P2638. Plasma trimethylamine-N-oxide is associated with atrial fibrillation

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Background/Introduction: Higher plasma trimethylamine-N-oxide (TMAO) concentrations are associated with cardiovascular disease (CVD). Any specific relationships with atrial fibrillation (AF) are not known.

Purpose: We evaluated potential associations between plasma TMAO with previous and incident AF among 4141 Norwegian patients undergoing coronary angiography for suspected stable angina pectoris.

Methods: We studied cross-sectional and prospective relationships between plasma TMAO and AF by Mann-Whitney U test and Cox regression, respectively. We explored improvement in risk prediction by calculating the continuous net reclassification index (NRI>0). Information on incident AF was obtained from public Norwegian health registries.

Results: Baseline plasma TMAO was associated with an adverse CVD risk profile. Median (25–75 percentile) plasma TMAO was 6.4 (4.4–11.6) and 5.6 (3.6–9.5) μmol/L among patients with (N=344) and without (N=3797) previous AF, respectively; P<0.001

Among patients without previous AF, 412 patients (10.9%) were diagnosed with incident AF during median 7.3 years of follow-up. The age-and gender adjusted hazard ratio (95% confidence interval (CI)) for incident AF was 1.16 (1.05–1.28); P=0.003 per 1 SD increase in log-transformed plasma TMAO. Similar risk estimates were obtained when adjusting for traditional AF risk factors (hypertension, body mass index, smoking and diabetes), and also when further controlling for left ventricular ejection fraction, estimated glomerular filtration rate, the extent of coronary artery disease at angiography, heart failure, serum high sensitive cardiac troponin T, as well as dietary intakes of total choline or betaine.

Adding TMAO to traditional AF risk factors yielded NRI>0 (95% CI) 0.106 (0.028–0.184); P=0.007.

Conclusions: Among patients with suspected stable angina pectoris, plasma TMAO was associated with previous and incident AF, and improved risk prediction of the latter. The prospective association was independent of traditional AF risk factors and potential confounders, as well as of dietary choline and betaine intake. Our findings suggest that higher plasma TMAO reflects metabolic alterations predisposing for AF.

P736. Relative downregulation of septal function and metabolism in TGA patients with atrial switch

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**Background:** In patients with transposition of the great arteries (TGA) and atrial switch, the right ventricle (RV) becomes the systemic ventricle. These patients have increased risk of heart failure. We have previously demonstrated reduced septal function by regional strain and work analyses.

**Purpose:** To determine whether reduced septal function in TGA-patients is reflected in reduced metabolism.

**Methods:** We included 10 TGA patients, age (30±5 years mean±SD), operated with atrial switch (Senning/Mustard) shortly after birth. Myocardial shortening was measured as longitudinal strain by speckle tracking echocardiography. Myocardial glucose metabolism was measured by 18F-fluorodeoxyglucose PET imaging (FDG-PET) by standard protocol, using SUV body mass (SUV:Standardized Uptake Value) as unit. These SUV were also normalized to the highest SUV value. Values presented are average SUV from volumes of interest (VOI) from the basal and mid segments for septum and RV free wall for both absolute and relative SUV.

**Results:** Septal longitudinal shortening was markedly reduced compared to the RV free wall (13±2 vs 20±3%, P<0.001) (Figure, panel A). Myocardial glucose metabolism, i.e. 18FDG-uptake, was also reduced in the septal segments compared to the RV free wall (SUV 5.1±1.8 vs 6.3±1.8, P<0.001). When SUV was normalised to the VOI with highest SUV, the septum had a mean of 0.75±0.09 vs 0.95±0.04 in the lateral wall (P<0.001) (Figure, panel B). In each patient, with no exception, the absolute value of SUV and strain were lower in the septum than in the RV free wall. In the typical example in panel C, there is normal metabolism in the RV free wall (homogenous red) and reduced metabolism is seen in the septum (pale red or yellow).

**Conclusions:** TGA patients demonstrated markedly reduced septal function which was accompanied by reduction in septal metabolism. Global function of the systemic right ventricle was maintained due to preserved function of the RV free wall. The change in septal function and metabolism may be early markers of decompensation of the systemic ventricle.

5924. Lack of the extracellular matrix proteoglycan lumican in mice exacerbates left ventricular dilatation and contractile dysfunction upon pressure overload

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Heart failure (HF) in response to pressure overload is characterized by cardiac remodeling. Lumican (LUM) is an extracellular matrix (ECM)-localized small leucine-rich proteoglycan (SLRP) with increased expression in hearts of HF patients and mice subjected to pressure overload by aortic banding (AB). To test the hypothesis that lumican is important for cardiac remodeling, lumican knock-out (LUM−/−) mice were subjected to AB and neonatal rat heart primary cultures exposed to LUM.

LUM exists as a non-glycosylated 38 kDa core protein and a 50–75 kDa proteoglycan in the mouse left ventricle (LV, n=3). When overexpressed in HEK293 cells, WT LUM was secreted into the culture medium, while the non-glycosylated N88A/N127A/N160A/N252A mutant was retained intracellularly (n=8). LUM+/− intercrosses (n=47) showed that out of 236 pups, 8 were LUM−/− (3% vs. expected 25%, p<0.0001), suggesting that LUM−/− predominantly is embryonic lethal. Echocardiography of adult LUM−/− mice showed no cardiac phenotype (n=9–26). LUM−/− exhibited exacerbated LV dilatation 1-10 weeks post-AB (n=3–14), with exacerbated contractile dysfunction 4–10 weeks post-AB. LV wall thickness was reduced 2 and 6–10 weeks post-AB. Importantly, Sirius Red staining of mid-ventricular sections (n=3–4) showed reduced fibrosis in LUM−/− 12 weeks post-AB.
P3339. Automatic measurements of tissue doppler indices to detect left ventricular dysfunction

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Introduction: With the increasing use of pocket-sized ultrasound devices by inexperienced users, automated measurements of left ventricular (LV) function will represent an advantage. LV longitudinal function is reduced in patients with systolic and diastolic dysfunction, and can be quantified by measuring the mitral annular plane systolic excursion (MAPSE), peak systolic (S’) and peak early (e’) and late (a’) diastolic mitral annular velocity. We have developed an algorithm that automatically measures these indices with a good precision, intended for inexperienced users.

Purpose: To evaluate the ability of the automatic algorithm to detect systolic and/or diastolic LV dysfunction, using experienced cardiologists’ echocardiographic evaluation of LV function as the reference.

Methods: 201 patients (126 males, median age 67 years) underwent echocardiographic examination by experienced cardiologists. LV dysfunction was defined as ejection fraction <50% or ejection fraction ≥50% and signs of elevated filling pressure. From apical four-chamber color tissue Doppler recordings, MAPSE, S’, e’ and a’ were measured automatically, from the basis of the septal and lateral LV walls. Septal and lateral measurements were averaged. The ability of the indices to detect LV dysfunction was studied in receiver operating characteristics (ROC) analyses. The area under the curve (AUC) for the different indices were compared. Sensitivity, specificity and positive (PPV) and negative predictive value (NPV) and cutoff values, with 95% confidence intervals (CI), were estimated by bootstrapping.

Results: 56 patients had LV dysfunction (47 systolic, 9 diastolic dysfunction). The best predictors of LV dysfunction were MAPSE (AUC=0.856) and S’ (AUC=0.838), with no significant differences between them (p=0.08). There were no statistically significant differences between a’ and S’ or e’ (p>0.191). The ROC curves are shown in Fig. 1. Table 1 shows specificity, PPV, NPV and cutoff values corresponding to 90% sensitivity.

Conclusions: Automatic measurements of mitral annular motion were helpful in detection of LV dysfunction. MAPSE and S’ were the best among the indices we assessed, but they should be evaluated in the context of other variables such as valvular function and be studied in other populations.

Table 1. Performance of indices used to detect LV dysfunction in 201 patients

<table>
<thead>
<tr>
<th>Indices</th>
<th>Sensitivity</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
<th>Cutoff (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>MAPSE</td>
<td>90%</td>
<td>62 (44-79) %</td>
<td>48 (36-63) %</td>
<td>97 (94-100) %</td>
<td>≤11 (10-12) mm</td>
</tr>
<tr>
<td>S’</td>
<td>90%</td>
<td>58 (35-73) %</td>
<td>46 (33-58) %</td>
<td>95 (91-98) %</td>
<td>≤5.7 (5.2-6.3) cm/s</td>
</tr>
<tr>
<td>e’</td>
<td>90%</td>
<td>37 (22-58) %</td>
<td>36 (28-47) %</td>
<td>93 (87-97) %</td>
<td>≤7.5 (6.3-7.9) cm/s</td>
</tr>
<tr>
<td>a’</td>
<td>90%</td>
<td>39 (21-66) %</td>
<td>37 (27-52) %</td>
<td>92 (87-96) %</td>
<td>≤8.0 (6.6-8.9) cm/s</td>
</tr>
</tbody>
</table>
P4581. Systemic cardiac troponin T is associated with incident atrial fibrillation among patients with suspected stable angina

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**Purpose:** Higher systemic cardiac troponin T (hs-cTnT) is associated with overall adverse prognosis for cardiovascular disease; however, the relationship with incident atrial fibrillation (AF) is less known. We studied this relationship among 3568 patients evaluated with coronary angiography for stable angina pectoris and without previous history of AF.

**Methods:** The prospective association between hs-cTnT categories (≤3 ng/L; n=1694; 4–9; n=1085; 10–19; n=614 and 20–30; n=175) were studied by Kaplan Meier plots and by Cox regression.

**Results:** The population consisted of 2535 (71.0%) males with a median (interquartile range) age of 61 (54 - 69) years. A total of 412 (11.5%) were diagnosed with AF. Kaplan Meier plots revealed a strong, graded association between hs-cTnT categories and risk of AF (Figure 1). In a Cox model adjusted for age, sex, body mass index, hypertension, diabetes mellitus, smoking, Apo A1, Apo B, estimated glomerular filtration rate, and left ventricular ejection fraction (%) (Model 1), hazard ratios (HRs) (95% confidence intervals [CIs]) were 1.53 (1.16-2.03), 2.03 (1.49-2.78) and 2.15 (1.40-3.31) when comparing the 2nd, 3rd and 4th to the 1st hs-cTnT group, respectively (P for trend <0.000001). The association was similar after further adjusting for severity of angiographic coronary artery disease (0–3) at baseline, medication (acylsalisylic acid, calcium blockers, beta blockers, loop diuretics, ACE-inhibitors and/or angiotensin receptor blockers and statins), previous peripheral artery disease or previous coronary intervention (Model 2).

**Conclusion:** In this large and well-defined cohort of patients undergoing elective coronary angiography, higher levels of hs-cTnT predicted increased risk of incident AF independent of traditional risk factors.

**Table 1. Hs-cTnT and incident AF**

<table>
<thead>
<tr>
<th>Hs-cTnT (ng/L)</th>
<th>Univariate</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio (95% CI)</td>
<td>P value</td>
<td>Hazard Ratio (95% CI)</td>
</tr>
<tr>
<td>&lt;4</td>
<td>Ref</td>
<td></td>
<td>Ref</td>
</tr>
<tr>
<td>4-9</td>
<td>2.23 (1.71-2.91)</td>
<td>&lt;0.000001</td>
<td>1.53 (1.16-2.03)</td>
</tr>
<tr>
<td>10-19</td>
<td>3.60 (2.72-4.72)</td>
<td>&lt;0.000001</td>
<td>2.03 (1.49-2.78)</td>
</tr>
<tr>
<td>20-30</td>
<td>4.27 (3.89-6.29)</td>
<td>&lt;0.000001</td>
<td>2.15 (1.40-3.31)</td>
</tr>
</tbody>
</table>

Figure 1. Kaplan-Meier plot of incident AF

Figure 2. Detection of LV dysfunction.
1194. 7-year change in physical fitness in healthy middle-aged men predicts stroke during 28 years follow-up

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Background: Little is known about temporal change in physical fitness and later risk of stroke in healthy individuals.

Methods: We performed a prospective cohort study of 2014 healthy Norwegian men aged 40–59 years, recruited during the period 1972–1975 and followed until 2007. Participants underwent a comprehensive assessment at baseline and at a 7-year follow-up visit, including a bicycle exercise test. Only participants who were healthy and able to complete the exercise test at both visits were included in the analyses. Physical fitness was measured as total work (kJ) divided by body weight (kg) and was age-adjusted. We calculated change in fitness from baseline to the 7-year visit, and divided the participants into quartiles of the delta value between the two visits. Data on stroke were collected from all later visits, medical records and the national death registry. We used Cox regression for analysis, adjusting for risk factors registered at the 7-year follow-up visit: age, systolic blood pressure, smoking, body mass index, resting heart rate, PR interval and physical fitness (at baseline).

Results: 1403 (70%) participants met the inclusion criteria. During 7 years 487 (35%) participants increased while 916 (65%) decreased their level of age-adjusted physical fitness. Mean change in physical fitness was -0.13 kJ/kg. 177 (13%) of the participants had a stroke during a median of 23 years follow-up. Compared to the quartile with largest decrease in physical fitness (Q1), the quartile with largest increase (Q4) had a hazard ratio of 0.44 for later stroke (95% CI 0.28–0.67, p<0.001, Figure 1).

Conclusion: Temporal change in physical fitness in middle-aged healthy men predicts stroke during long-term follow-up and into old ages.

P1441. Left ventricular mechanical dispersion, a novel marker for ventricular arrhythmic events, is increased in conditions with enhanced risk for cardiovascular disease. Data from the ACE 1950 study

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Background: Increased mechanical dispersion (MD) has proven to predict ventricular arrhythmic events in patients with established cardiovascular disease (CVD). Little is known about MD in the general population.

Purpose: To investigate if increased MD is present in individuals with established risk factors for CVD in a middle-aged general population.

Methods: The Akershus Cardiac Examination (ACE) 1950 cohort included 3706 men and women born in 1950 from Akershus County, Norway. Baseline examination included evaluation for CV risk factors and two-dimensional speckle tracking imaging echocardiography. We measured left ventricular (LV) global longitudinal strain (16 segments) and calculated MD from these measurements. MD is the standard deviation of contraction duration of the 16 segments, and is a measure of LV contraction heterogeneity. We assessed the association between established clinical conditions for CV risk and MD by multivariate linear regression analyses.

Results: In total 2525 subjects (68%) had echocardiographic images suitable for strain analyses. The median value for MD was 38 ms (IQR 17.25). Baseline characteristics according to MD are outlined in the table. Subjects with supra-median MD had a higher prevalence of CV risk factors. In a multivariate model we found a significant association between increased MD and hypertension (B=4.11; p<0.001), CAD (B=7.40; p<0.001), renal failure (B=6.80; p<0.01), diabetes (B=2.23; p<0.05), obesity (B=1.40; p<0.05) and COPD (B=2.50; p<0.05), but not stroke/TIA.

Conclusion: The present study demonstrates that increased LV MD is frequently present in subjects with clinical conditions at risk of CVD. This finding may indicate that individuals who fall into these categories are more prone to ventricular events.
Patients with left bundle branch block are hypersensitive to afterload: moderate elevation of systolic pressure caused marked depression of left ventricular function

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Introduction: In epidemiological studies left bundle branch block (LBBB) in otherwise healthy individuals carries a good prognosis, whereas LBBB in patients with arterial hypertension is associated with increased morbidity and mortality. We hypothesized that elevated blood pressure has a direct depressive effect on left ventricular (LV) function in individuals with LBBB.

Purpose: To test the hypothesis that subjects with LBBB have reduced tolerance to elevation in arterial pressure.

Methods: Eleven otherwise healthy LBBB-patients were compared to 11 age-matched controls with similar LV ejection fraction (EF). Inflatable cuffs were placed around both thighs and one arm and a handgrip dynamometer was used for static exercise. Global longitudinal strain was measured by speckle tracking echocardiography and LVEF by biplane Simpson’s method. Arterial pressure was increased by simultaneous cuff inflation and handgrip.

Results: The intervention increased systolic pressure by 34±13 mmHg in LBBB patients and 38±12 mmHg in controls (NS). This was associated with a reduction in LVEF from 52±4 to 41±6% (p<0.01) in LBBB and from 54±4 to 49±5% (p<0.01) in controls (p<0.02 LBBB vs controls). Global longitudinal strain decreased from 16.9±2.4 to 12.3±1.9% (p<0.01) in LBBB and from 20.8±2.5 to 18.4±2.4% (p<0.01) in controls, (p<0.01 LBBB vs controls). The figure shows strain traces from a representative patient and illustrates that the decrease in global LV function with elevated blood pressure in LBBB patients was due to a marked decrease in septal systolic shortening, whereas LV free wall shortening was maintained.

Conclusions: Moderate elevation of afterload in patients with LBBB caused marked depression of LV systolic function. This was attributed to aggravation of septal function. Future studies should investigate if a similar load dependency is present in hypertensive patients with LBBB and during right ventricular pacing which similar to LBBB, causes abnormal septal motion.
P6363. Abnormal left ventricular geometry in ankylosing spondylitis

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**Background:** Abnormal left ventricular (LV) geometry is a strong precursor for cardiovascular disease. Patients with ankylosing spondylitis (ASp) have increased risk for cardiovascular disease, but whether they also have increased prevalence of subclinical cardiac disease like abnormal LV geometry is unknown.

**Purpose:** To assess the prevalence and covariables of abnormal LV geometry in patients with ASp.

**Methods:** Clinical and echocardiographic data from 139 ASp patients, and 126 age- and sex matched control subjects were used. LV geometry was classified as abnormal if LV hypertrophy (LV mass index ≥ 49.2 g/m² in men and ≥ 46.7 g/m² in women) or concentric geometry (LV relative wall thickness ≥ 0.43) was present.

**Results:** ASp patients were on average 49 years old, and 40% were women. The prevalence of hypertension (35% versus 41%) and diabetes (5% versus 2%) were similar among ASp patients and controls, but ASp patients had lower rates of obesity (8% versus 17%, p=0.03). Patients with ASp had higher prevalence of LV hypertrophy (15% vs 6%, p=0.01) compared to controls, in particular of the eccentric type (Figure). Control subjects had more concentric remodelling than ASp patients (19% versus 8%, p=0.008) (Figure). In multivariable logistic regression analysis, having ASp was associated with LV hypertrophy independent of significant associations with presence of hypertension and obesity (odds ratio 6.4, 95% confidence interval 2.1–19.4, p=0.001). ASp disease characteristics or use of anti-inflammatory medication were not associated with abnormal LV geometry.

**Conclusion:** ASp patients have higher prevalence of LV hypertrophy, in particular eccentric LV hypertrophy, which may contribute to the reported increased risk of cardiovascular events in patients with ASp.

P4528. Bystander cardiopulmonary resuscitation after out-of-hospital cardiac arrest in children with congenital heart defects

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**Background:** Congenital heart defects (CHDs) are common birth defects, and children with congenital heart defects have increased risk of out-of-hospital cardiac arrest (OHCA) compared to healthy individuals. The outcome of OHCA in children is generally poor. Bystander cardiopulmonary resuscitation (BCPR) may prevent death, but previous studies have reported a low rate of BCPR following OHCA in children. In this nationwide cohort study, we describe the rate of BCPR and the rate of survival after OHCA in children 2-18 years old with CHDs.

**Methods:** Data concerning all live births in Norway in 1994–2009 were retrieved from the Medical Birth Registry of Norway, the patient administrative systems at all hospitals in Norway, the University Hospital’s Clinical Registry for Congenital Heart Defects and the Norwegian Cause of Death Registry. Survivors were followed through 2012, and supplementary information for the deceased children was retrieved from medical records at Norwegian hospitals. Cardiac arrests within 30 days of a cardiac surgical procedure were excluded.

**Results:** Among the 943 871 live births in Norway 1994–2009 were retrieved from the Medical Birth Registry of Norway, the patient administrative systems at all hospitals in Norway, the University Hospital’s Clinical Registry for Congenital Heart Defects and the Norwegian Cause of Death Registry. Survivors were followed through 2012, and supplementary information for the deceased children was retrieved from medical records at Norwegian hospitals. Cardiac arrests within 30 days of a cardiac surgical procedure were excluded.

**Conclusion:** The rate of bystander cardiopulmonary resuscitation after out-of-hospital cardiac arrest among children with congenital heart defects is low.
defects was high in Norway 1994–2012. The survival was comparable to the reported rate in the general child population.

Methods: We included 187 HCM subjects of which 121 (65%) had left ventricular hypertrophy, hence HCM phenotype positive (HCM+) (47 Females/ 74 Males) and 66 (35%) were HCM genotype positive, phenotype negative (HCM−) (40 Females/ 26 Males). We defined physical activity ≥6 metabolic equivalents as vigorous exercise and recorded lifetime vigorous exercise. Subjects with vigorous exercise for ≥4 hours/week for ≥6 years were defined as athletes. By echocardiography we assessed left ventricular (LV) maximum wall thickness (MWT), LV end diastolic (EDVI) and end systolic (ESVI) volume index.

Results: Mean age was 49±16 years, with no difference between females and males (p=0.99).

HCM+ patients were more frequently male (Male: 61%, Female: 39%, p=0.001) and HCM− subjects were more frequently female (Male: 36%, Female: 64%, p=0.001).

HCM males had accumulated more lifetime vigorous exercise than females (HCM+: 2886 (0–35776) hours vs. 0 (0–9464) hours, p<0.001; HCM−: 2535 (0–10208) hours vs. 1356 (0–10384) hours, p=0.05).

Lifetime vigorous exercise correlated moderately with EDVI (Figure) and ESVI (HCM+: rho 0.33, p=0.03; HCM−: rho 0.43, p=0.006) in females. In contrast, lifetime vigorous exercise did not correlate with EDVI (figure) or ESVI (HCM+: rho 0.21, p=0.08; HCM−: rho 0.24, p=0.28) in males.

There was no significant correlation between lifetime vigorous exercise and MWT in females or in males (Female HCM+: p=0.08, Female HCM−: p=0.67, Male HCM+: p=0.79, and Male HCM−: p=0.36).

Female HCM athletes had larger EDVI than non-athletes (HCM+: 46±11ml/m² vs. 35±9ml/m², p=0.009; HCM−: 56±11ml/m² vs. 43±11ml/m², p<0.001), while male HCM athletes had similar EDVI to non-athletes (HCM+: p=0.30; HCM−: p=0.30). Female HCM+ athletes had thinner MWT than non-athletes (15±1mm vs. 19±4mm, p=0.03), but there was no difference in MWT between female HCM− athletes and non-athletes (18±1mm vs. 18±1mm, p=0.81). There was no difference in MWT between male HCM athletes and non-athletes (HCM+: 9±1mm vs. 9±1mm, p=0.47; HCM−: 19±4mm vs. 19±4mm, p=0.81).

Conclusions: Females with HCM+ and HCM− had accumulated less lifetime vigorous exercise than males, but exercise was associated with larger LV volumes only in females. MWT was smaller in female HCM+ athletes compared to non-athletes, but similar between athletes and non-athletes in female HCM−, male HCM+ and male HCM−.

These results indicate gender differences in the effects of exercise on heart morphology and/or gender differences in lifestyle adaption to HCM diagnosis.

P2528. Exercise and gender differences in hypertrophic cardiomyopathy
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Introduction: Hypertrophic cardiomyopathy (HCM) is an autosomal dominant disease with doubled penetrance in males versus females. Competitive sports are discouraged in phenotype positive, due to possible increased risk of arrhythmias and sudden cardiac death. Relation between exercise and heart morphology in HCM is not known.

Purpose: We aimed to investigate the relation between lifetime exercise and phenotype expression in HCM females and males.
Exercise dose and threshold for adverse outcome in arrhythmogenic cardiomyopathy

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Background: Vigorous exercise is known to aggravate arrhythmogenic cardiomyopathy (AC). However, the relationship between exercise dose and adverse outcome in AC is poorly described.

Purpose: We aimed to explore the exercise dose and its threshold related to ventricular arrhythmia (VA), right ventricular (RV) dilation, RV dysfunction and left ventricular (LV) dysfunction in AC.

Methods: AC patients with history of regular exercise were included in a cross-sectional study. Exercise dose was expressed as metabolic equivalents (METs) x minutes/week. VA was defined as sustained ventricular tachycardia, ventricular fibrillation, or aborted cardiac arrest. By echocardiography, RV dilation was defined as proximal RV outflow tract (RVOT) diameter >35mm or basal RV diameter (RVD) >41mm. RV dysfunction was defined as fractional area change (FAC) <35% or tricuspid annular plane systolic excursion (TAPSE) <17mm. LV dysfunction was defined as ejection fraction (EF) lower than 54% in females and 52% in males, or global longitudinal strain (GLS) worse than -18%.

Results: We included 100 AC patients with history of regular exercise (40±16 years old, 42 female). Median exercise dose was 840 MET-minutes/week (range 180–5400). Exercise doses correlated with RVOT diameter (R=0.30, p=0.003), RVD (R=0.34, p=0.001), FAC (R=0.32, p=0.002), TAPSE (R=0.30, p=0.003), EF (R=0.50, p=0.001) and GLS (R=0.35, p=0.001). A large proportion of patients had adverse outcome (Figure). These patients had higher exercise doses than patients without adverse outcome (VA: 2325 vs. 720, p=0.002, RV dilation: 1200 vs. 720, p=0.01, RV dysfunction: 2400 vs. 840, p=0.002 and LV dysfunction: 2700 vs. 840 MET-minutes/week, p=0.001). Exercise threshold values for adverse outcome by ROC analysis were ≥870 MET-minutes/week (equivalent to 2.5h moderate intensity exercise/week) for VA and RV dilation (AUC 0.69, 95% CI 0.58–0.80, and 0.62, 95% CI 0.51–0.74, respectively) (Figure).

Conclusion: Higher exercise doses were associated with adverse outcome in AC patients. ≥2.5h moderate intensity exercise/week was the threshold for VA and RV dilation, and double the exercise dose (≥4.9h moderate intensity exercise/week) was the threshold for RV and LV dysfunction. These results confirm the close relationship between exercise and outcome in AC, and indicate that VA and RV dilation occur at lower exercise doses than RV and LV dysfunction.
P4304. Feasibility, accuracy and clinical influence of pocket-sized imaging by experts of the carotid arteries in patients with stroke and transitory ischemic attack

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On behalf: Centre for Innovative Ultrasound Solutions

Background/Introduction: Imaging of the carotid arteries is mandatory in stroke and transitory ischemic attack (TIA) patients and may have therapeutic influence.

Purpose: We aimed to study the feasibility, accuracy and clinical influence of the use of a point-of-care pocket-sized imaging device (PSID) by experts for assessment of carotid artery disease in patients with suspected stroke and TIA.

Methods: 80 patients admitted to a stroke unit with suspected stroke or TIA were examined with PSID by cardiologists experienced in carotid ultrasound. Utilizing a linear transducer, grey scale and colour Doppler images were displayed and stored. Reference method was high-end triplex ultrasound by cardiologists, blinded for the PSID study, and was performed in all patients. Computer tomography (CT) angiography of the neck arteries was performed on clinical indication.

Results: The final diagnosis was ischemic stroke or TIA in 76% of the patients. Median (range) age was 72 (23–93) years. Evaluation of all three carotid segments were judged feasible in 95% of patients. In 76% of the PSID examinations, a significant carotid stenosis (≥50% diameter reduction) was excluded and no further diagnostic tests were considered necessary. Sensitivity and specificity for diagnosing significant stenosis was 92% and 93%, respectively. PSID examinations missed 1 of 12 with significant stenosis. In this case the operator was not able to assess the carotids adequately due to image quality. All 4 patients in need of surgery had significant stenosis revealed by PSID examinations. Compared to CT angiography, sensitivity and specificity was 87% and 83%, respectively.

Conclusions: Point-of-care examinations of the carotid arteries by experts using PSID were feasible, accurate and could significantly reduce the need for high-end ultrasound examination in stroke and TIA patients. This may improve diagnostic workflow.

P487. Pulmonary vein stenosis after ablation treated by stent implantation - long term outcome

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Introduction: A rare but feared complication after catheter ablation of atrial fibrillation (AF) is symptomatic severe pulmonary vein stenosis (PVS). It is not clear which treatment option (pulmonary vein (PV) angioplasty (with or without drug eluting balloons) or PV stenting) should be preferred.

Purpose: We wanted to investigate the clinical outcome of nine patients treated with stent implantation which is the first choice in our centre.

Methods and results: Nine patients (7 paroxysmal, 2 persistent) in appr 3000 ablated patients (2001–2015) developed symptomatic PVS (all men, mean age 46±10 years). After a mean of 2,2±0,8 ablations three patients had recurrent pneumonia and the remaining patients slightly but highly symptomatic reduced functional capacity (NYHA 2). Imaging was performed before the stenting procedure (CT (n=7), MR (n=5), transoesophageal echocardiography (n=6) and angiography (n=9)). A total of 10 PV were stented 11±4 months after the last ablation and 11 stents were implanted (one patient received 2 stents in 2 consecutive procedures, one patient needed snare removal and later new stent implantation). All patients are now in NYHA functional class 1 (p<0,05) after a mean follow up of 52±32 (6–120) months and no further pneumonia was diagnosed. A slight increase in working capacity (208 versus 252 Watt, ns) could be demonstrated and 2 patients were ablated for their AF after stent implantation. Two patients still have paroxysmal atrial fibrillation.

Conclusions: Stent implantation in symptomatic PVS after ablation demonstrates good clinical effect during long term follow up and AF ablation can be performed in patients previously stented for PVS.
P1439. Mechanical dispersion predicts survival after ST-segment elevation myocardial infarction in patients treated with thrombolysis or percutaneous coronary intervention

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Background: New echocardiographic techniques have demonstrated improved prediction of cardiovascular events after revascularization of STEMI. The aim of this study was to investigate whether addition of strain echocardiography to conventional echocardiographic assessment of left ventricular function may improve prediction of outcome in patients with STEMI treated with thrombolysis or PCI

Methods: We included 184 patients with STEMI. 61 patients treated with thrombolysis in 2004 and 123 patients treated with primary PCI in 2014 and followed them for 12 months. Death and ventricular arrhythmia were registered as clinical events during follow up. Echocardiography was performed after STEMI treatment and before discharge from the acute event. We assessed left ventricular function by left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS). Mechanical dispersion (MD) was calculated by standard deviation of time to maximum myocardial shortening in a 16-segment LV model.

Results: LVEF (45±10% vs 46±7%, p=0.50), GLS (-14.9±4.4% vs -14.4±3.1%, p=0.28) and MD (55±15ms vs 52±14ms, p=0.18) at 3.1±3 days vs 2.8±6 days after STEMI did not differ between patients treated with thrombolysis and PCI. Ventricular arrhythmia and death within 12 months occurred in 7 (12%) patients treated with thrombolysis and in 2 (1.6%) patients treated with PCI (p<0.01). MD was more pronounced in patients with ventricular arrhythmia and death compared to patients without events (66±17 ms vs. 52±14 ms, p=0.01) while LVEF (39±14% vs 46±7%, p=0.06) and GLS (-12±5.9% vs -14.7±3.4%, p=0.09) did not differ significantly.

Kaplan Meier analysis demonstrated improved outcome in patients with MD <65 ms (log rank p<0.01)

Conclusions: Mechanical dispersion predicts adverse clinical events and indicates that increased heterogenous myocardial deformation after STEMI may affect outcome. This difference, however, was not reflected by LVEF and GLS which were similar in both revascularization groups. STEMI patients treated with thrombolysis had increased risk of ventricular arrhythmia and death compared to patients treated with primary PCI.

4794. Presentation, detection and treatment of Lotus valve thrombosis

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Background: Transcatether aortic valve replacement (TAVR) is an established treatment option for symptomatic, severe aortic stenosis in intermediate and high surgical risk patients. The occurrence of both clinically overt and silent valvular thrombosis has been reported.

Purpose: To evaluate the clinical presentation, diagnostics, imaging modalities, treatment options and prognosis of patients treated at our institution using the Lotus, second-generation tri-leaflet, bovine tissue valve.

Methods: A total of 98 patients underwent TAVR using the Lotus system at our institution from September 2014 until September 2016. All patients were included in a safety and quality control registry from which data was obtained and analyzed. Clinical follow-up including transthoracic echocardiography (TTE) was scheduled at 1, 6 and 12 months. Multidetector computed tomography (MDCT) was obtained when symptoms and/or TTE findings suggested valvular dysfunction. Continuous variables are presented as mean (SD).

Results: Following successful device implantation, n=7 (7%) patients presented after 8.5 (6.6) months with valve thrombosis either during planned follow-up visits or clinically driven evaluation (range 1 to 18 months). The presence of thrombus was not significantly associated with larger bioprosthesis size (one 23 mm, two 25 mm and 4 27 mm). All but one had symptoms with dyspnoe and/or angina. TTE pre- and immediately post-TAVR showed a mean pressure gradient (MPG) of 51.1 (11.3) mmHg and 12.0 (3.3) mmHg respectively. Upon presentation with thrombosis MPG was 33.9 (14.9) while subsequent MDCT showed reduced leaflet mobility and perileaflet
hypodense mass(es) consistent with thrombus. All patients were treated with vitamin K antagonist (VKA) in addition to single platelet inhibition with resolution of symptoms, gradients (MPG 10.9 (2.2) mmHg) and MDCT findings within 2.1 (1.1) months. There were no recorded cerebrovascular or systemic embolic events, nor was surgery required.

**Conclusion:** Thrombosis of the Lotus valve is not uncommon and associated with significant valvular dysfunction and morbidity. MDCT is crucial in both detection and monitoring of therapeutic intervention and should be obtained promptly when symptoms and/or TTE gradient suggest valvular thrombosis. In our experience VKA appears to be an efficient treatment option.

**P3242.** Prolonged release of cardiac troponin I after endurance exercise could indicate silent coronary artery disease in recreational athletes: the NEEDED study 2014

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**Background:** A physiological increase in cardiac Troponins (cTn) occurs after prolonged endurance exercise. We have previously linked high post-exercise levels of cardiac troponin I (cTnI) >201ng/l with the presence of asymptomatic coronary artery disease (CAD).

**Methods:** 1009 healthy subjects (46.9 (40.1–52.7) years (median (IQR)), 77.4% males) who participated in a 91-km endurance mountain bike competition (the North Sea Race 2014) were included. Clinical status, blood samples, ECGs, blood pressure and demographics were obtained 24 h prior to the race, 3 h after the race, and 24 h after the race for all participants. All participants with symptoms of CAD or ECG changes suggestive of CAD at any time point were excluded from the study. CT coronary angiography (CTCA) or conventional angiography were performed in the 80 subjects with highest cTnI (group 1 (G1)), roughly corresponding with the proposed cut-off of 201 ng/l. A control group (G2) of 40 subjects with cTnI values <201 ng/l matched for age, sex, body mass index and race performance also underwent CTCA.

**Results:** Endurance exercise was associated with a marked but transient increase in cTnI (Table). In G1, 10 (12.5%) participants had significant CAD (including myocardial bridging) whereas in G2, only 1 (2.5%) participant had significant CAD (p=0.097). At 3 and at 24 h after the race, those with CAD had significantly higher cTnI-values than the rest of G1 and G2 (p=0.026 at 3 h after the race and p=0.001 at 24 h after the race (Table)). This association was also significant at 24 h within the group of subjects (n=80) with the highest cTnI (G1); those with CAD had cTnI of 160 (108.1–214.2) vs 55.6 (31.7–115.4) (p=0.002).

**Conclusion:** Subjects with CAD had significantly higher cTnI values 24 h after endurance exercise. This finding suggests that the subjects with highly increased cTnI values after prolonged exercise should be further investigated even in the absence of symptoms or significant ECG changes.

**Table 1.** cTnI values according to findings of significant CAD in a total of 120 subjects that underwent CT- or conventional coronary angiography

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=109)</th>
<th>Significant CAD (n=11)</th>
<th>Mann-Whitney U test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline cTn</td>
<td>2.6 (1.6–6.8)</td>
<td>2.8 (1.7–7.2)</td>
<td>0.808</td>
</tr>
<tr>
<td>3 h after race cTn</td>
<td>216.7 (107.2–296.5)</td>
<td>269.2 (206.3–998.5)</td>
<td>0.026</td>
</tr>
<tr>
<td>24 h after race cTn</td>
<td>35.5 (18.8–81.6)</td>
<td>151.3 (101.9–195.9)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
P1624. Cardiovascular risk profile at the age of 40 in women with previous hyperemesis gravidarum or hypertensive disorders in pregnancy

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Background: Hyperemesis gravidarum is the most common cause of hospitalisation in first trimester and has been associated with placental dysfunction. Hypertensive disorders in pregnancy, which are also associated with placental dysfunction, are associated with increased cardiovascular (CV) risk. CV risk after hyperemesis has not yet been systematically explored.

Purpose: To investigate if hyperemesis gravidarum or hypertensive disorders in pregnancy are associated with increased maternal CV risk at the age of 40.

Methods: Population-based study. CV risk factors at the age of 40 among women with previous births were studied through linkage of the Norwegian Health Service screening program “Age 40” and the Norwegian Birth Registry. Women with a history of hyperemesis or hypertensive disorders in pregnancy were compared to women without such history.

Results: Among 178 231 women included in the study, 2 140 (1.2%) had experienced hyperemesis, 13 348 (7.5%) had experienced hypertensive disorders in pregnancy and 189 (0.1%) had experienced both. The mean time from first pregnancy to attending the “Age 40” Program was 17.9 years. Women with hyperemesis had lower mean systolic blood pressure and were less likely to smoke compared to women without any of the explored pregnancy complications. Hyperemesis was associated with higher BMI and being more inactive. Most of the CV risk factors studied were increased for women with previous hypertensive disorders in pregnancy; except physical activity and smoking (Table 1).

Conclusion: Women with previous hypertensive disorders in pregnancy had increased levels of most CV risk factors at the age of 40, but we found no consistent evidence of increased CV risk among women who suffered from hyperemesis gravidarum.

P5272. Concomitant heart failure (HF) and type 2 diabetes (T2D) - a deadly duo

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Background/Aims: Diabetes and heart failure (HF) are both global epidemics with tremendous costs on society with increased rates of HF hospitalizations and worsened prognosis when co-existing, making it a significant “deadly duo”. The evidence for pharmacological treatment of HF in patients with type 2 diabetes mellitus (T2D) stems typically from either subgroup analyses of patients that were recruited to randomized controlled trials of HF interventions, usually in patients with reduced EF, or from subgroup analyses of HF patients recruited to cardiovascular (CV) outcome trials (CVOT) of glucose lowering agents involving patients with T2D. We explored the incremental effect on mortality/morbidity of co-existing HF and T2D in these trials.

Methods: This work summarizes the literature on interventions aiming to reduce the HF burden in T2DM and includes 7 HF trials of ACEi, digoxin, β blocker, ARB, If-blocker, MRA, and ARNI involving 38600 patients, with or without prevalent

Table 1. Cardiovascular risk factors

<table>
<thead>
<tr>
<th>Pregnancy complications</th>
<th>Cardiovascular risk factors at the age of 40 [Mean (SD) or n (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Body mass index (kg/m²)</td>
</tr>
<tr>
<td>No HG or HT (ref)</td>
<td>24.2 (3.7)</td>
</tr>
<tr>
<td>HG</td>
<td>24.4 (3.8)*</td>
</tr>
<tr>
<td>HT</td>
<td>26.4 (4.9)*</td>
</tr>
<tr>
<td>Both HG and HT</td>
<td>26.5 (5.1)*</td>
</tr>
</tbody>
</table>

Abbreviations: HG, hyperemesis gravidarum; HT, hypertensive disorders in pregnancy; ref, reference group. *p-value <0.01, tested with t-test or Chi-squared test.
P3673. Differences in mortality between patients referred to coronary angiography with stable angina or unstable angina

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Introduction: New, high-sensitivity troponins detects very small amounts of myocardial necrosis, uncovering myocardial infarctions in patients previously diagnosed with unstable angina (UA). Consequently, the mortality and morbidity in the UA population is falling, leading some to suggest that the diagnosis of UA will become redundant in the future. The difference in mortality between patients presenting with UA and stable angina remains unclear.

Purpose: To investigate differences in mortality between patients presenting to coronary angiography (CAG) as UA and stable angina.

Methods: Study participants were recruited from the clinical registry of all CAGs performed at the sole providing hospital in the region. We included all procedures performed in patients with UA (n=961) and stable angina (n=2,400) in the primary catchment area from 2005 to 2010, and followed them until April 2013. Unstable angina was defined as troponin T ≤14 ng/L. High-sensitive troponin T was implemented in July 2009; standard troponin values measured up to that time was multiplied by a factor of three to adjust for lower sensitivity. Cox regression models was used to calculate the hazards ratios of death adjusted for age, sex, known coronary artery disease (CAD), kidney function and stratified for obstructive CAD, non-obstructive CAD and no CAD.

Results: During a median follow-up of 5.3 years, death occurred in 256 patients. The crude mortality of patients referred to CAG with presumed UA was 2.0%, compared to 1.8% in patients referred with presumed stable angina. Patients with UA did not have a significantly higher mortality, neither in an unadjusted model (hazard ratio (HR) 1.09; 95% confidence interval (CI) 0.83–1.43) or adjusted for age, sex, kidney function, and known CAD (HR 1.21; 95% CI 0.87–1.62). Obstructive CAD was prevalent in 51% of UA patients and 60% of stable angina patients. These patients had a higher mortality than patients with non-obstructive or no CAD (HR 1.52; 95% CI 1.08–2.15), but again with no difference between UA and stable angina (HR 1.21; 95% CI 0.82–1.79, ref. stable angina). Further, there was no significant difference in mortality between UA and stable angina in patients with obstructive CAD in the main stem, proximal LAD or in all three coronary vessels (HR 1.65; 95% CI 0.88–3.12, ref. stable angina). In subgroup analyses, UA patients with obstructive CAD and no prior CAD had non-significantly higher mortality than patients with stable angina (HR 1.59; 95% CI 0.98–2.60).

Conclusion: In the era of high-sensitive troponins, we found no difference in mortality between patients referred to CAG as UA and stable angina. A better identification of acute angina patients which safely can be referred to elective CAG is warranted.
P4944. Markers of gut leakage are associated with cardiovascular events in a high-risk population

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On behalf: Center for Clinical Heart Research

Background: The endotoxin lipopolysaccharide (LPS) elicits a strong proinflammatory response when it interacts with the innate immune system. This interaction is facilitated through lipopolysaccharide binding protein (LBP) and the co-receptor CD14. LBP-CD14 complex promote atherogenic and proinflammatory properties through toll-like receptor 4 (TLR4), which is a transmembrane receptor mainly on mononuclear immune cells.

The source of plasma LPS in healthy is thought to derive from the gut. Diseases which challenge the intestinal walls integrity facilitate leakage of LPS into the bloodstream, and studies have shown that smoking, high fat meals and metabolic disturbances may induce low-grade gut-related endotoxemia.

Purpose: We want to investigate whether circulating levels of LBP and CD14 (sCD14) are associated with cardiovascular events and all-cause mortality in a high risk population.

Methods: We examined 484 elderly men, aged between 65–75 years, at high cardiovascular risk who were followed for 3 years for clinical outcome. At inclusion, 16% were diabetics, 33% smokers, 18% had a previous myocardial infarction and 31% were treated for hypertension.

Blood samples were collected at inclusion in fasting condition. LBP and sCD14 were analyzed by commercial ELISAs. In total 55 patients suffered new cardiovascular (CV) events and 30 patients died.

Results: The concentration of LBP was significantly higher in patients who suffered a new CV event compared to individuals without (median 14.16 vs 12.68 ug/ml, respectively; p=0.006). sCD14 levels were significantly higher in patients who died compared to survivors (median 1456 vs 1286 ng/mL, respectively; p=0.009). When dichotomizing levels at medians, the group above the median of LBP (>12.92 ug/mL) had an unadjusted OR of 2.45 (95% CI 1.34–4.47), p=0.004 for having a new CV event and the group with the highest CD14 levels (>1297 ng/mL) had an unadjusted OR of 2.91 (CI 1.27–6.68), p=0.012 for death. When adjusting for relevant covariates (age, smoking, diabetes, CRP, systolic blood pressure, BMI and previous myocardial infarction) in multivariable logistic regression analyses, LBP remained significantly associated with a new CV event (OR 2.33 (CI 1.23–4.40), p=0.009), whereas sCD14 did no longer remain significantly associated with all-cause mortality (OR 2.10 (CI 0.88–5.02), p=0.06).

Conclusion: The significant association between markers of gut leakage and clinical outcome in individuals at high risk of CV disease, indicate gut-related endotoxemia to be of importance.

P5514. Pitfalls in automated QTc measurements. Experience from a manual review

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Background: To accurately determine the corrected QTc interval is an important but difficult task for most physicians. Automated ECG interpretation could be a useful tool, but is it reliable in everyday practice?

Purpose: We wanted to investigate the accuracy of automated measurements of the QTc interval compared to manual assessment in ECGs where the automated measurement suggests marked QTc prolongation.

Methods: Our institution has used an electronic ECG database since 2004. The database contains >250,000 ECGs. We searched the database for ECGs with QTc ≥500 ms and HR >30 and <100, absence of atrial fibrillation or flutter, absence of acute STEMI, QRS ≤120 ms and age ≥15 years.

All identified ECGs were manually reviewed and we compared the manually recorded QTc to the automated value. After review the ECGs were classified into the following 8 categories. QTc ≥500 ms and ΔQTc <10 ms, QTc ≥500 ms and ΔQTc ≥10 ms, false QTc value due to electromagnetic noise, false QTc value due to inclusion of P or U wave in QT interval, false QTc due to PVC in bigemini, false QTc due to short SVT, non-identified atrial fibrillation or flutter or other reasons.

Results: We identified ECGs from 1855 unique patients. After review ECGs from 324 patients were excluded and the cohort consisted of 1531 ECGs. In 1493 ECGs manual and automated QTc was in agreement while QTc was adjusted to a higher value in 15 cases and to lower value in 23 cases (Table 1).

Conclusion: Agreement between manually and automated QTc measurement was 88% in ECGs in sinus rhythm and with adequate technical quality indicating reliable automated QTc in absence of atrial fibrillation and other rhythm disturbances.
P6343. Sex-specific covariates of aortic valve calcification by echocardiography: relation to outcome in aortic stenosis

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Objective: Sex differences in covariates of aortic valve calcification (AVC) by echocardiography have not been reported from a large prospective study in aortic stenosis (AS).

Methods: AVC was assessed using a prognostically validated visual score and grouped into none/mild or moderate/severe AVC in 1725 men and women with asymptomatic AS in the Simvastatin Ezetimibe in Aortic Stenosis study. The severity of AS was assessed by the energy loss index (ELI) taking pressure recovery in the aortic root into account.

Results: More men than women had moderate/severe AVC at baseline despite less severe AS by ELI (p<0.01). Moderate/severe AVC at baseline was independently associated with lower aortic compliance and more severe AS in both sexes, and with increased high-sensitive C-reactive protein (hs-CRP) only in men (all p<0.05). In Cox regression analyses, moderate/severe AVC at baseline was associated with a 2.6-fold (95% CI 1.70–3.93) higher hazard rate of major cardiovascular events in women, and a 2.2-fold higher hazard rate in men (95% CI 1.55–3.17) (both p<0.001), after adjustment for age, hypertension, study treatment, aortic compliance, left ventricular mass and systolic function, AS severity and hs-CRP. Moderate/severe AVC at baseline also predicted a 1.8-fold higher hazard rate of all-cause mortality in men (95% CI 1.04–3.06, p<0.05) independent of age, AS severity, LV mass and aortic compliance, but not in women.

Conclusions: In conclusion, AVC scored by echocardiography has sex-specific characteristics in AS. Moderate/severe AVC is associated with higher cardiovascular morbidity in both sexes, and with higher all-cause mortality in men.

P4894. Completeness and correctness of myocardial infarction diagnoses in a medical quality register and an administrative health register

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Background: Health registers are used for administrative purposes, disease surveillance, quality assessment, and research. The value of the registers is entirely dependent on the quality of their data.

Purpose: The aim of the study was to investigate and compare the completeness and correct-
ness of the acute myocardial infarction (AMI) diagnosis in the Norwegian Myocardial Infarction Register and in the Norwegian Patient Register.

**Methods:** All Norwegian patients admitted directly at St. Olav Hospital, Trondheim University Hospital during July 1st – December 31st 2012 and who had plasma levels of cardiac troponin T measured during their hospitalization (n=5582), were included. The electronic medical records were reviewed to define cases of AMI in the Norwegian Myocardial Infarction Register and the Norwegian Patient Register as true positive, false positive, false negative, and true negative. We calculated sensitivity, positive predictive value (PPV), specificity, and negative predictive value (NPV) with 95% confidence intervals.

**Results:** Data in the Norwegian Myocardial Infarction Register and Norwegian Patient Register were both rather complete (sensitivity 86.2% vs. 85.6%) and highly correct (PPV 97.9% vs. 95.1%, and specificity 99.9% vs. 99.7%) regardless of patient gender and age.

**Conclusion:** The Norwegian Myocardial Infarction Register and the Norwegian Patient Register showed high degree of completeness and correctness. We conclude that both registries may be used for administrative purposes, disease surveillance, quality assessment, and research.

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**P1520. Maternal cardiovascular status after pregnancies complicated by preeclampsia or diabetes**

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**Background:** Women with a history of a preeclampsia (PrE) or diabetes mellitus (DM) pregnancies are at increased risk of cardiovascular (CV) disease although the underlying mechanisms and longitudinal changes of CV phenotypes in these at-risk cohorts remain to be described.

**Purpose:** We sought to comprehensively describe the CV phenotype of women at risk.

**Methods:** We compared demographics, blood pressure, echocardiography and vascular function in women 1 year after normal versus abnormal pregnancy complicated by PrE or DM at a large tertiary university hospital.

**Results:** See table: In PrE, but not in DM, multiple CV abnormalities suggest evolving cardiac hypertrophy and vascular stiffening.

**Conclusions:** Our data show multiple significant structural and functional CV abnormalities in women at 1 year after pregnancy complicated by PrE. These findings suggest increased clinical vigilance for evolving CV disease in these women.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n=38)</th>
<th>PrE (n=44)</th>
<th>DM (n=8)</th>
</tr>
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<tbody>
<tr>
<td>Age (y)</td>
<td>35±1</td>
<td>35±1</td>
<td>36±1</td>
</tr>
<tr>
<td>MAP, mean arterial blood pressure (mmHg)</td>
<td>78±1</td>
<td>87±1*</td>
<td>82±2</td>
</tr>
<tr>
<td>HR, heart rate (beats/min)</td>
<td>67±1</td>
<td>71±2</td>
<td>66±3</td>
</tr>
<tr>
<td>Rate-pressure product (mmHg/min)</td>
<td>7159±617</td>
<td>8450±292*</td>
<td>7280±436</td>
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**Echocardiography**

<table>
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<th>Controls (n=38)</th>
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</thead>
<tbody>
<tr>
<td>IVSD, interventricular septum diameter (mm)</td>
<td>6.2±0.1</td>
<td>6.9±0.1**</td>
<td>6.4±0.4</td>
</tr>
<tr>
<td>LVEDD, LV end-diastolic diameter (mm)</td>
<td>48.5±0.6</td>
<td>47.7±0.6</td>
<td>48.8±0.9</td>
</tr>
<tr>
<td>RWT, relative wall thickness</td>
<td>0.26±0.01</td>
<td>0.29±0.01**</td>
<td>0.26±0.02</td>
</tr>
<tr>
<td>LVM, LV mass (g)</td>
<td>98±3</td>
<td>108±3*</td>
<td>97±6</td>
</tr>
<tr>
<td>LVEF, LV ejection fraction (%)</td>
<td>63±0.5</td>
<td>63±0.5</td>
<td>64±1.3</td>
</tr>
<tr>
<td>LSVS, LV stroke volume (mL)</td>
<td>68±2</td>
<td>64±1*</td>
<td>66±3</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.83±0.06</td>
<td>1.68±0.06*</td>
<td>1.86±0.15</td>
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<tr>
<td>LV global myocardial performance (Tei) index</td>
<td>0.38±0.02</td>
<td>0.43±0.02*</td>
<td>0.37±0.03</td>
</tr>
<tr>
<td>LVSW, LV stroke work (mL)</td>
<td>92±2</td>
<td>100±3*</td>
<td>89±5</td>
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**Vascular function**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n=38)</th>
<th>PrE (n=44)</th>
<th>DM (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWV, pulse wave velocity (m/s)</td>
<td>6.1±0.1</td>
<td>6.5±0.2*</td>
<td>6.4±0.3</td>
</tr>
<tr>
<td>AIX, augmentation index (%)</td>
<td>10.5±19</td>
<td>15.4±13*</td>
<td>10.9±3.9</td>
</tr>
<tr>
<td>AoBPsys, systolic aortic blood pressure (mmHg)</td>
<td>94.8±1.3</td>
<td>104.5±18***</td>
<td>98.9±3.4</td>
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</table>

LV, left ventricle. Values are means ± SEM. *P<0.05, **P<0.01, ***P<0.0001, aP<0.1; PrE or DM versus controls (unpaired t-test).
P3978. Validation of a novel 3D holographic display for non-invasive quantification of mitral annular dynamics

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Introduction: A novel holographic display (Setred AS, Oslo, Norway) offers a 3-dimensional (3D) echocardiographic presentation. We have developed a virtual semi-automatic, semi-transparent annulus plane (3D VSAP) for quantification of mitral annular dynamics.

Purpose: Validation of the non-invasive 3D VSAP method using sonomicrometric crystals as reference method.

Methods: In 11 anesthetized open chest pigs 8 sonomicrometric crystals were sewn to the mitral annulus; AL and PM commissures and at each corresponding scallop (A1-A3 and P1-P3). Left atrial and ventricular pressures were measured by high-fidelity catheters. Adjustments of pre-and afterload were done by constriction of the vena cava inferior and the ascending aorta, respectively. 3D epicardial echo was obtained from an apical view and data were converted to the display for further analysis. Area of the annulus plane, non-planar angle and the annular height (AH)/ commissural width (CW) ratio (AHCWR) were measured in mid-systole and late diastole.

Results: Table 1 summarizes measurements by both methods.

Conclusion: The non-invasive 3D VSAP method correlates well with sonomicrometry over a wide range of loading conditions and may represent a new powerful tool for quantifying mitral annular dynamics.

Table 1. Measurements by both methods at baseline, caval- and aortic constrictions

<table>
<thead>
<tr>
<th></th>
<th>Sono-Syst</th>
<th>Sono-Diast</th>
<th>3D VSAP-Syst</th>
<th>3D VSAP-Diast</th>
<th>ΔSono (%)</th>
<th>Δ3D VSAP (%)</th>
<th>r-value</th>
<th>p-value</th>
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<tr>
<td>Baseline (n=11)</td>
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<td></td>
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<tr>
<td>Annulus plane area (mm²)</td>
<td>57.0</td>
<td>74.5</td>
<td>59.3</td>
<td>74.9</td>
<td>23.5</td>
<td>20.8</td>
<td>0.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-planar angle (°)</td>
<td>135.2</td>
<td>148.9</td>
<td>133.0</td>
<td>146.5</td>
<td>9.2</td>
<td>9.2</td>
<td>0.85</td>
<td>&lt;0.001</td>
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<tr>
<td>AHCWR</td>
<td>0.20</td>
<td>0.12</td>
<td>0.19</td>
<td>0.12</td>
<td>NA</td>
<td>NA</td>
<td>0.84</td>
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<td>Caval constriction (n=10)</td>
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<tr>
<td>Annulus plane area (mm²)</td>
<td>44.9</td>
<td>57.2</td>
<td>46.2</td>
<td>56.8</td>
<td>21.5</td>
<td>18.7</td>
<td>0.85</td>
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<tr>
<td>Non-planar angle (°)</td>
<td>134.3</td>
<td>145.6</td>
<td>135.4</td>
<td>146.8</td>
<td>7.8</td>
<td>8.4</td>
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<tr>
<td>AHCWR</td>
<td>0.17</td>
<td>0.14</td>
<td>0.16</td>
<td>0.12</td>
<td>NA</td>
<td>NA</td>
<td>0.76</td>
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<td>Aortic constriction (n=9)</td>
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<tr>
<td>Annulus plane area (mm²)</td>
<td>55.1</td>
<td>74.3</td>
<td>58.4</td>
<td>74.0</td>
<td>25.8</td>
<td>21.1</td>
<td>0.93</td>
<td>&lt;0.001</td>
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<tr>
<td>Non-planar angle (°)</td>
<td>134.2</td>
<td>149.0</td>
<td>135.4</td>
<td>147.7</td>
<td>9.9</td>
<td>8.3</td>
<td>0.87</td>
<td>0.002</td>
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<tr>
<td>AHCWR</td>
<td>0.17</td>
<td>0.11</td>
<td>0.17</td>
<td>0.11</td>
<td>NA</td>
<td>NA</td>
<td>0.81</td>
<td>0.01</td>
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</table>

P4945. Circulating interleukin-8 levels are associated with myocardial injury, left ventricular function and future clinical adverse events in patients with ST-elevation myocardial infarction

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Background: High interleukin-8 (IL-8) levels have been shown to be associated with adverse clinical outcome in heart failure (HF) patients, and with attenuated improvement in left ventricular (LV) function in patients with ST-elevation myocardial infarction (STEMI), suggesting a role in LV remodelling.

Purpose: In order to further elucidate a possible role of IL-8 in STEMI patients our aims were to evaluate 1) the temporal profile of IL-8 during STEMI, 2) possible associations between IL-8 and infarct size, microvascular obstruction (MVO), and LV function and remodelling, measured by cardiac magnetic resonance imaging (CMR), and 3) possible associations with clinical adverse events.

Methods: 272 patients with first-time STEMI, treated with primary percutaneous coronary intervention (PCI) were included. Blood samples for measurement of IL-8 were drawn before and immediately after the PCI procedure, at Day 1 (median 18.3 hours after PCI), and at 4-month follow-up. CMR was performed in the acute phase.
phase and after 4 months. Large infarct was defined as >30% of LV volume, reduced LV ejection fraction (LVEF) as <50%, and adverse LV remodelling as an increase in end-diastolic volume (EDV) of >15%. Clinical events were registered at 12-month follow-up and a composite end point was defined as all-cause mortality, MI, stroke, unscheduled revascularisation after >3 months, or rehospitalisation for HF. Additional long-term data for all-cause mortality were collected from clinical records.

Results: There was a significant increase in IL-8 levels from the PCI procedure to Day 1 with a subsequent decline from Day 1 to 4-month follow-up. Patients with high IL-8 levels (> median) measured both immediately after the PCI procedure and at Day 1 had significantly larger final infarct size, lower LVEF, larger increase in EDV and higher frequency of MVO. In multivariate logistic regression models, high IL-8 levels at Day 1 were associated with an increased risk of developing a large myocardial infarct (OR 6.5, 95% CI 1.6–26.3, p=0.008) and having reduced LV EF (OR 3.5, 95% CI 1.4–8.4, p=0.006) at 4 months, also after adjustment for peak troponin value. High levels of IL-8 were not associated with adverse LV remodelling. There were 19 clinical end points during 12 months of follow-up and a total of 27 patients died during a median follow-up time of 70 months. There were significant differences in overall survival between patients with high or low IL-8 (> median) at all sampling Points (Figure 1). Additionally, patients with high IL-8 levels (> median) measured before PCI and at Day 1 were more likely to have a clinical event during the first 12 months (before PCI: OR 6.0, 95% CI 1.7–21.2, p=0.005; day 1: OR 6.3, 95% CI 1.8–22.3, p=0.004).

Conclusions: High circulating IL-8 levels in STEMI patients were associated with large infarct size, impaired recovery of LV function and adverse clinical outcome.

P4930. Hypertension is associated with subclinical left ventricular dysfunction in ischemic stroke survivors (the NOR-SYS study)

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1Haukeland University Hospital, Department of Cardiology - Bergen - Norway, 2Haukeland University Hospital, Department of Neurology - Bergen - Norway, 3University of Bergen, Department of Clinical Science - Bergen - Norway,

On behalf: Bergen Hypertension and Cardiac Dynamics group

Background: Hypertension is highly prevalent in stroke patients, but the impact on subclinical left ventricular (LV) dysfunction by strain imaging has not been reported.

Methods: Conventional and speckle tracking echocardiography was performed in 270 ischemic stroke patients (aged 15–60 years) included in the Norwegian Stroke in the Young Study (NOR-SYS). Peak systolic LV global longitudinal strain (GLS) was measured by averaging segments from apical 4 and 3 chamber views. Clinic and ambulatory blood pressure were recorded to diagnose hypertension.

Results: Hypertension was found in 67% of patients. Hypertensive patients were older, had higher body mass index, LV mass, carotid intima-media thickness and arterial stiffness, and included higher proportions of men and subjects with diabetes compared to the normotensive group (all p<0.01) (Table). Hypertensive patients also had lower peak systolic GLS, while GLS was on average normal in normotensive patients (p<0.001) (Table). In multivariable linear regression analysis, lower peak systolic GLS was associated with the presence of hypertension (β=0.38, p<0.001) independent of significant association of LV hypertrophy (β=0.25, p=0.001), higher age (β=0.20, p<0.012) and triglycerides (β=0.16, p=0.03) (Multiple R2=31, p<0.001).

Conclusion: Hypertensive stroke survivors had greater burden of cardiovascular disease risk factors and markedly reduced peak systolic GLS, reflecting subclinical LV dysfunction. The prevalent subclinical LV dysfunction may contribute to the observed higher cardiovascular event rate in stroke survivors.
Table 1. Characteristics of normotensive and hypertensive ischemic stroke patients

<table>
<thead>
<tr>
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<th>Normotensives</th>
<th>Hypertensives</th>
<th>P</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>45±11</td>
<td>52±8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male (%)</td>
<td>56</td>
<td>73</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.8±3.1</td>
<td>28.4±5.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>1.3±0.9</td>
<td>1.8±1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean common carotid IMT (mm)</td>
<td>0.75±0.63</td>
<td>0.90±0.29</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Pulse wave velocity (m/s)</td>
<td>6.8±1.3</td>
<td>8.3±1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricular mass index (g/m²)</td>
<td>32.9±8.2</td>
<td>42.4±12.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>64±7</td>
<td>63±7</td>
<td>NS</td>
</tr>
<tr>
<td>Peak systolic GLS (%)</td>
<td>-19±2</td>
<td>-16±3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

GLS, global longitudinal strain; IMT, intima-media thickness.

P1095. Modeling of cardiac ischemia and reperfusion injury: a human-based in vitro model using iPS-derived cardiomyocytes

J. Pinho, N.R. Scrimgeour, T. Stolen, K. Solvang-Garten, A. Sharma, D. Miranda Fonseca, G. Smith, M. Hoydal, Norwegian University of Science and Technology, Department of circulation and medical imaging - Trondheim - Norway, 2Norwegian University of Science and Technology, Proteomics and Metabolomics Core Facility (PROMEC) - Trondheim - Norway, 3University of Glasgow, Institute of Cardiovascular and Medical Sciences - Glasgow - United Kingdom.

Background: Ischemia-reperfusion (I/R) injury is a major contributor to myocardial damage generated during myocardial infarction (MI). Establishing an understanding of the pathological processes occurring during MI and developing effective therapeutic approaches requires methodologies that consistently recapitulate the pathophysiological changes associated with MI. The generation of induced pluripotent stem derived cardiomyocytes (iPS-CM) has provided unprecedented opportunities for studying disease in human cardiomyocytes.

Aim: We sought to develop and characterize a human-based in vitro model of cardiac I/R injury, using cardiomyocytes derived from human iPSCs (hiPS-CM).

Methods: To simulate I/R in vitro, hiPS-CM were subjected to 48h hypoxia (1% O2) followed by 2 h of reoxygenation (H/R). Cells under normoxic culture conditions served as baseline group (N). We have fully characterized the hiPS-CM in terms of calcium (Ca2+)-handling properties using fluorescence microscopy; investigated for hypoxia, apoptotic and necrotic markers by qPCR and probed their proteome using liquid chromatography-mass spectrometry (LC-MS).

Results: hiPS-CM display spontaneouos contraction, Ca2+ handling and electrophysiological properties resembling human adult cardiomyocytes, including a rapid upstroke of 5.05±0.95 ms, 90% of action potential repolarization of 160.9±12.7 ms, Ca2+ time to rise of 279±4.2 ms, and spatial dispersion of time to 90% of Ca2+ decay of 305.3±41.5 ms, suggesting adequately functional sarcolemmal and sarcoplasmic reticulum Ca2+ handling. Transcript levels of key Ca2+-handling proteins, including SERCA2a, CACNA1C and NCX, were not significantly affected by H or H/R. Hypoxia increased HIF-1α mRNA expression and activated the downstream targets proapoptotic BNIP3 (6-fold), proangiogenic VEGFA (1.5-fold) and antiangiogenic MMP2 (2.5-fold). Reoxygenation partially reversed the effect of hypoxia by decreasing the levels of VEGFA transcript. Antiapoptotic BCL-2 mRNA levels increased 5-fold in hypoxic hiPS-CM and were not changed after reoxygenation. From a total of 257904 MS/MS spectra collected over 9 LC-MS/MS runs (3 replicates per sample, 4-hour gradient), 3215 unique protein groups were confidently identified with a false discovery rate of 1%. Of these, 937 proteins were consistently up- or down-regulated under hypoxia or hypoxia/reperfusion. The data cover large numbers of regulatory proteins, including transcription factors, kinases, phosphatases, ubiquitin-associated and ribosomal proteins. Analysis of KEGG pathways associated with hypoxia and hypoxia/reperfusion revealed that these proteins were related with mitochondrial proton-transporting ATP synthase complex (17), proteins associated with proton-transporting ATP synthase complex (17) and cardiac muscle contraction (28).

Conclusion: Taken together, the data presented in this study lend support to the use of hiPS-derived cardiomyocytes as a relevant model system to investigate I/R injury.

P5346. Worst lead residual ST-deviation 60 minutes after primary PCI for STEMI is associated with infarct size and myocardial salvage on cardiac magnetic resonance imaging

Introduction: In earlier studies it has been shown that various metrics of ST-segment deviation are predictive of final infarct size and long term ventricular function after STEMI. Cardiac magnetic resonance (CMR) imaging is considered the gold standard for determining infarct size, myocardial salvage and microvascular obstruction after reperfusion therapy. However, CMR is not utilized as routine clinical practice in most hospitals when treating STEMI-patients. The residual ST-deviation in the worst lead on ECGs taken post-PCI is easily measured by clinicians.

Objective: To characterize the associations between worst lead residual (WLR) ST-segment deviation one hour after percutaneous revascularization (without reference to the baseline ECG) and CMR measures of myocardial salvage, infarct size and microvascular obstruction in STEMI patients included in the MITOCARE trial.

Methods: Worst lead residual ST-segment deviation was defined as the absolute magnitude of residual ST-deviation increasing for each mm of ST-deviation, measured manually at the J-point to the nearest 0.5 mm, in the most affected lead from ECGs obtained 60 minutes after revascularization. Infarct size, myocardial salvage and microvascular obstruction were measured by CMR 3–5 days after primary percutaneous coronary intervention. Logistic regression modelling was used to explore the associations between WLR (expressed for each increasing mm of ST-deviation) and CMR measures of myocardial damage.

Results: In the MITOCARE trial, 88 patients underwent CMR within 3–5 days after STEMI and were included in this substudy. The MITOCARE trial included patients with a first time STEMI and infarct size, myocardial salvage and microvascular obstruction measured 60 minutes after revascularisation of a first time STEMI and infarct size, myocardial salvage and microvascular obstruction.

Conclusion: Significant associations were detected between worst lead residual ST-deviation measured 60 minutes after revascularisation of a first time STEMI and infarct size, myocardial salvage and microvascular obstruction.

Figur 1. WLR for prediction of myocardial damage.

P651. Cardiac function in newborns of obese women and the effect of an exercise intervention during pregnancy

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Background: Almost two thirds of pregnant women are obese or overweight. Pre-pregnancy obesity is associated with later cardiometabolic disease in the child and the underlying pathogeneses begin in early life. Therefore, pregnancy and infancy are key periods for potential intervention.

Purpose: To investigate the cardiac function in newborns of obese women and the effect of an exercise intervention during pregnancy.

Methods: 55 pregnant women with a pre-pregnancy BMI ≥30 kg/m² were randomized to exercise training (n=29) or control (standard maternity care) (n=26). Participants were offered 3 weekly supervised sessions of 35 minutes of moderate intensity endurance exercise and 25 minutes of strength training, from pregnancy week 14 until delivery. All newborns had an echocardiogram done 1–3 days and 6–8 weeks after delivery. The results were compared with newborns of normal weight women (n=20).

Results: Newborns of obese women had an impaired systolic and diastolic cardiac function with reduced global strain, strain rate, tissue Doppler velocities as well as a thicker septum and a smaller left ventricle (LV) at birth and after 6–8 weeks after delivery (except for size of LV) (Table). Exercise had no effect; however the adherence to exercise was low with 1.3±1.2 sessions per week at the lab.

Conclusions: Newborns of obese women had reduced cardiac function compared to normal weight women. Exercise during pregnancy had no effect, maybe due to low adherence. Future studies should focus on pre-pregnancy exercise as well.
Hoydal 1, 1 Norwegian University of Science and Technology - Trondheim - Norway, 2 Ulleval University Hospital, Department of Cardiology - Oslo - Norway, 3 Ulleval University Hospital, Department of Cardiology - Oslo - Norway, 4 Oslo Sports Trauma Research Center - Oslo - Norway, 5 Norwegian University of Science and Technology - Trondheim - Norway.

Background: Matrix metalloproteinases (MMP) have a crucial role in degradation of ECM and remodeling of the heart during the process of heart failure development. Both MMP-2 and 9 are important biomarkers of myocardial infarction. Recently microRNA (miR)-451a has been found to inhibit the expression of both MMP2 and MMP9 in human malignancies, but its role in human HF we performed qPCR analyses in the left ventricle (LV) from post myocardial infarction (MI) HF patients. To further determine the role of miR-451a on regulating MMP2 and MMP9 in cardiac cells has not yet been investigated. We hypothesized that miR-451a is an important modulator of MMP2 and MMP9 levels in human cardiomyocytes.

Method: To verify the regulation of miR-451a in human HF we performed qPCR analyses in the left ventricle (LV) from post myocardial infarction (MI) HF patients. To further determine the role of miR-451a on regulation of MMP2 and MMP9 in human cardiomyocytes (hIPS-CM) we established two models including key components of pathological cardiac remodeling in human inducible pluripotent stem cell cardiomyocytes (hiPSC-CM): 1) endothelin-1 (ET-1) stimulation vs. vehicle control and 2) 48h hypoxia (1% O2) vs. normoxia. Both cell models were transfected with synthetic miR-451a mimics or mismatch-controls. Regulation of MMP2 and MMP9 was determined both by qPCR and protein MMP2/9 activity assay.

Results: Analyses in LV samples from patients with post MI HF displayed significant reduced expression levels of miR-451a (73% reduced vs. controls, p<0.0001). hiPSC-CM stimulated by hypoxia caused a two-fold increase in both MMP2 and MMP9 expression levels compared to normoxia (p<0.05), whereas ET-1 stimulation only increased the MMP9 level compared to vehicle controls (p<0.05), and not MMP2. Following transfection of miR-451a mimics, MMP2 and MMP9 expression levels remained not different from normoxic controls; compared to hypoxic hiPSC-CM treated with mismatch-controls, MMP2 was significantly reduced (p<0.05), whereas MMP9 only displayed a tendency. Transfection of miR-451a mimic in ET-1 stimulated hiPSC-CM confirmed, however, a significant reduction in MMP9 levels (p<0.01). MMP2 levels were unaffected by ET-1 stimulation and did not display any further reduction by miR-451a mimic treatment. Furthermore, to determine the effect of changes observed at the mRNA levels we performed a separate experiment on MMP2/9 protein activity. We found that protein activity of MMP2/9 was significantly lower in ET-1 stimulated hiPSC-CM treated with miR-451a mimic compared to mismatch-controls.

Conclusion: The present data support an important role of miR-451a on regulating MMP2 and 9 in human cardiac cells. In both our experimental models, hiPSC-CM stimulated either with ET-1 or hypoxia, both MMP2 and 9 remained at expression levels not different from miR controls following treatment by miR-451a mimics. The effect of increasing miR-451a is further verified by reducing the MMP2/9 protein activity. Taken together our data therefore suggest that increasing the low expressed miR-451a verified in human post MI HF patients may have a potential for further verification as targeted treatment of HF.

P5389. MicroRNA-451a regulate expression and activity of matrix metalloproteinases 2 and 9 in human cardiomyocytes

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Table 1. Cardiac variables in newborns

<table>
<thead>
<tr>
<th>Cardiac variables</th>
<th>NNW 1–3 days</th>
<th>NOW exercise 1–3 days</th>
<th>NOW control 1–3 days</th>
<th>NNW 6–8 weeks</th>
<th>NOW exercise 6–8 weeks</th>
<th>NOW control 6–8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global strain LV, %</td>
<td>-23.1±2.0**</td>
<td>-17.1±4.0</td>
<td>-16.9±3.9</td>
<td>-24.2±1.3*</td>
<td>-20.9±3.6</td>
<td>-20.3±3.4</td>
</tr>
<tr>
<td>Global strain rate LV, s⁻¹</td>
<td>-2.00±0.33*</td>
<td>-1.62±0.29</td>
<td>-1.68±0.30</td>
<td>-2.22±0.20*</td>
<td>-1.78±0.27</td>
<td>-1.81±0.36</td>
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<tr>
<td>Global strain RV, %</td>
<td>-26.8±2.8*</td>
<td>-20.6±4.8</td>
<td>-18.8±5.0</td>
<td>-31.6±4.8*</td>
<td>-22.2±6.7</td>
<td>-21.7±5.7</td>
</tr>
<tr>
<td>Global strain rate RV, s⁻¹</td>
<td>-2.71±0.71*</td>
<td>-1.87±0.44</td>
<td>-1.73±0.40</td>
<td>-3.24±0.70</td>
<td>-2.49±0.88</td>
<td>-2.09±0.61</td>
</tr>
<tr>
<td>S', cm/ s</td>
<td>6.4±1.1*</td>
<td>4.4±0.9</td>
<td>4.2±0.9</td>
<td>8.2±1.3*</td>
<td>6.1±1.2</td>
<td>6.2±1.3</td>
</tr>
<tr>
<td>e', cm/ s</td>
<td>7.4±2.1**</td>
<td>5.7±1.3</td>
<td>5.5±1.1</td>
<td>12.1±2.7</td>
<td>9.5±2.2</td>
<td>8.9±2.1</td>
</tr>
<tr>
<td>TAPSE, mm</td>
<td>10.0±1.5***</td>
<td>9.2±1.3</td>
<td>9.0±1.5</td>
<td>15.2±1.2***</td>
<td>13.9±2.2</td>
<td>14.2±2.1</td>
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<tr>
<td>Septum d, mm</td>
<td>3.1±0.8**</td>
<td>3.7±1.0</td>
<td>4.0±1.3</td>
<td>3.4±0.1**</td>
<td>4.1±0.8</td>
<td>4.1±0.1</td>
</tr>
<tr>
<td>LVId d, mm</td>
<td>19.2±2.0***</td>
<td>18.3±1.7</td>
<td>18.1±1.6</td>
<td>22.8±2.6</td>
<td>22±1.9</td>
<td>21.8±2.3</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>38.2±3.3</td>
<td>37.2±4.3</td>
<td>35.9±7.3</td>
<td>37.8±3.2</td>
<td>35.1±5.4</td>
<td>35.0±5.6</td>
</tr>
</tbody>
</table>

NNW, newborns of normal weight women; NOW, newborns of obese women; LV, left ventricle; RV, right ventricle; S', peak systolic tissue Doppler velocity (TDV); e', peak early diastolic TDV; d, end diastole; LVId, LV internal diameter. *p<0.001, **p<0.01, ***p<0.05 between NNW and NOW.

P2532. Value of blood pressure measurements in both arms in olympic and paralympic athletes

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Background: Hypertension is the most prevalent risk factor for cardiovascular disease in elite athletes. ESC guidelines recommend that BP...
measurement during preparticipation screening should be performed according to “best clinical care”, and the International Olympic Committee recommends that BP should be measured in both arms. However, no studies have assessed the value of routine bilateral measurements.

**Purpose:** To determine BP in elite athletes using standardised methods, and to assess the added value of BP measurements in both arms.

**Methods:** We measured BP in athletes preparing for the Olympic and Paralympic Games in Rio 2016, as part of the preparticipation screening. After five minutes’ rest, BP was measured with appropriate cuff size in a sitting position in a quiet room on a day without prior training. An automated BP device (Watch BP office, Micro-life) measured BP three times simultaneously in both arms, with one minute’s intervals. We calculated mean values (±SD) of the last two measurements, and graded BP according to ESC guidelines (see Figure). We used independent and paired T-test to compare between groups and within individuals, respectively.

**Results:** 100 Olympic and 20 Paralympic athletes participating in 18 different sports disciplines were included (49 males (40.8%), mean age 26.8±6.4 years, BMI 23.2±2.9 kg/m²). Nine (7.5%) had high BP, (five of them in one arm only), and 22 (18.3%) had high-normal BP. 36 athletes (30.0%) had a difference of >5 mm Hg in systolic BP between arms (mean 8.4±4.3 mm Hg), included five (4.2%) with a difference of >10 mm Hg. There were no significant differences between Olympic and Paralympic athletes.

**Conclusions:** One quarter of Olympic and Paralympic athletes had high or high-normal BP, and one third had a BP difference of >5 mm Hg between arms. BP is an important part of preparticipation screening of athletes. Elevated BP can easily be missed if BP is measured in one arm only, and BP should therefore be measured in both arms.

**P2534. Cardiovascular incidents, including sudden cardiac arrests, in professional male football players with negative preparticipation cardiac screening results: 8-year follow-up**

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**Background:** The aim of pre-participation cardiac screening of athletes is to detect cardiovascular disease at an early stage to prevent sudden cardiac arrests and deaths. Few studies have focused on the consequences of false negative findings.

**Purpose:** To identify cardiovascular incidents in a cohort of male professional football players with negative screening results.

**Method:** Retrospective 8-year follow-up of 604 players who underwent pre-participation cardiac screening by experienced cardiologists, including electrocardiography and echocardiography, in January-April 2008. We performed a media search to identify cardiovascular incidents (sudden cardiac arrest or death, angina pectoris or myocardial infarction, transient ischemic attack, cerebral hemorrhage or infarction, atrial flutter or fibrillation, blood clot, myocarditis or pericarditis) in Norwegian football between January 1st 2008 and February 13th 2016. Incidents were cross-checked with the hospital records of the players affected.

**Results:** Six of the 572 players with negative cardiac screening results, had experienced serious cardiovascular incidents during follow-up (median age 30 yrs, 27–36). Three players had suffered sudden cardiac arrest (62 per 100 000 athlete years), one had myocardial infarction, one had transient ischemic attack and one had atrial flutter. Four of the incidents occurred during or directly after a match, and one during football training. Three of the players ignored chest pain, paresis, dyspnea and near-syncope, two completed the match before seeking medical assistance, one was misinterpreted and received inappropriate treatment initially, and two were discharged from hospital without proper follow-up, despite serious symptoms. Prompt cardiopulmonary resuscitations saved all three lives. None of the 32 players with initially positive screening results, who all were subsequently cleared to play, experienced any cardiovascular incidents.

**Conclusions:** Based on our findings, we cannot recommend routine pre-participation cardiac screening of professional male football players in Norway. A comprehensive protocol (including ECG and echocardiography) performed by experienced cardiologists was not sufficient to
detect cardiovascular disease at an early stage. Negative screening results may have delayed proper medical assistance. However, our study emphasizes that symptoms and findings indicative of cardiovascular disease should be evaluated carefully also in elite athletes. Immediate first-responder treatment with cardiopulmonary resuscitation saves lives, and a comprehensive medical emergency plan, including automated external defibrillators, should be available in all football arenas.

**P4392. Heart rate prediction of outcome in heart failure following myocardial infarction depend on heart rhythm status**


**Background:** Heart rate has been reported to be associated with adverse outcome in heart failure (HF) and myocardial infarction (MI), but conflicting evidence exists regarding its impact in patients with associated atrial fibrillation (AF).

**Objectives:** We investigated the differential impact of heart rate on clinical outcomes according to the presence or absence of AF in patients with reduced systolic function and/or HF after MI.

**Methods:** We studied the association of heart rate with outcome using Cox-models in a merged dataset (n=28,771) of four randomised trials (CAPRICORN, EPHELUS, OPTIMAAL, and VALIANT).

**Results:** At baseline, 3736 (13%) patients had AF. We identified a significant interaction between AF and heart rate, and a decreasing effect of heart rate with time (both p for interaction <0.001). We report associations with outcome separately in patients with and without AF. A 10-bpm increase in heart rate conferred increased risk for all-cause mortality (1.27 [1.21 to 1.33], p=0.0001), CV-mortality (1.28 [1.22 to 1.34], p=0.0001), and HF-hospitalisation (1.25 [1.19 to 1.31], p=0.0001) in patients without AF. In contrast, in patients with AF, the incremental risk for 10-bpm increase in heart rate was attenuated for all-cause (1.14 [1.06 to 1.23], p=0.0007), CV-mortality (1.12 [1.03 to 1.22], p=0.006), and HF-hospitalisation (1.16 [1.07 to 1.26], p=0.0006, p for interaction with AF <0.001 for all outcomes).

**Conclusions:** In patients with reduced systolic function and/or HF post-MI, higher heart rate predicts increased major cardiovascular events during the first year following MI in patients without AF. This association is markedly attenuated in subjects with AF.

**2860. The association between carotid plaque burden and adiposity: results from a large population-based study**

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**Background:** Carotid plaque burden is associated with increased CVD risk. However, large population-based studies investigating the determinants of carotid plaque burden are scarce. In particular, little has been reported on the association between adiposity and carotid plaque burden.

**Purpose:** To investigate the associations between presence of carotid plaque, and total plaque area (TPA), with measures of adiposity: body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR).

**Method:** We analyzed cross-sectional data from 4978 subjects aged 50+ years collected in the Norwegian population-based Tromsø 5 study. The carotid artery ultrasound examinations were conducted to determine presence of carotid plaque presence and TPA. Measures of adiposity were converted to SD units to allow direct comparison of effect sizes. TPA was log transformed as it was left skewed. Logistic and linear regressions were used. Model 1 was adjusted for age, sex and smoking. Model 2 was additionally adjusted for factors that might be on the causal pathway between adiposity and plaque (ie SBP, HDL and non-HDL cholesterol and glucose).

**Results:** Mean age of participants was 67 years and 44% were male. The means (SD) for BMI, WC and WHR were 26.9 kg/m^2 (4.2), 90.7 cm (12.3) and 0.89 (0.09). 63.5% had carotid plaque. There was some evidence that the presence/absence of plaque was associated with WHR. However, among the 3130 with carotid plaque, there was strong evidence that burden (measured as log TPA) was associated with all three measures of adiposity. On additional adjustment for factors that might be on the causal pathway between adiposity and plaque (ie SBP, HDL and non-HDL cholesterol and glucose).

**Conclusions:** The measures of adiposity examined do not appear to be strongly predictive of presence of carotid artery plaque. However, they are associated with the extent of plaque burden, with
Table 1

<table>
<thead>
<tr>
<th>Adiposity per 1 SD</th>
<th>Model 1 p-value</th>
<th>Model 2 p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>1.02 (0.96, 1.09)</td>
<td>0.45</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>1.03 (0.96, 1.10)</td>
<td>0.44</td>
</tr>
<tr>
<td>Waist/Hip ratio</td>
<td>1.11 (1.03, 1.20)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WHR (a measure of abdominal adiposity)</th>
<th>Model 1 p-value</th>
<th>Model 2 p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>0.033 (0.006, 0.060)</td>
<td>0.02</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.053 (0.024, 0.082)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist/Hip ratio</td>
<td>0.079 (0.047, 0.112)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results: We intriguingly found 5h after CNI injection an important reduction (~50%) of cardiac contractility (End-systolic elastance; Ees) that was confirmed in vitro with a down-regulation of beta-adrenergic signaling upon adult primary cardiomyocyte stimulation with CNI (4h). Interestingly, these effects were completely absent after the same treatment in transgenic mice and cardiomyocytes with inhibited enzymatic function of PI3Kg (PIKg KD), and in mice and cardiomyocytes treated simultaneously with PI3Kg selective inhibitor. Following up these findings, we have also observed an acLQTS that was also significantly reduced in mice treated with PI3Kg inhibitor. In addition, whereas the observed side effects of CNI were correlated with higher mortality, the group of mice simultaneously treated with PI3Kg inhibitor interestingly exhibited a better survival rate (p<0.05).

Conclusion: In this study, we observed an acute cardio-depressive effect of CNI associated with acLQTS, sudden death and established the rationale for PI3Kg inhibition as a potential therapeutic approach to those effects.

2220. Sham or no-sham control in trials of renal denervation for treatment resistant hypertension: a systematic meta-analysis

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1Oslo University Hospital - Oslo - Norway, 2Capital Medical University - Beijing - China People’s Republic of, 3University of Leuven, KU Leuven Department of Cardiovascular Sciences - Leuven - Belgium, 4Université Catholique de Louvain - Brussels - Belgium, 5Oslo University Hospital, and University of Oslo - Oslo - Norway,

On behalf: European Network COordinating research on Renal Denervation (ENCOREd)

Background: Number of patients, study design and patients and physician related confounders have hampered studies of renal denervation (RDN) in patients with treatment resistant hypertension (rHT). It remains uncertain whether RDN lowers BP. We aimed to investigate
whether the use of sham control is essential in RDN studies or whether systematic use of 24-hour ambulatory BP provides enough information thereby making an invasive sham control redundant.

**Methods:** We meta-analyzed summary statistics of randomized clinical trials on RDN in rHT. For continuous outcomes, we assessed heterogeneity by Cochran’s Q test and used random-effect models weighted for the inverse of the variance. On top of the randomized trials reviewed earlier, we additionally included two new studies reported in 2016, one conducted in Spain (24 patients, RDN vs. spironolactone) and one conducted in Denmark (69 patients, sham controlled). We analyzed office and 24-hour ambulatory BP in 3 sham controlled studies vs. 6 no sham controlled studies.

**Results:** The meta-analysis of 9 studies at 6-month follow-up showed 2.85 mmHg (p=0.60) and 1.16 mmHg (p=0.52) reductions in office and in 24-hour systolic BP, respectively. Meta-analysis of 24-hour systolic BP in the 3 sham-controlled studies showed a reduction of 2.24 mmHg (95% confidence intervals (CIs) -4.70 to 0.22 mmHg, n=396 vs. 230, p=0.07). For the 6 no sham controlled studies there was no difference in 24-hour systolic BP (+0.42 mmHg; 95% CIs -2.50 to 3.34 mmHg, n=162 vs. 174, p=0.90). The test for sub-group heterogeneity showed no significant interaction (p=0.46). Removing one trial at a time produced confirmatory results.

**Conclusion:** Pooled effects of 9 randomized and controlled studies of RDN showed no significant effect on BP. In addition analysis does not support the use of sham control but rather suggests extensive use of 24-hour ambulatory BP in studies of RDN in resistant hypertension.

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5935. Effects of empagliflozin on cardiac and vascular hemodynamic markers by subgroups of age, sex and hypertension in patients with T2DM and high CV risk: EMPA-reg outcome

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**Background:** Empagliflozin (EMPA) significantly reduced the risk of CV death in the EMPA-REG OUTCOME trial.

**Purpose:** We explored for differential effects on cardiac and vascular hemodynamic markers by age, sex, and systolic BP (SBP) subgroups.

**Methods:** Pts with T2D and high CV risk were randomized to receive placebo (PBO) or 2 doses of EMPA. Changes in indices of arterial stiffness, vascular resistance and cardiac workload (pulse pressure (PP), mean arterial pressure (MAP) and the double product (DP)), and SBP were assessed across subgroups of age, sex, and SBP, using a mixed model repeated measures analysis in randomized pts who received ≥1 dose of study medication.
drug using all measurements obtained until study end.

**Results:** 2333, 2345 and 2342 pts received PBO, EMPA 10 mg or 25 mg and mean±SE baseline SBP was 135.79±0.36, 134.91±0.35, 135.65±0.35 mmHg, respectively whereas mean (SE) heart rate was 70.74±0.23, 70.96±0.22 and 70.52±0.22 beats per minute. There were significantly greater reductions in markers of arterial stiffness, vascular resistance, cardiac workload and SBP among pts treated with either EMPA dose vs. PBO across age, sex, and SBP groups (Table above).

**Conclusions:** EMPA consistently improved SBP and cardiac and vascular hemodynamic markers, irrespective of age, sex, or baseline SBP. Further analyses will determine the potential contribution of these changes to the CV mortality benefit with EMPA.

P1448. 3D shape assessment from 2D echocardiography using machine learning

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In the context of cardiac remodelling, shape assessment of the heart is important for diagnosis and follow up. Despite offering a full view of the heart, 3D imaging presents some disadvantages, such as the poor acoustic window of 3D echography, ionisation in the case of Computed Tomography, and the cost in the case of Magnetic Resonance. Given that 2D echocardiographic data are widely available, we investigated the feasibility of machine learning for assessing the 3D left ventricular (LV) end-diastolic shape from 2D measurements enriched with clinical information.

We used a dataset consisting of 116 preadolescents, 45 with intrauterine growth restriction (IUGR) and 71 controls. A complete 2D echocardiographic study was performed and 3D LV shape was extracted using 3D echocardiography. The measurements related to the LV shape were long axis, end-diastolic volume, basal diameter and internal dimension. As a clinical variable, the fact of having IUGR or not during fetal life was used.

A statistical shape model was computed from the 3D echocardiography shapes through Principal Component Analysis (PCA), leading to a template shape and deformations from that template. In the IUGR dataset, most of the shape variation was explained by (1) overall size variability, (2) radial scaling, (3) an inclination of the apex with respect to the base. Those shape variations can be seen in the Figure.

Linear Regression was performed to predict each deformation coefficient from the available 2D measurements. We could predict most of the overall size (R² =0.75, p value <1e-5) and some of the radial scaling (R² = 0.3, p value<1e-5) while the other deformations could not be predicted. Introducing the IUGR label to the regression improved the quality of the radial scaling prediction to R²=0.4. This confirms that IUGR is related to LV sphericity, and that clinical and functional data can indirectly assess the 3D ventricular shape.

The effect of (Gaussian) noise on the results was also investigated using a synthetic dataset, which includes non-symmetrical bulging of the septal wall. As with the real dataset, we could not recover the asymmetrical modes even with total absence of noise. Comparing the results of the size and radial scaling R² coefficients, we estimated the level of noise in the real dataset to be around 10%. The plot in the figure shows the effect of noise in the regression quality. Adding new 2D measurements that are not in the guidelines allowed us to recover the asymmetrical shape.

In conclusion, using only the recommended 2D measurements limited ventricular shape prediction to the symmetric components. The prediction deteriorated with increased measurement noise. However, adding extra measurements, or relevant clinical information, some asymmetrical components can be regressed. We believe that this work is a promising first step towards deriving more complete shape measurements from routinely available 2D data.
Differences in two-year outcomes according to type of atrial fibrillation: results from the GARFIELD-AF registry

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On behalf: GARFIELD-AF Investigators

Purpose: Atrial fibrillation (AF) burden and type of AF have not been established as major differential predictors of stroke and death. The aim of this work was to analyse outcomes by type of AF and by antithrombotic therapy.

Methods: 28,628 adults (≥18 yrs) with nonvalvular AF and ≥1 investigator-defined stroke risk factor were enrolled in the ongoing, prospective GARFIELD-AF registry from 32 countries in Mar 2010–Oct 2014. Patients classified as having paroxysmal (n=10,473, 48.5%), persistent (n=6020, 27.9%), or permanent AF (n=5117, 23.7%) by 4 mos were included in the analysis of baseline characteristics, antithrombotic therapy, and 2yr incidence of outcomes.

Results: Patients with permanent AF had slightly higher CHA2DS2-VASc (3.5 vs both 3.1) and HAS-BLED (1.6 vs both 1.4) vs those with paroxysmal or persistent AF, and they were most likely to be ≥75 yrs (48.3% vs 33.6% vs 34.3%). Compared to patients with other AF types, those with paroxysmal AF were less likely to be obese (26.7% vs 30.9% vs 33.2%) or to have LVEF<40% (6.0% vs 12.0% vs 14.4%) or severe HF (NYHA Class III/IV; 25.3% vs 33.0% vs 38.8%), but they were as likely to have history of vascular disease: stroke/transient ischaemic attack 12.2% vs 10.7% vs 13.5%; carotid occlusive disease 2.9% vs 2.8% vs 4.1%; ACS 9.4% vs 8.3% vs 9.6%. Patients with paroxysmal AF were less likely to receive anticoagulant (AC) therapy (+antiplatelets, AP) vs those with persistent or permanent AF and more likely to receive AP only or no antithrombotics (Tab). Compared to patients with paroxysmal AF, those with persistent

Antithrombotic therapy by type of AF

<table>
<thead>
<tr>
<th>%</th>
<th>Paroxysmal AF (n=10,473)</th>
<th>Persistent AF (n=6,020)</th>
<th>Permanent AF (n=5,117)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA +/- AP</td>
<td>38.0</td>
<td>53.9</td>
<td>57.1</td>
</tr>
<tr>
<td>FXaI +/- AP</td>
<td>13.1</td>
<td>9.8</td>
<td>9.0</td>
</tr>
<tr>
<td>DTI +/- AP</td>
<td>7.0</td>
<td>7.7</td>
<td>5.8</td>
</tr>
<tr>
<td>AP only</td>
<td>26.8</td>
<td>19.7</td>
<td>19.7</td>
</tr>
<tr>
<td>None</td>
<td>15.1</td>
<td>9.0</td>
<td>8.3</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist.

Fig 1. Adjusted HRs for 2yr outcomes by AF type
or permanent AF had higher risks of all-cause mortality, stroke/systemic embolism (SE) and major bleeding. However, only the difference in mortality persisted after adjustment (Fig). Adjusted HRs also showed higher mortality for non-paroxysmal vs paroxysmal AF and for permanent vs paroxysmal/persistent AF (Fig). We found no interaction between type of AF and AC therapy.

**Conclusion:** Persistent and permanent AF were associated with higher mortality risk vs paroxysmal AF but had similar adjusted risks of stroke/SE and major bleeding in 2 yrs of follow-up.

**P5464. Mechanical dyssynchrony assessment improves the prognostic value of current guidelines based patient selection for CRT**

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**Background:** Candidate selection for cardiac resynchronization therapy (CRT) should aim at a high response rate of this costly and invasive therapy without denying therapy to potential responders. Current ESC guidelines rely solely on ejection fraction (EF), QRS width and morphology as well as NYHA functional class. Echocardiographic signs of mechanical dyssynchrony, such as apical rocking (ApRock) and Septal Flash (SF) are not taken into account, although they have shown to be associated with CRT response and increased long term survival.

**Purpose:** To determine if incorporation of mechanical dyssynchrony assessment could improve the prognostic value of current European guidelines based patient selection.

**Methods:** We analyzed data from a multicenter registry of 1060 patients who received CRT between 1999 and 2012. All patients were retrospectively classified according to the 2016 ESC guidelines for CRT implantation. Patients had been examined by echocardiography before and 12±6 months after implantation. Mechanical dyssynchrony, defined as presence of ApRock or SF, as well as presence and extent of myocardial scar were visually assessed by three blinded readers at the baseline examination. Response was defined as ≥15% reduction in left ventricular end systolic volume at follow-up. Patients were followed for a median of 44 months (Interquartile range: 26–48 months) for the occurrence of death of any cause.

**Results:** Applying current ESC guidelines, 65% of the patients had been implanted with a class I indication, 18% with class IIa, 9% with class IIb, 6% with class III while 2% remained unclassifiable. In class I, 64% of patients responded to therapy, 51% in class IIa, 39% in class IIb and 34% in class III. Mechanical dyssynchrony predicted 97% of responders in class I, 96% in class IIa, 64% in class IIb and 69% in class III. Patients in class I had the most favorable survival, followed by class IIa, class IIb and then class III respectively (Log-rank P=0.07). In guideline classes I, IIa and IIb, presence of mechanical dyssynchrony at baseline predicted long term outcome better than the guideline class (Log-rank P<0.0001, 0.01 and 0.01 respectively; figure).

**Conclusion:** The current guideline criteria for CRT candidate selection can be improved by incorporating assessment of mechanical dyssynchrony. ApRock and SF have an added predictive value and are associated with better response and outcome after CRT.
99. Predictors of ventricular arrhythmias in the Nordic arrhythmogenic right ventricular cardiomyopathy registry: first experience from the prospective multicenter Scandinavian cohort

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Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is characterised by myocardial and genetic heterogeneity and variable clinical course of the disease, which affects development of strategies for risk stratification and primary prevention of sudden death. While most of data regarding the course of the disease comes from retrospective cohort studies, long-term follow-up studies of prospectively recruited cohorts remain limited. We aimed to assess predictors of ventricular arrhythmias in patients with definite ARVC prospectively enrolled in the Nordic ARVC registry.

Methods: Patients recruited in the registry from 8 sites in Denmark, Norway and Sweden with newly diagnosed ARVC fulfilling 2010 Task Force Criteria constituted the prospective cohort (n=92, 62% male, median age at diagnosis 45 years [IQR 33–60]). Genetic analysis was performed in 86%, of whom 62% appeared to be genotype-positive with plakophyllin-2 being the most common affected gene (61%) followed by desmoglein-2 (23%). Primary endpoint was defined as a time to first ventricular tachycardia (VT) documented by ECG or appropriate ICD therapy and assessed using Kaplan-Meier curve analysis and multivariate Cox regression. Median follow-up duration was 3.1 [IQR 1.8–3.9] years.

Results: At baseline, 54 patients had ICD implanted, 9 of whom received it for secondary prevention after aborted cardiac arrest; 40 patients had no history of arrhythmias, 11 had syncope with or without VT and remaining 41 patients had documented VT. During follow-up, 23% patients developed VT while the vast majority remained asymptomatic. Age <45 years, history of syncope or VT with left bundle branch QRS morphology (LBBB) and superior axis, and T-wave inversion in any of the inferior leads II, III or aVF were predictive of the primary endpoint during follow-up (Table). However, in the multivariable analysis, only VT with LBBB and superior axis morphology and inferior T-wave inversion remained independent predictors of ventricular arrhythmias (Figures).

Conclusion: In a Scandinavian cohort of prospectively enrolled patients with definite ARVC, over two thirds of patients remained asymptomatic during mid-term follow-up. In agreement with observations from other ARVC registries, history of VT or syncope and the presence of advanced repolarization abnormalities were associated with VT during follow-up. Our data further support repolarization abnormalities in inferior leads as an emerging risk indicator that independently predicted VT in our cohort.
3877. Primary prevention of sudden death with ICD therapy in the Nordic arrhythmogenic cardiomyopathy registry

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Background: Implantable cardioverter-defibrillator (ICD) therapy remains a cornerstone of sudden death (SCD) prevention in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC). However, risk stratification and predictors of ICD interventions are not fully clarified. We aimed to assess predictors of appropriate ICD interventions in AC patients who received ICD implants for primary prevention of sudden death enrolled in the Nordic ARVC registry.

Methods: Of the 203 ICD-carriers with definite ARVC enrolled in Denmark, Norway and Sweden, 27 received the implant after aborted cardiac arrest and were excluded from analysis. The remaining 176 patients (70% male, age at first implant 42±15 years) from 148 families constituted the study group. Task Force 2010 diagnostic criteria, ECG characteristics at baseline and history of syncope or documented ventricular tachycardia (VT) prior to ICD implant were assessed as predictors of appropriate ICD therapy defined as either antitachycardia pacing (ICD-ATP) or shock (ICD-Shock) using Kaplan-Meier curve analysis and multivariable Cox regression. Median follow-up duration was 8.3 years.

Results: Prior to ICD implantation, 94 patients (53%) had either sustained or non-sustained VT and 43 (24%) had syncope. Appropriate ICD therapy was detected in 104 patients (59%). While neither imaging nor depolarization criteria showed any significant association with the outcome, ICD therapy was independently predicted by history of syncope (HR 1.64, 95% CI 1.07–2.49, p=0.022), documented VT prior to ICD implant were assessed as predictors of appropriate ICD therapy defined as either antitachycardia pacing (ICD-ATP) or shock (ICD-Shock) using Kaplan-Meier curve analysis and multivariable Cox regression. Median follow-up duration was 8.3 years.

Conclusion: While history of VT and syncope are well accepted indications for ICD therapy in patients with ARVC, our data further support the role of ECG markers of electrical instability of ventricular myocardium such as T-wave inversion in the precordial leads meeting major repolarization criterion according to the Task Force 2010 definitions.

2897. Sex difference in cardiovascular risk is offset by presence of left ventricular hypertrophy

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Background: The notion that women have better cardiovascular (CV) outcome than men is consolidated by strong evidence. However, whether or not this sex-specific protection persists also in the presence of hypertensive target organ damage such as left ventricular (LV) hypertrophy (LVH) is unclear.

Purpose: Our objective was to assess whether the presence of LVH alters the outcome difference between men and women with treated arterial hypertension.

Methods: Clinical, echocardiographic and outcome data from 5,395 women and 6,937 men free from prevalent CV disease from the prospective Campania Salute Network registry were used. Median follow-up was 49 months. LVH was identified from prognostically validated sex-specific cut-off values of LV mass index (47 g/m² for women and 50 g/m² for men). The presence of any of these three risk factors was a strong predictor of appropriate ICD therapies (HR=2.89, 95% CI 1.43–5.57, p=0.003, Figure).

Conclusion: While history of VT and syncope are well accepted indications for ICD therapy in
presence or absence of LVH, using Cox regression analysis and reported as hazard rates (HR) and 95% confidence intervals (CI).

**Results:** Women were older, more obese, had higher systolic blood pressure (BP), total and high density lipoprotein cholesterol, and lower diastolic BP, serum triglycerides and glomerular filtration rate compared to men (all p<0.01), while the prevalence of smoking did not differ. LVH was more prevalent in women than men (43.2 vs. 32.4%, p<0.001). Incident MACE occurred in 3.5% of men and 2.8% of women during follow-up (p=0.040). In Cox regression analysis among subjects without LVH, adjusting for baseline differences in CV risk factors, women without LVH had a 32% lower HR for MACE (95% CI 0.49–0.95), p=0.025) than men without LVH (Figure, Panel A). Running the same model in subjects with LVH, women with LVH did not have a significantly lower HR for MACE (HR 0.79 [0.59–1.06], p=0.110) than men with LVH (Figure Panel B).

**Conclusions:** In hypertension, presence of LVH attenuates the sex difference in CV risk.

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**P2620. Sudden death in primarily asymptomatic patients with aortic valve stenosis**

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**Background:** The risk of sudden cardiac death (SCD) in patients with asymptomatic aortic stenosis (AS) is thought to be approximately 1%/year and may be dependent on AS severity. We retrospectively analyzed outcome data from the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) study with the aim to assess the incidence and potential risk factors of SCD in this prospectively followed cohort of asymptomatic patients.

**Methods:** Of the 1873 patients included in the trial, 1204 (64%) with mild to moderate aortic stenosis (jet velocity 2.5–4.0 m/s), complete clinical, echocardiographic, and follow up data remained event-free (except for sudden death) throughout the study period.

**Results:** SCD occurred in 19 patients during a mean follow-up of 26.6±13.2 months (0.7%/year). Patients with SCD were older (p=0.01), had a higher left ventricular (LV) mass (p<0.001), tended to be female (p=0.11) and leaner (p=0.06) than surviving asymptomatic patients. None of the echocardiographic parameters of stenosis severity (or their development over time) were associated with SCD (e.g. jet velocity 3.1±0.4 vs. 2.9±0.5 m/s, p=0.33). Cox regression analysis identified age (HR 1.077, 95% CI 1.012–1.145 per year), LV mass (HR 1.013, CI 1.007–1.019 per gram), and BMI (HR 0.836, CI 0.721–0.968 per kg/m2) as independent risk factors of SCD (all p<0.02).

**Conclusion:** Sudden cardiac death in asymptomatic patients with aortic stenosis is rare and strongly related to left ventricular mass but not stenosis severity.

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**P6200. Getting a grip on heart failure: the nexus between multimorbidity, physical frailty and 12-month mortality in 765 patients hospitalised with heart failure**

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**Background:** In an increasingly ageing patient population, multimorbidity and physical frailty in those hospitalised with chronic heart failure (CHF) represent potentially important contributors to all-cause 12 month mortality.

**Purpose:** To characterise the pattern of the ten most common forms of multimorbidity and physical frailty in relation to 12-month mortality in a high-risk cohort of patients hospitalised with CHF.

**Methods:** A prospective analysis was conducted on data collected on 765 CHF participants at baseline in a large CHF management multicentre randomised control trial. Participants received a minimum of 12 months follow up to determine all-cause mortality. The analysis was conducted using handgrip strength and multimorbidity...
being the 10 most common concurrent conditions in CHF. We identified frailty according to the lowest quintile of handgrip strength with the highest quintile of handgrip strength.

**Results:** The mean age was 74±12 years (42% female), with left ventricular systolic dysfunction (65%), and NYHA Class III/IV (28%). Overall, there is a linear trend for the majority of the 10 comorbidities across the quintile handgrip strength. Patients with the lowest handgrip strength had the highest prevalence of anaemia (81% in the lowest handgrip strength quintile vs 23% in the highest grip strength quintile), cognitive impairment (63% vs 51%) and depression/anxiety (78% vs 69%). The 12-month mortality was 22% in males and 17% in females. There was a downward trend in handgrip strength and 12-month mortality in males, at 33%, 24%, 14% and 12% for quintile groups 1, 2, 3, 4 and 5 respectively (P=0.007). There was no trend in females (P=0.749). After adjustment for age and the 10 CHF comorbidities, multivariate logistic regression analysis showed that handgrip strength had a significant impact on 12-month mortality in males independent of age (P=0.020), but not in females (P=0.114).

**Conclusion:** Physical frailty measured by handgrip strength is a promising predictor of 12-month mortality in men with CHF, independent of age and the common comorbidities associated with CHF. Further research is needed to identify determinants of muscular strength in CHF patients, and to test whether improvement in strength reduces mortality.

**P2408. Impact of mitral regurgitation correction (mitraclip vs surgical repair) on left ventricular myocardial performance according to baseline left ventricular ejection fraction**

**Table 1**

<table>
<thead>
<tr>
<th>EF at baseline &lt;40% (n=24)</th>
<th>EF at baseline ≥40% (n=8)</th>
<th>EF at baseline &gt;50% (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>35±15</td>
<td>33±14</td>
</tr>
<tr>
<td>6-month follow-up</td>
<td>56±11</td>
<td>45±14</td>
</tr>
<tr>
<td>GLS (%)</td>
<td>-10.2±4.6</td>
<td>-10.0±4.2</td>
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<tr>
<td>Mechanical Dispersion (ms)</td>
<td>95±50</td>
<td>89±36</td>
</tr>
<tr>
<td>GW (mmHg %)</td>
<td>84±1405</td>
<td>937±436</td>
</tr>
<tr>
<td>PW (mmHg %)</td>
<td>999±399</td>
<td>112444</td>
</tr>
<tr>
<td>NW (mmHg %)</td>
<td>-116±124</td>
<td>-52±112</td>
</tr>
</tbody>
</table>

*p values assessed by Student’s paired t-test. All values expressed as mean ± standard deviation. LVEF: left ventricular ejection fraction; GLS: global longitudinal strain; GW: global work; PW: positive work; NW: negative work.*
Increased bleeding events in patients co-administered rivaroxaban and either cyp3A4 or P-gp inhibitors

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Background: The ROCKET AF trial established the non-inferiority of rivaroxaban compared to warfarin for prevention of thromboembolic events in patients with non-valvular atrial fibrillation. Reduced dosing is recommended for patients with renal insufficiency. However little is known about clinical outcomes when rivaroxaban is used with cytochrome P450 CYP3A4 or P-glycoprotein (P-gp) inhibitors. Hepatic CYP3A4 and renal P-gp are thought to play important roles in rivaroxaban degradation and renal excretion respectively. Both are subject to competitive inhibition by a number of commonly prescribed cardiac medications. We hypothesized that bleeding rates might increase when patients take rivaroxaban in combination with either CYP3A4 or P-gp inhibitors.

Methods: We reviewed the records of patients prescribed rivaroxaban over a 5-year period between January 1st, 2011 and December 31st, 2015. Patients were included in the study if they (1) had a prescription for rivaroxaban for at least 90 consecutive days, (2) were prescribed at least one concomitant medication of interest, and (3) had a medical bleeding event occurring at least 7 days after the prescription date of the interacting medication. In addition to CYP3A4 and P-gp inhibitors, the impact of platelet aggregation inhibitors (PAIs) and non-steroidal anti-inflammatory drugs (NSAIDs) on bleeding was evaluated. Bleeding-related diagnoses, classified by individual ICD codes, were used to tabulate the number of bleeding events. Chi-square tests were used to compare the proportion of patients with bleeding events in the group that had concomitant interacting medications versus the group that did not.

Results: 1674 patients were identified who were prescribed rivaroxaban and either a CYP3A4 inhibitor, P-gp inhibitor, PAI, or NSAID. The most commonly co-prescribed class of drugs was P-gp inhibitors (49.8% of patients). 10.1% of patients on rivaroxaban were co-prescribed PAIs, 13.6% CYP3A4 inhibitors and 26.6% NSAIDs. The greatest bleeding risk was observed with CYP3A4 inhibitors (40.0% vs. 17.1% on rivaroxaban alone; p<0.01). Increased bleeding rates were also seen with co-administration of PAIs (28.4%, p<0.1), P-gp inhibitors (24.1%, p<0.01) and NSAIDs (21.1%, p=0.01).

Discussion: Concomitant use of either CYP3A4 or P-gp inhibitors with rivaroxaban was associated with increased bleeding risk. CYP3A4 inhibitors were associated with the greatest risk, while P-gp inhibitors were associated with an increased risk similar to that seen for patients prescribed NSAIDs or PAIs. Our data is limited by the number of patients available for analysis and use of ICD codes to determine bleeding. However, our study provides evidence that co-administration of rivaroxaban with either CYP3A4 or P-gp inhibitors may be associated with an increased risk of bleeding.

P2404. Percutaneous mitral valve repair in secondary mitral regurgitation improves cardiac work

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Background: Left ventricular (LV) pressure-strain loops (PSLs) have been recently validated as a non-invasive index of myocardial performance. Aim is to compare LV function, myocardial work, and energy dispersion in patients with severe mitral regurgitation (MR) and decreased left ventricular ejection fraction (LVEF) before percutaneous mitral valve repair (PMVR, by Mitraclip® system) and at 6-month follow-up (FU).

Methods: We included 32 patients (mean age: 71±10 years) with secondary MR (18 with ischemic cardiomyopathy, 14 with dilated cardiomyopathy) undergoing PMVR. All patients underwent echocardiography before PMVR and at FU. Strain traces and valvar event times were used to calculate LV-PSLs and Global cardiac Work (GW), Positive Work (PW), and Negative work (NW) were therefore obtained.

Results: The main results are shown in table 1. Despite a strong decrease of NYHA class (2.6 vs 1.8; p<0.001), no significant difference in LV function and remodeling parameters was observed at FU. Interestingly, while GW and NW remained unchanged, PW significantly improved at FU (999 vs 1112 mmHg.%; p=0.05).

Conclusion: Patients with severe MR and high surgical risk undergoing PMVR experienced a significant improvement in symptoms which was associated to an increase in PW. No classical parameters of LV function/remodeling were ameliorated at FU. It support the hypothesis that the estimation of PW by LV-PSLs might be more sensible that commonly used index of myocardial performance to detect early improvement in myocardial function.
Background/Purpose: There are very few data published on long-term outcomes of patients with spontaneous echo contrast, left atrial/left atrial appendage (LA/LAA) thrombus, and complex aortic plaque in those with atrial fibrillation (AF) receiving chronic oral anticoagulation. Therefore, we explored the relationship between these 3 specific echocardiographic findings and clinical outcomes, as well as the comparative efficacy and safety of apixaban and warfarin for each of them.

Methods: Patients from the ARISTOTLE trial with spontaneous echo contrast, LA/LAA thrombus, or complex aortic plaque, diagnosed by either transthoracic or transesophageal echocardiography (TEE), were compared with patients with none of these findings by TEE.

Results: A total of 1251 patients were included: 217 had spontaneous echo contrast, 127 had LA/LAA thrombus, 241 had complex aortic plaque, and 746 had none of these findings on TEE. The rates of stroke or systemic embolism were not significantly different among patients with and without these echocardiographic findings (HR 0.96, 95% CI 0.25–3.60 for spontaneous echo contrast; HR 1.27, 95% CI 0.23–6.86 for LA/LAA thrombus; HR 2.21, 95% CI 0.71–6.85 for complex aortic plaque). Rates of ischemic stroke, myocardial infarction, cardiovascular death, and all-cause death were also not different between patients with and without these echocardiographic findings (Figure). There was no evidence of a differential effect of apixaban compared with warfarin on the majority of outcomes, in patients with any of the specific echocardiographic findings.

Conclusions: In anticoagulated patients with AF and at least 1 risk factor for stroke the presence of spontaneous echo contrast, LA/LAA thrombus, and aortic plaque do not add to the risk of thromboembolism.
P1077. High-risk cluster of multimorbidity in elderly patients hospitalised with chronic heart failure

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Background: Multimorbidity is not only common in elderly patients with heart failure (HF), but also adversely affect health outcomes. Delineating risk of poor health outcomes within this complex population represents a major clinical issue.

Purpose: To test the hypothesis that independent of extent of multimorbidity, there are distinctive clusters of coexisting conditions that convey increased risk for 30-day all-cause readmission or death in hospitalised HF patients.

Methods: Study data were derived from a multicentre trial of HF management program comprising 787 hospitalised patients. Classification and regression tree (CART) analysis was used to identify distinctive combinations of comorbidities associated with 30-day all-cause readmission or death. Ten HF comorbidities as outlined in the expert-derived ARISE-HF (Acknowledge, Routinely profile, Identify, Support, and Evaluate Heart Failure) framework, were tested in the CART model; comprising anaemia, arrhythmias, cognitive dysfunction, depression or anxiety, diabetes or obesity, musculoskeletal disorders, renal impairment, respiratory disease, sleep disorders and thyroid disease.

Results: Mean age was 74±12 years and 41% were female, 65% had HFrEF (LVEF 31.4±8.9%) and 28% were NYHA Class III/IV at hospital discharge. Multimorbidity was common comprising - with depression or anxiety (70%), arrhythmias (64%), diabetes or obesity (63%), renal impairment (60%), cognitive impairment (58%) and anaemia (55%) the six most common comorbidities. Most patients (87% in men, 91% in women) had ≥3 concurrent conditions. All-cause readmission or death within 30 days of index hospital discharge occurred in 219 patients (28%), including 8 deaths. Patients with arrhythmias, depression or anxiety, and renal impairment had higher 30-day readmission/death rates (30% to 31%) than those without these three conditions (23% to 24%, P<0.05).

There was an upward trend in 30-day readmission/death rates as the number of chronic conditions increased - 11%, 22%, 29% and 47% for those with 0–1, 2–4, 5–7 and 8–9 comorbidities (P=0.006), respectively. The presence of arrhythmias was the most important predictor for 30-day readmission or death, and the risk of 30-day readmission or death was varied across 7 distinctive clusters of comorbidities detected from CART model (Figure 1). Compared to those with diabetes or obesity, but without arrhythmias or cognitive impairment who had the lowest readmission/death rate (16%), patients with arrhythmias, renal impairment and respiratory disease simultaneously had significantly higher readmission/death rate (42%, RR=3.4).

Conclusion: We have identified a “malignant” cluster of comorbidities (arrhythmias, renal impairment and respiratory disease) associated with significantly increased risk of immediate rehospitalisation or death in HF patients. These data may be critical in the delivery of HF management programs to improve health outcomes in particularly high risk patients.

Figure 1. Multimorbid clusters and outcomes

P5233. Is a simpler approach to the diagnosis of cardiotoxicity accurate? Comparison of single-view and standard assessment of global longitudinal strain

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Background: Global longitudinal strain (GLS) is a sensitive marker of LV dysfunction that facilitates early detection of cancer therapeutics related cardiac dysfunction (CTRCD). Standard GLS is derived from 3 apical views. However, as patients require repeated testing and CTRCD is a diffuse process, single view GLS could improve efficiency.

Purpose: We sought whether 4 chamber view GLS (4CV_LS) could substitute GLS for the detection of CTRCD in an international multicenter study.

Methods: In patients receiving Anthracycline-based chemotherapy, enrolled from 17 international institutions (7 Europe, 2 North America, 5 Asia and 3 Australia), ejection fraction (EF), GLS and 4CV_LS were measured at baseline and follow-up, and the differences between them were calculated. Asymptomatic CTRCD was defined as EF>0.10 decrease with to <0.55, or GLS>12% decrease. A Bland-Altman plot (BA plot) was used for evaluation of concordance.

Results: Of 108 patients (54±13 years, 101 women), 95 had breast cancer, 13 had hematologic malignancy. There were good correlations between GLS and 4CV_LS at baseline and follow-up (r=0.86 and 0.89, both p<0.0001). BA plots demonstrated minimal bias (0.21 at baseline; 0.03 at follow-up) but modest limits of agreement (2.54% and 2.19%). Of 47 patients developing CTRCD, 4CV_LS yielded 15 (14%) false negatives and 9 (8%) false positives, resulting in a discordance rate of 22% to detect CTRCD (Figure).

Conclusions: 4CV_LS has good correlation with GLS, but our study indicates that it could lead to significant misdiagnoses. We recommend standard GLS from multiple apical views for patients with risk for CTRCD.

P3568. Low apolipoprotein al is significantly associated with decreased risk of cardiovascular events in anticoagulated patients with atrial fibrillation: insights from the ARISTOTLE trial

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Background: Dyslipidemia is a major contributor to cardiovascular disease. The prognostic importance of lipoproteins in patients with atrial fibrillation (AF) is not well understood.

Purpose: Our aim was to explore the prognostic value of the levels of apolipoprotein A1 (ApoA1) and B (ApoB) in relation to ischemic cardiovascular events in patients with AF.

Methods: ApoA1 (a main component of HDL) and ApoB plasma levels were measured at baseline in 14,884 patients with AF from the ARISTOTLE (Apixaban for the Prevention of Stroke in Subjects with Atrial Fibrillation) trial which compared apixaban with warfarin. The median length of follow-up was 1.9 years. The association of ApoA1 and ApoB concentrations with cardiovascular events was evaluated using Cox analyses adjusted for established cardiovascular risk factors, randomized treatment, concomitant medication (statins, aspirin and ACE-inhibitors/ARB), and other prognostic cardiovascular biomarkers (troponin, NT-proBNP, cystatin C, CRP, and IL-6) in AF. A composite ischemic outcome consisting of ischemic stroke, systemic embolism, myocardial infarction, and cardiovascular death (excluding bleeding) was used as the primary endpoint.

Results: The median ApoA1 level was 1.10 g/L (interquartile range 0.93–1.30), and 0.70 g/L (0.55–0.85) for ApoB. In the fully adjusted analyses, ApoA1 was independently associated with a reduction in the composite ischemic outcome with a HR of 0.66 (95% CI, 0.52–0.82, p=0.0004) comparing the highest with the lowest quartile group (Table). Similar results were seen for the individual components of the composite ischemic outcome. ApoB was not
significantly associated with the composite ischemic outcome, HR 0.95 (0.77–1.16, p=0.6132) comparing the same quartile groups. Neither ApoA1 nor ApoB were associated with major bleeding. There was no significant interaction with randomized treatment.

**Conclusion:** In patients with AF on oral anticoagulation, the level of ApoA1 is independently associated with decreased risk of ischemic cardiovascular outcomes. Investigating therapies targeting dyslipidemia may thus be useful to improve cardiovascular outcomes in patients with AF.

**1255. Matching delivery of heart failure management to overcome individual barriers to optimal health care: A case of so CLOSE and yet so far**

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**Background:** Despite a tendency to apply different models of heart failure (HF) management according to a patient’s proximity to health services, a number of other factors (beyond geography) influence a patient’s ability to access care.

**Purpose:** To characterize the barriers to care among rural and metropolitan-dwelling patients requiring post-discharge, HF management and their ideal model of care according to the novel CLOSE framework.

**Methods:** We applied Clinical, LOcation and Socio-Economic status (CLOSE) profiling to a typical cohort of patients requiring post-discharge HF management following an acute admission to 4 geographically dispersed hospitals. They were then designated as proximal (<25km) or remote (≥25km) to specialist care. Patients were also designated as either independently able to access health care or facing significant barriers according to the presence of 3 or more of the following factors - 1) aged >75 years, 2) living alone, 3) Non-English speaking, 4) Age adjusted Charlson Index Score of ≥5, 5) Cognitive Impairment (Montreal Cognitive Score <26) and 6) NYHA Class III/IV at discharge. These two main categories were then combined to produce 4 CLOSE groups: GROUP 1: Independent and proximal to healthcare services; GROUP 2: Independent but living remotely; GROUP 3: Barrier to health care despite living proximal to healthcare services; and GROUP 4: Barriers to healthcare and living remotely.

**Results:** In total, 809 patients (59% male aged, 74±12 years and 65% HFrEF) of whom 19% were living remote from specialist care, were profiled and categorised into the 4 CLOSE groups; with 68% of patients having ≥3 barriers to health care (the majority having 2–4 barriers) overall. On an individual basis, these barriers typically affected 29% (NYHA III/IV) to 84% (high multimorbidity) of patients with only 6% completely independent (no barriers) according to CLOSE criteria. Figure 1 shows these four CLOSE groups and the ideal model of HF management based on their combination of geographic, clinical and socio-economic barriers. Overall, 59% of those living proximal or remote to services (this being the worse combination for accessing health care) had significant barriers to care that prompted our recommendations for additional management better suited to their needs.

**Conclusions:** A majority of health care services primarily focus on providing care to those who are independently mobile and who are proximal to services. However, many high risk HF patients

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<td>4521</td>
<td>258 (3.02)</td>
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**Table 1. The association of Apolipoprotein A1 at baseline with the ischemic composite outcome**

**Figure 1. CLOSE Groups Recommendations**
are still vulnerable to poor health outcomes. In the case of remote dwelling patients with significant barriers to care, for example, face-to-face contact supplemented by remote management techniques would be preferable to remote management alone.

288. Prognostic impact of increase arterial stiffness in hypertensive patients: the Campania Salute Network

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Background: Increased arterial stiffness has been associated with advanced atherosclerosis, abnormal left ventricular (LV) geometry and diastolic dysfunction. Recently, increased arterial stiffness has been also related to subclinical systolic dysfunction probably due to abnormal vascular-ventricular coupling. While increased arterial stiffness is associated with incident adverse cardiovascular (CV) event, independent of major confounders and CV risk factors, whether this prognostic effect is also independent of LV geometry still needs to be clarified.

Purpose: We evaluated whether a measure of arterial stiffness, the pulse pressure (PP)/stroke index ratio (SVi) predicts incident CV event independently of LV geometry, in patients with treated arterial hypertension, from a large observational registry in southern Italy.

Methods: Hypertensive participants from the Campania Salute Network (n=9692) without prevalent coronary or cerebrovascular disease, with ejection fraction >50% and no more than stage III CKD were followed for a median of 49 months for the occurrence of cardiovascular events (fatal and non-fatal stroke and myocardial infarction, and atrial fibrillation). PP/SVi was divided into sex specific quartiles. The highest sex specific quartile was considered normalized by allometric signal of height (2.04). LV hypertrophy (LVH) was defined as LV mass thickness ≥ 50 g/m² in men or ≥ 47 g/m² in women. LV hypertrophy and concentric geometry, high PP/SVi predicted 35% increased hazard ratio of (Figure 1). Linear variance inflation was <2 for all variables used in Cox modeling.

Conclusions: In hypertensive patients, higher PP/SVi is associated with increased CV risk, independently of demographics, presence of LV hypertrophy and concentric geometry.

P5443. The lack of clinical awareness towards the diagnosis of mitral regurgitation. Insights from a European survey

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Background: Mitral regurgitation (MR) is the most frequent valvular disease in the community. However, the current knowledge and application of Guidelines on diagnosis and evaluation of MR are not well known.

Purpose: The Education Committee of the ESC and AXDEV Group performed a mixed-methods educational needs assessment, which included a case-based evaluation, in a wide panel of practitioners in Europe.

Methods: The quantitative portion of the needs assessment included 3 case scenarios (asymptomatic severe primary MR, symptomatic severe primary MR in the elderly and symptomatic severe secondary MR) and was conducted online from March to May 2016 in 7 countries: France, Germany, Italy, Poland, Spain, Sweden and the United Kingdom. 554 practitioners participated in the study, 51 in the exploratory qualitative phase, and 503 in the quantitative phase. The qualitative phase case scenarios were answered by 108 primary care physicians (PCP), 203 general and 192 sub-specialized cardiologists.

Results: Cardiac auscultation was performed systematically by 54% of PCPs and only in the presence of cardiac symptoms by 31%. In addition, 40% of PCPs did not perform systematic auscultation after mitral valve repair. 20% of
PCPs considered that the lack of symptoms was discordant with severe MR. In an elderly patient with severe MR and comorbidities, dyspnoea was more frequently considered as severe by PCPs (69% of participants) than by cardiologists (29% of participants). Cardiologists appropriately interpreted echocardiographic findings with regards to mechanism and quantitation of symptomatic primary MR (75% and 75%, respectively) and of asymptomatic primary MR (87% and 86%, respectively). The diagnosis of secondary MR was correct in 93% of cases, although it was based on left ventricular dysfunction in 79% of cases and on analysis of leaflet structure and movement in only 14%. In contrast, secondary MR was quantitated as severe by only 44% of cardiologists. Only 44% of cardiologists requested the measurement of tricuspid annulus diameter before surgery for asymptomatic severe primary MR.

Conclusions: The early detection of primary MR in asymptomatic patients suffers from the underuse of systematic auscultation by PCPs. Systematic auscultation is also insufficiently performed during follow-up after mitral valve repair. Symptom perception differs between PCPs and cardiologists. Interpretation of echocardiography by cardiologists is good for primary MR but less satisfying for secondary MR, in particular concerning quantitation. Increased awareness is needed on the tricuspid valve. These findings identify important targets for future educational programmes.

2035. Mid- and long-term outcome of the EXPLORE trial: investigating the impact of CTO PCI versus no-CTO PCI in STEMI patients with a concurrent CTO

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On behalf: EXPLORE Trial

Background: At 4 month follow-up (FU) the EXPLORE trial showed no difference on the primary endpoint left ventricular (LV) function comparing early percutaneous coronary intervention of the chronic total occlusion (CTO PCI) to standard medical treatment (no-CTO PCI) in ST-elevation myocardial infarction (STEMI) patients. However, the long-term effects of CTO PCI versus no-CTO PCI are currently unknown.

Purpose: To investigate the effect of CTO PCI versus no-CTO PCI in STEMI patients on mid- and long-term LV function and clinical outcome.

Methods: At 1, 2, 3, 4, and 5 years, clinical follow-up was obtained on: angina status, dyspnoea status, all events and major adverse cardiac events (MACE); composite of cardiac death, myocardial infarction and coronary artery bypass graft surgery. Moreover, patients underwent cardiac magnetic resonance imaging (CMR) at 1 year. An independent corelab analysed all CMR data. All events underwent independent monitoring and were adjudicated by an independent critical events committee. For the incidence of MACE, Kaplan-Meier curves were constructed and compared using the log-rank test.

Results: In the EXPLORE Trial there were 148 patients randomized to CTO PCI within 7 days and 154 patients to no-CTO PCI. There were no differences in baseline characteristics between both arms. One year LV function was comparable between CTO PCI patients (n=45) and no-CTO PCI patients (n=49) (LVEF 45.5±9.1% versus 44.6±10.7%, p=0.66, LVEDV 198.0±44.8ml versus 208.1±50.9ml, p=0.31). One year clinical follow-up was complete for all patients. MACE rates were comparable between CTO PCI and no-CTO PCI (6.8% versus 5.3%, p=0.56). In the no-CTO PCI group 27 patients (17.6%) underwent an additional CTO PCI after obtaining the primary endpoints. The median long-term follow-up of all patients is 3.9 (IQR 2.9) years.

Conclusion: The EXPLORE trial is the first randomized clinical trial investigating the impact of revascularization of a CTO. The primary outcome (LVEF and LVEDV) of the EXPLORE Trial was not met at four months. Furthermore no benefit of CTO PCI on 1 year LV function was seen. There was no significant difference in MACE between the 2 treatment groups. Long-term follow-up is currently being analyzed and we will be able to present the long-term clinical outcome at ESC 2017.

Figure 1. MACE at 1 year follow-up