NORSKE ABSTRAKTER PRESENTERT I PARIS

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138: The association between leisure time physical activity and atrial fibrillation in the general population - a longitudinal study

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Purpose: To determine the effect of self-reported physical activity on the risk of AF in subjects without concomitant heart disease in a longitudinal population study.

Methods: Three population-based surveys using standardized methods undertaken during 1974-2003 were merged. The present analysis comprises 428 519 participants, alive and aged 30-81 years by the end of 2003. Having at least one prescription of flecainide dispensed January 1st 2004 until December 31st 2009, was used as proxy for AF based on the Norwegian Prescription Database, established in 2004. Flecainide is mainly used for prevention of AF recurrence, and structural heart disease is a contra-indication. Subjects with prescription of flecainide or sotalol at survey were excluded from the analyses. Hazard ratios were estimated by Cox' proportional hazards regression with time from January 1st 2004 until first dispensed prescription of flecainid as the time variable.

Results: During the follow-up period, 1183 men and 609 women with prescribed flecainide for the first time constitute the AF cases. The risk of AF increased with increasing level of physical activity in men, whereas no such association was observed among women (Table). The majority of the AF cases were 50-69 years old,non-smokers, and had higher education. Resting heart rate was inversely related to the risk of having AF.The male cases had also lower levels of the major cardiovascular risk factors.

Conclusion: There was a graded independent increase in the risk of AF with increasing levels of physical activity in this population based study among men with ostensibly no other heart disease.

Physical activity and AF hazard ratio

Adjusted for:	Walking, etc. for at least 4 hrs/week		Light sports, heavy gardening		Hard exercise several times/week	
	HR	95% CI	HR	95% CI	HR	95% CI
Men (N=204,897)						
Age	1,21	1,03, 1,44	1,47	1,23, 1,76	2,94	2,25, 3,84
Age+height	1,18	1,00, 1,40	1,41	1,18, 1,70	2,84	2,17, 3,71
Age+bmi	1,21	1,02, 1,43	1,46	1,22, 1,76	2,92	2,23, 3,82
Age+education	1,20	1,01, 1,42	1,42	1,18, 1,70	2,75	2,11, 3,60
Age+height+bmi+educ.	1,18	1,00, 1,40	1,39	1,16, 1,67	2,75	2,10, 3,60
Women (N=223,622)						
Age+height+bmi+educ.	1,00	0,82, 1,23	0,78	0,56, 1,08	NA	NA

156: Risk of ventricular arrhythmias in patients with idiopathic dilated cardiomyopathy can be identified by left ventricular global strain

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Purpose: Identification of patients at risk of ventricular arrhythmias in patients with idiopathic dilated cardiomyopathy (iDCM) is demanding. Indications for primary prevention ICD therapy are based on LV ejection fraction (EF) <35%. Myocardial strain by echocardiography

can accurately quantify ventricular function. We therefore hypothesized that global strain may be a better marker of ventricular arrhythmias in patients with iDCM.

Methods: In all, 58 consecutive patients with iDCM were prospectively included. QRS duration was recorded from ECG. By speckle tracking echocardiography, global strain was calculated as average peak strain from a 16 LV segments model. LVEF and body surface corrected LV mass were assessed from standard echocardiography.

Results: During 39 (16-63) months of follow up, 9 patients had arrhythmic events defined as sustained VT or cardiac arrest. Global strain was reduced in iDCM patients with arrhythmic events compared to those without (-7.2±5.9% vs. -12.2±5.9%, p=0.02). iDCM patients with arrhythmias had higher LV mass index (191±54 g/m^2 vs. 149±42g/m^2, p=0.01) and prolonged QRS compared to those without arrhythmic events (138±38ms vs. 97±32ms p=0.002). EF was slightly lower in those with arrhythmic events (32±15% vs. 41±15%, p=0.08). By ROC analysis, global strain could better discriminate between those with and without arrhythmic events compared to EF (AUC 0.79 (95%CI 0.63 to 0.95) vs 0.68 (95%CI 0.47 to 0.89) p=0.04) (Figure 1).

Conclusions: Global strain, LV mass and QRS duration were markers of arrhythmias in patients with iDCM. Global strain was superior to EF in identifying arrhythmic events. Global strain by echocardiography may provide additional value for risk assessment of ventricular arrhythmias in iDCM patients.

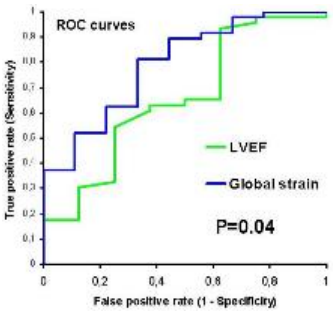

Figure 1. Identifying arrhythmic events in 58 pts.

P251 : Soluble gp130 predicts outcome in chronic heart failure: analysis from the controlled rosuvastatin multinational trial in heart failure (CORONA)

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Purpose: Circulating levels of interleukin-6 family cytokines, including soluble glycoprotein 130 (gp130), their common signal-transducing receptor subunit, are elevated in patients with chronic heart failure (HF), with increasing levels according to disease severity. We investigated whether gp130 provided independent prognostic information in patients with chronic HF and examined possible interactions with statin therapy.

Methods: Gp130 as a risk factor for the primary endpoint (cardiovascular[CV] death, nonfatal myocardial infarction, nonfatal stroke; n=408), all-cause mortality (n=422), CV mortality (n=344), death from HF (n=102) or sudden death (n=194), total- (n=804) or HF hospitalizations (n=327) was investigated in 1447 patients (≥ 60 years, New York Heart Association [NYHA] class II-IV, ischemic systolic HF, optimal pharmacological therapy) in the CORONA population, randomly assigned to 10 mg rosuvastatin or placebo.

Results: In multi-variable analyses, adjusting for left ventricular ejection fraction, NYHA class, age, body mass index, diabetes, sex, intermittent claudication, heart rate, estimated glomerular filtration rate, and ApoB/ApoA-1-ratio, gp130 (continuous variable, adjusted by the standard deviation of gp130) was significantly associated with all end-points (HR from 1.10 to 1.39 for the different end points), except the primary endpoint. When NT-proBNP was added to the

model, gp130 still provided independent predictive information for all-cause mortality [HR 1.19 (1.06-1.33), p=0.004], CV mortality [HR 1.15 (1.01-1.31), p=0.034] and death from HF [HR 1.50 (1.20-1.86), p<0.0001], but not for hospitalizations. We observed no interactions between gp130 levels and effect of rosuvastatin treatment on outcomes.

Conclusions: Soluble gp130 independently predicts mortality, and especially death due to worsening HF, in older patients with advanced chronic systolic HF of ischemic etiology.

P556 : Economic impact of smoking cessation among motivated quitters in Norway

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Background: Tobacco use is the most important health-risk that can be prevented, and an important cause of premature death. More than 10% of all deaths from cardiovascular disease (CVD) are due to smoking. After diagnosed CVD, around 50% of smokers continue to smoke. Smoking cessation (SC) is potentially the most cost-effective life-saving intervention for patients with CVD, and costs of interventions for SC are small in comparison with the long-term benefits both in terms of prevention, mortality, morbidities and treatment costs for smoking-related diseases. The purpose of this study is to explore the economic impact of SC by treating motivated quitters with varenicline (Champix).

Method: An Excel-based model was developed to compute per-member-per-year costs associated with SC among motivated quitters in general population. The model assumes that smokers make only one SC attempt using varenicline. Model inputs on smoking-related costs were 80 billion NOK per year and 2-3 billion NOK reduced costs per year per % reduction in smoking prevalence, both in accordance with cost data from the Norwegian Health Directorate. Inputs included also smoking prevalence, drug costs and the proportion of motivated quitters. Norwegian statistics on smoking prevalence, Medline search for statistics regarding motivated quitters and varenicline effect as shown by the Norwegian Knowledge Center for Health Services (NKCHS). The primary model outcome will be costs of treating with varenicline and costs avoided.

Result: If 50.000 of 900.000 Norwegian daily smokers use varenicline in one SC attempt, 13.000 will remain smoke free after one year. This will reduce the smoking prevalence in Norway by 1.4%. Since reduced costs per year per % reduction in smoking prevalence is 2-3 billion NOK, the cost-effectiveness is substantional as treatment cost for medicines is 115 million NOK. Net gain from SC in motivated quitters amount to 2.8-4.2 billion NOK in year one. Assuming the applied average cost is too high, the model predicts a "first year break even cost" of 8.800 NOK per patient.

Conclusion: Our analysis demonstrates that the alarmingly high smoking-related costs can be influenced by significant cost savings already in year one. Reduced smoking prevalence, also among smokers with CVD, will have substantial short- and long-term cost-effects as both disease progression and smoking related CVD deaths will be influenced, and the CVD related treatment costs will be reduced.

P762 : Cardiac hemodynamics and 6-minute walk distance in patients with chronic obstructive pulmonary disease

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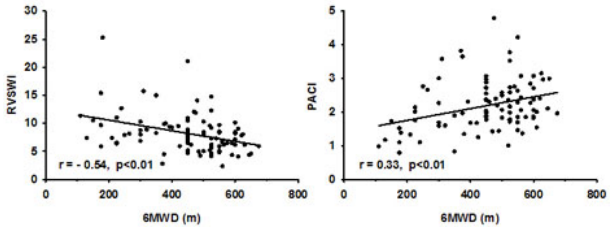
Aim: To evaluate the association between cardiac hemodynamics determined by right heart catheterization (RHC) and 6-minute walk distance (6MWD) in patients with chronic obstructive pulmonary disease (COPD) and pulmonary hypertension (PH).

Methods: RHC with measurements of mean pulmonary artery pressure (mPAP), mean pulmonary capillary wedge pressure (mPCWP), mean right atrial pressure (mRAP), and 6MWD were performed in 98 COPD patients without left sided heart diseases, age 64 (7) years, 50% men. PH was defined as mPAP at rest ≥ 25mmHg and mPCWP ≤15 mmHg. Right ventricle stroke work index (RVSWI) was calculated as stroke volume index (SVI) x (mPAP-mRAP) x 0.0136. Indexed pulmonary artery compliance (PACI) was calculated as SVI/PP (PP=pulse pressure).

Results: RVSWI was significantly increased (p<0.01) in the group of COPD patients with PH compared to the group with no PH (10.9±3.2 vs. 6.9±2.1), and PACI was significantly (p<0.01) decreased (1.7±0.6 vs. 2.2±0.7). For those with PH (n=26), 6MWD was significant reduced (343±149 m) compared to no PH (489±113 m) (p<0.01). Moreover, 6MWD correlated with RVSWI, r=0.5 (p<0.01), PACI, r=0, 3 (p<0.01)

and mPAP, r=0.5 (p<0.01) (fig.1). Significant differences (p<0.01) in following parameters in PH group, mPAP, mPCWP, mRAP, 29±4, 11±3, 7±3 mmHg vs. no PH group, 18±3, 8±4, 5±3 mmHg, respectively. No significant differences in SVI.

Conclusion: Exercise capacity as evaluated by 6MWD in COPD with PH is reduced. In these patients we observed increased RVSWI and reduced PACI. The increased RVSWI is caused by PH, since there is no difference in SVI between COPD patients with or without PH. Reduced compliance contributes to deterioration in RV-PA coupling and increases RV afterload in PH group, and likely generates a higher workload at the right ventricle.



P764 : Prevalence of established and exercise induced pulmonary hypertension in moderate to severe chronic obstructive pulmonary disease

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Purpose: The prevalence of pulmonary hypertension (PH) in chronic obstructive pulmonary disease (COPD) is uncertain. This inconsistency can be explained by dissimilarities in definitions of PH as patient population studied and mixing of pre and post-capillary reasons for PH. We aimed to describe prevalence of pre-capillary PH at rest and exercise induced pulmonary hypertension (EIPH) in a population of stable smoke associated COPD without left sided heart diseases.

Methods: 98 patients, 64±7 yrs and 50% men, were prospectively recruited and classified according to GOLD (Global initiative for Obstructive Lung Disease) criteria. Right heart catheterization with exercise protocol was done with the following pressure measurements: Mean pulmonary artery pressure (mPAP) and capillary wedge pressure (mPCWP), and pulmonary vascular resistance (PVR) were calculated. Pulmonary artery compliance (PAC) was defined as stroke volume/puls pressure (PP). Pre-capillary PH at rest was defined as mPAP ≥25 mmHg and PCWP ≤15 mmHg. Pre-capillary EIPH was defined as an increase in mPAP combined with abnormal exercise responses both in PVR (unchanged or increased value from rest to exercise) and PAC (reduced value from rest to exercise) with an increase in mPCWP ≤20 mmHg.

Results: 26 (27%) patients, mPAP 29±4 mmHg, had pre-capillary PH at rest. Categorized by GOLD stages, PH at rest was found in 2 (5%) in GOLD II, 8 (28%) in GOLD III, and 16 (52%) patients in GOLD IV. PCWP was normal at rest, 11±3 mmHg. During maximum effort 60 of 72 (83%) patients showed normal response in mPCWP, and 12 (17%) showed pathological increase in mPCWP (23±2 mmHg) at maximum effort. Among the 60 patients with normal rise in mPCWP, EIPH was found in 30 (50%). In this group of patients mPAP at rest and exercise were 18±3 and 38±7mmHg, respectively; 15 patients were allocated to GOLD II, 11 to GOLD III, and 4 to GOLD IV. Accumulated prevalence of pathological response of the pulmonary artery pressure (PH at rest with normal PCWP and EIPH with normal rise in PCWP) was found in 56 (58%) of all the 98 patients.

Conclusion: There was a high prevalence, even in patients with GOLD 2, of PH and EIPH of pre-capillary type in this COPD population. In lack of upper normal limit for mPAP during exercise we suggest a combined evaluation of PAC and PVR to determine if increase in mPAP is a pathologic or an expected physiologic response to exercise.

P766 : Pulmonary artery pressure rise during exercise in COPD with normal pressure at rest is accompanied by pathologic responses in pulmonary artery compliance and in pulmonary vascular resistance

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Background: The majority of COPD patients have normal resting mean pulmonary artery pressure (mPAP). The aim of the present study was to investigate if these patients showed abnormal pulmonary pressure rise during exercise.

Methods: 112 patients (47% male), in age 63±7 (mean ± SD) years with smoke associated COPD, and normal LV function, were included. Right heart catheterization at rest and during supine bicycle exercise was performed to exhaustion. End expiratory mPAP, mean pulmonary arterial wedge pressure (mPCWP) and cardiac output (CO) were measured. Pulmonary vascular resistance (PVR) was calculated as (mPAP-mPCWP)/CO. Pulmonary artery compliance (PAC) was calculated as stroke volume /pulse pressure.

Results: 74 patients had normal mPAP at rest (18±3 mmHg), which increased to 37±7 mmHg (p<0.01) during max effort (Wattmax 35±21). CO increased from 5.2±1.0 to 10.8±3.0 L/min (p<0.01) and stroke volume increased from 71.2±16.7 to 98.7±24.2 ml/beat (p<0.01). There was a significant decrease in PAC from rest 4.0±1.5 to exercise 3.0±1.2 (p= <0.01). There was no significant change in PVR (exercise 2.1±1.1 vs. 1.9±0.9 wu at rest). There was a significant correlation between PACmax and PVRmax, r=0.7 (p<0.01) and between PACmax and mPAPmax, r= 0.5 (p<0.01).

Conclusion: We have demonstrated a significant increase in pulmonary artery pressure on exercise at low workload, which was accompanied by a reduction in PAC and a lack of reduction in PVR. These findings might support the existence of an early clinical phase of pulmonary hypertension in patients with COPD and normal mPAP at rest.

P802 : Anemia is not a predictor of all-cause mortality in outpatients with advanced heart failure or severe renal dysfunction

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Purpose: Anemia is identified as an independent prognostic marker in patients with heart failure. The effect of anemia on mortality is assumed to decrease with increasing creatinine levels. We wanted to evaluate the prognostic impact of baseline anemia in outpatients with chronic heart failure attending their first visit at specialized heart failure clinics, and specifically investigate the prognostic utility of anemia in patients with severe renal dysfunction or advanced heart failure.

Methods: Multivariate Cox regression analyses were used to investigate the prognostic effect of baseline anemia in 4144 patients with heart failure from 21 outpatient heart failure clinics in Norway. Severe renal failure was defined as eGFR ≤45 ml/min per 1.73 m^2 and advanced heart failure as NYHA class IIIb and IV. Interaction analyses by product terms were used to test for differences in HR of anemia in paients with severe renal dysfunction and advanced heart failure compared to the rest of the population.

Results: Median age was 70 years and 71% of patients were men. Twenty-four percent had anemia at baseline as defined by WHO criteria. In the whole population anemia was a strong predictor of all-cause mortality with a crude HR of 1.87 (95% CI 1.66-2.11, p<0.001) and adjusted HR of 1.30 (95% CI 1.09-1.56, p=0.004). Anemia was not an independent predictor of all-cause mortality in the 752 patients with severe renal dysfunction (HR 1.08, 95% CI 0.77-1.51, p=0.662) or in the 528 patients with advanced heart failure (HR 0.87, 95% CI 0.56-1.34, p=0.542). HR of anemia was significantly lower in patients with severe renal dysfunction (p=0.022) and advanced heart failure (p=0.002) compared to the rest of the population.

Conclusions: Baseline anemia is an independent predictor of all-cause mortality in outpatients with heart failure. In patients with advanced heart failure or severe renal dysfunction other prognostic variables seem to be more important than anemia. These patients might benefit from different therapeutic strategies in the management of anemia.

P807 : Prognostic significance of change in diastolic function defined by mitral Doppler - a prospective cohort study - the Tromsø Study 1994-2009

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Diastolic dysfunction (DD) of the left ventricle (LV) is a known risk factor for all cause death. Few have documented change in diastolic function (DF) over time and its prognostic significance.

A population sample of 1337 subjects aged ≥55 years with LV ejection fraction ≥0.5 had mitral Doppler echocardiography done in 1994 and 2001. Validated cut-off values for mitral EA-ratio and mitral E-wave deceleration time (EDT) were used to classify the subjects into five groups with increasing degree of DD from group 1 (normal) to 5. Group 1 was defined as EA-ratio 0.75-1.50 and EDT ≥140ms, group 2 EA-ratio≥1.51 and EDT≥140ms, group 3 EA-ratio ≤0.74 and any EDT, group 4 EA-ratio 0.75-1.50 and EDT≤139ms and group 5 EA-ratio≥1.51 and EDT≤139ms.

1292 subjects (96.6%) could be classified according to these groups both in 1994 and 2001. Change in group from 1994 to 2001 was recorded and subjects were classified as having stable, improved or deteriorated DF.

End-point was all-cause mortality with follow-up until 31 Jan 2009. There were 191 deaths of all-causes. Cox regression analysis was used to calculate hazard ratios (HR) for change in group with 95%-confidence interval (CI) for all cause mortality and p-values for trend.

The table displays that when adjusted for age, sex and degree of DF in 1994 (model I), there was a significant trend towards increasing mortality with deterioration in DF. However, adjusted for degree of DF in 2001 (model II) this effect was absent. In conclusion, this illustrates that the degree of diastolic function has predictive power, whereas change in DF per se does not.

Change in group of diastolic function	n	HR (CI) Model I*	HR (CI) Model II**
Improved	142	0.76 (0.44-1.30)	1.15 (0.72-1.85)
Stable	869	1	1
Deteriorated by 1 group	58	1.19 (0.58-2.43)	0.96 (0.46-2.01)
Deteriorated by 2 groups	197	1.65 (1.13-2.41)	1.08 (0.68-1.73)
Deteriorated by 3 groups or more	26	2.56 (1.24-5.28)	1.28 (0.51-3.18)

**Model I: Adjusted for age, sex and group of diastolic function in 1994 - p-trend = 0.014. **Model II: Adjusted for age, sex and group of diastolic function in 2001 - p-trend = 0.943.*

P836 : CXCL16 is associated with both death and hospitalization due to worsening of heart failure in patients with chronic heart failure

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Purpose: Both experimental and clinical studies indicate a role for inflammation in the development of myocardial failure. Thus, we recently demonstrated increased production of CXCL16 in experimental and clinical heart failure indicating a role in vascular remodeling and development of HF. We hypothesized that soluble CXCL16 concentrations are associated with long-term outcome in patients with HF.

Methods: The importance of plasma CXCL16 as a risk factor for the primary endpoint (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke; n= 318 events) and for all-cause mortality (n= 329) and all-cause mortality and hospitalization for worsening of heart failure (WHF; n= 475) was investigated in a total of 1464 patients at least 60 years of age [mean age 72±7 (SD), 341 (23%) women], in NYHA class II-IV, with ischaemic systolic HF receiving optimal pharmacological therapy in the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA) population, randomly assigned to receive 10 mg rosuvastatin or placebo once daily and followed for a median 32.8 months.

Results: In multi-variable analyses, baseline CXCL16 as a continuous variable, added no significant predictive information for the risk estimation of the primary endpoint, all-cause or CV-mortality, or hospitalization due to WHF beyond demographic, clinical and biochemical variables (left ventricular ejection fraction, NYHA class, age, body mass index, diabetes, sex, intermittent claudication, heart rate, serum creatinine, apoA1 and NT-proBNP). However, the change in CXCL16 from baseline to 3 months, added independent predictive information for CV-mortality [HR 1.19 (1.04-1.35), p=0.009] and in particular death due to WHF [HR 1.34 (1.08-1.66), p=0.008] when adjusting for the variables mentioned above, including NT-proBNP. Finally, the change in CXCL16 was

associated with hospitalization due to WHF [HR 1.10 (1.00-1.20), p=0.046) after adjustment for all variables excluding NT-proBNP.

Conclusion: Baseline CXCL16 levels was poorly associated with long-term outcome. However, the change in CXCL16 during follow-up was associated with both death and hospitalization due to WHF in patients with advanced chronic systolic HF of ischemic etiology supporting a role for CXCL16 the pathogenesis and progression of chronic myocardial failure.

P893 : Detrimental effect of biventricular and left ventricular pacing in acute heart failure with narrow QRS and mechanical dyssynchrony

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Purpose: Pacing therapy for heart failure (HF) patients with narrow QRS has gained increasing interest. We investigated responses to biventricular pacing (BVPace) and left ventricular lateral wall pacing (LVPace) in a dog model.

Methods: In 6 anaesthetised dogs with micromanometers, acute HF was induced by microembolisation of the left main coronary artery. Segment lengths were recorded by sonomicrometry and timing of peak systolic strain (PSS) was measured. Electrical and mechanical dyssynchrony was assessed by intersegmental time delay (ITD) calculated by subtracting the latest from the earliest regional measurement in each individual for intramyocardial electromyograms (IM-EMG) and PSS, respectively. Stroke work (SW) and regional work were calculated from pressure-volume and pressure-segment length loops. Measurements were performed during baseline, HF and HF with BVPace and LVPace.

Results: Coronary microembolisation decreased SW by 37±14% ($p<0.01$). No electrical dyssynchrony appeared, as ITD for IM-EMG remained unchanged. However, ITD for PSS increased by 56±13 ms ($p<0.01$), indicating mechanical dyssynchrony. During HF, LVPace and BVPace decreased SW by 18±16% and 10±8.5%, respectively ($p<0.05$). LVPace increased ITD for IM-EMGs by 28±15 ms ($p<0.01$), indicating electrical dyssynchrony. This caused a redistribution of segmental work with a reduction in lateral wall work (smaller loop area in the figure), and an increase in septal work (larger loop area).

Conclusion: In acute HF with normal electrical conduction and mechanical dyssynchrony, LVPace and to a lesser degree BVPace, reduced systolic function due to dispersion in electrical activation and a non-uniform distribution of segmental work. This emphasises the importance of caution when considering CRT for HF patients with narrow QRS.

933 : Metabolic syndrome and cardiovascular outcomes in statin-treated, stable coronary patients with low LDL cholesterol levels of the TNT and IDEAL studies

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Purpose: The usefulness of metabolic syndrome (MetS) in cardiovascular (CV) disease risk prediction among statin-treated patients has recently been challenged and it is unclear whether MetS has predictive value in patients who reach their low-density lipoprotein cholesterol (LDL-C) goal. Our objective was to investigate whether statin-treated patients with MetS reaching low LDL-C levels are at increased risk compared to those without MetS in two large randomized trials of stable coronary patients.

Methods: We used a Cox proportional hazard model adjusted for age, sex, and smoking to assess the predictive value of MetS in 8,500 patients of the TNT study and in 7,819 patients of the IDEAL study, two trials comparing the efficacy of high-dose vs. standard-dose statin therapy on cardiovascular outcomes. Individuals

with diabetes were excluded. Patients with LDL-C levels <100 mg/dL (2.59 mmol/L) at baseline were considered as having low LDL-C levels. The primary endpoint was the time to the first occurrence of a major CV event (MCVE), defined as coronary heart disease death, nonfatal, non-procedure-related myocardial infarction, resuscitated cardiac arrest, and fatal or nonfatal stroke.

Results: The prevalence of the MetS was 51.2% in TNT and 41.5% in IDEAL. A total of 744 (8.8%) and 943 (12.1%) patients had a MCVE during the follow-up, respectively in TNT and IDEAL. In TNT patients with low LDL-C levels (n=4,739), the hazard ratio (HR) for MCVE comparing those with vs. without MetS was 1.34 (95%CI, 1.09-1.63, p=0.005). In IDEAL patients with low LDL-C levels (n=1,986), the corresponding HR was 1.49 (1.13-1.96, p=0.0004). In TNT, LDL-C categories (< or >100 mg/dL) and MetS presence (yes or no) had an additive impact on CV risk (p [interaction]=0.63 and p [linear trend]=0.0002). In IDEAL, the predictive value of MetS appeared to be greater in patients with low LDL-C than in those with higher LDL-C levels (p [interaction]=0.07 and p [linear trend]=0.002). In both studies, significant trends between the number of MetS components and risk of MCVE were observed in patients with low LDL-C (p=0.0002 in TNT and p=0.01 in IDEAL) and in those with higher LDL-C levels (p=0.003 in TNT and p=0.01 in IDEAL).

Conclusions: In stable coronary patients without diabetes treated with statins, metabolic syndrome is an important predictor of CV risk, even in those with low LDL-C levels, and should be targeted accordingly.

1023 : Serial measurement of pentraxin-3 is a strong predictor of outcome in heart failure: results from the CORONA and GISSI-HF trials

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Purpose: Pentraxin-3 (PTX3) is an acute phase protein that, in contrast to CRP, is widely expressed under inflammatory stimuli in the heart and blood vessels. Circulating PTX3 is a marker of severity and outcome in acute MI, but little is known in chronic HF.

Methods: PTX3 was measured in a core laboratory (ELISA, Perseus Proteomics) at baseline and 3- month follow-up in 2690 patients with chronic HF enrolled in the GISSI-HF (1233) and CORONA (1457) trials. Overall 22% were females, mean age was 69±9 y (±SD) and LVEF 32±8%. The clinical determinants of elevated logPTX3 were identified with multivariable regression analysis. The prognostic value of PTX3 at baseline or its relative changes over 3 months (%) was tested in multivariable Cox regression models that included NT-proBNP or hsCRP.

Results: The median plasma concentration of PTX3 was 5.33 [3.55-7.64] ng/mL. Advanced NYHA classes and age, low BMI, ischemic etiology and LVEF were associated with elevated PTX3. 3-month changes in PTX3, but not baseline PTX3, independently predicted incident all-cause mortality (629 events) and CV mortality (483), after adjustment for clinical risk factors, including NT-proBNP (Table) or hsCRP.

Conclusions: A representative cohort of contemporary patients with HF from 2 independent trials consistently shows that (1) PTX3 is related to severity and outcomes in HF, (2) the prognostic value of 3-month changes is stronger than that of a single measurement, and (3) PTX3 emerges as a prognostic marker independent from CRP.

Cox proportional hazard models

Variable	All-cause mortality		CV mortality	
	Wald χ^2	p	Wald χ^2	p
3-month changes in PTX3 (%)	28	<0.0001	15	<0.0001
Baseline PTX3 (ng/mL)	0.3	0.58	1	0.27
Baseline PTX3 (ng/L)	111	<0.0001	103	<0.0001
Age (year)	23	<0.0001	11	0.001
Sex	18	<0.0001	11	0.001
BMI (kg/m^2)	4	0.04		
LVEF (%)	5	0.03	5	0.03
NYHA class	40	<0.0001	19	<0.0001
eGFR (mL/min/1.73 m^2)	16	<0.0001	19	<0.0001
Trial (CORONA vs. GISSI-HF)	0.1	0.71	0.1	0.72

1275 : Self-reported atrial fibrillation in still active old cross-country skiers - the Birkebeiner aging study

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Background: Long-term strenuous endurance training seems to predispose to lone atrial fibrillation (LAF) in middle-aged athletes, but previous studies are conducted in smaller cohorts of athletes. LAF among still active old athletes has not been studied before.

Purpose: 1) To explore the prevalence of atrial fibrillation (AF) and LAF in still active old cross-country skiers with a history of strenuous endurance training through decades; 2) to compare prevalence in still active old athletes with controls from a general Norwegian population.

Methods: 483 men and women ≥ 65 years who completed The Birkebeiner cross-country ski race (54 kilometres) in 2009 were invited to participate. Health status, physical activity and other life-style factors were assessed using a questionnaire. Participants were asked if they had experienced AF at least once, several times or if they had permanent AF. LAF was defined as self-reported AF in absence of coronary heart disease, diabetes, antihypertensive medication and an alcohol-intake above the recommended number of units/week. Study participants and controls from The Tromso-VI health survey were matched for age and sex.

Results: 423 (87%) persons participated in the study, only 32 were female. Median age was 67 (range 65 – 89) years. The overall prevalence of AF was 14% (59/422) in the skiers and 12% (47/398) in the controls (OR[95%CI]: 1.21[0.81, 1.83], p=0.41, n.s.). The prevalence of LAF was 13% (43/334) and 6% (11/190) in skiers and controls respectively (OR[95%CI]: 2.41[1.21, 4.28], p 0.01).

Conclusion: The prevalence of self-reported LAF was significantly higher in still active old cross-country skiers compared with the general population. The overall prevalence of AF, though, did not differ significantly between still active old skiers and the general population. Our results indicates that etiology of AF in still active old athletes differ from etiology of AF in the general population and that long-term strenuous endurance training might have contributed to the higher prevalence of LAF in the still active old cross-country skiers compared with the general population.

P1451 : Predictors of one year mortality in heart transplant recipients

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Purpose: Prediction of one year mortality in heart transplant (HTx) recipients is challenging. Different clinical diagnostic tools have been introduced. Although speckle-tracking strain has been used in a growing number of clinical situations, the association between reduced left ventricular (LV) global longitudinal strain (GLS) and risk for mortality in HTx recipients is unclear. We aimed to test different clinical diagnostic tools for the ability to predict one year mortality in HTx recipients.

Methods: We included 176 consecutive adult primary single organ orthotopic HTx recipients. Creatinine and CRP, the hemodynamic parameters: mean pulmonary artery pressure, pulmonary capillary wedge pressure (PCW), cardiac output and pulmonary vascular resistance (PVR) were measured and echocardiography was performed 13±6 days post HTx. Peak systolic myocardial strain by two-dimensional speckle-tracking echocardiography was assessed in 16 LV segments, and averaged to global strain – an index of global LV function.

Results: During the first year, 16 (10%) patients died 82±72days after HTx. Recipient and donor age, CRP, all hemodynamic parameters except PCW were increased, while LVEF and LV GLS were decreased in non-survivors compared to survivors ($p<0.05$). However, LV GLS was the only significant ($p=0.02$) non-invasive and PVR was a significant ($p<0.001$) invasive predictor of 1 year mortality in a multivariate Cox analysis (Table 1).

Conclusions: Reduced LV function by global longitudinal strain and increased pulmonary vascular resistance are related to poor prognosis in HTx recipients. Early assessment of LV GLS might be a non-invasive predictor of 1 year mortality in these patients.

Table 1. Multivariate Cox regression analyses

	Univariate	Cox Regression		Multivariate Cox Regression		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (years)	1.08	1.00–1.15	0.04	1.02	0.92–1.12	0.72
PVR (WU)	4.56	2.65–7.86	<0.001	3.88	1.84–8.17	<0.001
LV GLS (%)	1.67	1.39–2.01	<0.001	1.44	1.06–1.94	0.02
LVEF (%)	1.92	1.46–2.52	<0.001	1.29	0.74–2.25	0.36
CRP (mg/ml)	1.02	1.01–1.03	<0.001	1.00	0.97–1.02	0.86

PVR = pulmonary vascular resistance; LV = left ventricular; GLS = global longitudinal strain; LVEF = LV ejection fraction; CRP = C-reactive protein.

P1505 : Impact of diabetes on LDL-cholesterol target achievement in patients with cardiovascular disease in clinical practice in Europe and Canada: results of the dyslipidemia international study

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Background: Chronic statin treatment is well established for patients with dyslipidemia and high risk for subsequent cardiovascular events and its use is widespread. Patients with documented cardiovascular disease (CVD) and diabetes are at extraordinary risk for subsequent events. Little is known about the impact of co-existing diabetes on achievement of recommended lipid targets in CVD patients in clinical practice.

Methods: Between June 2008 and February 2009, 2,987 primary care physicians, cardiologists, endocrinologists and internists in 11 European countries and Canada enrolled 22,063 consecutive statin-treated outpatients into DYSIS (Dyslipidemia International Study) to assess the prevalence of dyslipidemia while on chronic statin treatment. ESC recommendations were used to classify patient's risk and define the LDL-C goal. We compared the level of LDL-C goal achievement of CVD patients with and without diabetes.

Results: A total of 11,520 patients had known CVD, of whom 4471 (38.8%) had diabetes mellitus. Patients with CVD + Diabetes were older, more often female, more often were obese and more often reported sedentary lifestyle. They had a higher prevalence of heart failure than patients without diabetes. Diabetics were more likely to be treated with simvastatin as with other statins. Patients with CVD and Diabetes more often reached the guideline recommended target of LDL-Chol < 100 mg/dl in clinical practice. The co-morbidity of diabetes in CVD was an independent predictor of LDL-Chol goal achievement (OR 1.39, p<0.01).

Conclusion: Patients with CVD and diabetes were more likely to reach the recommended LDL-goal as compared to patients without diabetes. Within CVD, diabetes was an independent predictor with a 39% higher chance to reach LDL-C < 100mg/dl in clinical practice.

	CVD + Diabetes n=4,471 (38.8%)	CVD w/o Diabetes n=7,039 (61.2%)	p-value
Age (years)	69	68	<0.01
Female Gender	32.7%	30.7%	<0.05
BMI ≥30 kg/m^2	44.9%	24.8%	<0.01
Ischemic heart disease	46.1%	34.5%	<0.01
Cerebrovascular disease	21.5%	18.6%	<0.01
Peripheral artery disease	27.1%	17.6%	<0.01
Heart Failure	23.1%	14.8%	<0.01
Sedentary Lifestyle	58.5%	47.4%	<0.01
Statin = Simvastatin	49.9%	46.7%	<0.01
Ezetimibe	12.3%	11.9%	0.56
LDL-Chol at goal (<100 mg/dl)	62.0%	55.8%	<0.01

P1518 : Symptoms of anxiety and depression after percutaneous coronary intervention are associated with decreased heart rate variability, impaired endothelial function and inreased inflammation

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Background: Depression and anxiety are prevalent risk factors for cardiac events in patients with coronary artery disease. However, little is known about the pathophysiological mechanisms responsible for this association.

Methods: Four weeks after successful revascularization by percutaneous coronary intervention for angina pectoris or an acute coronary syndrome 94 patients completed the Hospital Anxiety and Depression Scale (HADS), underwent ultrasound based measurement of endothelial function, assessment of heart rate variability by 24-hour Holter registration and measurement of plasma levels of C-reactive protein (CRP).

Results: Twenty-three patients showed a HADS-anxiety (HADS-A) score ≥8 and 19 patients had a HADS-depression (HADS-D) score ≥5. Those patients had significant lower means of heart rate variability measures reflecting parasympathetic activity (root mean square of differences between successive NN intervals (rMSSD) and the percentage of differences between adjacent NN intervals that are >50 msec (pNN50), impaired endothelial function (flow mediated dilation (FMD)) and higher plasma levels of CRP compared to patients with normal HADS scores (Table 1). Seven patients with a HADS-A score ≥8 had a cardiovascular event, while there were six events in the group with normal HADS-A scores during 30±10 months follow-up (p=0.017).

Conclusions: Depressive and anxiety symptoms after revascularization for coronary artery disease are prevalent and are associated with decreased parasympathetic mediated heart rate variability, impaired endothelial function and increased inflammation, potentially contributing to explain the association between anxiety and depression and the increased risk for cardiac events in this patient population.

Table 1

	Normal HADS score	HADS-A score ≥8	HADS-D score ≥5
rMSSD (ms)	40±19	23±14***	20±9***
pNN50%	11±10	3±4***	3±2***
FMD (%)	9±5	5±5**	4±4**
CRP	2.1±1.9	3.8±2.9*	3.8±2.9*

**p<0.05, **p<0.01, ***p<0.001.*

P1621 : Interleukin-1b is a major determinant of LV remodelling following STEMI treated by primary PCI

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Purpose: Increased levels of interleukin (IL)-1-related molecules are seen during myocardial infarction (MI), but data on their relation to infarct size and left ventricular (LV) remodeling are lacking.

Methods: Forty-two patients with first time ST segment elevation MI (STEMI) with a single occluded vessel, successfully treated by percutaneous coronary intervention (PCI), were recruited. Cardiac magnetic resonance (CMR) was used for assessment of infarct size and LV remodeling at 2 days, 1 week, 2 months and 1 year. Plasma levels of IL-1β, IL-1 receptor antagonist, IL-18 and caspase-1 were analyzed until 2 months after PCI.

Results: Univariate analysis showed that IL-1-related mediators were strongly (IL-1β), moderately (caspase-1), slightly (IL-1Ra), associated with impaired myocardial function and non-infarct mass, but not infarct size, one year after STEMI (Table - demonstrates only IL-1β relationships). In multivariate analyses, troponin T predicted ($p<0.001$) LV ejection fraction (LVEF), infarct size, LV end-diastolic and end-systolic volume indexes (LVEDVi, LVESVi). However, significant additional variance was explained by IL-1β, IL-18 and caspase-1. IL-1β levels at 2 months ($p<0.05$), IL-18 at 2 days ($p<0.01$) and pre-PCI caspase-1 ($p<0.05$) were predictors of LVEF. Caspase-1 ($p<0.01$) and in particular IL-1β at 2 days ($p<0.01$) were the only predictors of non-infarct mass. IL-1β ($p<0.01$) at 2 days and IL-18 ($p<0.01$) at 2 days were predictors of LVEDVi, while pre-PCI levels of IL-1β ($p<0.01$)contributed to prediction of LVESVi. In contrast, pro-B-type natriuretic

peptide and C-reactive protein had no significant association with these CMR parameters.

Conclusions: IL-1β levels after STEMI were strongly associated with impaired myocardial function and non-infarct LV mass after 1 year. This finding suggests a role for IL-1β in maladaptive myocardial remodeling following MI.

Table. IL-1β and CMR findings at 1 year

	Infarct mass	Non-infarcted mass	LVEDVi	LVESVi	LVEF
IL-1β					
Pre PCI	0.05	0.24	0.36*	0.39*	-0.33
2 days	0.19	0.40*	0.41**	0.35*	-0.36*
1 week	0.13	0.35*	0.41**	0.34*	-0.23
2 months	0.05	0.09	0.33*	0.36*	-0.39*

**p<0.05, **p<0.01.*

P1740 : Soluble ST2 predicts outcome in heart failure of ischemic aetiology

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Purpose: Soluble ST2 (sST2) is a decoy receptor for interleukin (IL)-33 and thus modifies inflammation. Serum levels of sST2 are elevated in patients with chronic heart failure (HF) compared with healthy controls.

We examined the prognostic value of sST2 in a sub-study involving approximately 30% of participants in the CORONA study (Controlled Rosuvastatin Multinational Trial in HF).

Methods: The prognostic value of sST2 was investigated in 1449 patients ≥ 60 years with ischemic, systolic HF, who were in NYHA class II-IV on optimal pharmacological therapy. They were randomly assigned to 10 mg rosuvastatin or placebo. The primary composite end point of the CORONA study was cardiovascular death, nonfatal myocardial infarction or stroke. By Cox proportional hazard analyses, adjusting for clinical and biochemical variables, we explored the association between baseline levels of sST2 and the primary end point as well as the following end points: Death from any cause, death from cardiovascular causes, sudden death, death from worsening of HF, death from other causes, any coronary event, all-cause hospitalization, hospitalization for cardiovascular causes and hospitalization for worsening of HF. sST2 and NT-proBNP levels were log-transformed prior to statistical analyses.

Results: Patients were on average 72 years old, 73% were male, 12% were smokers and 26% were diabetics, most were in NYHA class 2 or 3, and mean left ventricular ejection fraction was 0.32±0.07. The median follow-up time was 2.6 (IQR 2.2 – 3.0) years. Median baseline sST2 was 21 (IQR: 13 - 25) ng/ml. 408 of 1449 patients met the primary end point. In multi-variable analyses, adjusting for 8 clinical and 2 biochemical variables, higher sST2-levels were associated with a higher risk of all the specified end points, including the primary end-point [HR 1.65 (1.38-1.98), p<0.001]. When N-terminal pro-B-type natriuretic peptide (NT-proBNP) was added to the model, the association between sST2 and the primary end point was attenuated and no longer significant. However, sST2 levels remained associated with all cause hospitalization, hospitalization for worsening of HF [HR 1.32 (1.06 – 1.64)] and death from HF [HR 1.68 (1.13 – 2.50)] even after adjusting for NT-proBNP. No treatment interaction was observed.

Conclusions: sST2 is associated with outcome in patients with chronic HF. sST2 is an independent predictor of worsening of HF as well as death from HF, indicating that the IL-33 pathway is a potential target for intervention in HF.

P1782 : Galectin 3 predicts mortality and response to statin therapy in chronic heart failure

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Purpose: Galectin-3 is a new biomarker involved in inflammation and fibrogenesis and could therefore contribute to myocardial remodeling. We examined the prognostic value of galectin-3 and its interaction with statin therapy in a sub-study involving approximately 30% of participants in the CORONA study (Controlled Rosuvastatin Multinational Trial in HF).

Methods: Patients (n=1462), >60 years with systolic, ischemic heart failure (HF) were randomized to 10 mg/day rosuvastatin or placebo. The primary composite endpoint was cardiovascular death, nonfatal myocardial infarction or stroke (n=408).

Results: In multi-variable analyses, adjusting for 8 clinical and 2 biochemical variables, higher galectin-3 concentration was associated with a higher risk of the primary end-point [HR 1.16 (1.03-1.31), p=0.012] as well as all cause- and cardiovascular mortality, sudden death, and the composite end-point of all-cause mortality and hospitalization for worsening of heart failure. When N-terminal pro-brain natriuretic peptide (NT-proBNP) was added to the model, the association between galectin-3 and these end-points was attenuated and no longer significant. There was a significant interaction between baseline galectin-3 concentration and the effect of rosuvastatin. In patients with galectin-3 < median (19.0 ng/mL), 72 patients (7.8%) on rosuvastatin and 97 patients (11.2%) on placebo had a primary endpoint: HR 0.65 (0.46-0.92). In patients with galectin-3 >median, 126 patients (15.1%) on rosuvastatin and 116 patients (14.2%) on placebo experienced this outcome: HR 1.07 (0.79-1.45); interaction p=0.019.

Conclusions: Galectin-3 was associated with the primary endpoint, and death in older patients with advanced chronic systolic HF of ischemic etiology. Furthermore, galectin-3 appeared to modify the effect of rosuvastatin, with the benefit from rosuvastatin confined to those with galectin-3 concentration below 19 ng/mL

P1822 : Single sheath lead extraction, a single centre experience of more than 900 lead extractions

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Our centre is serving most of Norway and Iceland for pacemaker and ICD lead extractions. We have adopted a single sheath technique, a variant of the dilating sheath technique described by Byrd.

Materials and methods: From 1998 to end of August 2010, we treated 551 patients, median age 64 years (range 7-95 years), with 904 leads. Fifty-one percent of the extractions were performed on infections, the rest were elective. Median age of all leads was 5 years (range 0,1 to 42 years). The single sheath technique was used in 69% of the extractions, in 26% we used traction alone, in 5% various fishing techniques and in 1% "Evolution" (Cook).

We start with a gentle traction and then proceed to single sheath technique after applying a locking stylet (Cook/Spectranetics/VascoMed). A single Cook polypropylene sheath is mounted with a Cook Pin Vise and is gently pushed down over the lead with rapid rotation. When serious resistance is met, the sheath size is increased. For larger diameter leads (ICD) we have also used "VisioSheath" (Spectranetics). If hard resistance/calcification is met under the clavicle, a steel sheath is used to gain access into the subclavian vein.

Results: Complete success was achieved with 96% of the leads. "Clinical success" (ie. removal of all of the lead except the distal 4 cm) was achieved in another 3% of the lead extractions. The overall procedural success was 99%. ICD-leads: 154 leads: 99% success, one major complication, resolved without sequelae.

Median "sheath-time" (ie. the time the sheath is applied) is 5 min., range 1 to 300 minutes. Complications: Major complications 2%, one fatal (0,2%). Minor complications 1%.

Conclusion: The single sheath technique was effective, with 99% procedural success. The technique appears to be a quick and effective alternative to laser sheath lead extraction. The complication rate of the single sheath technique was low.

1881 : High normal blood pressures predict incident atrial fibrillation in healthy middle-aged men, a 35 year follow-up study

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Purpose: Hypertension is a prevalent risk factor for development of atrial fibrillation (AF), but the blood pressure (BP) levels that impose a significant increased risk of AF have so far not been established. We aimed to study long-term impact of different BP levels on incident AF in a population-based study.

Methods: From 1972-1975, 2014 healthy men aged 40-59 years were included in a prospective cardiovascular survey in Oslo, Norway and underwent a clinical examination including standardized BP measurements. During 35 years follow-up, 272 men were documented with AF by scrutinizing all hospital discharges.

Results: Risk estimation for incident AF was analyzed in quartiles (Q) of BP using Cox proportional hazards adjusted for age and body mass index. Additional adjustments for smoking, resting heart rate, maximal heart rate during exercise and physical fitness did not influence the results. Compared with reference quartile with systolic BP <118 mm Hg the adjusted long- term risk of incident AF was increased by 45% (HR 1.45, 95% CI 1.01–2.08) and 58% (HR 1.58, 95% CI 1.10-2.28) for men with baseline systolic BP 128-138 mm Hg (Q3) and 140-220 mm Hg (Q4), respectively. Diastolic BP <80 mm Hg was associated with lower risk of incident AF compared with significantly increased risk in the three higher quartiles, HR 1.60 (1.10-2.37), HR 1.66 (1.14-2.50) and HR 1.82 (1.24-2.69), respectively.

Conclusions: Systolic BP ≥128 mm Hg and diastolic BP ≥80 mm Hg are independent long-term predictors of incident AF in healthy middle-aged men.

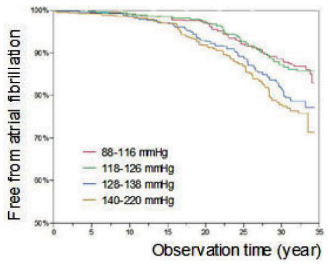

Figure. Men free from AF related to systolic BP

1893 : Reduced life expectancy after myocardial infarction in women and men: smoking is most harmful in women

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Purpose: It has been debated whether smoking is more harmful in women than in me. The aim of the study was to investigate possible gender differences in loss of life-years after an acute myocardial infarction (MI) and, furthermore, to explore how smoking affects life expectancy in the two genders.

Methods: In the 8-year period from 1998 to 2005 data on 2,281 consecutive MI patients (36.8% women) who were discharged from or died in one hospital with a diagnosis of MI were included in the study. The hospital admits virtually all MI patients in a well-defined catchment area, thus a sample representative of an unselected MI population was obtained. Surviving patients were followed for a mean of 8 years and time of death was recorded for those who died. The age of death for each individual patient was compared with the average projected age of death for individuals in the general population with a similar age as the patient had at the time of the MI, also taking into account gender and county of habitation. The latter was provided by The National Bureau of Statistics. The actual age at death was subtracted from the projected age of death to yield time lost/gained after MI for those who died, and then analyzed for gender, smoking, and other risk factors. This is a novel method that, to our knowledge, has not been used before.

Results: The average age at admission for the MI was 70.4±12.7 years for men and 76,5±11.5 years for women. During follow up 55% of the patients had died. The patients in the categories non-smoker, ex-smoker and current smoker at admission lost 5.4, 6.4 and 10.3 life-years, respectively. Analysis of current smoker and ex-smoker combined, showed the following loss of life-years: men 7.4 (SE 0.3) and women 9.5 (SE 0.5), P<0.001. Multivariate regression analysis (including gender, age, history of smoking, hypertension, history of stroke, and diabetes mellitus) showed that women lost 1.3 life-years more than men, and female current smokers lost an additional 1.1 years compared with male current smokers (p<0.001 and p<0.005, respectively).

Conclusion: Suffering a MI entailed loss of life-years, but with a heavier loss in current smokers

than in ex-smokers and non-smokers. Smoking reduced life expectancy more in women than in men, indicating that smoking has a more detrimental cardiovascular effect in the female gender.

1909 : Prevention of peptic ulcers with once-daily esomeprazole 20 mg and 40 mg in low-dose acetylsalicylic acid users at gastrointestinal risk: outcome analysis by cardiovascular risk (OBERON)

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Purpose: Esomeprazole prevents peptic ulcer (PU) in low-dose acetylsalicylic acid (LDASA) users at gastrointestinal risk (OBERON: NCT00441727). A retrospective assessment of PU prevention by baseline cardiovascular (CV) risk factors was undertaken.

Methods: 2426 pts taking LDASA (75–325 mg) were randomised to receive daily oral esomeprazole 20 mg, 40 mg or placebo for 26 wks. Pts fulfilled at least one of the following criteria: age ≥65y; age ≥18y with history of gastric/duodenal ulcer; age ≥60y with stable coronary artery disease or dyspeptic symptoms and ≥5 gastric/duodenal erosions, or LDASA treatment begun within 1 month prior to randomisation. Pts with a history of ulcer complications, gastric/duodenal ulcer or reflux esophagitis (LA grade C or D) on baseline endoscopy, continuous use of NSAIDs or Helicobacter pylori infection were excluded. Endoscopy-confirmed PU frequency after 26 wks was assessed according to baseline CV risk factors. Baseline CV risk factors and treatment outcome interaction was assessed by the Cox-proportional hazards model.

Results: 2250 pts had ≥1 CV risk factor at baseline, most commonly hypertension (79%). 15% pts had a history of myocardial infarction. Esomeprazole 20 mg and 40 mg reduced PU occurrence by 26 wks compared to placebo in all CV risk factor groups (Table). None of the baseline CV risk factors showed a significant interaction with the effect of treatment (all p>0.05).

Conclusions: Esomeprazole was effective in the prevention of PU in all the investigated CV risk factor sub-groups.

Cardiovascular risk factor	Total patients (n)	Number of patients (%) with peptic ulcer at week 26		
		Esomeprazole 20 mg (n=804)	Esomeprazole 40 mg (n=817)	Placebo (n=805)
Hypertension	1784	7/600 (1.2)	9/593 (1.5)	40/591 (6.8)
Hypercholesterolemia	1036	4/335 (1.2)	5/362 (1.4)	25/339 (7.4)
Age >70 years	867	3/286 (1.0)	4/299 (1.3)	16/282 (5.7)
Body mass index >30 kg/m^2	625	2/212 (0.9)	4/210 (1.9)	13/203 (6.4)
History of myocardial infarction	328	1/116 (0.9%)	1/111 (0.9%)	4/101(4.0%)
Percutaneous coronary intervention (past)	317	0/103 (0.0)	0/112 (0.0)	5/102 (4.9)
Coronary artery bypass graft (past)	251	2/85 (2.4)	0/85 (0.0)	8/81 (9.9)
Smoker	223	1/73 (1.4)	0/77 (0.0)	6/73 (8.2)
History of stroke	145	0/50 (0.0%)	1/53 (1.9%)	3/42 (7.1%)

Pts could have >1 CV risk factor.

P2659 : NT-proBNP predicts new-onset atrial fibrillation in patients with asymptomatic aortic stenosis - a SEAS substudy

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Background: Brain natriuretic peptides (BNP) is a biomarker for cardiovascular conditions including heart failure and aortic stenosis (AS). NT-proBNP is elevated in atrial fibrillation, however the association between NT-proBNP and development of new-onset atrial fibrillation (AF) in asymptom-

atic patients with mild to moderate AS remains unclear.

Methods: 566 patients with mild to moderate AS and no previous history of AF were inluded from the SEAS Study (Simvastatin and Ezetimibe in Aortic Stenosis). The primary endpoint for this substudy was time to new-onset AF adjudicated by 12-lead ECG at a core lab reading center, according to NT-proBNP level.

Results: New-onset AF occurred in 35 (6.2%) patients (13.8 per 1,000 person-years follow-up) who at baseline in comparison with patients in sinus rhythm were older (71.7±9.6 vs. 65.8±9.6 years, p<0.001), had larger left ventricular (LV) mass (108.9±34.1 vs. 97.9±27.5 g/m^2, p=0.031) and higher NT-proBNP level (504.9±464.4 vs. 222.6±274.6 pg/ml, p<0.001). In a multivariable Cox model adjusted for LV mass, LV ejection fraction, left atrial size, age and gender NT-proBNP predicted new-onset AF (HR:2.1[95%CI:1.5-3.0], p<0.001) and the combined endpoint of new-onset AF and death (HR:2.1[95%CI:1.5-3.0], p<0.001). Baseline NT-proBNP of 189 pg/ml was found as the best threshold to predict new-onset AF with an area under the curve of 0.72, a sensitivity of 71% and a specificity of 63%. NT-proBNP ≥189 pg/ml predicted new-onset AF (HR:3.4[95%CI:1.6-7.5], p<0.001). Same results were found in competing risk models.

Conclusions: In patients with asymptomatic aortic stenosis NT-proBNP baseline level was significantly higher in patients who subsequently developed AF. Baseline NT-proBNP significantly predicted new-onset AF and the combined endpoint of new-onset AF and death.

P3252 : Apolipoprotein E polymorphism modifies the effects of smoking and physical inactivity on coronary heart disease (CHD) risk

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Purpose: Apolipoprotein E (ApoE) has 3 major isoforms coded by alleles ε2, ε3 and ε4, and is important for lipid metabolism and CHD risk, but underlying mechanisms and interactions with the environment are not well known. We examined if ApoE polymorphism modifies the effects of the lifestyle factors smoking, physical inactivity and overweight on low density lipoprotein cholesterol (LDL-C) levels and CHD risk.

Methods: We used pooled data from 2 large case-control studies, including 3833 men and 2680 women. Of these, 1790 were subjects with a CHD event (myocardial infarction or unstable angina). Smoking and physical activity data were obtained by questionnaire. Interaction between ApoE and each lifestyle factor was evaluated by likelihood ratio tests comparing models with and without a product term of the 2 factors.

Results: With never-smoking ε3 homozygotes as reference, the odds ratio (OR) for CHD in ever-smoking ε2 carriers was 1.30 (95% CI 1.02-1.67), whereas ever-smoking ε3 homozygotes had OR 2.34 (1.98-2.77) and ever-smoking ε4 carriers had OR 2.39 (1.97-2.90). In female ε4 carriers, smoking was associated with a particularly high CHD risk (OR 3.69, 2.33-5.83 versus never-smoking). The ApoE interaction with smoking was statistically significant in the whole population (p=0.04) and in women separately (p=0.006) and was independent of BMI, physical activity and LDL-C levels. With physically active ε3 homozygotes as reference, physically inactive ε2 carriers were at lower risk of CHD (OR 0.65, 0.45-0.93), whereas physically inactive ε3 homozygotes had an OR of 1.36 (1.13-1.64) and physically inactive ε4 carriers an OR of 1.80 (1.41-2.30), interaction p-value=0.07. No interaction was seen between ApoE and overweight on CHD risk, or between ApoE and any of the lifestyle factors on LDL-C levels.

Conclusions: Our results provide confirmatory evidence of the interaction between ApoE and smoking on CHD risk, here demonstrated also in women. Carriers of the ε2 allele were partly protected from the smoking-related CHD risk in both sexes, whereas the increased smoking-related risk in ε4 carriers was seen clearly only in women. Similarly, ε2 carriers were protected from CHD risk related to physical inactivity. The observed interactions are unlikely to be directly mediated by differences in LDL-C levels. Instead, a possible mechanism is that the stronger anti-oxidative effect of the ApoE E2 isoform reduces the increased oxidative stress following smoking or physical inactivity.

P3271 : SCORE OP: derivation and validation of a function for estimating CVD risk in older people

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Background: Estimation of CVD risk is of critical importance in prevention of CVD in clinical practice. SCORE (Systematic Coronary Risk Evaluation) is the risk estimation system recommended by the European guidelines on CVD prevention. It is intended for use in the 40 to 65 year old age group. Risk estimation is known to be inaccurate in the older age groups. We hypothesized that the reason for the inaccuracy is the assumption, inherent in current risk estimation systems, that risk factors function similarly in older and younger age groups.

Objective: To derive and internally validate a risk estimation function, similar to SCORE, sorely from data from individuals aged over 65 years.

Methods: Data from three representative, prospective studies of the general population which were included in the original SCORE dataset (Belgium, Denmark, Italy) were combined with data from the CONOR (Cohort of Norway) prospective study to derive the function. Only those aged over 65 years and without pre-existing CHD were included. Cox proportional hazards model was used.

Results: 20,704 men and 20,121 women were included. The variables which remained statistically significant and were included in the SCORE OP model were: age, total cholesterol, HDL cholesterol, systolic blood pressure, smoking status and diabetes. SCORE OP showed good discrimination, AUROC 0.74 (95%CI: 0.73 to 0.75). Calibration was also good, hosmer lemeshow test goodness of fit test: 17.16 in men, 22.70 in women. Compared to the original SCORE function extrapolated to the over 65 year old age group there was superior performance, p=0.05 in men, p<0.001 in women. Simple charts were constructed.

Conclusion: SCORE OP, a risk estimation system derived exclusively from data from the older age group estimates CVD risk better than the original SCORE function. The likely explanation for this is the use of age-specific risk factor weightings. SCORE OP provides a useful tool in the assessment of CVD risk in this rapidly expanding section of society.

P3274 : What are the implications of the Universal definition of acute myocardial infarction from 2007 and the changing definitions during the last decade?

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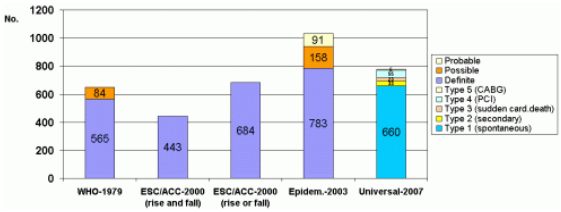
Purpose: To analyse the impact of four different international definitions of acute myocardial infarction (AMI) that have been applied during the last decade for the incidence of AMI.

Methods: We examined AMI incidence according to four different definitions of AMI, including the unauthorised "rise or fall" version of the ESC/ACC-2000 definition, among 2011 hospital admissions to our Hospital during 1 March 2002 to 28 February 2003. Eligible patients were those with a discharge diagnosis of a first or subsequent AMI, or at least one elevated cardiac troponin I (cTnI) during admission. cTnI levels ≥0,10 μg/L (the 99th percentile of a healthy population) were considered elevated indicating AMI. All cTnI values were evaluated according to the criteria of rise and/or fall, defined as a change >20% from the index value. Difference in incidence of AMI according to different definitions were tested using McNemar test.

Results: The original ESC/ACC-2000-definition resulted in 443 AMIs among the 2011 admissions and was used as reference. Excluding possible and probable AMIs (WHO-1997 and Epidemiological-2003 definitions), the number of AMIs were: 565 (+27.5%) by WHO-1979, 684 (+54.4%) by the unauthorised version "rise or fall" ESC/ACC-2000, 783 (+76.7%) by the Epidemiological-2003, and 776 (+75.2%) by the Universal-2007 definition (all p<0.001) (Figure 1).

Conclusion: The changing definitions of AMI during the last decade have had a great impact



on the incidence of diagnosed AMIs in hospitalized patients. We found an increase of 75% from the original ESC/ACC-2000 definition to the Universal-2007 definition. It is important to correct for this variability when trends in incidence and case fatality are studied.

P3277 : The prognostic impact of HDL-cholesterol for coronary heart disease is independent of physical fitness

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Purpose: To test the hypothesis that physical fitness (PF) influences the prognostic impact of high density lipoprotein cholesterol (HDL) for coronary heart disease (CHD) and also CHD-, cardiovascular disease- (CVD) and all-cause-death. High density lipoprotein cholesterol and PF have both been shown to predict CVD, particularly CHD. Improved PF is associated with increased HDL and may partly explain the benefit of HDL.

Methods: HDL was measured 1979-1982 in 1357 healthy men aged 44-69 years followed up to 28 years and, PF was measured using bicycle exercise test. Hazard ratios (HR) adjusted for age, smoking, systolic blood pressure, and total cholesterol and further for PF between quartiles of HDL were calculated using Cox proportional-hazard modelling. A possible interaction between HDL and PF was tested using separate analyses for our main endpoint, CHD, for men with age adjusted PF above and below median.

Results: The highest quartile of HDL was associated with lower risk of CHD (angina pectoris, non-fatal myocardial infarction and CHD-death), CHD-, CVD- and all-cause-death compared to the lowest quartile, HR=0.57 (95% CI 0.43-0.74), 0.54 (0.35-0.83), 0.63 (0.45-0.87) and 0.80 (0.65-0.99), respectively. Adjustments for PF did not change the results except for all-cause-death which was not significantly different between HDL quartiles. Beneficial effects of HDL were similar above and below median age adjusted PF.

Conclusions: HDL is a strong predictor of long-term risk of CHD, CHD-death and CVD-death in healthy middle aged men. Physical fitness has no impact on the ability of HDL to predict CVD.

Table 1. Relative risks of the composite endpoint of coronary heart disease (CHD) including angina pectoris, non-fatal myocardial infarction and coronary heart death in quartiles of HDL-cholesterol compared to the lowest quartile (Q1) as hazard ratios (95% confidence interval)

	Q1	Q2	Q3	Q4
	(0.81-1.30 mmol/l)	(1.31-1.51 mmol/l)	(1.52-1.71 mmol/l)	(1.71-3.30 mmol/l)
	n=348	n=325	n=344	n=340
Multiple adjusted{†} without PF	1.00	0.80 (0.62-1.02)	0.58 (0.44-0.75)	0.57 (0.44-0.74)
Multiple adjusted{†} with PF	1.00	0.83 (0.64-1.06)	0.60 (0.46-0.79)	0.61 (0.47-0.80)

{†}Adjusted for age, smoking status, systolic blood pressure and total cholesterol.

P3547 : Rate of LV pressure rise is an important confounder when assessing left ventricular electrical dyssynchrony by onset of myocardial shortening

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Background: During left bundle branch block (LBBB) delay in onset of left ventricular (LV) free wall shortening (OS) exceeds delay in regional electrical activation (REA). We investigated the hypothesis that timing of OS is determined not only by electrical conduction but also by rate of change of LV pressure (dP/dt) at the time of REA.

Methods: In an experimental dog model (n=7) with LBBB and in patients (n=8), with CRT devices, we measured OS by sonomicrometry and tissue Doppler strain echocardiography, respectively, and pressure by micromanometry. REA was assessed by implanted myocardial electrodes (dogs) and pacemaker leads (patients). Excitation-contraction coupling time was measured from REA to onset active force by pressure-strain analysis. Measurements were done in the septum and LV lateral wall (Fig 1).

Results: In the dogs with LBBB, delay in OS between septum and LV lateral wall (82+12 ms) exceeded the delay in REA (54+8 ms, p=0.002). There was no significant correlation between time to OS and LV pressure at time of electrical activation. There was, however, a strong correlation between time to OS and LV dP/dt at time of electrical activation (r=0.88, Fig 2). Excitation-contraction coupling time by onset active force remained unchanged. Similar findings were observed in the patients (Fig 2).

Conclusions: Mechanical dyssynchrony in LBBB reflects the combined effect of delay in electrical conduction and delay in onset shortening due to faster rate of rise in LV pressure at the time of contraction in late activated segments. In late activated segments which contract at higher LV dP/dt, this mechanism may cause additional delay in onset of shortening, and thus aggravating mechanical dyssynchrony. These findings suggest that changes in LV contractility may modify mechanical dyssynchrony.

3904 : Apixaban in patients with atrial fibrillation and their risk for cardiovascular hospitalization: insights from the AVERROES trial

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Background: The AVERROES trial randomized 5599 patients with atrial fibrillation (AF) at increased risk of stroke and unsuitable for vitamin K antagonist (VKA) therapy to receive, double-blind, apixaban 5 mg twice daily or aspirin 81 to 324 mg once daily. Apixaban was superior in preventing strokes with no increase in major bleeding. This analysis evaluates the incidence, baseline predictors and prognostic implications of cardiovascular hospitalizations (CVH) in AVERROES.

Methods and results: 2809 patients received apixaban, 2791 aspirin. There were 410 (14.7%) CVH in patients on aspirin and 331 (11.8%) in patients on apixaban (Relative Risk (RR) 0.88, 95% CI: 0.77-0.99). The reduction in CVH in the apixaban group was mainly driven by fewer admissions for stroke (RR 0.50, 95% CI 0.35-0.71, p<0.0001) and non-CNS embolisms (RR 0.18, 95% CI 0.04-0.82). There were no significant differences in rates of hospitalization for other reasons. Multivariable analyses revealed that in addition to treatment with apixaban, independent predictors of CVH were age >75 vs. ≤75 years (RR 1.35), CHADS2 score ≥3 vs. ≤1 (RR 1.46) and 2 vs. ≤1 (RR 1.36), treatment with antiarrhythmic vs. no antiarrhythmic drugs (RR 1.25), history of heart failure vs. no heart failure (RR 1.20), and systolic blood pressure >135 vs. ≤135 mmHg (RR 1.16). Compared with those who were not hospitalized, patients who were hospitalized during the study had a significantly higher unadjusted risk of subsequent mortality: hospitalization for stroke: RR of death 19.42; hospitalization for MI or new angina: RR of death 7.66; hospitalization for non-CNS embolism: RR of death 4.19; hospitalization for other CVH: RR of death 7.8; hospitalization for non-CVH: RR of death 7.28.

Conclusions: Apixaban compared with aspirin significantly reduced CVH in AF pts unsuitable for therapy with VKA. Risk factors for CVH mirrored stroke risk factors. All causes of CVH were associated with high subsequent mortality.

P4066 : Diagnostic accuracy and feasibility of bedside pocket-sized ultrasound examination in patients admitted to an internal medicine department

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Background: The use of pocket-sized ultrasound may improve patient care and hospital workflow. Our aim was to study the reliability and feasibility of echocardiographic evaluation with pocket-sized ultrasound (POCKET) performed bed-side in patients admitted to an internal medicine department.

Methods: 108 patients were scanned bed-side with POCKET shortly after admission and later with a high-end scanner (HIGH) in the echo-lab for comparison. Median delay to HIGH exam was 17 hours. The POCKET examinations were done bed-side by 1 of 3 experienced cardiologists on their ward rounds using a standardized screening protocol. Assessments of global left ventricular (LV) function, right ventricular (RV) function and valvular function were visually classified as 1) normal/near normal, 2) moderate dysfunction or 3) severe dysfunction). Left atrial (LA) size was classified as (normal< 40mm or dilated ≥40mm), the pericardium and pleura were classified as presence or absence of fluid, the abdominal aorta (AA) was classified as 1) normal (< 35 mm) or 2) aneurysmatic (≥35 mm).

Results: Median time used for bedside screening with POCKET was 4.2 minutes (range 2.3-13.0). The concordance between POCKET and HIGH is illustrated in left part of the table by kappa statistics, and the feasibilty of POCKET examinations is illustrated in right part of the table.

Conclusions: Semi quantitative evaluation of cardiac anatomy and function with POCKET at the bedside had a high feasibility and almost perfect agreement with reference echocardiographic examination for most indices. Routine bedside screening by experts with POCKET of 4 minutes length may improve patient care and workflow in an internal medicine department.

Accuracy and feasibility of POCKET

Agreement	Kappa	Anatomic structure	Assessed to satisfaction*
LV global function	0.83	Left ventricle	108 (100%)
LV regional function	0.92	Right ventricle	107 (99%)
RV function	0.84	Pericardium	108 (100%)
Valvular function	0.86	Left atrium	105 (97%)
LA size	0.55	Valves	107 (99%)
Pericardial effusion	0.94	Pleura	102 (94%)
Size of the AA	1	AA	77 (71%)
Pleural Effusion	0.84		

**Number of patients (percentage of total).*

P4085 : Important change in the diagnosis of 1 in 5 patients admitted to a medical department after screening with pocket-sized ultrasound

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Purpose: The aim of this study was to investigate the potential of a an early diagnostic screening of patients admitted to a medical department, to see in what extent this may favor an early correct diagnosis and so on enhance patient care and hospital workflow.

Methods: Patients admitted to a non-university hospital in Norway in the period from March 1st 2010 to September 30th 2010 were screened with pocket-sized ultrasound with b-mode and color flow imaging (size of unit: 135×73×28mm). After a principal diagnosis was set, the patients underwent the cardiac and abdominal ultrasound screening performed by one of three performing physicians, all cardiologists with some experience in abdominal ultrasound. Inclusion was restricted by the preset days these cardiologists were on second call. Diagnostic corrections were made and all findings were confirmed by standard diagnostic methods.

Results: 196 patients were included (male=57%, 68.1±15.0 years old). The time used for the ultrasound examinations was 4.3±1.6 min for the cardiac screening and 2.5±1.1 min for the abdominal screening. In 36 (18.4%) patients this examination resulted in a major change in diagnosis compared to the initial diagnosis set by the doctor examining the patient in the emergency room. In 38 patients (19.4%) the initial diagnosis was verified and in 18 patients (9.2%) an additional diagnosis was made.

Conclusions: By performing a cardiovascular and an abdominal screening by pocket-sized ultrasound lasting less than 10 minutes we changed, verified or added important diagnosis in 47% of patients admitted to a general medical department. In one out of five patients the diagnosis was changed in a way that resulted in a com-

pletely different treatment strategy and so on enhanced patient care and hospital workflow.

P4313 : The modern epidemiology of valvular aortic stenosis

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Background: Epidemiological data concerning valvular aortic stenosis (AS) are limited. Retrospective prevalence studies have been performed, but to our knowledge there are no proper incidence data.

Methods and results: Over a 14 year span we performed 3 repeated echocardiography examinations (1994/95, 2001 and 2008) of a random sample of initially 3273 men and women who were enrolled in a population based prospective survey (The Tromsø Study). Data from the only hospital serving the population were included. This allowed us to assess prevalence, incidence and prognosis of degenerative valvular aortic stenosis in the population.

The total number of subjects with AS was 161, with a mean age of 66 years at the start of the study. At the end of the observation time 72 were defined as mild AS (mean gradient ≥ 15mmHg/ flow rate ≥ 2.5m/sec.), 46 had developed moderate AS (mean gradient ≥ 30 mmHg) and 43 severe AS (mean gradient ≥ 50 mmHg).

In all 3 screenings we consistently found an increase in prevalence with age, average values being 0.35% in the 50-59 year cohort, 1.3% in the 60-69 year cohort, 3.4% in the 70-79 year cohort and 11.3% in the 80-89 year cohort.

Incidence rates in the two observation periods 1994-2001 and 2001-2008 were 3.3‰/year and 2.9‰/year. For the total study period 1994-2008 it was 3.3‰/year (95% CI 2.6–4.0) and when hospital information was added the incidence rate increased to 5‰/year (95% CI 4.6–5.4).

Of the 161 participants with AS 53 died during follow up. The remaining 3121 without AS had a mean age of 59 years and during the course of the study 752 died. There was no excessive mortality in the asymptomatic AS-group nor in those who received aortic valve replacement (n=30) when adjusted for age and compared with the rest of the study population.

Conclusions: This is the first study to document the incidence of new-onset AS in a general population. The prognosis of AS seems to be fully comparable with that of the normal population both in the asymptomatic stage and after successful surgery, indicating that the follow up regime and timing of surgery has been adequate for this patient group.

P4338 : The predictive value of troponin, C-reactive protein and brain natriuretic peptide in patients with symptomatic aortic stenosis

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The mechanisms of disease progression as well as risk factors are suspected to be similar in aortic stenosis (AS) and atherosclerosis. Biomarkers are important prognostic variables in various forms of cardiovascular diseases. We hypothesised that the combined use of high sensitive troponin T (hsTnT), N-terminal pro brain natriuretic peptide (NT-proBNP) and high sensitive C-reactive protein (hsCRP) could be useful in risk stratification in patients with advanced AS.

136 patients referred for evaluation of AS were enrolled in the study (57% men, mean age 74 years, aortic valve area 0,62 cm^2, transaortic gradient 54 mm Hg and left ventricular ejection fraction 63%). The relationship between hsTnT, hsCRP and NT-proBNP, different echocardiographic measures of AS and cardiac function, were investigated as well as their relation to all-cause mortality.

103 patients were scheduled for aortic valve replacement (AVR) while surgical intervention was declined in 33. During follow-up 29 patients died; 12 in the non-surgical group and 17 in the group who underwent surgery.

Non-survivors were older; more often had diabetes mellitus, atrial fibrillation or renal impairment. hsTnT and NT-proBNP levels were markedly increased and less so hsCRP. They had lower

effective aortic valve area, ejection fraction and cardiac output.

hsCRP and hsTnT showed no correlation with aortic pressure gradient and aortic valve area, NT-proBNP was inversely correlated with aortic pressure gradient and positively correlated with aortic valve area. hsTnT and NT-proBNP was significantly correlated with several echocardiographic parameters of myocardial function.

Both hsTnT and NT-proBNP were individually correlated with prognosis. The optimal cut of point for NT-proBNP was 142 pmol/L and for hsTnT 32 ng/l. Multivariable stepwise Cox regression analysis identified diabetes and the combination of hsTntT and NT-proBNP as significant predictors of all-cause mortality. When analysing patients without surgery separately, only the combination of hsTnT and NT-proBNP was identified as a significant predictor of all-cause mortality in multivariable analysis.

In AS NT-pro-BNP and hsTnT seem to be of value in risk stratification in patients with advanced AS. Combination of these two biomarkers had an even better predictive value. These findings indicate that biomarkers may improve the management of patients with AS and may potentially also be helpful in timing of AVR and possibly also when selecting patients to traditional surgery or transcatheter aortic valve implantation (TAVI).

P4343 : Lower left ventricular stroke volume predicts cardiovascular events in asymptomatic aortic stenosis (the SEAS study)

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Purpose: Mean aortic gradient is used to assess aortic stenosis (AS) severity and cardiovascular (CV) risk. Theoretically, lower left ventricular (LV) stroke volume may lead to reduced mean aortic gradient and cause underestimation of CV risk. The aim of the study was to assess the added prognostic information by including assessment of LV stroke volume in follow-up of asymptomatic AS.

Methods: The prognostic impact of LV stroke volume was assessed by Cox regression analysis in 1752 patients (mean age 67±10 years, 39% women) included in the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) study, using Doppler derived stroke volume indexed for hight in the allometric power (2.04) at baseline and annual follow-up visits. The mean follow-up was 4.3 years.

Results: Lower stroke volume index at baseline was associated with older age and lower mean aortic gradient and LV mass (all p<0.01). During follow-up a total of 624 CV events occurred. Lower baseline LV stroke volume index predicted increased risk of major CV events [HR 1.028 (95% confidence interval 1.017-1.040), p<0.01], independent of significant associations with mean aortic gradient and LV mass. To account for the change in mean aortic gradient and LV mass during progression of AS, a time-varying Cox regression model was also used. In this model, lower LV stroke volume index during follow-up retained its predictive value [HR 1.016 (95% confidence interval 1.006-1.026, p=0.001] independent of study treatment and significant associations with in-study mean aortic gradient, LV mass and baseline LV stroke volume index (Table).

Conclusion: During follow-up of patients with initial asymptomatic AS, lower LV stroke volume index or reduction in LV stroke volume index both predicted higher rate of CV events independent of AS severity and changes in LV mass.

Table 1

	Hazard ratio	95% Confidence Interval	p-value
Stroke volume index* (ml/h(2.04))	1.016	1.006–1.026	0.001
Mean aortic gradient* (mmHg)	1.021	1.017–1.026	<0.01
LV mass* (g)	1.002	1.001–1.003	<0.01
Study treatment	1.051	0.898–1.230	0.536
Baseline stroke volume index (ml/h(2.04))	1.014	1.002–1.026	0.017

**In-study.*

P4375 : Remodelling of left ventricular mechanic in dilated cardiomyopathy: a two-dimensional speckle tracking echocardiography study

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Aim of the study was to asses myocardial function based on speckle tracking echocardiography (2D-STE) in patients with dilated cardiomyopathy (DCM).

Methods: One hundred patients (mean age 49±10 years) with DCM, defined as ejection fraction (EF) < 45% and left ventricular end-diastolic diameter (LVEDd) >27 mm/m^{2}BSA were recruited retrospectively after receiving heart failure therapy for more than 6 months resulting in a considerable improvement of the EF in some of the patients. All patients underwent echocardiograpic examination and were divided according to the EF as following: EF 55-45%, EF 44-35% and EF < 35%. Twenty-five subjects with normal LV function served as control group. Greyscale cine-loops were obtained from three apical views and two short axis planes of the left ventricle (LV) and the right ventricular (RV) free wall was recorded. Based on 2D-STE the following parameters were extracted: strain (S), systolic (SRs) and diastolic strain rate (SRe). LV twist was calculated as difference between rotation of the apical and basal LV short axis planes.

Results: The results are displayed in Table 1.

Conclusions: 1. Patients, who have recovered from DCM, still show a significant reduction of regional systolic longitudinal and circumferential function compared to normal subjects. 2. 2D-STE surrogate parameters for regional myocardial function and overall LV twist decrease gradually with the reduction of the EF.

Table 1

	Normal group (n=25)	Pat. group 1 EF 55–45% (n=24)	Pat. group 2 EF 44–35% (n=19)	Pat. group 3 EF <35% (n=57)
LV_longitudinal Strain (%)	-20±2	-17±4*	-14±3*	-8±3*°{†}
LV_longitudinal SRs (1/sec)	-1.18±0.19	-0.98±0.24*	-0.77±0.17*°	-0.50±0.17*°{†}
LV_longitudinal SRe (1/sec)	1.77±0.27	1.25±0.41*	1.07±0.28*	0.72±0.34*°{†}
LV_circumferential Strain (%)	-20±4	-17±6*	-12±3*°	-8±3*°{†}
LV_circumferential SRs (1/sec)	-1.59±0.28	-1.46±0.37	-1.33±0.44	-0.96±0.5*°
LV_circumferential SRe (1/sec)	2.08±0.51	1.53±0.41*	1.22±0.27*	1.01±0.42*°
RV Strain (%)	-33±10	-27±6	-24±9*	-17±8*°{†}
RV SRs (1/sec)	-2.19±0.78	-1.59±0.61*	-1.49±0.49*	-1.09±0.46*°
RV SRe (1/sec)	2.63±1.02	1.87±0.77*	1.43±0.59*	1.27±0.65*°
LV_Twist (degree)	13±4	10±3	6±5*	3±5*°

**p<0.05 vs. normal group, °p<0.05 vs. group 1, {†}p<0.05 vs. group 2.*

P4376 : Evidence for impaired left ventricular contractility during normal pregnancy

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Purposes: During pregnancy cardiovascular adaptations facilitate the increased metabolic need of the mother and fetus. The effects on LV contractility have not been well defined. In this non-invasive study, we evaluated, LV contractility serially by analysis of LV shortening incorporating pre- and afterload status during a normal pregnancy and at a 6 month post partum follow-up (reference time point).

Methods: 65 women, aged (mean±SD) 32±5 years, underwent echoDoppler including tissue Doppler and 2D speckle tracking strain analysis, as well as calibrated subclavian arterial pulse trace to obtain central aortic end-systolic pressure, at gestational weeks 14-16, 22-24, 36, and 6 months postpartum.

Results: During pregnancy, cardiac output (CO) and LV end-diastolic volume increased by 20% and 23%, respectively (both p<0.01). LV EF, global peak systolic strain (GS%), and rate corrected LV velocity of circumferential fiber shortening (Vcfc), a preload insensitive measure of LV shortening, were reduced by 11%, 6%, and 6%, respectively (all p<0.01). Afterload obtained as meridional end systolic wall stress (ESWS) increased by 12% (p<0.01). By plotting Vcfc versus afterload (ESWS), Vcfc was found left- and downward displaced during pregnancy (22-24w) as compared to 6 months postpartum indicating that LV contractility was significantly reduced (Table).

Conclusions: Cardiovascular adaptations during NP are characterized by large shifts in loading conditions. Although CO increases, our analysis of LV contractions incorporating loading, indicates

	14–16 weeks	22–24 weeks	36 weeks	6 months PP	p
CO (L/min)	5.7±1.1*	6.0±1.0*	6.0±0.9*	4.8±1.0	<0.01
LV EDV (mL)	92±22*	97±23*	101±26*	78±19	<0.01
LV EF biplane (%)	61±6	59±9	54±8 *#{†}	60±7	<0.01
GS (%)	-19.0±3.2	-19.6±2.2	-18.1±2.4{†}	-19.2±2.7	0.02
Vcfc (circ/s)	1.22±0.16	1.14±0.15*	1.18±0.21	1.24±0.14	<0.01
ESWS (kdyn/cm^2)	90.2±22.6	87.3±26.8*	99.5±23.3{†}	99.1±19.9	<0.01

*Mean ±SD. p<0.05 vs *6 mo postpartum, #14–16 w, {†}22–24 w, {$}36 w.*

that LV contractility temporarily is reduced during NP. This is a novel observation that should be relevant for future evaluation of cardiac function during any pregnancy.

Results: Table.

P4380 : Alterations in ventriculo-arterial coupling and systemic arterial properties during normal pregnancy

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Purpose: During normal pregnancy (NP) increased cardiac output (CO), and reduced blood pressure and vascular resistance, facilitate the metabolic need of mother and fetus. Whether changes in arterial properties and ventriculoarterial coupling (VAC) are part of this adaptation, is unknown. We performed serial follow-up of arterial properties and VAC during NP and 6 months postpartum (PP).

Methods: 65 (32±5) with NP were examined at weeks 14-16, 22-24, 36 and PP. LV end-systolic volume (LVESV) and stroke volume (SV) calculated by Doppler echocardiography (indexed by body surface area). Aortic root pressure and flow obtained by calibrated right subclavian artery pulse traces and aortic annular Doppler flow. Arterial compliance (C), arterial elastance (Ea), characteristic impedance (Z0), and peripheral arterial resistance (R) were obtained from aortic root pressure and flow data using 4-element windkessel model and Fourier analysis. VAC index was obtained as the ratio between the indexed arterial and LV elastance, Eal/ELVI = ESVI/SVI.

Results: During NP, mean arterial blood pressure was reduced 10% (p<0.01). R and Ea were reduced by 5% and 20% (p<0.01). Z0 and C did not change. Eal/ELVI increased 30% during pregnancy (p<0.01) (increased Eal (21%, p<0.01) and reduced ELVI (29%, p=0.05)).

Conclusions: During NP there is reduction in peripheral arterial resistance and mean arterial blood pressure, whereas central aortic properties are but little altered. VAC index increases and indicates a transition from maximal cardiac efficiency towards maximal external work during pregnancy.

Results: Table

	14–16 weeks	22–24 weeks	36 weeks	6 months PP	P
Mean arterial pressure(mmHg)	82.8±6.6	80.0±6.2*#	84.8±7.1#{†}	88.0±7.3	<0.01
R (mmHg ml^{-1}s^{-1})	0.85±0.18*	0.81±0.16*	0.92±0.23*{†}	1.10±0.29	<0.01
Z_o (10^{3}mmHg ml^{-1} s^{-1})	43±18	51±36	45±23	55±21	0.168
C WK (ml mmHg^{-1})	1.45±0.33	1.56±0.45	1.55±0.46	1.40±0.45	0.220
Ea (mmHg ml^{-1})	1.05±0.25*	1.02±0.24*	1.19±0.28{†}	1.27±0.28	<0.01
ESVI (mL/m^2)	21±6	23±7*	26±9*#	18±4	<0.01
Eal (mmHg/ml·m^2)	1.99±0.56*	1.85±0.53*	2.16±0.43{†}	2.34±0.50	<0.01
E_{LV} I (mmHg/ml·m^2)	4.65±1.87	3.83±1.29*#	3.82±1.76*#	5.40±1.68	<0.05
Eal/E_{LV} I	0.45±0.14	0.53±0.17	0.64±0.23*#{†}	0.45±0.14	<0.01

*Mean ±SD. p<0.05 vs *6 mo post partum, #14-16 w, {†}22-24 w, {$}36 w. C WK = C obtained using windkessel model fit.*

P4700 : Cardiovascular screening by pocket-sized ultrasound among patients admitted to cardiac department at a Norwegian non-university hospital

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Purpose: The use of pocket-sized ultrasound may improve and change hospital workflow and in this study we wanted to study the usefulness of cardiovascular screening with pocket-sized ultrasound (pUS) in patients admitted to a cardiac department with respect to diagnostic accuracy and adjustment.

Methods: 119 persons (20-89 years, median 67 years), admitted to the cardiac department were screened with b-mode and color flow imaging with pocket-sized ultrasound (size of unit: 135×73×28 mm) at admission. The examinations were performed bed-side by three experienced cardiologist. The pUS screening included assessment of left ventricular global and regional function, right ventricular size and function, valvular function, the pericardium and pleura, as well as the abdominal aorta and inferior vena cava. Prior to pUS screening a tentative diagnosis was made by residents based on usual care. The usefulness of pUS with respect to correct the diagnosis was classified as 1) change of tentative diagnosis, 2) verification of tentative diagnosis, 3) additional diagnosis made and 4) no diagnostic change. Verification of pUS usefulness was made by the Study Committee in each case. Validation of pUS screening was done by high-end echocardiography in a subpopulation of 90.

Results: The diagnostic influence of pUS is summarized in the Table. The tentative diagnosis was changed in 19 patients (16%), and only in 54 patients (45%) the pUS screening had no diagnostic usefulness. Time used for pUS screening was median 4.4 (range 2.0-13.0) minutes. Kappa statistics ranged 0.7 to 1, except for left atrial diameter were K=0.5.

Conclusions: Cardiovascular screening by pocket-sized ultrasound changed, verified or added important diagnosis in 55% of patients admitted to a cardiac department. Thus, a bed-side examination with pocket-sized ultrasound of 4 minutes length may improve patient care and workflow in cardiac departments. However, how this corresponds to non-expert users has to be proven.

Diagnostic influence of pUS screening

	Number (%)
Change of tentative diagnosis	19 (16%)
Verification of tentative diagnosis	34 (29%)
Additional important diagnosis made	12 (10%)
No diagnostic influence	54 (45%)

pUS = pocket-sized ultrasound.

P4877 : Myocardial salvage is reduced in primary PCI-treated STEMI patients with microvascular obstruction, demonstrated by early and late CMR

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Purpose: Restoration of epicardial blood flow by primary PCI is no guarantee for normalization of myocardial tissue perfusion. Microvascular obstruction (MVO), as defined by cardiac magnetic resonance (CMR), has been shown to be associated with large infarct size (IS). However, it is not known whether MVO is associated with myocardial salvage.

Methods: The study population consisted of 94 patients with acute ST elevation myocardial infarction (STEMI) treated by primary PCI. CMR was performed within 1-5 days (early) and repeated after 4 months (late). Myocardium at risk (MaR) (early CMR), ejection fraction (EF) and final IS (late CMR) were compared in patients with and without MVO, respectively. Myocardial salvage was defined as: ((MaR – final IS) × 100)/MaR. A multivariate analysis was also performed in order to adjust for clinical covariates at baseline.

Results: MVO was present in 52% of the patients and was associated with significantly larger IS and lower EF, also after adjusting for potential confounders, including differences in MaR, in a multivariate model. Myocardial salvage was associated with MVO, also after adjustment for differences in clinical characteristics.

Conclusions: The results indicate that the presence of MVO is associated with large final IS and low EF, also after adjustment for MaR. Myocardial salvage after primary PCI is impaired in patients with MVO.

Table 1. Final IS, EF and myocardial salvage in patients with and without MVO

	With MVO (n=49)	Without MVO (n=45)	P-value
Infarct size at 4 months (ml)	17.7 (14.2-25.6)	6.6 (2.8-12.5)	<0.00001
Ejection fraction (%)	50 (43-54)	64 (59-70)	<0.00001
Myocardial salvage (%)	39.8 (25.3-51.4)	65.4 (50.5-79.6)	<0.0001

P5058 : AAI mode pacing in patients with sick sinus syndrome. 20 years follow-up data from a single Norwegian non-university hospital

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Purpose: Guidelines recommend either the use of atrial mode (AAI) or dual (atrial and ventricular) mode (DDD) pacing with minimized ventricular pacing in case of sick sinus node syndrome (SSS). However, most centers prefer the use of DDD mode. We aimed to study the long term outcome of a restrictive use of DDD mode in patients with SSS.

Methods: In a single Norwegian non-university hospital we studied 190 persons (118 women) with median (range) age 76 (27-95) years that were treated with pacemakers (AAI or DDD) for SSS between 1990-2009. The policy of the hospital was to use AAI mode if there was no sign of atrioventricular (AV) block, except for grade 1 or bundle branch block. This policy was unchanged in the whole study period, and totally four different cardiologists performed the implantations. 139 patients were treated with AAI mode, and 51 were treated with DDD mode. Follow-up data was taken from the Norwegian Pacemaker Registry and the hospitals patient journal system.

Results: Median age was 77 (AAI) and 73 (DDD) years. with p-value for difference 0.04. The proportion of women was higher in the AAI group, p-value for difference 0.001. In total 1,265 patient years (982 years with AAI) was yielded in the study period. In total 8 (6%) patients had their AAI upgraded to DDD pacemakers due to the development of higher degree of AV block after mean 4.5 (range 0-17) years. 2 out of these 8 patients had higher degree of AV block prior to AAI implantation and should, following the hospitals policy, had DDD mode pacing. Thus, by strict following the policy of using AAI mode pacing when no higher degree of AV block was detected prior to implantation only 6 patients (4%) needed upgrading to DDD mode. Any kind of AV block, except incomplete right bundle branch block and hemi block developed in 8 (6%) of those in AAI mode. 71 patients died in the study period. Median survival time was 9.4 (AAI) and 10.0 (DDD) years, and there was no significant difference between the groups. Other complications were deep vein thrombosis in 2 patients (both AAI) and pacemaker infections in 2 (AAI: 1).

Conclusions: In our long term follow-up data AAI mode pacing in sick sinus syndrome equals DDD mode pacing with respect to mortality and complications. Infrequently there is a need for upgrading to DDD mode. Thus, in our data AAI mode in sick sinus syndrome is non-inferior to DDD mode pacing, and we hypothesize that the much cheaper and easier AAI mode is underused in the everyday clinical practice.

5186 : Prothrombotic markers in patients with acute myocardial infarction and left ventricular thrombus formation treated with dual antiplatelet therapy

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The aim of the present study was to compare selected circulating prothrombotic markers in patients with acute myocardial infarction (AMI) and left ventricular (LV) thrombus with similar patients without thrombus formation.

Methods: One hundred patients with acute ST-elevation myocardial infarction treated with percutaneous coronary intervention on the left descending coronary artery and dual antiplatelet therapy were included. LV thrombus formation was detected by echocardiography and/or MRI in 15 patients during the first 3 months, most of them within the first week. Patients with LV thrombus were anticoagulated with low molecular weight heparin followed by warfarin. Fasting blood samples were drawn 4-5 days (baseline), 5-6 days, 7-8 days, 2-3 weeks and 3 months after the AMI for determination of selected prothrombotic markers.

Results: We found higher levels of soluble tissue factor (sTF) in the LV thrombus group at baseline, after 7-8 days and 3 months compared to the patients without LV thrombus. Patients with sTF levels above the upper quartile at baseline had significantly higher risk for developing LV

thrombus (odds ratio 4.6; 95% confidence interval 1.5 -14.4; p=0.01). Similar pattern was shown for d-dimer with higher levels in the LV thrombus group except at 3 months where the levels were lower. On the contrary, the levels of prothrombin fragment 1+2 (F1+2) and endogenous thrombin potential (ETP) were significantly lower in the thrombus group after 7-8 days (only ETP), 2-3 weeks and 3 months. The levels of plasminogen activator inhibitor 1 did not differ at the various time points between the groups.

Conclusion: In conclusion, in the very acute phase of AMI, we found higher levels of sTF and d-dimer in the LV thrombus group that may be of importance for the generation of mural thrombus. Lower levels of F1+2, ETP and d-dimer in the LV thrombus group late during follow-up are probably induced by ongoing anticoagulation therapy and thereby less thrombin generation.

Hazard ratios (95% confidence interval) of new onset diabetes mellitus in tertiles (T1–3) of fasting serum triglycerides compared to the lowest tertile (T1)

	T1 (0.23-1.00 mmol/l) n=677	T2 (1.01-1.15 mmol/l) n=630	T3 (1.16-11.57 mmol/l) n=655
Unadjusted	1.00	1.44 (0.95-2.19)	3.27 (2.30-4.73)
Multiple adjusted{†} without PF	1.00	1.18 (0.78-1.79)	1.86 (1.29-2.73)
Multiple adjusted{†} with PF	1.00	1.13 (0.75-1.72)	1.70 (1.18-2.49)

n = number of men each tertile, PF = age adjusted physical fitness. {†}Adjusted for body mass index, fasting blood glucose and maternal diabetes.

5322 : Serum triglycerides predict new onset diabetes mellitus independent of physical fitness

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Purpose: Both fasting serum triglycerides (TG) and physical fitness (PF) have been shown to be predictors of new onset diabetes mellitus (NOD). We aimed to test the hypothesis that TG predicts NOD also when adjusted for PF in healthy individuals.

Methods: Fasting serum triglycerides were measured 1972-1975 in 1962 healthy men with fasting blood glucose (FBG) in the non-diabetic range (venous whole blood glucose < 6.1mmol/l) aged 40-59 years followed up to 35 years. PF was measured using a symptom limited bicycle exercise test; with starting load 100 W and 50 W increase every 6th minute. PF was defined as the total work divided by the body mass (J/kg). Survival models were adjusted for body mass index, FBG, maternal diabetes and further for age adjusted PF.

Results: The incidence of NOD was 202 cases (10.3%) during 35 years. An increase of 1SD in log TG was associated with a 30% (95% CI, 1.13-1.50) increased risk of NOD when adjusted without PF, and 27% (1.10-1.46) with age adjusted PF in the model. The highest tertile of TG was associated with 86% increased risk of NOD compared to the lowest. Only small changes in risk were observed when adjusting for PF (Table, Relative risk of diabetes)

Conclusions: Fasting serum triglycerides is a strong long-term predictor of new onset diabetes mellitus, even after adjustments for physical fitness.

5360 : Quantification and visualization of right and left ventricular wall motion and blood flow by 3D MRI

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Purpose: Assessing the wall motion in the left ventricle is important for detecting regional left ventricular dysfunction. For the right ventricle, the contraction and the dilatation as well as the filling are dependent of the left ventricle. Therefore, the right ventricle cannot be studied isolated and should be investigated together with the left ventricle. Further, dysfunctional wall motion may also influence on the blood flow pattern and should also be evaluated together with the ventricle wall. The aim of this study was to develop an improved tool for visualization and quantification of regional ventricular wall motion and blood flow in the left and right ventricle.

Methods: Velocity measurements of the left and right ventricle were obtained by three-dimensional phase shift velocity mapping. Slices were acquired using a 3.0T GE Signa Excite scanner. Sequence parameters were: TR=11 ms, TE=4 ms and Flip Angle=20°. The acquired matrix was 256×256 with a resolution of 320×320 mm^2 giving 0.8 pixels per mm in both directions. Slice thickness was 0.8 mm. For every point of time, slices were stacked to provide a full time-dependent three-dimensional volume throughout the cardiac cycle.

The blood and ventricular walls were segmented to provide regions of interest (ROI) in each time-dependent image by implementing a discrete contour model. Interactive planes were created that could be positioned in any direction through the volume. In these planes, colored three-dimensional velocity vectors within the ROIs were calculated and presented in a separate window to study the three directional myocardial and blood flow velocities anywhere within the ventricles.

Results: By utilizing three-dimensional phase shift velocity mapping the software was able to construct a time-dependent 3D volume and present velocity information for both left and right ventricular wall as well as blood flow in arbitrary positioned planes. Planes can be added and interactively repositioned to construct different myocardial segments.

Conclusions: This software utilizes three-dimensional MRI velocity mapping and improves the ability to study the simultaneous regional contraction of the myocardium in the left and right ventricle and compare this to the time dependent intracavity blood flow throughout the cardiac cycle. The technique may reveal hypokinetic and akinetic contractions, as well as asynchronous and dyscinetic wall movements in the right and left ventricle.

5374 : Exercise stress testing is associated with an increase in cardiac troponin T levels in patients with suspected coronary artery disease

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Purpose: To assess the profile of circulating troponin T levels during exercise stress testing in patients with stable and unstable coronary artery disease (CAD).

Methods: We included 198 consecutive patients undergoing a maximal bicycle exercise stress test with single-photon emission computed tomography (SPECT) for suspected myocardial ischemia. Levels of high sensitive troponin T (hs-cTnT) were measured before (baseline), immediately after, and 1.5 hours and 4.5 hours after stress testing. A clinical events committee blinded to hs-cTnT data categorised patients into three groups; unstable, stable and no CAD based on results from SPECT and on patient records.

Results: Of the 198 patients, 44 were classified as having unstable CAD, 41 as having stable CAD, and 113 as having no CAD. Baseline levels of hs-cTnT were higher in patients with unstable vs. no CAD [median 8.8 (quartile (Q) 1-3: 5.5, 14.8) ng/L vs. 4.7 (Q1-3: 3.0, 8.0) ng/L, p<0.001], and in patients with stable vs. no CAD [8.6 (Q1-3: 3.6, 11.9) ng/L vs. 4.7 (Q1-3: 3.0, 8.0) ng/L, p=0.001]. hs-cTnT levels did not differ between the patients with unstable and stable CAD at baseline (p=0.43). After 4.5 hours the median hs-cTnT levels increased in patients with no CAD [4.7 (Q1-3: 3.0, 8.0) ng/L to 6.3 (Q1-3: 3.9, 11.00) ng/L, p<0.001] and in patients with stable CAD [8.6 (Q1-3: 3.6, 11.9) ng/L to 11.0 (Q1-3: 6.2, 15.7) ng/L, p<0.001], while the increase in patients with unstable CAD was of borderline significance [8.8 (Q1-3: 5.5, 14.8) ng/L to 9.8 (Q1-3: 6.9, 15.0) ng/L, p=0.060]. There was no difference in the magnitude of hs-cTnT increase between the patient groups.

Conclusion: Exercise stress testing is associated with an increase in hs-cTnT from baseline to 4.5 hours after stress testing, regardless of the presence or absence of unstable, stable or no CAD. Mechanisms other than reversible myocardial ischemia may play a role for this increase.

P5409 : Is athletic training-induced bradycardia caused by a downregulation of the Ca2+ clock pacemaker mechanism in the sinoatrial node?

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Introduction: Athletic training has myriad established cardiovascular benefits. However, recently concern has arisen about the potential for training to do cardiovascular harm. Accumulating reports of exercise-induced sudden cardiac death, myocardial damage and ECG abnormalities (including atrial fibrillation and bradyarrhythmias caused by nodal dysfunction) have led to significant consternation. We used a rat model of exercise training to investigate our hypothesis that training can alter the functioning of the heart's pacemaker, the sinoatrial node (SAN), via altered gene expression.

Methods: Male Wistar rats were assigned to either sedentary (n=7) or exercise groups (n=8). Rats in both groups underwent implantation of telemetry devices. Sedentary rats remained caged for 24 hours/day. Exercised rats underwent training based on their maximum O2 uptake, VO2,max - they exercised for 1 hour 5x/week for 10 weeks. Training intensity was adjusted following fortnightly checks on VO2,max. Following training, all animals were sacrificed by approved methods, their hearts removed and samples of SAN, right atrium (RA) and ventricle (RV) were dissected and frozen in liquid N2 for subsequent qPCR mRNA analysis.

Results: VO2,max corrected for body weight showed a 20% increase in the trained group compared to a 13.3% decrease in the sedentary group ($p<0.05$). In trained animals, in vivo baseline cycle length was significantly increased by training (161 ms before vs 181 ms after; $p<0.05$). It was not affected in sedentary animals. qPCR revealed no change in the pacemaker ion channel, HCN4, in the SAN in trained animals. However, a number of important changes in gene expression were observed. In the SAN of trained animals, Cav3.1 (ion channel carrying T-type Ca^{2+} current, ICa,T), RyR2 (sarcoplasmic reticulum (SR) Ca^{2+} release channel) and NCX1 (Na^{+}–Ca^{2+} exchanger) were all downregulated ($p<0.1$) compared to sedentary animals. In the RA, the same transcripts were downregulated and, in addition, SERCA2A (SR Ca^{2+}-pump) was downregulated ($p<0.05$). In the RV, RyR2 was again downregulated, whilst Cav3.1 and NCX1 were upregulated ($p<0.1$).

Conclusion: In rats, as in humans, a programme of athletic training leads to the development of in vivo bradycardia. In the SAN, this was accompanied by a downregulation in an ion channel and Ca^{2+}-handling proteins involved in the "Ca^{2+} clock" mechanism of pacemaking. It is possible, therefore, that athletic training-induced bradycardia is caused by downregulation of the Ca^{2+} clock pacemaker mechanism, and not by "high vagal tone" as commonly believed.

P5459 : Impact of aortic valve stenosis and hypertension on radial strain in multiple myocardial layers

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Purpose: In young healthy individuals, left ventricular (LV) radial strain is gradually increasing from the subepicardial to the subendocardial layer. In patients with aortic stenosis (AS), LV global systolic function by either ejection fraction or midwall shortening decreases in response to chronic pressure overload. Our aim was to investigate regional changes in myocardial layer function measured as radial strain in AS.

Methods: Systolic strain was assessed in three layers in the inferior LV wall by tissue Doppler imaging in 70 patients with AS (73±10yrs, 41 women, 50% hypertensive). Three small regions of interest (size 2×6 mm, strain length 2 mm) were tracked for peak systolic radial strain measurements. 37 patients had mild/moderate and 33 severe AS by aortic valve area corrected for pressure recovery.

Results: Strain was significantly lower in the subepicardial layer (33.8±40.7%), but similar in the mid-myocardial and subendocardial layers: 52.8±39.3 vs. 55.2±41.5%, both $p<0.001$. In all three layers, strain was lower in patients with severe AS compared to those with mild/moderate AS ($p<0.05$). In multivariate regression analyses, strain in the mid-myocardium was attenuated by the presence of hypertension independent of age, gender, LV mass, severity of AS and subepicardial strain (Table 1). Strain in the subendocardium was significantly influenced by severe AS only (Table 1).

Conclusions: In patients with AS, AS severity mainly influences subendocardial strain, while concomitant hypertension primarily influences mid-myocardial strain. Chronic pressure overload in AS is associated with changed strain gradient across the LV myocardial wall.

Table 1

	Mid-myocardial strain		Subendocardial strain	
	(R^2=0.36, p<0.001)		(R^2=0.24, p<0.01)	
	Beta	p	Beta	p
Age (yrs)	0.02	0.85	-0.15	0.21
Gender	0.14	0.27	0.26	0.06
LV mass (g)	-0.07	0.55	-0.14	0.29
Hypertension	-0.20	0.05	-0.05	0.64
Severe AS	-0.12	0.28	-0.27	0.03
Subepicardial strain (%)	0.50	0.01	0.10	0.39

P5516 : Systolic torsion, twist rate and global systolic LV strain are reduced at rest in professional soccer players

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Purpose: Left ventricular (LV) torsional function augments cardiac performance during exercise. We studied LV torsional function and global systolic strain at rest in a large cohort of highly trained athletes with anticipated adaptive LV remodeling.

Methods: 103 male professional soccer players from the two top Norwegian leagues underwent echocardiography, and were compared with age-matched healthy controls (n=46). LV rotation was obtained at basal and apical short axis levels using speckle-tracking imaging (STI). LV torsion was defined as the net difference between apical and basal LV rotation, while rotational rates and twisting rates were derived from integrating rotation or torsion over time. Time-to-peak (TTP) data were normalized to systole duration (i.e. the time from QRS onset to aortic valve closure =100%). LV global systolic strain was computed by 2-dimensional STI from apical standard views.

Results: Soccer players and controls displayed similar body mass index, body surface area, blood pressure, and LV ejection fraction, but lower heart rates (50±1 vs 63±2 min^{-1}). Moreover, players exhibited greater computed LV mass (173±3 vs 150±5 g) and LV enddiastolic volumes (LVEDV, 158±3 vs 125±4 mL, both P<0.001), indicating LV remodeling. Peak basal and apical rotation was not different between groups. Absolute values of systolic torsion were comparable (14.3±0.5 vs 15.2±0.9 deg; players vs controls, respectively). However, when indexed to LV size (i.e., LVEDV), torsion was significantly lower in players (P<0.01). Moreover, peak basal rotational rate was lower (-55.9±2.1 vs -65.1±3.7deg/s, P<0.02) and occurred earlier in players (TTP, 57.5±1.0 vs 62.1±2.2%, P<0.05), while magnitude and timing of apical rotational rate was similar in both groups. Peak systolic twisting rate was significantly lower in players (86.4±2.8 vs 101.9±5.2 deg/s, P<0.01) with unaltered timing. Peak diastolic untwisting rate was enhanced in players (-124.5±4.2 vs -106.9±6.7 deg/s, P<0.05) and occurred significantly earlier (TTP, 112.7±0.8 vs 117.4±2.4%, P<0.02). Absolute values of LV global systolic strain were comparable (-19.3±0.2 vs 19.0±0.4%), but significantly lower in players when indexed to LVEDV (-126.4±3.8 vs -165.9±7.4%/L, p<0.0001).

Conclusions: Systolic torsion and global systolic LV strain were reduced at rest in professional soccer players when LV size is taken into account. Also, systolic twist rate was reduced. Diastolic untwisting rate was increased in players even at rest and may contribute to enhanced LV early diastolic function.

P5556 : Predictors for VO2 peak in heart transplant recipients - "how strong you kick can determine the peak you reach"

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Introduction: Heart transplant (HTx) recipients have impaired muscle strength and are deconditioned as compared to age-matched values in normal subjects. Previous studies have reported VO2 peak in the range of 50-70% of predicted. Several factors might be involved in this limitation of which chronotropic incompetence is regarded as the most important factor. However, in general few factors that could contribute to reduced exercise capacity have been considered at the same time. The aim of the present study was to evaluate the current level of aerobic capacity and to look for several factors that could be predictive for VO2 peak.

Methods: 52 HTx patients, underwent exercise testing on a treadmill with gas exchange

measurements 1-8 years after HTx. We obtained clinical and laboratory data, ECG, blood pressure, lung function tests, isokinetic muscle strength, and echocardiography.

Results: Mean age was 52±16 years, 71% men, mean time after HTx was 4.1±2.2 years. Peak VO2 was 27.7±6.3 ml/kg/min (84±22% of predicted). 51% achieved a VO2 peak >80% of predicted values. Patients with VO2 peak >80% had significantly lower BMI and triglycerides and significantly higher muscle strength (quadriceps/hamstrings), HDL-cholesterol, peak ventilation and O2 pulse. Donor and recipient age, sex, medication, lung function, renal function, ischemic time, and heart rate (HR) response during exercise were similar. Patients with or without VO2 peak >80% had a mean percentage of age predicted maximum heart rate >90% and a mean chronotropic response index >1.1

Linear regression analysis (corrected for age and gender) showed that muscle strength (TW=total work), BMI, level of HDL and HR reserve explained 66% of the variation in peak VO2 values (R2 Change= 0.662). R2 for the model as a whole = 0.701 (p<0.001). (See table).

Conclusion: A modern population of HTx recipients has only mildly impaired chronotropic response. Muscle strength (TW), BMI, level of HDL and HR reserve explain the variation in VO2 peak, with TW and BMI clearly as the most important predictive factors.

Model summary

Model		Beta	p	R2 Change	p
1	Gender	0.004	0.972	0.040	0.388
	Age	-0.134	0.184		
2	Muscle strength	0.459	<0.001	0.662	< 0.001
	BMI	-0.446	<0.001		
	HR reserve	0.265	0.008		
	HDL	0.245	0.020		< 0.001
1 & 2				0.701 (R2)	< 0.001