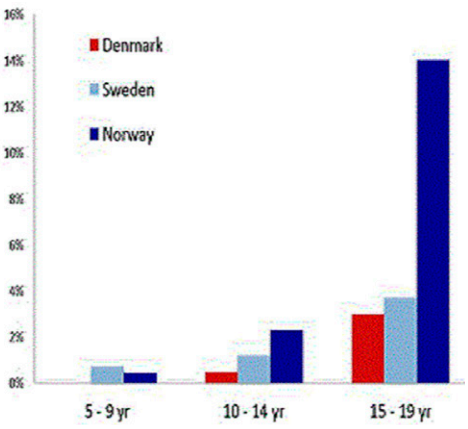
dren who were treated according to the national registries were calculated. We also calculated changes between 2006 and 2016.

Results: As shown in Table 1, 1086 children 5-19 years in Scandinavia used statins in 2016. In the ages 10-19 years, statins were more frequent used in Norwegian FH children than in children from Denmark and Sweden (figure 1). Nevertheless, the number of children aged 5-19 years using statins increased from about 2% to 4% between 2006 and 2016 in Sweden and Denmark (n=109 and n=136 respectively) and from about 5% to 10% in Norway (n=340).

Discussion: We observed a modest increase in statin users aged 5-19 years in the Scandinavian countries during a 10-year period. Nevertheless, our findings indicate that it will take decades to implement the current Statin-recommendation. Possible reasons for the difference in the degree of treatment between the countries will be discussed during the presentation, in particular with respect to genetic testing and cascade screening.

Conclusions: Despite increased statin use during the last years, there is still a severe undertreatment of children with FH in the Scandinavian countries.

Age (year)	Male, N (%)		Female, N (%)		Both Sexes N (%)	
5 - 9	36	(3)	30	(3)	67	(6)
10 - 14	158	(15)	127	(12)	294	(27)
15 - 19	327	(30)	395	(36)	725	(67)
0 - 19	521	(48)	552	(51)	1 086	(100)



P2500 The high-sensitivity cardiac troponin I and T response following strenuous activity is attenuated by smokeless tobacco: The North Sea Race Endurance Exercise Study (NEEDED) 2014

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Background: Use of snus, a smokeless oral tobacco product, is increasing among athletes and recreational exercisers in Scandinavia. Strenuous physical activity is associated with an acute increase in high-sensitivity cardiac troponins (hs-cTn) in healthy individuals. Current smoking is associated with lower baseline hs-cTn concentrations in current smokers in the general population, but whether tobacco affects the hs-cTn response to exercise remains unknown.

Methods: We measured serial cTnI and cTnT concentrations in 1002 healthy recreational athletes before, 3 and 24 h after a 91 km bicycle race. Self-reported snus habits were reported as: non-current (n=794) and current (n=118). The association between snus use and change in log hs-cTnI and hs-cTnT (differences between concentrations at baseline and 3 h (?3 h) and 24 h (?24 h)) were assessed by multivariable linear regression analysis.

Results: Current snus use was associated with lower cTnI (current users of snus vs non-current: median, 1.7 ng/l; interquartile range (IQR), 1.6-2.3 vs 2.0 ng/L; IQR 1.6-3.2; p=0.020) and cTnT (current users of snus vs non-current: median, 3.0 ng/L, IQR, 3.0-3.5 vs 3.0 ng/L, IQR 3.0-4.3; p=0.021) concentrations at baseline. Both in unadjusted and fully adjusted linear regression models, users of snus had significantly lower ?3 h and ?24 h cTnI and cTnT concentrations (Table).

Conclusion: The exercise-induced cTn response in healthy recreational cyclist is attenuated in users of smokeless tobacco compared to never users. These findings extend observations of lower hs-cTn concentrations in tobacco smokers in the general population.

Association between snus use and change in concentrations of hs-cTnI and hs-cTnT, (95% CI)

	Model 1	Model 2	Model 3	Model 4
ΔcTnI 3 h				
Current snus	-28% (-46% to -10%), p=0.003	-33% (-51% to -14%), p=0.001	-31% (-49% to -13%), p=0.001	-29% (-47% to -11%), p=0.002
ΔcTnI 24 h				
Current snus	-38% (-62% to -15%), p=0.002	-36% (-59% to -12%), p=0.003	-32% (-56% to -9%), p=0.007	-30% (-54% to -7%), p=0.010
ΔcTnT 3 h				
Current snus	-28% (-10% to -46%), p=0.003	-33% (-51% to -14%), p=0.001	-31% (-49% to -13%), p=0.001	-29% (-47% to -11%), p=0.002
ΔcTnT 24 h				
Current snus	-20% (-4% to -36%), p=0.015	-23% (-39% to -8%), p=0.004	-21% (-36% to -5%),p=0.009	-19% (-34% to -14%), p=0.013

Model 1 unadjusted; Model 2 adjusted for sex and age; Model 3 adjusted for Model 2 and systolic blood pressure, body mass index, low-density lipoprotein and estimated glomerular filtration rate; Model 4 adjusted for the same variables as in Model 3 but also race duration and resting heart rate

P6239 Late adverse effects of residual platinum concentrations on cardiac function in testicular cancer survivors: a 30-year follow-up study

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Background: Cisplatin-based chemotherapy (CBCT) is essential in the treatment of testicular cancer (TC), and platinum can be detected in TC survivors decades after cessation of treatment. CBCT has been implicated as a risk factor in cardiovascular morbidity and mortality.

Purpose: Our study aimed to assess the relationship between residual serum platinum concentrations and changes in cardiac function and morphology in TC survivors 30 years after CBCT.

Methods: Seventy TC survivors diagnosed and treated with CBCT (1980-1994) were recruited from the longitudinal Norwegian Cancer Study in Testicular Cancer Survivors. Serum platinum concentration was measured twenty years after CBCT. Patients were then allocated to either a high or low platinum concentration group. Echocardiography was performed in all subjects.

Results: The participants were on average 60±9 years old. There was a trend towards smaller left ventricular (LV) volumes in the high residual platinum concentration group (Table). No intergroup difference in cardiac function was found. Six (9%) participants had reduced EF (<52%) and 14 (20%) participants had reduced LV global longitudinal strain (> -18.0%), however, there was no intergroup difference. Neither cumulative cisplatin dose nor residual serum platinum concentration showed any correlation with LV or right ventricular functional parameters.

Conclusion: Our 30-year follow-up study of testicular cancer patients could not demonstrate impact on cardiac function caused by cumulative cisplatin dose or residual serum platinum concentrations.

	Low residual Pt concentration >85 ng/L (n=35)	High residual Pt concentration <85 ng/L (n=35)	p-value
Cumulative cisplatin dose, mg/m^2	680±249	814±271	<0.05
Residual Pt concentration, ng/L	44±22	136±44	<0.001
3D LV end-diastolic volume, ml/m^2	66±17	60±8	0.07
3D LV end-systolic volume, ml/m^2	29±15	24±5	0.08
3D ejection fraction, %	57±9	59±6	0.24
LV global longitudinal strain, %	- 19.2±3.3	- 20.0±2.0	0.26
LV global circumferential strain, %	- 21.1±4.2	- 22.1±1.8	0.30
E/e'	10.6±4.4	9.2±2.2	0.10
TAPSE, mm	2.2±0.4	2.3±0.4	0.22
RV fractional area change, %	40±7	41±7	0.67

Data are presented as mean±SD. The P-values were derived from the Student's t-test. LV, left ventricle; MV, mitral valve; Pt, platinum; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

P3681 Apparent sex differences in risk of life-threatening events in arrhythmogenic cardiomyopathy are related to exercise habits

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Background: Arrhythmogenic cardiomyopathy (AC) is an inheritable heart disease characterized by high risk of ventricular arrhythmias and exercise intolerance. Male sex is associated with higher risk of life-threatening events. However, this may be challenged by the fact that men exercise more than women.

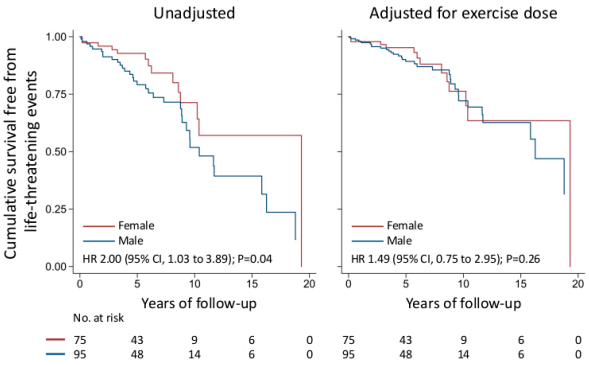
Purpose: To assess whether the sex differences in arrhythmic outcome in AC-patients are driven by sex differences in exercise exposure.

Methods: We included AC-patients diagnosed between 1997 and 2017 in a longitudinal cohort study. We assessed exercise habits during the preceding 3 years before inclusion, and exercise dose was expressed as metabolic equivalent hours per week (MET-hours/week). Life-threatening events were defined as sustained ventricular tachycardia, aborted cardiac arrest or appropriate therapy from an implantable cardioverter-defibrillator at the time of diagnosis and prospectively during follow-up.

Results: We included 170 AC-patients (52% probands, 44% female, age 41±16 years). Males had higher exercise doses than female patients (36 [IQR, 14 to 54] vs. 12 [IQR, 8 to 22] MET-hours/week; P<0.001). Fifty-seven patients (34%) had previous life-threatening events, and 45 (26%) had life-threatening events during 5.7 (IQR, 2.8 to 9.4) years of follow-up. Male sex seemed to be a marker of previous life-threatening events (OR 2.0 [95% CI, 1.0 to 3.8]; P<0.05), but not when adjusted for exercise dose (Adjusted OR 1.3 [95% CI, 0.6 to 2.7]; P=0.44). Male sex also seemed to be a predictor of life-threatening events during follow-up (HR 2.0 [95% CI 1.0 to 3.9]; P=0.04) (figure, left panel), but not when adjusted for exercise dose (Adjusted HR 1.5 [95% CI 0.8 to 3.0]; P=0.26) (figure, right panel).

Conclusions: Sex differences in arrhythmic risk in AC were attributable to higher exercise doses in male AC-patients. This highlights the importance of exercise assessment in these patients, and challenges the current opinion of male sex as a risk factor in itself. Risk stratification based on sex may underestimate the risk of physically active female AC-patients.

Kaplan Meier curves for life-threatening arrhythmic events in 170 AC patients stratified by sex. No sex differences in arrhythmic events were found when adjusting for exercise dose.



1175 Structural progression increases the risk of ventricular arrhythmias in patients with arrhythmogenic cardiomyopathy

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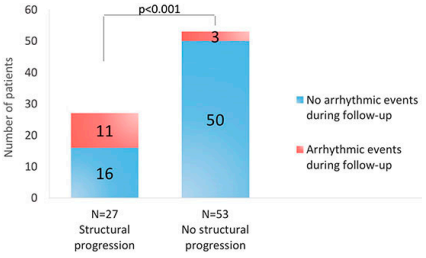
Background: Arrhythmogenic cardiomyopathy (AC) is an inheritable cardiomyopathy with incomplete penetrance, variable phenotype severity and poorly described disease progression. It is characterized by high risk of life-threatening ventricular arrhythmias and sudden cardiac death in young individuals. Risk stratification and selection of patients presenting without history of life-threatening arrhythmic events for cardioverter-defibrillator implantation in primary prevention remains challenging.

Purpose: We aimed to assess the impact of disease progression on arrhythmic outcomes in AC patients.

Methods: We included consecutive AC probands and mutation-positive family members with at least one complete follow-up evaluation. Echocardiographic and electrical parameters were defined according to the 2010 Revised Task Force criteria at inclusion and at last follow-up. Structural progression was defined as development of new echocardiographic diagnostic criteria. Electrical progression was defined as the development of new diagnostic depolarization, repolarization and/or premature ventricular complex count criteria during follow-up. Non-sustained ventricular tachycardia or ventricular tachycardia occurring during follow-up defined incident ventricular arrhythmic events.

Results: We included a total of 144 patients (48% female, 47% probands, 40±16 years old). At inclusion, 54 patients (37%) had a history of arrhythmic events, 30 patients (21%) had overt structural disease and 114 (79%) had no or minor structural disease. During 7.0 (IQR: 4.5 to 9.4) years of follow-up, 49 patients (43%) with no or minor structural disease at inclusion developed new structural criteria being defined as progressors. Among 80 participants with no or minor structural disease and no arrhythmic history at inclusion, a first arrhythmic event occurred in 14 (17%). The incidence of arrhythmic events was higher in progressors (11/27, 41%) than in non-progressors (3/53, 6%) (p<0.001) (figure). Structural progression was associated with higher risk of first arrhythmic events during follow-up when adjusted for sex, age at inclusion and follow-up duration, independent of electrical progression (7.6, 95% CI [1.5, 37.2], P=0.01).

Conclusion: Almost half of patients without overt structural cardiac disease at genetic diagnosis develop new structural criteria during 7 years follow-up and 17% experienced their first ventricular arrhythmic event. Structural progression was independently associated with ventricular arrhythmic events during follow-up. These findings highlight the increased risk of arrhythmias when structural abnormalities are detected. Their finding may initiate the evaluation for primary prevention cardioverter-defibrillator implantation.



P1238 Acute re-distribution of myocardial work by cardiac resynchronization therapy determines long-term remodelling of the left ventricle

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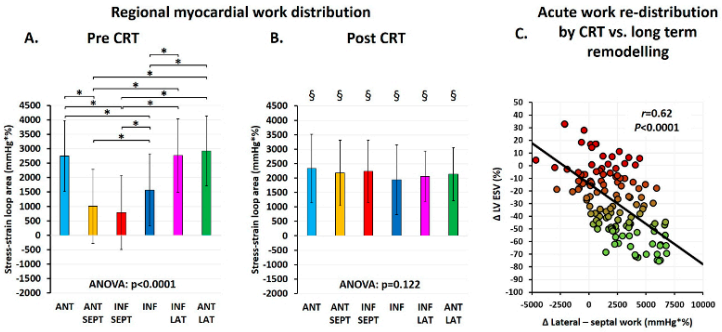
Background: In patients with dilated cardiomyopathy and left bundle branch block (LBBB), different regions of the left ventricle (LV) have been shown to perform different amounts of work. In this study, we investigate the acute impact of cardiac resynchronization therapy (CRT) on regional LV work distribution and its relation to long-term reverse-remodelling.

Methods: We recruited 130 heart failure patients, referred for CRT. Regional myocardial work was calculated from non-invasive echocardiographic segmental stress-strain-loop-area before and immediately after CRT. The magnitude of volumetric reverse-remodelling was determined from the change in LV end-systolic volume (ESV), 11±2 months after implantation. Characteristics of patients with the lowest and highest quartile of LV ESV reverse remodelling (? LV ESV < -9% and ? LV ESV > -48%) were compared.

Results: Before CRT, myocardial work showed significant differences among the walls of the LV (figure A). CRT caused an acute re-distribution of myocardial work, on average with most increase in the septum and most decrease laterally (all walls p<0.05) and lead to a homogeneous work distribution (figure B). The acute change in the difference between lateral and septal wall work (? lateral – septal work) correlated best and significantly with LV ESV reverse-remodelling



(r=0.62, p<0.0001). The smallest changes in work were seen in the patients with the least LV ESV reverse remodelling (figure C, red markers), while patients with the most LV ESV reverse remodelling showed the largest changes in work (figure C, green markers). In a multivariate-linear-regression-analysis, including pre-implant QRS duration, LVEF, LV EDV and GLS, the re-distribution of work remained as the strongest determinant of volumetric reverse-remodelling after CRT (r=0.63, p<0.0001).

Conclusions: The acute re-distribution of regional myocardial work between the septal and lateral wall of the left ventricle is the main determinant of long term reverse-remodelling after CRT-implantation. Our data suggest that modification of regional loading is the mode of action of CRT treatment.

P2458 Restricted left atrial motion as a result of atrial stiffening in patients with cardiac amyloidosis

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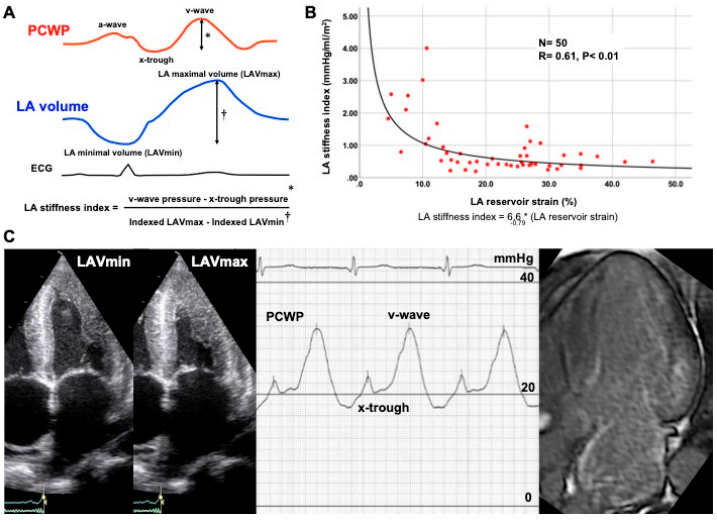
Background: Left atrial (LA) involvement of abnormal amyloid fibrils could induce LA dysfunction and stiffening in patients with cardiac amyloidosis (CA). Thus, the assessments of LA function and stiffness might be a potential approach to diagnose CA phenotype among patients with hypertrophied hearts.

Purpose: We sought to determine whether LA reservoir strain with speckle tracking echocardiography could be used a marker of LA stiffness in a derivation cohort. Furthermore, we tested to our hypothesis that LA reservoir strain could differentiate CA patients from hypertrophic cardiomyopathy (HCM) in an independent validation cohort.

Methods: In the derivation cohort, echocardiography was performed simultaneously with measurements of pulmonary capillary wedge pressure (PCWP) in 50 patients with suspected or established heart failure and relatively preserved left ventricular (LV) ejection fraction (56 ± 10%). LA maximum and minimum volume index, and reservoir strain were measured from apical four-chamber view. LA stiffness index was computed as a pressure rise from x-trough to v-wave divided by an increase from minimum to maximum indexed LA volume (Figure A). In an independent validation group, we studied a total of 33 biopsy-proved CA patients and 127 HCM patients (LV ejection fraction: 57 ± 11% vs. 66 ± 10%, P<0.01) in sinus rhythm on the date of comprehensive echocardiographic study. Among them, cardiac magnetic resonance imaging (CMR) could be evaluated in 17 CA patients and 98 HCM patients. Furthermore, right heart catheterization was performed with 12 CA patients and 12 HCM patients in the CMR group.

Results: The derivation cohort study found that there was a significant curvilinear correlation of LA reservoir strain to LA stiffness index (figure B). In the validation cohort, LA reservoir strain was reduced in patients with CA compared with HCM in all participants (11.6 ± 5.6% vs. 18.5 ± 6.9%, P<0.01), although there was no significant difference of LA maximal volume index between 2 groups (37 ± 16 ml/m2 vs. 37 ± 12 ml/m2, p=0.89). In the CMR group, the late gadolinium enhancement was observed in the LA wall in 16 patients with CA (94.1%) as shown in figure C. In contrast, the LA enhancement revealed only in 1 patient with HCM (1.0%). Among patients with invasive measures, LA stiffness index [median (interquartile range)] was higher in patients with CA than that in patients with HCM [1.1 (0.4-2.8) vs. 0.2 (0.1-0.6), P=0.01].

Conclusions: LA reservoir function was fairly limited in patients with CA compared with HCM. Restricted LA motion might be related to atrial amyloid deposits or fibrosis, which potentially provokes atrial chamber stiffening.



P3470 Comparative effectiveness and safety of non-vitamin K oral anticoagulants and warfarin in non-valvular atrial fibrillation - a cohort study in 3 Nordic countries

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Background: Non-vitamin K oral anticoagulants (NOACs) are an alternative to warfarin in the prevention of stroke in non-valvular atrial fibrillation (NVAF). Nordic countries have high quality of warfarin treatment, making them an especially suitable setting for assessing effectiveness and safety of NOACs against warfarin.

Purpose: The BEYOND Pooled (BEnefit of NOACs studY of nOn-valvular AF patieNts in NorDic countries) study compared risks of ischaemic or haemorrhagic stroke/systemic embolism (S/SE), and risk of bleeding with acute hospitalisation with an overnight stay (bleeding) in NVAF patients treated with apixaban, dabigatran or rivaroxaban, each compared with warfarin treatment.

Methods: A cohort study of treatment-naïve adult NVAF patients dispensed apixaban, dabigatran, rivaroxaban or warfarin was identified from 01 Jan 2013 to 31 Dec 2016. The population and study variables were identified from national registries in Denmark, Norway and Sweden. After 1:1 propensity score (PS) matching for each NOAC-warfarin comparison, individual-level data were pooled across the countries. Cox proportional-hazards regression was used to estimate adjusted hazard ratios (aHRs) of the endpoints.

Results: PS matched NOAC cohort sizes were: apixaban (55,696) dabigatran (28,526) and rivaroxaban (30,701), and the total follow-up in the PS-matched population was 291,171 years (mean 1.3 years). During the follow-up, 35,450 oral anticoagulation (OAC) patients had a S/SE and 38,620 OAC patients had bleeding. Adjusted HRs for the two endpoints are presented in the table. PH assumption has not been formally tested but cum incidence curves did not indicate substantial differences in the effects over time.

Conclusions: Relative to warfarin, apixaban and dabigatran were associated with lower rates of bleeding whereas rivaroxaban was associated with a higher rate. The three NOACs had comparable rates of stroke and systemic embolism relative to warfarin.

Endpoint	Apixaban vs Warfarin: aHR (95% CI)	Dabigatran vs Warfarin: aHR (95% CI)	Rivaroxaban vs Warfarin: aHR (95% CI)
Stroke/SE	0.93 (0.85-1.03)	0.89 (0.80-1.00)	0.97 (0.88-1.08)
Bleeding	0.72 (0.67-0.77)	0.87 (0.80-0.95)	1.12 (1.04-1.20)

Adjusted hazard ratios (aHR) of stroke/systemic embolism and bleeding for non-vitamin K oral anticoagulants versus warfarin.

P2766 Increased right ventricular burden in patients with chronic thromboembolic disease

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Introduction: Patients with chronic thromboembolic disease (CTED) have residual perfusion defects after pulmonary embolism (PE) but not increased pulmonary artery (PA) pressure. These patients suffer from functional limitation and have a higher risk of venous thromboembolism recurrence.

Purpose: In this study we wanted to explore if CTED patients had signs of increased PA pressure and right heart burden by echocardiography

Methods: Inclusion criteria were history of PE, age 18 - 75 years and PE diagnosed 6 – 72 months prior to inclusion. Patients with left ventricular systolic or diastolic heart failure, valvular disease, chronic pulmonary disease and chronic thromboembolic pulmonary hypertension were excluded. All patients underwent echocardiography with standard and novel methods and ventilation/perfusion (VQ)-scan. The echocardiographic examinations were blinded to the result of the VQ-scan. VQ-scan were analyzed according to the European Association of Nuclear Medicine-criteria, and deemed either positive or negative. Data are presented as mean ±SD or median ±IQR as appropriate. Independent sample t-test or Mann-Whitney U test was used

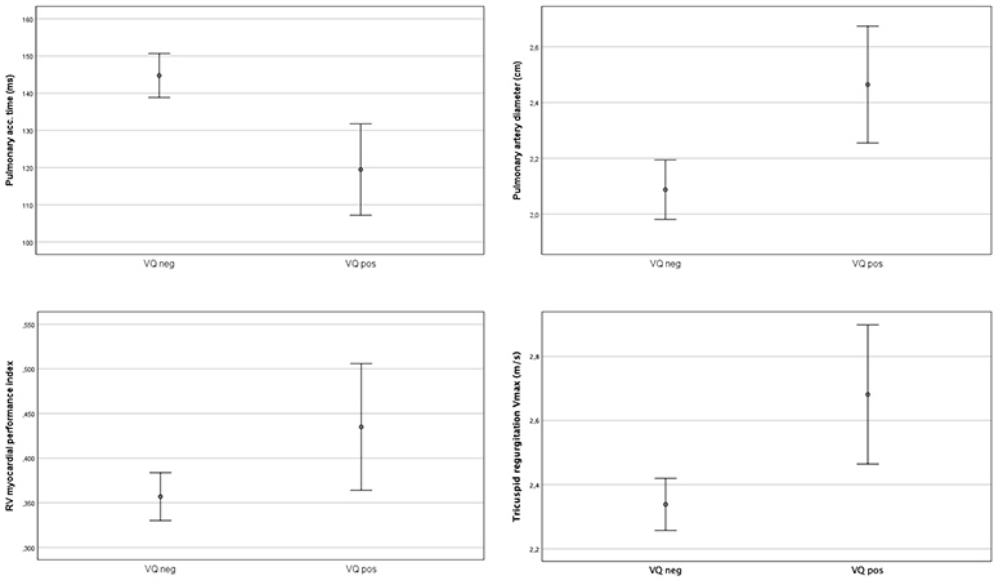
for the primary statistical analysis. Multiple linear regression was used to adjust for age, BMI and systolic blood pressure.

Results: (table)

Conclusion: Patients with CTED after PE have increased PA pressure and impaired RV systolic and diastolic function compared to those without residual perfusion defects. These findings indicate that CTED patients should be more thoroughly followed up.

	VQ negative n=58	VQ positive n=20	p-value	adjusted
Age (years)	59 ±8	67 ±6,5	0,71	
Time since PE event (months)	37 ±19	33 ±17	0,42	
Pulmonary artery acceleration time (ms)	145 ±22	119,5 ±26	<0,001	<0,001
Pulmonary artery diameter (mm)	21 ±3,3	25 ±3,6	<0,01	<0,01
TAPSE (mm)	25,7 ±3,6	24,9 ±4,0	0,45	
RV (right ventricle) S´(cm/s)	12,7 ±2,3	12,8 ±2,7	0,78	
RV isovolumic relaxation time (ms)	33 ±23,9	50 ±22	<0,01	<0,01
RV myocardial performance index	0,36 ±0,10	0,44 ±0,15	0,04	0,02
Tricuspid regurgitation maximum velocity (m/s)	2,3 ±0,3	2,7 ±0,4	<0,001	<0,001
LV (left ventricle) ejection fraction (%)	62,5 ±4,2	61,3 ±6,0	0,41	
E/A	1,02 ±0,26	0,90 ±0,23	0,09	
E/e´	6,8 ±2,0	6,5 ±2,2	0,75	

E/A: Ratio between transmitral pulsed doppler peak early (E) diastolic and atrial (A) velocity; E/e´: Ratio between E and peak early velocity (e´) by tissue velocity



P691 Left ventricular systolic function in long term survivors of allogeneic hematopoietic stem cell transplantation

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Introduction: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is increasingly utilized in young patients. Allo-HSCT usually requires myeloablative therapy that is potentially cardiotoxic. In addition, allo-HSCT survivors have a high prevalence of cardiovascular risk factors.

Purpose: We aim to describe left ventricular systolic function in long term survivors after allo-HSCT.

Methods: This study included 104 patients, aged (mean±SD) 18 ± 10 years at allo-HSCT, and follow-up time was 17 ± 6 years. 74% were sufferers of malignant disease. Pre-transplantation therapies consisted of anthracyclines (AnT) in 44% and mediastinal radiotherapy in 2%. Conditioning regimes consisted of cyclophosphamide with bulsulfsan in 77%. 22% received anti-lymphocyte globulin and 6% received total body irradiation. Left ventricular (LV) function was evaluated by 2D and 3D echocardiography. Healthy controls matched for age, sex and BMI were used in group comparisons. Group comparisons were performed by t-tests and chi-square. A linear regression was used to identify contributing factors to reduced systolic LV function in allo-HSCT survivors.

Results: Most parameters of LV systolic function including 2D and 3D LV ejection fraction (LVEF), global longitudinal strain (GLS), mitral annulus excursion (MAPSE) and s' were all significantly impaired after allo-HSCT as compared to the control group. Significant ($p<0.05$) contributors to LVEF in the multivariate regression analysis were age, AnT dosage, graft versus host disease (GVHD, occurring in 67%) and hypertension (HT, occurring in 31%).

	Allo-HSCT	Control	p value
n	104	55	-
Gender (female)	56 (54)	29 (53)	0.89
Age (yr)	35 ± 12	36 ± 11	0.44
BMI (kg/m^2)	25 ± 5	24 ± 3	0.57
Fractional Shortening (%)	31 ± 6	32 ± 4	0.26
2D LVEF (%)	55 ± 6	59 ± 3	<0.005
3D LVEF (%)	54 ± 5	58 ± 3	<0.005
MAPSE (mm)	13 ± 2	15 ± 2	<0.005
Mean s' (mm)	81 ± 17	89 ± 17	<0.005
2D GLS (%)	-17 ± 2	-20 ± 2	<0.005

values: mean±SD or n(%), t-test or chi-square

Conclusion: LV systolic function is reduced in long term survivors of allo-HSCT. Pre-transplantation AnT, HT and GVHD are significantly associated with increased risk of cardiotoxicity.

P3835 Improvement of myocardial energetic efficiency during treatment in hypertensive patients: the life study

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Background. Myocardial energetic efficiency (MEE) per unit of left ventricular (LV) mass significantly predicts composite of cardiovascular (CV) events in treated hypertensive patients and specifically heart failure in an event-free population-based cohort with normal ejection fraction, independently of LV hypertrophy (LVH).

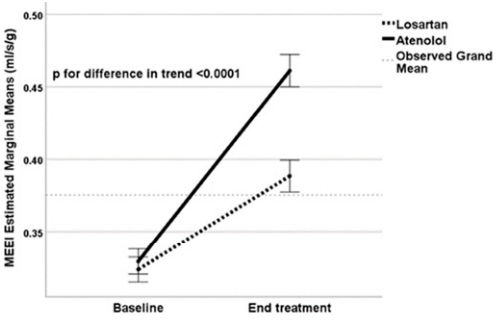
Purpose. To investigate whether MEEi changes over time in treated hypertensive patients, and whether different treatments have different effects.

Methods. From the Losartan Intervention For Endpoint study (LIFE Echo Sub-study) we selected 744 hypertensive patients (age 66±7 years; 45% women) with LVH at ECG, without atrial fibrillation, previous or incident myocardial infarction and with normal echocardiographic ejection fraction (>50%). MEE was estimated as the ratio of stroke work to the "double" product of heart rate times systolic blood pressure (BP), simplified as the ratio of stroke volume to heart rate, as previously reported. MEE was normalized for LVM (MEEi) and analyzed in quartiles at baseline and at the end treatment, according to an «intention-to-treat» protocol.

Results. Age and proportion of women were not significantly different from the highest to the lowest quartiles (from 65 ±7 to 66±7 years, p for trend=0.352; from 45% to 42%, p=0.946, respectively), whereas diastolic blood pressure (from 97± 8 to 100± 9 mmHg, p=0.006), prevalence of obesity (from 14 to 31%, p=0.001) and diabetes (from 4 to 14%, 0.004) progressively increased. Prevalence of concentric LV geometry and echocardiographic LVH also progressively increased from the highest to the lowest

quartile (from 14 to 70%, and 61 to 90%, both p<0.0001). MEEi increased over time (p<0.007), independently of initial diastolic BP, diabetes and obesity, significantly more in patients treated with atenolol than with losartan (p<0.0001) (figure), due to both increased stroke volume and decreased heart rate (both p<0.0001).

Conclusions: In a randomized clinical study, MEEi improves with anti-hypertensive therapy. Improvement is more evident in patients with atenolol than with losartan-based treatment, possibly providing pathophysiologic explanation of the comparable performance in prevention of ischemic heart disease previously reported in the LIFE study.



P606 High intermodality variability in ejection fraction measured by echocardiography, cardiac magnetic resonance and single photon emission computed tomography in chronic coronary artery disease patients

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Background: Clinical treatment strategies are often based on measurement of left ventricular ejection fraction (LVEF). There is limited evidence about variations in LVEF when measured by different imaging modalities.

Purpose: To investigate the intermodality variability of LVEF measured by two-dimensional echocardiography (2DE), three-dimensional echocardiography (3DE), cardiac magnetic resonance (CMR), and single photon emission computed tomography (SPECT) in patients with chronic coronary artery disease (CAD).

Methods: Patients from a multicenter study (DOPPLER-CIP - Determining optimal noninvasive parameters for the prediction of left ventricular remodeling in chronic ischemic patients) with chronic CAD were included. LVEF was measured by CMR and at least one additional modality. In each modality, LVEF was measured by a core laboratory independently of the other modalities. Measurements of LVEF by CMR were compared to 2DE, 3DE and SPECT using correlation and Bland-Altman plots.

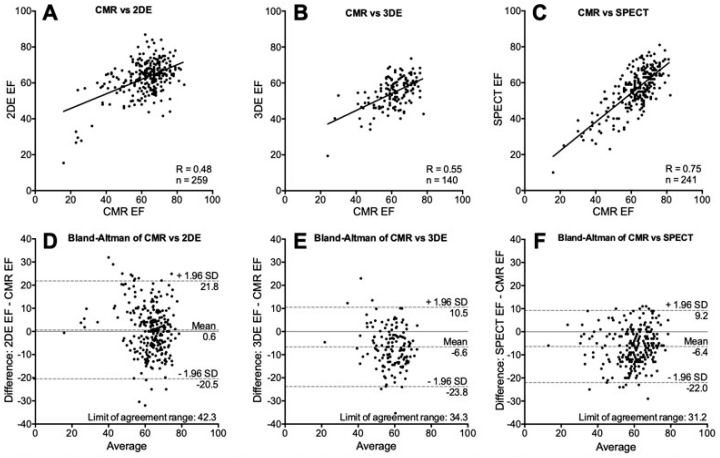

Figure. Correlation plots comparing left ventricular ejection fraction measured by cardiac magnetic resonance with 2-dimensional echocardiography **(A)**, 3-dimensional echocardiography **(B)**, and single photon emission computed tomography **(C)**, respectively. Corresponding Bland-Altman plots showing the mean difference and 95% limits of agreement **(D-F)**. R = Pearson correlation coefficient.

Results: A total of 343 patients were included. Mean age was 63.9 ± 8.3 years and 253 (74%) were males. Mean LVEF by CMR was 61.8 ± 11.6%. Correlations between CMR LVEF and other modalities were moderate for 2DE and 3DE, and good for SPECT (FIGURe A-C). CMR had significantly greater correlation to SPECT, compared to 2DE and 3DE. Bland-Altman plots indicated relatively wide limits of agreement between all modalities, ranging from 31% to 42% (FIGURe, D-F). Mean absolute difference of LVEF between CMR and other modalities were 8.5% for 2DE, 9.0% for 3DE, and 8.3% for SPECT. The percentage of measurements that fell within a range of 5% difference compared to CMR LVEF was 41% for 2DE, 34% for 3DE and 37% for SPECT (all p > 0.05).

Conclusions: In a multicenter study with chronic CAD patients, LVEF assessed by CMR had better correlation to SPECT, compared to 2DE and 3DE. However, there was considerable variability among all three modalities that were compared to CMR. Awareness of these variations are important in clinical management.

P1231 Loss of function in cytoskeletal genes associates with early onset atrial fibrillation

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Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia. It carries an increased risk of serious complications and an increased mortality. Genome Wide Association Studies have demonstrated that variants in several structural genes are associated with AF, and recently two landmark papers have implicated loss of function (LoF) variants in titin (TTN), a gene associated with dilated cardiomyopathy (DCM), in patients with early onset AF. An atrial cardiomyopathy syndrome has been proposed as a mechanism in the development of AF.

Purpose: We hypothesized that genes encoding structural proteins that were associated with DCM, could also be involved in atrial cardiomyopathy and contribute to AF.

Materials and methods: We performed targeted deep sequencing of structural genes associated with DCM. The genes were grouped by cellular function, and the burden of LoF variants was examined in a cohort of 540 early onset AF patients and compared to a control group (n=383). The patients were below age 49 with normal echo, and no other cardiovascular disease at onset of AF. Patient inclusion in the cohort is still ongoing, and we are working on obtaining a CRISPR/CAS9 modified zebra fish model with LoF variants in cytoskeletal proteins.

Results: We identified a total of 6 carriers of LoF variants in 3 genes thought to encode cytoskeletal proteins (DMD, PDLIM3 and FKTN). The burden of variants in cytoskeletal genes was significantly increased in patients with early onset AF compared with controls (p=0.0385). Four carriers had LoF variants in the dystrophin gene (DMD), while there was 1 carrier of LoF variants in PDLIM3 and FKTN respectively. All carriers with LoF variants in DMD developed persistent AF before age 30.

Conclusion: Our data suggest that rare mutations in cytoskeletal genes previously associated with DCM, may also play a role in the development of early onset AF. The data supports that AF is a part of an atrial cardiomyopathy syndrome.

P5976 Prediction of ventricular arrhythmias with mechanical dispersion assessed by strain echocardiography: A systematic review and meta-analysis

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Background: Recent studies have demonstrated that left ventricular mechanical dispersion (LVMD) assessed by speckle tracking might be a powerful marker in risk stratification for ventricular arrhythmias (VA). We sought to perform a systematic review and meta-analysis to i) assess the prognostic value of this parameter (previous studies were predominantly single-center), ii) define the value relative to other parameters, iii) identify the most appropriate cutoff for designating risk.

Purpose: To assess the association between LVMD and the incidence of VA.

Methods: A systemic review of studies reporting the predictive value of LVMD for VA was undertaken from a search of Medline and Embase. LVMD was defined as the standard deviation of time from Q/R on ECG to peak negative strain from each LV segment. VA events were defined as sudden cardiac death, cardiac arrest, documented ventricular tachyarrhythmia, and appropriate implantable cardioverter defibrillator therapy. Hazard ratios (HRs) were extracted from univariable and multivariable models reporting on the association of LVMD and VA and described as pooled estimates with 95% confidence intervals (CIs). In a meta-analysis, the predictive

value of LVMD was compared to that of left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS).

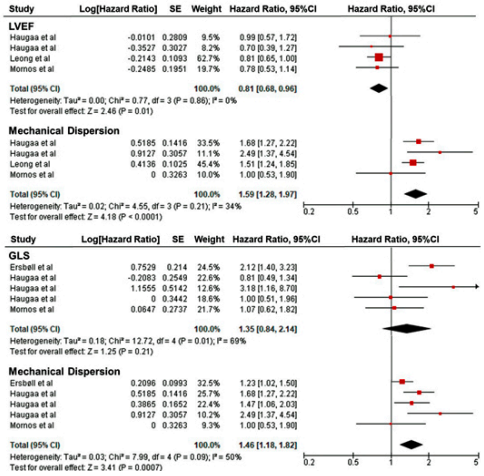
Results: Among 3198 patients (weighted mean, 63 years, 30% female; 82% ischemic heart disease) in 12 published articles, 387 (12%) had VA events over a follow-up (17-70 months). Patients with VA events had a significantly greater mechanical dispersion compared with those without VA events (weighted mean difference, -20.3 ms; 95% CI, -27.3 to -13.2; p<0.01); 60 ms was found to be the optimal cutoff LVMD value for predicting VA events. Each 10 ms increment of LVMD was significantly and independently associated with VA events (HR, 1.19; 95%CI, 1.09 to 1.29; p<0.01). The predictive value of LVMD was superior to that of LVEF or GLS (figure).

Conclusion: LVMD assessed by speckle tracking provides important predictive value for VA in patients with a number of cardiac diseases and appears to have superior predictive value to LVEF and GLS for risk stratification.

Figure

LVEF vs LVMD (per 1-SD increase)

GLS vs LVMD (per 1-SD increase)



2177 Cardiac resynchronization therapy in patients greater than 75 years of age - results from the European Society of Cardiology Survey II with 11 088 patients

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Background: Cardiac Resynchronization Therapy (CRT) reduces morbidity and mortality in selected patients with heart failure (HF) and electrical dyssynchrony. The median age for patients included in the CRT landmark trials ranged from 62–68 years, therefore limited trial evidence exists on CRT in patients =75 years of age.

Purpose: To assess similarities and differences in patient demographics and implantation practice in different age groups implanted with a CRT device.

Methods: Between 2015 and 2017, two European Society of Cardiology (ESC) associations, European Heath Rhythm Society and the Heart Failure Association, conducted the CRT Survey II, a survey of CRT implantations in 11,088 patients in 42 ESC member states.

Results: In our survey 32% of patients included were =75 years of age. These patients were more frequently in NYHA Class III or IV, had more comorbidity (including hypertension, atrial fibrillation, anaemia and renal dysfunction) and had significantly higher NT-pro BNP levels than younger patients. Slightly fewer patients =75 years of age had LBBB but all groups had the same median QRS duration. Despite substantially more patients =75 years of age having HF of ischaemic aetiology compared with those <65 year of age, far fewer patients in oldest age group category were implanted with a CRT-defibrillator (CRT-D) compared with those in the youngest group.

Conclusions: Patients =75 years of age had greater comorbidity and experienced more symptoms from their heart failure. However, they did not suffer more complications or adverse events

Demographics	Age <65 years	Age 65-74 years	Age ≥75 years
N	3478 (32%)	4025 (36%)	3536 (32%)
NYHA class III & IV	52%	59%	66%*
Ischaemic HF aetiology	33%	49%	50%*
Atrial fibrillation	17%	27%	33*
NT proBNP (pg/ml, median, IQR)	1651 (670, 3811)	2319 (1070, 5169)	3510 (1647, 7631)*
CRT-D	81%	76%	52%*
Peri-procedural complications	5%	6%	6%
Adverse Events during hospitalization	4%	5%	5%

*CRT–D (Cardiac resynchronization therapy –defibrillator), HF- heart failure, IQR –interquartile range, *differences between groups is significant with p<0.001*

during the index hospitalization, suggesting that CRT may safely be offered to elderly patients.

P2247 Pregnancies and childbirth in women with arrhythmogenic right ventricular cardiomyopathy are associated with low risk of ventricular arrhythmias

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Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is associated with a risk of ventricular arrhythmias (VA) and sudden cardiac death (SCD). Even though female patients with ARVC are considered to be at lower risk of VA, the impact of pregnancy and child birth on the arrhythmic risk and development of arrhythmic substrate in the context of ARVC remains insufficiently studied.

Objective: To assess the risk of VA in relation to childbirth in women with ARVC and the impact of multiple pregnancies on progression of arrhythmic manifestations of the disease.

Methods: The study included 186 females with definite ARVC (n=107, 70 probands) or unaffected mutation-carriers (n=79) with median age at the end of follow up of 48 (IQR 34-60) years. Seventeen women had 1, 59 had 2 and 29 had =3 child births by the age of 40 years. VA was defined as ventricular tachycardia, appropriate ICD therapy, aborted cardiac arrest or SCD. Proportions of patients who experienced VA by the age of 40 years were compared between nulliparous women (n=81) and those with reported child births (n=105). VA-free survival after accomplished pregnancies was assessed for women =40 years of age (n=119). Cumulative probability of VA for each pregnancy (n=230) was assessed from conception through 2 years after child birth and compared between those that occurred before ARVC diagnosis (Pre-Ds, n=164), after it (Post-Ds, n=11) and in unaffected mutation carriers (No-Ds, n=55).

Results: The nulliparous women had lower age at ARVC diagnosis (37 vs 44, p=0.023) and more often had VA before the age of 40 (31% vs 13%, p=0.003) while the number of child births was not related to the prevalence of VA (18% among women with 1 childbirth, 12% in those with 2 and 14% in those with 3 or more, ns). Three women suffered SCD before the age of 40. VA-free survival after 40 years did not differ between nulliparous and those who gave birth (figure A). Only four pregnancy-related events were documented (figure B): 1 in the Post-Ds group and three in the Pre-Ds group. No pregnancy-related events were reported in the unaffected mutation carriers.

Conclusion: In this Scandinavian cohort of women with ARVC we observed no indication of an increased VA risk either associated with pregnancies or during long-term follow up after the last child birth.

P992 Incidence, predictors, and success of ventricular tachycardia catheter ablation in arrhythmogenic right ventricular cardiomyopathy (ARVC): A long-term cohort study from the Nordic ARVC registry

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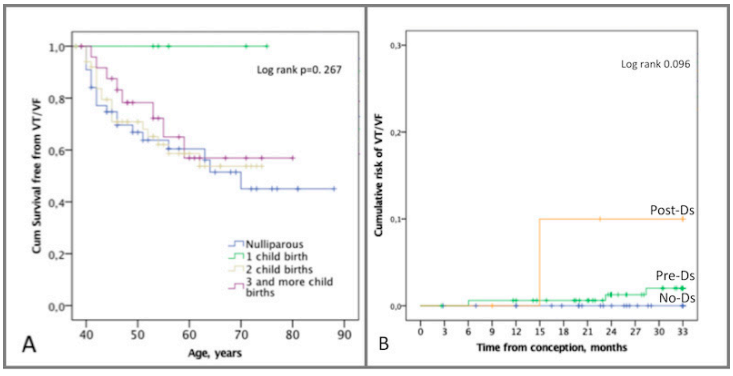

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Background: Catheter ablation may reduce ventricular tachycardia (VT) burden in arrhythmogenic right ventricular cardiomyopathy (ARVC) patients. However, little is known about factors predicting need for ablation and various outcomes have been reported.

Purpose: We sought to investigate predictors and use of VT ablation and to evaluate the post-procedural outcome in ARVC patients.

Methods: We studied 435 patients from the Nordic ARVC registry including 220 probands with definite ARVC according to the 2010 task force criteria and 215 mutation-carrying relatives identified through cascade screening. Patients were followed until first-time VT ablation, death, heart transplantation, or January 1st 2018. Additionally, patients undergoing VT ablation were further followed from the time of ablation for recurrent ventricular arrhythmias.

Results: Cumulative use of VT ablation was 4% (95%CI 3%-6%) and 11% (95%CI 8%-15%) after 1 and 10 years. All procedures were performed in probands in whom the cumulative use was 8% (95%CI 5%-12%) and 20% (95%CI 15%-26%). In adjusted analyses restricted to probands, only young age predicted need for ablation. In patients undergoing ablation, risk of recurrent arrhythmias was 59% (95%CI 44%-71%) and 74% (95%CI 59%-84%) 1 and 5 years after the procedure. Despite high recurrence rates, the burden of ventricular arrhythmias was reduced after ablation (p=0.0042). Young age, use of several antiarrhythmic drugs and inducibility to VT immediately after ablation were associated with an unfavorable outcome.

Conclusions: Twenty percent of ARVC probands developed a clinical indication for VT ablation within 10 years after diagnosis whereas mutation-carrying relatives were without such need. Although the burden of ventricular arrhythmias decreased after ablation, risk of recurrence was substantial.

P4154 MicroRNA Signatures Predict Early Major Coronary Events in Middle Aged Men and Women

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Background. The role of microRNA as biomarkers able to predict major coronary events (MACE) has not been fully elucidated, reproducibility being a critical issue.

Aim. To identify circulating microRNA signatures able to predict MACE.

Methods. We employed a PCR-based method to screen 754 microRNAs in a cohort of 60-year-olds (60YOs) from Stockholm, using a nested case-control design (100 cases vs 100 matched controls). The association of microRNAs and their interaction with the risk of MACE (myocardial infarction (MI), angina and sudden cardiac death) was estimated with random-effect logistic regression and expressed as OR with 95% CI. A bioinformatics approach identified microRNA clusters based on predicted targets. Main findings were tested in 58 MI and 60 age and sex matched referents from the the Nord-Trøndelag Health (HUNT) Study, a longitudinal population health study conducted in Norway.

Results. Fifty-five microRNAs were found to be associated with risk of MACE in the 60YO. MicroRNA-145-3p was associated with the largest estimated risk increase of MACE after adjustment for the common CV risk factors (OR: 2.18; 95% CI: 1.27–3.75). Interaction analysis revealed that increasing plasma levels of microRNA-320b modulated the association of 16 microRNAs with risk of MACE. As an example the estimated MACE risk associated with microRNA-145-3p was 1.47 (0.87-2.47) in the presence of low (<25th percentile) and 4.00 (1.79- 8.93) in the presence of high (> 75th percentile) miRNA 320b expression levels. Sixteen microRNA pairs could be classified in 4 functional clusters with 492 predicted gene targets, mainly involved in the regulation of inflammation, thrombosis and lipid metabolism. Eight miRNAs interacting pairs belonging to cluster 2 and 4 showed a similar association trend with MI risk in the HUNT study.

Conclusions. We report the identification of microRNA signatures predicting risk of MACE in middle-aged Scandinavian men and women. These signatures could be a valuable tool to improve CV disease prediction in the aged.

P3779 NT-proBNP adds incremental predictive information on incident atrial fibrillation in patients with asymptomatic aortic stenosis

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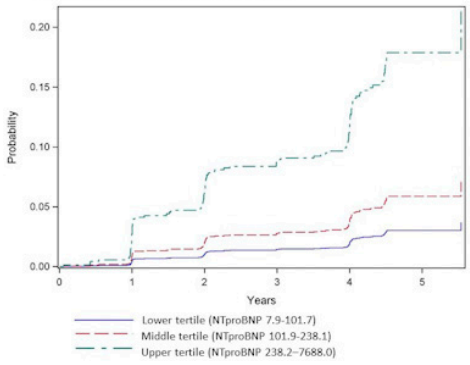
Background: Incident atrial fibrillation (AF) marks an adverse shift in the prognosis of patients with aortic stenosis (AS). Identifying risk factors for AF is therefore of paramount importance for timely intervention in patients with AS. In patients without AS, brain natriuretic peptides (BNP) is a well-established biomarker for left ventricular pressure overload on the pathway to heart failure and atrial fibrillation. However, a potential role of NT-proBNP to predict risk of new-onset AF in asymptomatic patients with mild to moderate AS is not well studied.

Methods: We included 1,434 patients with mild to moderate AS from the SEAS Study (Simvastatin and Ezetimibe in Aortic Stenosis) without AF or clinically overt heart failure at baseline. The primary endpoint for this substudy was time to incident AF, as determined by the first annual in-study 12-lead ECG with AF. Multivariable Cox model were adjusted for other important predictors of incident AF as selected by Bayesian statistics. Fine and Gray competing risk regression was used to evaluate the influence of all-cause mortality on selected predictor variables of incident AF.

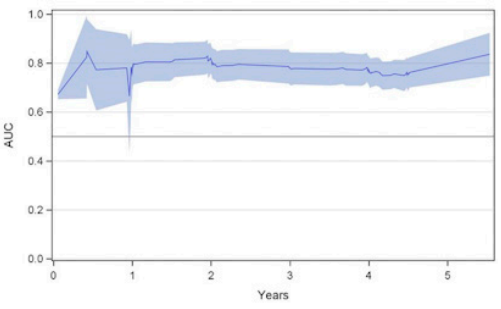
Results: During a median follow-up of 4.3 years (range 0.1-6.9 years), incident AF occurred in 114 (6.1%) patients (13.8 per 1,000 person-years of follow-up), who at baseline were older (69±10 vs. 67±10 years, p<0.001), had larger systolic left atrial diameter (46±24 vs. 34±18 mm, p<0.001) and higher NT-proBNP level (286 [132; 613] vs. 154 [82; 297] pg/ml, p<0.001); but same left ventricular ejection fraction (66±6 mm vs. 67±6, p=0.4). In multivariable Cox regression, adjusted for age, circumferential end-systolic stress, left atrial volume and ECG PR interval, Ln(NT-proBNP) was associated with higher risk of new-onset AF (HR: 1.9 [95%CI: 1.6-2.3], p<0.001). Similar results were found when using Fine and Gray estimates with all-cause mortality (HR: 2.0 [95%CI: 1.7-2.4], p<0.001 (FIGURe, panel A). NT-proBNP level added incremental predictive information on incident AF over the other important, as selected by Bayesian statistics, predictor variables (C-index 0.81, p<0.001, FIGURe, panel B). There was no interaction with aortic valve area (p>0.05).

Conclusions: In patients with asymptomatic aortic stenosis and sinus rhythm at baseline, NT-proBNP levels were significantly higher in patients who subsequently developed AF. NT-proBNP significantly improved prognostic information of incident AF over other important predictor variables. This supports the notion that incident AF is a marker of left ventricular pressure overload and possibly a novel marker of timely intervention with aortic valve replacement.

Panel A. Competing risk estimates of new-onset atrial fibrillation probability according to baseline NTproBNP tertiles, during a median follow-up of 4.3 years



Panel B. Time-dependent area under the curve (95% confidence limits)



NTproBNP: N-terminal prohormone of brain natriuretic peptide

P5296 A healthier lifestyle increases circulating pro-atrial natriuretic peptide concentrations in overweight children

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Background: Higher concentrations of atrial natriuretic peptides (ANP) are associated with a poor prognosis among patients with cardiovascular disease (CVD). Counter-intuitively, higher ANP concentrations in healthy populations are associated with an ideal American Heart Association Cardiovascular Health score, which includes high level of physical activity, normal body mass index (BMI), optimal levels of lipids, blood pressure (BP) and glucose. Along this line, overweight individuals have lower than expected ANP concentrations, and it has been proposed that this natriuretic handicap could play a role in overweight related disorders. The mechanism behind the natriuretic handicap is still not clear, but presence of insulin resistance with hyperinsulinemia has been implicated.

Purpose: We investigated whether an intensive lifestyle intervention with an intended weight loss, including an increased level of physical activity and a healthy diet, could increase plasma concentrations of mid-regional pro-ANP (MR-proANP), a stable marker of ANP secretion, in overweight children. In a mechanistic perspective, we investigated metabolic changes associated with increases in MR-proANP concentrations.

Methods: This study is an extension of the Odense Overweight Intervention Study (OOIS) which included 99 overweight children (11-13 years, 55% girls). The children were randomised to a Day Camp Intervention Arm (DCIA) and a Standard Intervention Arm (SIA) for 6 weeks. DCIA included 3 hours physical activity per day and a healthy diet according to Danish recommendations. SIA included 1 weekly fun-based physical activity session and 1 lifestyle education session. OOIS included measurements of anthropometry, body composition, lipids, BP, glucose and insulin. Linear regression analyses, expressed as unstandardized regression coefficients, were used to examine between-group differences in MR-proANP concentrations and to examine the associations between changes in MR-proANP and variables of interest. As we wanted to study physiological relationships, we pooled both arms to one group to increase power in the latter.

Results: At week 6, children in DCIA had lower BMI (-2.4kg/m2) and lower total body fat (-6.5%) but higher level of fitness (4.1 ml/O2/min/kg) compared to children in SIA. From baseline to week 6 DCIA increased MR-proANP concentrations (B (95% CI): 5.7 (1.2 to 10.2) pmol/l, P= 0.014) more than SIA. Of the variables studied, we found an inverse association between fall in insulin and increase in MR-proANP concentrations (B (95% CI): -0.52 (-1.02 to -0.02) pmol/l/mIU/ml,P= 0.041). None of the other associations between changes in variables reached statistical significance.

Conclusion: A healthier lifestyle, based on a healthy diet and a higher level of physical activity, increases MR-proANP among overweight children. In a mechanistic perspective, improved insulin sensitivity with lower insulin appears to be a factor that leads to higher MR-proANP.

P668 Aspirin for primary prevention of cardiovascular disease

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Background: Platelet inhibition by aspirin reduces ischemic events but increases the risk of bleeding events. Yet, the role of aspirin in primary prevention of cardiovascular disease remains unclear.

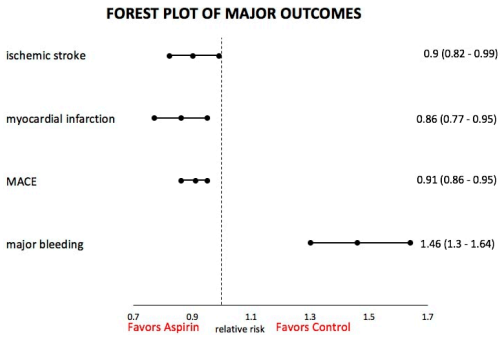
Purpose: To produce a clinically relevant benefit-risk assessment of aspirin for primary prevention of cardiovascular disease.

Methods: We performed a meta-analysis of aspirin effects in primary prevention of cardiovascular disease comprising 13 randomized-controlled trials in 164.225 patients comparing aspirin versus placebo/control during a mean follow-up period of 6.4 years. Using a random effect model, relative risks and 95% confidence intervals were calculated for each outcome.

Results: Aspirin reduced the relative risk of ischemic stroke by 10% (RR: 0.90; 95%CI: 0.82-0.99), myocardial infarction by 14% (RR: 0.86; 95%CI: 0.77-0.95) and the major adverse cardiovascular events by 9% (RR: 0.91; 95%CI: 0.86-0.95) but was associated with a 46% relative risk increase of major bleeding events (RR: 1.46; 95%CI: 1.30-

1.64). Aspirin did not reduce the risk of cardiovascular mortality (RR: 0.99; 95%CI: 0.90-1.08), all-cause mortality (RR: 0.98; 95%CI: 0.93-1.02) or cancer (RR 1.05; 95% CI, 0.87-1.26). Aspirin use did not translate into a net clinical benefit adjusted for event-associated mortality risk (mean 0.034%; 95%CI: -0.18 to 0.25%).

Conclusions: Aspirin use in primary prevention is associated with a reduced risk of stroke and myocardial infarction, but at a cost of an increased risk of major bleeding.



P4542 Revisiting the obesity paradox in heart failure: percent body fat as predictor of biomarkers and outcome

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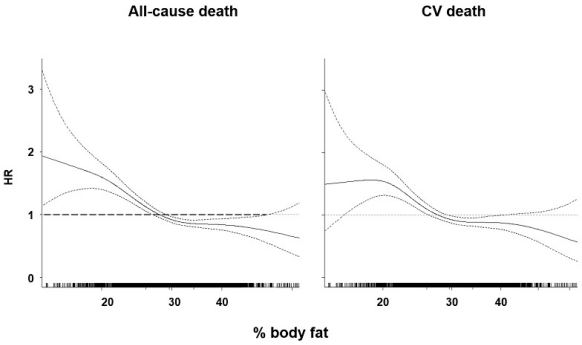
Background: Obesity defined by body mass index (BMI) is characterized by better prognosis and lower plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) in heart failure (HF). We assessed whether another anthropometric measure, percent body fat (PBF), reveals different associations with outcome and HF biomarkers (NT-proBNP, high-sensitivity troponin T [hs-TnT], soluble suppression of tumorigenesis-2 [sST2]).

Methods: In an individual patient dataset, BMI was calculated as weight(kg)/height(m)2, and PBF through the Jackson-Pollock and Gallagher equations.

Results: Out of 6468 patients (median 68 years, 78% men, 76% ischaemic HF, 90% reduced EF), 24% died over 2.2 years (1.5-2.9), 17% from cardiovascular death. Median PBF was 26.9% (22.4-33.0%) with the Jackson-Pollock equation, and 28.0% (23.8-33.5%) with the Gallagher equation, with an extremely strong correlation (r=0.996, p<0.001). Patients in the first PBF tertile had the worst prognosis, while patients in the second and third tertile had similar survival. The risks of all-cause and cardiovascular death decreased by up to 36% and 27%, respectively, per each doubling of PBF. Furthermore, prognosis was better in the second or third PBF tertiles than in the first tertile regardless of model variables. Both BMI and PBF were inverse predictors of NT-proBNP, but not hs-TnT. In obese patients (BMI =30 kg/m2, third PBF tertile), hs-TnT and sST2, but not NT-proBNP, independently predicted outcome.

Conclusion: Patient prognosis improves with either BMI or PBF. Obesity, assessed with BMI or PBF, is associated with lower NT-proBNP but not hs-TnT or sST2. hs-TnT or sST2 are stronger prognostic predictors than NT-proBNP among obese patients.



P2650 Antihypertensive treatment with calcium channel blockers in patients with moderate or severe aortic stenosis: relationship with all-cause mortality

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Background: Hypertension is prevalent in patients with aortic stenosis (AS) and optimal blood pressure (BP) control is advised to reduce arterial load and avoid cardiovascular events. Whether calcium channel blockers (CCB) are safe is not known.

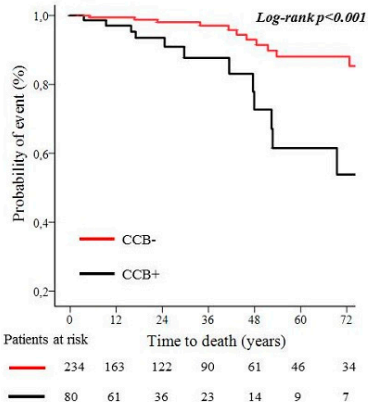
Methods: A total of 314 patients (age 65±12 y, 68% men) with moderate or severe asymptomatic AS were included.

Results: The prevalence of hypertension was 73.6%, and 65% took antihypertensive treatment. Patients who used a CCB (25%) (CCB+) were older, had higher clinic systolic BP, were more likely to have hypercholesterolemia and coronary artery disease (CAD), and to use a diuretic or alpha blocker compared to CCB- patients (all p<0.05) (Table). During the baseline ETT, patients who used a CCB achieved a lower peak heart rate, a shorter exercise time and were more likely to have a blunted BP response compared to those who did not use a CCB (all p<0.05) (Table). Event-free survival was significantly lower in CCB+ than CCB- patients (Fig) (all-cause mortality 16 [20.3%] versus 13 (5.6%); p<0.001). In a multivariable Cox regression model, CCB+ was associated with a 6.8-fold increased hazard ratio (HR) for all-cause mortality (HR 6.77 95% CI 1.66-27.54, p=0.008), independent of age, gender, systolic BP, hypertension, diabetes, CAD, hypercholesterolemia and aortic valve area.

Conclusion: The use of calcium channel blockers was associated with an adverse effect on treadmill exercise and reduced survival in apparently asymptomatic patients with moderate or severe AS.

	CCB- (n=234)	CCB+ (n=80)	p
Age, y	64±12	70±10	<0.001
CAD, %	45	66	0.006
Hypercholesterolemia, %	62	78	0.015
Clinic systolic BP, mmHg	139±19	150±17	<0.001
Left atrial diameter, cm	3.7±0.7	3.9±0.6	0.007
LV end-diastolic diameter, cm	4.5±0.7	4.8±0.6	0.002
LV mass index, g/m^2.7	50±17	57±17	0.007
Aortic valve area, cm^2	0.94±0.22	0.93±0.22	0.716
LV stroke work, g-m/bmp	155±46	175±69	0.046
Peak HR at baseline ETT, bmp	138±24	120±25	<0.001
Blunted BP response, %	33	49	0.013
Exercise duration, min	10.1±4.5	8.3±3.7	0.001
Double Product, mmHg · bmp	1.85±0.43	2.08±0.54	<0.001

Table. Baseline characteristics of patients.



P6226 Association of functional iron deficiency with incident cardiovascular diseases and mortality in the general population

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Background: Functional iron deficiency (FID) has been established as a risk factor in patients with cardiovascular diseases (CVD). As opposed to absolute iron deficiency, it reflects stored iron as well as utilized iron and allows for a more accurate evaluation of individual iron status. However, evidence is scant on the

relevance of FID to the incidence of CVD in the general population.

Aim: This study aimed to evaluate the association of FID with incident cardiovascular diseases and mortality endpoints in a large population-based cohort.

Methods: FID was defined as either ferritin below 100 µg/L or ferritin between 100 and 299 µg/L and transferrin saturation below 20%. Only individuals free of CVD at baseline from three population-based European cohorts were included. Multivariable-adjusted sex- and cohort-stratified Cox regression analyses were performed to evaluate the association of functional iron deficiency with incident cardiovascular diseases (coronary heart disease, cerebral infarction, heart failure and atrial fibrillation) as well as with all-cause and cardiovascular mortality. Adjustments were performed for sex (as strata), age (as time scale), smoking, total cholesterol, systolic blood pressure, diabetes, body mass index and high-sensitive C-reactive protein.

Results: In total, N=12146 individuals were included in the analysis with a median age of 59.0 years (25thpercentile 45.0, 75thpercentile 68.0), and 45.2% men. Incidence of FID was 64.3%. Median follow-up times were 12.3 to 21.8 years, with an all-cause mortality rate of 18.2% and a cardiovascular mortality rate of 6.2%. Incident coronary heart disease, cerebral infarction, heart failure and atrial fibrillation were observed in 8.7%, 6.5%, 5.9% and 11.7%, respectively.

FID was significantly associated with all-cause mortality (hazard ratio (HR) 1.12, 95% confidence interval (CI) 1.01–1.24, p = 0.034), cardiovascular death (HR 1.26, 95% CI 1.03-1.54, p=0.027) and incident coronary heart disease (HR 1.23, 95% CI 1.06-1.43, p<0.01). There was no significant association with the other tested endpoints.

Conclusion: In our analysis of population-based cohorts, FID showed a significant positive association with all-cause as well as cardiovascular mortality and incident coronary heart disease. Further research is needed to validate the role of FID as a cardiovascular risk factor in the general population and to evaluate the impact of iron supplementation on gender and outcome.

P4526 Implant procedure and lead handling characteristics of a novel active fixation quadripolar lead: Results from the Attain Stability Quad clinical trial

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Background: Dislodgements of left ventricular (LV) leads are still a challenging problem in cardiac resynchronization therapy (CRT). The Attain Stability Quad (ASQuad) MRI SureScan 4798 steroid-eluting, quadripolar LV lead has a side-helix to enable the lead to be actively fixated to the vessel wall. The uniquely designed active fixation can be advantageous in vessels that are wide or have short take-offs. Further, the helix easily elongates to allow for future extraction.

Purpose: To report on the handling, performance and safety of ASQuad LV lead in a large clinical study.

Methods: The ASQuad clinical study is a prospective clinical trial from 50 centers in 10 countries enrolling CRT candidates implanted with the ASQuad LV lead. Aside from evaluating safety and effectiveness of the LV lead, the trial specifically collected data on parameters related to lead stability during and post implant.

Results: Of 440 enrolled patients (74.8% male, average age 70 ± 11 years) that underwent an implant attempt, 426 (96.8%) were successfully implanted. The helix was mostly affixed in the mid to basal lateral position (62%), followed by mid to basal posterior position (29%). The lead tip placement was most often mid lateral or mid posterior (77%), and in a vein with diameter greater than the pacing electrode diameter (> 5.1 French) in the majority (60%) of procedures. Among all subjects (n=421) who underwent pacing capture thresholds (PCT) tests before and immediate after guide catheter slitting, 98% reported = 1 V difference in PCT, and 86% were within 0.5 V. The interquartile range for the difference in PCT was -0.1 to 0.1 V. The mean PCT at implant for all subjects at the final selected LV pacing vector was 1.15 ± 0.70 V at 0.5 ms pulse width. The average LV lead implant time was 16 ± 21 minutes. Targeted pacing location was achieved in 97% of successful implants, and 98% of implanters reported good or fair stability after guidewire removal. The overall handling of the LV lead was rated as acceptable by implanters in 99% of cases. Three patients (0.7%) experienced LV lead dislodgement post implant, and these complications were resolved by repositio-

ning of the lead (0 and 1-day post implant) in two and by lead replacement when noted at 90 days follow-up in one.

Conclusions: The ASQuad LV lead was implanted with a high rate of success and ability to achieve the targeted pacing location. Lead handling and stability following guidewire removal were rated as acceptable by nearly all implanters. The side-helix likely improved LV lead stability since 98% of the subjects had =1 V difference in PCT before and after catheter slitting during implant procedures, and by demonstrating a low post implant lead dislodgement rate.

P5608 Acute respiratory failure after type A aortic dissection repair: data from the International Registry of Aortic Dissection (IRAD)

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Background: Acute Respiratory Failure (ARF) has been noted in up to 20% of patients undergoing cardiac surgery and is associated with increased mortality. Cardiopulmonary bypass (CPB) is often followed by pulmonary dysfunction, although literature on the subject in the setting of Type A acute aortic dissection (TAAAD) is limited.

Methods: this study identified the incidence of ARF after TAAAD, associated risk factors, and the impact of ARF on early and late outcomes. All data have been derived from the International Registry of Acute Aortic Dissection (IRAD).

Results: Postoperative ARF (defined as ventilator support for = 3 days, tracheostomy, and/or pneumonia) occurred in 434 (24.6%) of 1764 surgically managed TAAAD patients (mean age 60.1 ± 14.2 years) from November 2001 until November 2017. Peripheral vessel procedures (6.4% v 2.8%, p=0.002), cerebral perfusion (89.2% v 82.3%, p<0.001), use of hypothermic circulatory arrest (93% v 87.7%), longer arrest time (median 39 (Q1-Q3 27-128 minutes) v 31 (Q1-Q3 22.0-52.9 minutes)), and lower extremity ischemia (18.8% v 6.7%, p<0.001) were more common in ARF patients.

On multivariable logistic regression analysis, age = 70 years (OR 1.019, 95% CI 1.005-1.034, p=0.008), current smoking (OR 1.744, 95% CI 1.184-2.570, p=0.005), peripheral vessel procedures (OR 2.457, 95% CI 1.132-5.334, p=0.023), presenting hypotension/shock (OR 2.036, 95% CI 1.336-3.102, p=0.001), lower extremity ischemia at surgery (OR 2.77, 95% CI 1.574-4.875, p<0.001), concomitant coronary artery bypass graft (CABG) (OR 2.982, 95% CI 1.597-5.568, p=0.001), pre-operative acute renal failure (OR 2.532, 95% CI 1.350-4.749, p=0.004), and prolonged circulatory arrest time in minutes (OR 1.005, 95% CI 1.003-1.007, p<0.001) were independently associated with ARF development. Patients with aortic valve replacement (AVR) were less likely to develop ARF (OR 0.497, 95% CI 0.308-0.802, p=0.004).

Post-operative complications were more common in ARF patients. In-hospital mortality was higher in the ARF cohort (16.4% v 4.7%, p<0.001). Multivariable logistic regression identified ARF (OR 2.686, 95% CI 1.647-4.381, p<0.001) as well as pre-operative hypotension (OR 1.89, 95% CI 1.130-3.159, p=0.015), lower extremity ischemia (OR 2.77, 95% CI 1.545-4.998, p=0.001), pre-operative myocardial infarction (OR 3.141, 95% CI 1.058-9.33, p=0.039), and CABG (OR 1.988, 95% CI 1.011-3.909, p-value 0.047) as independent predictors of death.

Conclusions: Post-operative ARF is common after TAAAD repair; in-hospital complications and death are higher in this cohort.

1154 FFR guided acute complete revascularization versus culprit lesion only treatment in patients presenting with STEMI and multi vessel disease; final 3-year outcome data from Compare-Acute trial

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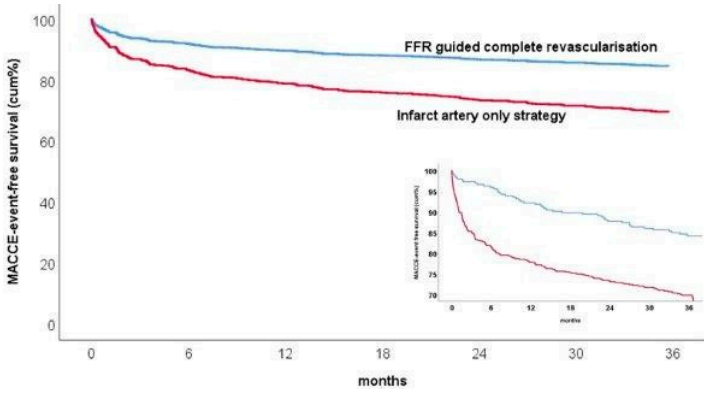
Background: Compare-Acute trial showed a 1-year superior outcome of FFR-guided acute complete revascularization (FFR-CR) compared to culprit-lesion-only revascularization (CLO) in patients presenting with ST-segment elevation myocardial infarction (STEMI) and multi-vessel disease (MVD). Long-term outcome results are unknown.

Purpose: To evaluate if FFR-CR strategy is superior to CLO strategy in terms of outcome at 3 year follow-up.

Methods: Compare-Acute is a multicenter, investigator-initiated prospective randomized controlled trial that involved 24 sites. Patients with STEMI and MVD were randomized, after successful primary PCI towards FFR-CR or CLO treatment strategies with a 1:2 ratio (295 pts vs 590 pts). All stenosis = 50% in the non-infarct artery were investigated by FFR in both arms. In the FFR-CR arm, all non-culprit (NC) lesions with a FFR = 0.80 were treated by PCI. In the CLO arm pts underwent blinded FFR procedure of the NC lesions. Further treatment of these lesions was based on symptoms and/or ischemia testing during follow-up with an allowed treatment window of 45 days. The primary endpoint was defined as a composite of all-cause mortality, non-fatal myocardial infarction, any revascularization and cerebrovascular events (MACCE) at 12 months. The major secondary endpoint is MACCE from both strategies up to 3-year follow-up.

Results: 1-year clinical outcomes have already been presented and published. At 36 months the composite end-point of MACCE occurred in 46 patients in the FFR-CR group vs 178 patients in the CLO group (15.6% vs 30.2%; HR 0.46 – 95% CI 0.29-0.59; p < 0.01), as shown in Fig. 1. The incidence of death (4 pts vs 10 pts; 1.4% vs 1.7%; HR 0.86 – 95% CI 0.39-1.8; p = 0.71), MI (20 pts vs 53 pts; 7.1% vs 9.3%; HR 0.74 – 95% CI 0.44-1.24; p = 0.25) and stroke (1 pt vs 7 pts; 0.3% vs 1.2%; HR 0.29 – 95% CI 0.03-2.3; p=0.24) was not significantly different in the two groups, but revascularizations were significantly higher in the CLO group: 37 patients in the FFR-CR group vs 149 patients in the CLO group (13.0% vs 26.0%; HR 0.45; 95% CI 0.31-0.64; p < 0.01). Furthermore, in a subgroup analysis, when we considered only patients with FFR positive non-culprit lesions in both arms, we found a higher incidence of MI at follow-up in the CLO arm compared to the FFR-CR arm: 30/224 vs 13/194 (13.4% vs 6.7%; p 0.03).

Conclusion: With this analysis of the Compare-Acute trial we confirm that the benefit of a FFR-guided complete revascularization strategy in patients with STEMI and MVD is maintained at 3 years of follow-up. This difference is mainly driven by increased revascularizations in the CLO arm, but also by increased incidence of MI in the CLO subgroup with FFR+ lesions that were left untreated.



P3515 Gender differences in plasma levels and prognostic value of NT-proBNP in chronic heart failure

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Background: Natriuretic peptides are established biomarkers of heart failure (HF). The existence of gender-related differences in circulating levels and prognostic value are still controversial.

Methods: Individual patient data from studies assessing cardiac biomarkers (N-terminal fraction of pro-B-type natriuretic peptide - NT-proBNP - and high-sensitivity troponin T) for risk prediction in stable chronic HF were analysed.

Results: Women (n=1964, 23%) had higher median [interquartile interval] NT-proBNP concentrations than men (1678 [659-4215] vs. 1294 [522-2973] ng/L, p<0.001). Female gender predicted higher NT-proBNP independently from age, body mass index, glomerular filtration rate, left ventricular ejection fraction (LVEF), and atrial fibrillation.

Over a 2.4-year follow-up (1.6-3.2), 2351 patients (27%) died, and cardiovascular death occurred in 1558/8271 (19%). HF hospitalization was recorded in 2088/7944 (26%) over 2.0 years (1.3-2.6). Women and men had similar areas under the curve for the 3 endpoints, with higher cut-offs among women: all-cause death, 2328 ng/L vs. 1319 ng/L; cardiovascular death, 2328 ng/L vs. 1413 ng/L; HF hospitalization, 1265 ng/L vs. 907 ng/L. In the prognostic model above, the risk of the three endpoints increased by 32%, 35%, and 17%, respectively, per doubling of NT-proBNP in women, and by 41%, 45%, and 30% in men.

Conclusions: Women with chronic HF display higher NT-proBNP levels than men in the whole population as well as across many patient subgroups. This difference is not entirely explained by heterogeneity in age, BMI, or renal function. NT-proBNP holds independent prognostic significance in both genders, although alternative prognostic cut-offs might be considered for women.

P2630 Incidence and prognostic impact of new-onset left bundle branch block in patients with heart failure and reduced ejection fraction

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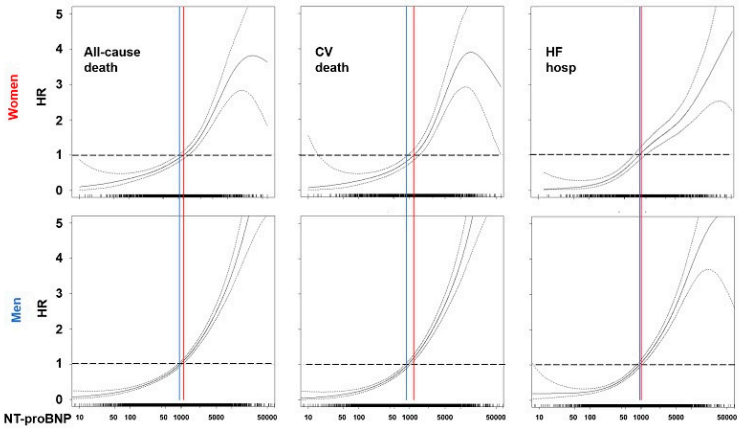
Background: Cardiac resynchronization therapy (CRT) improves survival in patients with heart failure, reduced ejection fraction (HFrEF) and left bundle branch block (LBBB). However, little is known about the incidence of LBBB in HFrEF and the risk factors for developing this. We addressed these questions in the PARADIGM-HF and ATMOSPHERE trials.

Methods: We identified 7703 patients with a non-paced rhythm on their baseline ECG, a QRS<130 ms, and at least one follow-up ECG (done at annual visits and end of study). Patients were stratified by baseline QRS duration (=100 ms - reference; 101-115 ms and 116-129 ms) and followed until development of QRS duration =130 ms with a LBBB conFIGURation or latest available ECG. The crude LBBB incidence rate per 100



person-years (py) was identified in the three QRS duration subgroups. Additionally, we examined risk of the primary composite outcome of cardiovascular death or HF hospitalization, and all-cause mortality, in patients with incident LBBB vs. no incident LBBB.

Results: Overall, 313 of 7703 patients (4%) developed LBBB during a mean follow-up of 2.7 years, yielding an incidence rate of 1.5 per 100 py. The rate ranged from 0.9 in those with QRS =100 ms to 4.0 per 100 py in patients with QRS 116-129 ms. Other predictors of incident LBBB included male sex, age, lower LVEF, HF duration and absence of AF. The risk of the primary composite endpoint was higher among those who developed incident LBBB vs no incident LBBB; event rates 13.5 vs 10.0 per 100 py, yielding an adjusted HR of 1.43 (1.05-1.96). For all-cause mortality the corresponding rates were 12.6 vs 7.3 per 100 py; HR 1.55 (1.16-2.07) (Table 1).

Conclusion: Among patients with HFrEF, the annual incidence of new-onset LBBB (and a potential indication for CRT), was around 1.5%, ranging from 1% in those with QRS duration below 100 ms to 4% in those with QRS 116-129 ms. Incident LBBB was associated with a much higher risk of adverse outcomes, highlighting the importance of repeat ECG monitoring in patients with HFrEF.

	No. events	Crude rate per 100py	Adjusted* HR (95% CI)
HF hospitalization or CV death			
No incident LBBB	2145	10.0 (9.6-10.4)	1.00 (ref.)
Incident LBBB	43	13.5 (10.0-18.2)	1.43 (1.05-1.96)
All-cause mortality			
No incident LBBB	1662	7.3 (6.9-7.6)	1.00 (ref.)
Incident LBBB	48	12.6 (9.5-16.7)	1.55 (1.16-2.07)

Table: Risk of outcomes according to incident LBBB during follow-up