

ABSTRAKTER PRESENTERT PÅ HØSTMØTET

Ischemic postconditioning in ST-elevation myocardial infarction. Results of the randomized, controlled POSTEMI trial

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Objectives: This study assessed the effect of ischemic postconditioning (IPost) on infarct size in patients with ST-elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PCI).

Background: Reduction of infarct size by IPost has been reported in smaller proof-of-concept clinical studies, but has not been confirmed in other smaller studies. The principle needs to be evaluated in larger groups of STEMI patients before implemented in clinical practice.

Methods: Patients with first-time STEMI, <6 h from symptom onset, referred to primary PCI were randomized to IPost or control groups. IPost

was administered by 4 cycles of 1 min reocclusion and 1 min reperfusion, starting 1 min after opening, followed by stenting. In the control group, stenting was performed immediately after reperfusion. The primary endpoint was infarct size measured by cardiac magnetic resonance after 4 months.

Results: A total of 272 patients were randomized. Infarct size (percent of left ventricular mass) after 4 months (median values and interquartile range) was 14.4 (7.7, 24.6) % and 13.5 (8.1, 19.3) % in the control group and IPost group, respectively ($p=0.18$). No significant impact of IPost was found when controlling for risk factors of infarct size in a multivariate linear regression model ($p=0.86$). The effects of IPost on secondary endpoints, including markers of necrosis, myocardial salvage and ejection fraction, as well as adverse cardiac events during follow-up, were consistently neutral.

Conclusions: In contrast to several smaller trials reported previously, we found no significant effects of IPost on infarct size or secondary study outcomes. At this stage, IPost cannot be recommended as adjunctive therapy in STEMI treated by primary PCI.

Effect of High Intensity Interval Training on Progression of Cardiac Allograft Vasculopathy

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Background: Cardiac allograft vasculopathy (CAV) is a progressive form of atherosclerosis occurring in heart transplant (HTx) recipients, leading to increased morbidity and mortality. Given the atheroprotective effect of exercise on traditional atherosclerosis, we hypothesized that high intensity interval training (HIT) would reduce the progression of CAV among HTx recipients.

Methods: Forty-three (mean \pm SD age 51 \pm 16 years, 67% males, time post HTx 4.0 \pm 2.2 years) clinically stable HTx recipients > 18 years old, were randomized to either HIT or control group (standard care) for one year. The effect of training on CAV progression was assessed by intravascular ultrasound (IVUS).

Results: IVUS analysis revealed a significantly less mean increase [95%CI] in percent atheroma volume (PAV) of 0.9 [-0.3, 1.9] % in the HIT-group as compared to the control group: 2.5 [1.6, 3.5] % ($p=0.021$). Similarly, mean increase [95% CI] in total atheroma volume (TAV) was 0.3 [0.0, 0.6] mm 3 /mm in the HIT-group versus 1.1 [0.6, 1.7] mm 3 /mm in the control group ($p=0.020$), and mean increase in maximal intimal thickness (MIT) were 0.02 [-0.01, 0.04] mm in the HIT-group versus 0.05 [0.03, 0.08] mm in the control group ($p=0.054$). Qualitative plaque progression (virtual histology parameters) and inflammatory activity (biomarkers) were similar between the two groups during the study period.

Conclusions: HIT among maintenance HTx recipients resulted in a significantly impaired rate of CAV progression. Further and larger studies should examine if exercise rehabilitation strategies should be included as part of CAV management protocols.

Exercise activity increases arrhythmic risk in subjects with arrhythmogenic right ventricular cardiomyopathy

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Purpose: Case reports indicate that athletic activity increases the risk of ventricular arrhythmias (VAs) in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC). The purpose of this study was to explore the frequency of exercise induced VAs in athletes with ARVC and compare to ARVC subjects without a history of athletic activity.

Methods: In total, 112 consecutive ARVC index patients and mutation-positive family members from the prospective Nordic ARVC registry were studied (42 \pm 17 years, 58% male). Subjects with former or actual history of physical activity level > 1440 metabolic equivalents (METs)- min/week or > 4 hours of vigorous activity a week during minimum 3 years were defined as athletes. Exercise induced VAs were defined as ventricular tachycardia during exercise.

Results: The definition of athlete status was fulfilled in 37 (33%), while 75 (67%) were non-athletes. Athletes were more frequently index patients compared to non-athletes (28/37, 76 % vs. 37/75, 49%, $p<0.01$). Athletes were younger at time of diagnosis than non-athletes (36 \pm 13 vs. 45 \pm 18 years, $p<0.01$). Exercise induced VAs occurred in 41 (37%) and were more frequent in athletes (28/37, 76%) compared to non-athletes (13/74, 17%) ($p<0.001$). Subjects with exercise induced VAs had higher levels of METs-min/ week than those without VAs ($p<0.001$) (Figure).

Activity level in ARVC subjects

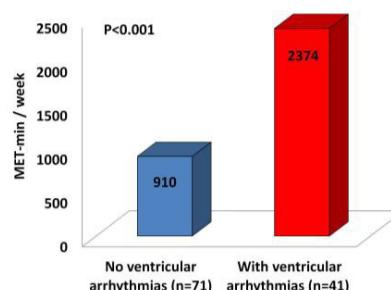


Figure. Among index patients ($n=65$), all athletes (100%) had exercise induced VA, while only 31% of non-athletes had exercise induced VA ($p<0.01$).

Conclusions: These findings confirm that exercise induced VAs are frequent in ARVC patients and even more frequent in those with athletic activity compared to non-athletes. Furthermore athletes were younger at diagnosis and more frequently index patients, indicating that athletic activity aggravate the onset of life threatening arrhythmias in ARVC.

Peripartum cardiomyopathy - evaluation of left ventricular reserve capacity by ergometric stressechocardiography 6-12 months postpartum.

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Background: Peripartum cardiomyopathy (PPCM) is cardiac failure with left ventricular ejection fraction (LVEF) <45% occurring in the last month of pregnancy or within five months postpartum (PP). The incidence is approximately 1 in 10'000 pregnancies. Maternal mortality is estimated to 20%. If LVEF is reduced one year PP, the risk of death in a subsequent pregnancy is approximately 20%. With normalized LV function, mortality in a subsequent pregnancy is small. However, there is a substantial risk of recurrence of PPCM. The aim of this study was to evaluate the LV reserve capacity for PP based on ergometric stress echocardiography (ESE) performance.

Methods: Women were studied while exercise testing on a specialized bicycle in a semi-supine position. A GE Vingmed vivid 7 or E9 scanner was used. Data is given as (mean±SD).

Results: 10 women (age 34 ± 7 years) with PPCM underwent ESE 10 ± 3 months PP. All received betablockers and ACE-inhibitors. All were asymptomatic at the time of ESE. ProBNP was almost normalized in 8 patients (541 ± 628 to 18 ± 13 pmol/l, p < 0.05). Resting LVEF (34 ± 8 to 53 ± 11%, p < 0.05) and global strain (-10.8 ± 3 to -16.7 ± 2 %, p < 0.05) was improved. Mean duration of the ESE was 8 ± 2 min and maximum work load was 82 ± 19 Watt. Heart rate increased from 78 ± 10 to 138 ± 13 bpm (p < 0.01) and blood pressure from 106 ± 19/68 ± 11 to 142 ± 18/84 ± 13 mmHg (p < 0.01). There was a slight improvement in global means of LV function (LVEF: 58 ± 8% vs 53 ± 8%, p < 0.05 and strain -18.1 ± 4.2% vs -16.7 ± 3.2 %, p < 0.05).

Conclusion: All women had improvement in LV function at 10 months PP. However, improvement of LV function during exercise was small. These findings suggest that women with PPCM have reduced LV reserve capacity despite normalization of ventricular function at rest. This might be a potential reason for the high risk of recurrence of PPCM.

Prevention of obesity-induced myocardial oxygen-wasting through NADPH-oxidase inhibition

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Obesity and diabetes are independent risk-factors for cardiovascular diseases, and associated with the development of a specific cardiomyopathy with altered myocardial substrate utilization (increased dependency on fatty acids as energy fuels) together with elevated myocardial oxygen consumption (MVO₂) and impaired cardiac efficiency. We have data suggesting a relationship between MVO₂ and reactive oxygen species (ROS) content in cardiac sections from lean and diet-induced obese (DIO) mice, supporting the notion that ROS may be involved in oxygen-wasting mechanisms. As the heart has several sources of myocardial ROS production, we have in this study used a pharmacological approach in order to elucidate a potential role of NADPH oxidase 2 (NOX2) in obesity-induced myocardial oxygen wasting. Mechanical function, myocardial substrate utilization and MVO₂ were monitored in isolated working hearts from DIO mice treated with or without the NOX2-inhibitor Apocynin. Left ventricular mechanical efficiency and mechanoenergetic changes were assessed by analyzing the relationship between cardiac work and MVO₂ under various workloads. This study demonstrated that Apocynin treatment improved glucose tolerance, mechanical efficiency and ventricular function in DIO mice. Analysis of ventricular tissue also showed a tendency for reduced myocardial ROS content following Apocynin treatment. These results therefore indicate that there may be a link between myocardial ROS and NOX2 activation in obesity-induced myocardial oxygen wasting.

Impaired left ventricular dia- stolic function and increased systolic contractions in type 2 diabetes compared to healthy controls: a case-control study.

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Background and aims: Left ventricular (LV) myocardial dysfunction is prevalent in type 2 diabetes (T2D). We aimed to compare myocardial systolic and diastolic function in T2D with matched healthy controls (CTRs).

Material and methods: This case-control study involved a clinical examination and detailed echocardiographic assessment, incl. tissue Doppler imaging (TDI) in patients with T2D. CTRs matched for age, gender, weight and systolic blood pressure (BP) were obtained from a population based health survey (HUNT). TDI measures were obtained from stored loops of color tissue Doppler from 2 apical LV views. Diastolic function was evaluated from E/A-ratio, deceleration time (DT) and mitral Doppler early (MVE) and late (MVA) diastolic velocities, and longitudinal myocardial early diastolic velocity (e'). Systolic function was assessed from biplane ejection fraction (EF), peak systolic longitudinal strain and strain rate.

Results: We included 100 patients with T2D (29% females, age/diabetes duration (mean \pm SD) 58 \pm 10/6 \pm 6 yrs, BMI 30.1 \pm 5.5 kg/m², hypertension 68 %, coronary artery disease 26 %, HbA1c 7.6 \pm 1.6%, LDL 2.9 \pm 0.9 mmol/L, BP 141 \pm 18/83 \pm 9 mmHg), and 100 matched healthy CTRs. Patients had higher resting heart rate (72 \pm 12 vs 67 \pm 10 bpm; p=0.001) and diastolic BP (83 \pm 9 vs 79 \pm 8 mmHg; p=0.005). LV cavity diameters were similar while interventricular septum was thicker in T2D (1.1 \pm 0.2 vs 1.0 \pm 0.2 cm, p<0.001). Diastolic function differed adversely in T2D with lower E/A-ratio (0.91 \pm 0.27 vs 1.12 \pm 0.38, p<0.001), deceleration time (195 \pm 49 vs. 242 \pm 72; p<0.001), and e' (5.7 \pm 2.0 vs. 6.6 \pm 1.8, p=0.001), and higher MVA (0.71 \pm 0.13 vs. 0.62 \pm 0.18; p<0.001). Patients with T2D had evidence of increased contractions with higher EF (62.8 \pm 7.7 vs. 55.2 \pm 7.6; p<0.001), longitudinal strain (16.4 \pm 3.9 vs. 15.6 \pm 2.4; p=0.065), and strain rate (1.22 \pm 0.32 vs. 1.04 \pm 0.21; p<0.001).

Conclusion: T2D was characterized by impaired LV diastolic function combined with augmented LV myocardial contractions. This supports that the acknowledged subclinical LV diastolic

dysfunction in T2D is in part compensated by a raised contractile state.

High intensity aerobic exercise in patients with ankylosing spondylitis reduces arterial stiffness: Results from a randomized controlled trial

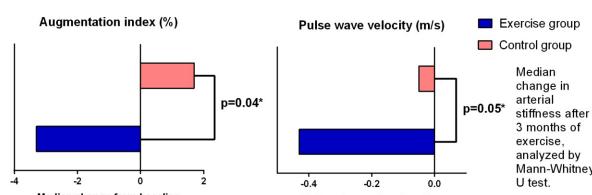
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Objective: Patients with ankylosing spondylitis (AS) are at increased risk of cardiovascular disease. The etiological mechanism or how to reduce risk is not known. Exercise can reduce cardiovascular risk in the general population. The objective was to test whether high intensity aerobic exercise reduces central arterial stiffness in AS patients.

Methods: A proof of concept randomized controlled pilot study. AS patients were allocated to exercise group (EG) or control group (CG). The 3 month exercise intervention, consisted of aerobic high intensity training 40 minutes 3 days a week and muscular strength training 20 minutes twice a week. The control group received care as usual. Augmentation Index (Alx) and pulse wave velocity (PWV) were assessed at baseline and after intervention. Statistical analyses (SPSS 20) were performed using Mann-Whitney U test to compare median change (from baseline to 3 months) of the parameters between EG and CG. Analyses were performed pr protocol.

Results: 28 AS patients were recruited, 24 patients fulfilled the study, 10 in the EG and 14 in the CG. There were some differences in demographics (EG vs. CG): age, years [median (range)] 43 (30-67) vs. 50 (26-68), male gender: 20% vs. 71%. After the study period, arterial stiffness was reduced in the EG compared CG, both significant for Alx (%) [median(range)] -3.3 (-24.5-2.5) vs. 1.7 (-13.5-10.3), p=0.04 and for PWV (m/s) median (range) -0.4 (-1.9-0.1) vs. -0.1 (-1.5-0.1), p=0.05 (figure). The estimated differences (95% CI) were Alx 5.3 (0.5-11.0) and for PWV 0.3 (0.0-0.7), all in favor of the EG.

Conclusion: In AS patients intervention with high intensity aerobic exercise over 3 months reduced arterial stiffness after 3 months compared to controls.



Global longitudinal strain at baseline predicts ventricular arrhythmias in heart failure patients eligible for cardiac resynchronization therapy

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Background: Markers of ventricular arrhythmias in heart failure patients eligible for cardiac resynchronization therapy (CRT) may be valuable for correct choice of CRT, with or without an implantable cardioverter defibrillator (ICD). Echocardiographic strain detects subtle myocardial dysfunction and is shown to predict ventricular arrhythmias in cardiomyopathies. We aimed to explore for echocardiographic predictors of ventricular arrhythmias in CRT-candidates.

Methods: Heart failure patients fulfilling CRT-indications were studied. We performed echocardiography before CRT-implantation. Myocardial function was assessed as ejection fraction (EF) and global longitudinal strain (GLS) from 2D speckle tracking method. Sustained ventricular tachycardia/fibrillation(VT/VF) were recorded during 2 year follow-up and defined as VT with rate ≥ 120 lasting ≥ 30 seconds or appropriate anti-tachycardia pacing or defibrillation.

Results: We included 73 patients (64 ± 10 years, NYHA class 2.8 ± 0.4 , EF $28 \pm 9\%$), 44% with ischemic etiology. Sustained VT/VF was documented in 10 patients (14%) during 2 year follow-up. Left ventricular function by GLS was worse in patients with VT/VF compared to those without (-4.8 ± 2.8 vs. $-8.7 \pm 3.7\%$, $p=0.002$). EF was not a marker of VT/VF (24 ± 8 vs. $29 \pm 9\%$, $p=0.14$). Receiver operating characteristic analysis showed that GLS at baseline had better ability to predict sustained VT/VF than EF with area under curve $0.81(0.67-0.94)$ vs. $0.66(0.46-0.85)$ ($p=0.02$).

Conclusions: Reduced myocardial function by GLS before CRT-implantation was a marker of subsequent ventricular arrhythmias in heart failure patients, while EF was not. Our results suggest that GLS may be part of risk prediction of ventricular arrhythmias in CRT-candidates and may help in the decision making for correct choice of CRT.

Treatment-Resistant Hypertension after Witnessed Intake of Medication before Qualifying Ambulatory Blood Pressure

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Objective: It is unknown whether the decline in blood pressure (BP) after renal denervation (RDN) is caused by denervation itself or concomitantly improved drug adherence. We aimed to investigate the BP lowering effect of RDN in true treatmentresistant hypertension by excluding patients with poor drug adherence.

Design and Methods: Patients with resistant hypertension ($n=18$) were referred for a thorough clinical and laboratory work-up. Treatment-resistant hypertension was defined as office systolic BP >140 mm Hg, despite maximally tolerated doses of ≥ 3 antihypertensive drugs, including a diuretic. In addition, ambulatory daytime systolic BP >135 mm Hg was required after witnessed intake of antihypertensive drugs to qualify. RDN ($n=6$) was performed with Symplicity Catheter System.

Results and conclusion: The mean office and ambulatory BPs remained unchanged at 1, 3 and 6 months in the 6 patients, whereas there was no known change in antihypertensive medication. Two patients, however, had a fall in both office and ambulatory BPs. Our findings question whether BP falls in response to RDN in patients with true treatment- resistant hypertension. Additional research must aim to verify potential BP lowering effect and identify *a priori* responders to RDN before this invasive method can routinely be applied to patients with drug-resistant hypertension.

Clinical Trial Registration - URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT01673516.

Echocardiography may facilitate exclusion of ACS

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Background: Many patients with suspected non-ST-elevation acute coronary syndrome (NSTE-ACS) does not have significant coronary artery disease. Current diagnostic approach with repeated ECG and cardiac biomarkers requi-

res observation for >6-12 hours. This strategy places a heavy burden to hospital facilities. The objective of this study was to investigate whether myocardial strain by echocardiography may exclude significant coronary artery stenosis in patients presenting with suspected NSTE-ACS.

Methods: 64 patients presenting with suspected NSTE-ACS without known coronary artery disease, inconclusive ECG and normal cardiac biomarkers at arrival to the emergency department were enrolled. 12-lead ECG, Troponin T assay and echocardiography were performed at arrival and all patients underwent coronary angiography, after median 26 (IQR 22) hours. ST-segment deviation >1 mm in any ECG lead or T-wave inversions in two or more consecutive leads, and Troponin t >30 ng/L were considered abnormal. Significant coronary stenosis was defined as >50 % luminal narrowing. Global myocardial peak systolic longitudinal strain (GLS) was measured using speckle-tracking echocardiography, as the average value of 16 segments. Left ventricular ejection fraction (LVEF), wall motion score index (WMSI) and GRACE-score were calculated.

Results: No significant stenosis in any coronary artery was found in 35 of these patients (55%). GLS (AUC 0.87) was superior to LVEF (AUC 0.68), WMSI (AUC 0.71) and GRACE score (AUC 0.68) in distinguishing patients with and without significant coronary artery stenosis, with sensitivity and specificity 0.93 and 0.78, respectively and positive predictive value and negative predictive value of 0.74 and 0.92, respectively. Accuracy for GLS was calculated to 78 %

Conclusions: Myocardial strain by echocardiography may become an easily available tool to facilitate exclusion of significant coronary artery stenosis among patients presenting with suspected non-ST-elevation acute coronary syndrome with inconclusive ECG and normal cardiac biomarkers.

Carotid artery plaques are associated with coronary atherosclerosis in patients with inflammatory joint diseases independent of several cardiovascular risk calculators

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Background/Purpose: Patients with rheumatoid arthritis (RA) and carotid plaque (CP) have increased risk of future acute coronary syndrome.

We have established a cardiovascular (CV) preventive clinic and during CV risk evaluation it is of clinical value to know if CP is associated with coronary atherosclerosis (CA) in addition to the CV risk algorithms in patients with inflammatory joint diseases (IJD). Our objective was to evaluate if CP was associated with CA in patients with IJD.

Methods: In a preventive cardio-rheuma clinic, 157 patients with IJD (98 with RA, 42 with ankylosing spondylitis and 17 with psoriatic arthritis) were referred for CV risk evaluation. Traditional CV risk factors were recorded. All patients underwent B-Mode ultrasound of the carotid arteries for evaluation of CP, and multi detector computer tomography (MDCT) coronary angiography for evaluation of CA.

Results: In a cross sectional analysis all patient characteristics as age, traditional CV risk factors and CRP/ESR were comparable across the various IJD, apart from gender ($p<0.01$) and disease duration ($p<0.01$). The presence of CP was also comparable across the various IJD [RA, n= 76 (77.6%), ankylosing spondylitis: 36 (85.7%), psoriatic arthritis 15 (88.2), $p=0.38$]. A total of 98 (62) had CA, while 59 (37.6) did not have CA and there was no difference between the 3 IJD groups. In logistic regression analyses, CP was significantly associated with CA (Figure) independent of the 3 CV risk calculators: SCORE, Framingham and Reynolds (Figure). When number of CP was added in the models, it increased the associations of CP with CA.

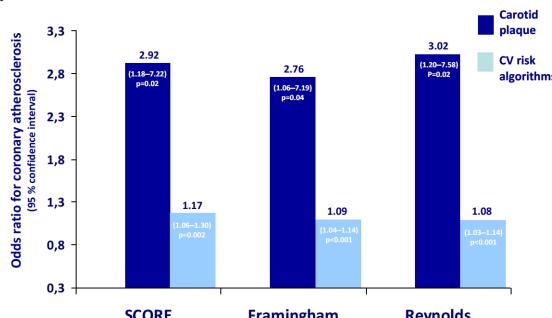


Figure. Odds ratios for coronary atherosclerosis when carotid plaque(s) was present

Conclusion: CP was independently associated with CA. CP can therefore be regarded as CV disease in patients with IJD and has direct clinical implications during CV risk evaluation and prevention.

Presence of chest pain is of limited importance during cardiovascular risk evaluation in patients with rheumatoid arthritis and ankylosing spondylitis

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Objectives: Clinical implementation of cardiovascular (CV) risk evaluation in patients with inflammatory joint diseases (IJD) is in an early phase, despite the high CV risk these patients experience. A vital symptom, which is always asked about during CV risk evaluation, is chest pain. Knowledge about the relation between chest pain and coronary disease in patients with IJD is not previously explored. The aim of this report was to evaluate associations between chest pain, CV risk factors and coronary atherosclerosis (CA) in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) who did not have established CV disease.

Methods: Detailed information concerning chest pain and CV risk factors was obtained in 335 patients with RA and AS. In addition, 119 of the patients underwent multi detector computer tomography (MDCT) coronary angiography.

Results: Thirty-one percent (104/335) reported chest pain. Only 6 patients (1.8%) had atypical angina pectoris (pricking pain at rest). In 69 patients without chest pain, two thirds had CA, while in those where chest pain was reported (n=50), equal many had and did not have CA (Figure). In a logistic regression analysis with CA (by MDCT coronary angiography) as the dependent variable, chest pain was not associated with CA ($p=0.28$). About 30% of CA was explained by any of the three following CV risk calculators: SCORE, Framingham or Reynolds in these models.

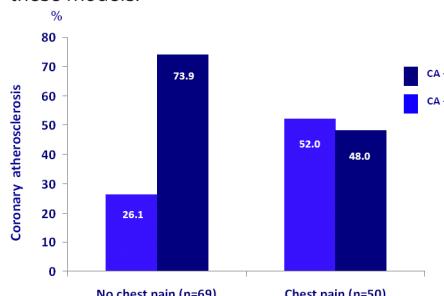


Figure. Chest pain and coronary atherosclerosis in RA and AS

Conclusion: Chest pain was infrequently reported considering the underlying RA or AS disease. Due to the poor association with CA, chest pain was of limited value during CV risk evaluation.

Systemic inflammation in patients with inflammatory joint diseases does not influence statin dose needed to obtain LDL-c goal in cardiovascular prevention

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Objectives: There is a lipid paradox in rheumatoid arthritis (RA) meaning that despite low lipids influenced by systemic inflammation, there is an increased cardiovascular (CV) risk. Our aim is to describe doses of statin needed to obtain recommended lipid goals in patients with inflammatory joint diseases (IJD). Further, to evaluate if baseline lipid levels and - systemic inflammation are associated with the statin dose sufficient to achieve lipid targets in patients with IJD.

Methods: CV risk stratification was performed at the first consultation in 197 patients. The patients were classified to either primary or secondary CV prevention with lipid lowering (LL) treatment, or to have low risk with no indication for medical intervention. LL treatment was initiated with statins and adjusted until at least two lipid targets were achieved. Any side effects/intolerance was recorded. Intensive LL treatment was defined as rosuvastatin > 20 mg, atorvastatin and simvastatin > 80 mg, and conventional LL treatment was defined as all lower doses.

Results: In an independent sample t-test, systemic inflammation (CRP/ESR: p-value 0.10 and 0.11, respectively) and lipid levels (low density lipoprotein cholesterol (LDL-c)/total cholesterol (TC): p-value 0.17 and 0.34, respectively)

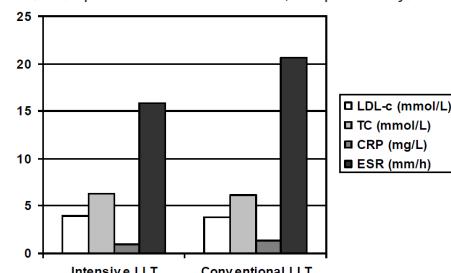


Figure: Doses of lipid lowering treatment (LLT) needed to achieve LDL-c goals

at baseline were not associated with the statin dose needed to achieve LDL-c targets (Figure). Overall, the adverse event rate was low.

Conclusions: Systemic inflammation or lipid levels did not influence statin dose needed to obtain guideline recommended lipid targets in CV prevention. Whether the background inflammation in IJD patients over time influences the CV risk reduction related to statins is yet unknown.

Impact of asymptomatic atherosclerosis on cardiovascular risk stratification and consequences for lipid lowering prevention in patients with inflammatory joint diseases

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Background/Objectives: Patients with carotid plaque (CP) should receive intensive lipid lowering treatment (LLT). Due to the high frequency of CP in patients with inflammatory joint diseases (IJD), we evaluated the impact of CP on cardiovascular (CV) risk stratification and consequences for lipid lowering prevention in patients with IJD.

Methods: CV risk stratification in IJD patients (n= 334) was performed using the systematic coronary risk evaluation (SCORE) algorithm, in addition to ultrasound of the carotid arteries. Cross-tabulations, Chi2 and ROC curves were used to calculate sensitivity and specificity for the SCORE algorithm. The ROC curves closest point (0.1) and 80 % sensitivity were used for optimizing CV risk classification.

Results: Two hundred and forty nine patients with IJD had a SCORE <5 %, indicating no need for LLT. However, 98 (39.4 %) of these patients had CP and should receive intensive LLT. In patients with a calculated SCORE >5 % & <10 % + LDL>2.5 mmol/L (n=58), where moderate LLT is recommended, 38 (65.5 %) patients had CP and should therefore be classified to receive intensive LLT. Thus, patients with CP who were

wrongly classified to receive no (low+moderate CV risk) or only moderate (high CV risk) instead of intensive LLT, was 39.4 % and 65.5 %, respectively. Taken together, 136/307 (44.3 %) of these patients would receive inadequate LLT (Table).

The sensitivity (correctly classifying patients with IJD + CP): 0.39 and the specificity: 0.83. Optimizing SCORE cut off for very high risk, by area under the ROC curves' closest point (0, 1) (resulted in SCORE 2%: sensitivity: 0.73, specificity: 0.62) or 80% sensitivity (resulted in SCORE 1.6%: specificity: 0.56) did not improve correct CV risk stratification in congruence with recommended standards.

Conclusion: Carotid ultrasound contributes to optimized CV risk classification with consequences for CV preventive LLT in patients with IJD.

Effects of physical exercise on coronary artery plaque structure and morphology assessed by grayscale and radiofrequency intravascular ultrasound: A randomized controlled trial.

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Aim: To investigate the effects of two different exercise protocols (aerobic interval training (AIT) versus moderate continuous exercise (MCT)) on coronary artery plaque structure and morphology.

Methods: 36 patients (7 women) on optimal medical treatment with at least one coronary artery stenosis requiring intracoronary stent implantation were included and randomized to AIT or MCT three times a week for 12 weeks. Grayscale- and radiofrequency intracoronary ultrasound was performed at baseline and follow-up. Aerobic capacity (VO_{2max}), endothelial function, and health-related Quality of Life were also assessed. Primary endpoints were analyzed offline at an independent corelab, and included

changes in total atheroma volume, plaque burden, necrotic core, and Virtual Histology morphological plaque classification.

Table

CV risk calculator: SCORE IJD patients (n=334)	Recommended treatment	CP present: Should receive intensive LLT	% classified to no or inadequate LLT
Low + Moderate risk <1% & <5%	No LLT	98/249	39.4
High risk > 5% & <10% + LDL >2.5 mmol/L	Moderate LLT	38/58	65.5
Very high risk >10% & LDL > 1.8 mmol/L	Intensive LLT	16/27	0

Data were analyzed using repeated measures analysis of variance and linear mixed models with maximum likelihood estimations.

Results: VO_{2max} increased more in the AIT group than in the MCT group ($p<0.05$), which arguments different training effects of the two interventions given. There were strong trends towards greater total atheroma volume reduction in distal coronary segments in the AIT group ($p=0.07$), and a reduced plaque burden of 10 percent independently of intervention group ($p=0.06$). Necrotic core volume was reduced in both groups ($p<0.05$), both in distal coronary segments and in morphological lesions. At follow-up, six and four morphological lesions, in the AIT- and MCT group respectively, were transformed into less vulnerable lesions, while three lesions in the MCT group increased vulnerability. Endothelial function and Quality of Life improved in both groups.

Conclusions: Although small, our study strengthens the scientific basis for beneficial effects of physical exercise on coronary artery plaque structure and morphology in optimal medically treated patients with moderate to advanced coronary artery disease.

ClinicalTrials.gov identifier NCT01228201

Baseline CRP but not NSAID-use predicts future increased arterial stiffness in ankylosing spondylitis: Results after 5-year follow up.

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Table

Variables	Univariate beta (95% CI)	p-value	Multivariate beta (95% CI)	p-value
Age (years)	0.7 (0.5-0.9)	<0.001	0.5 (0.3-0.7)	<0.001
Gender, male	-12.0 (-17.3- -6.7)	<0.001	-10.9 (-14.4- -7.5)	<0.001
Education>12 years	-1.0 (-5.3-3.3)*	0.63		
Baseline predictors 2003				
Current smoking	3.9 (-0.5-8.3)*	0.08		
BMI (m ² /kg)	0.8 (0.0-1.6)*	0.04		
NSAID	2.7 (-2.5-7.8)*	0.30		
DMARD	-3.2 (-8.3-1.9)*	0.22		
CRP (mg/l)	0.2 (-0.0-0.3)*	0.06	0.2 (0.0-0.3)	0.02
Current factors 2008				
Height (cm)	-0.3 (-0.5- 0.0)*	0.03		
CMAP (mmHg)	0.3 (0.1-0.5)*	<0.001	0.3 (0.1-0.4)	<0.001
Statins	6.2 (0.9-11.6)*	0.02	6.3 (1.5-11.2)	0.01
Antihypertensives	0.8 (-3.9-5.5)*	0.74		

*adjusted age and gender

Objective: Patients with ankylosing spondylitis (AS) have increased risk of cardiovascular disease (CVD), but do not have a worsened risk profile regarding traditional cardiovascular risk factors. The objective was to investigate whether baseline CRP predicts future increased central arterial stiffness.

Methods: 5-year follow-up study of hospital recruited AS patients, examinations in 2003 and 2008-2009. Demographics, co-morbidities and medication were assessed from questionnaires. Baseline CRP was measured in 2003. Arterial stiffness, measured as Augmentation index (Alx), was recorded in 2008-2009 (Sphygmocor apparatus). We used SPSS 20 for statistical analyses. Univariate associations between Alx and baseline predictors (education, smoking habits, BMI, use of NSAID and disease modifying anti-rheumatic drugs (DMARD), CRP) and factors known to have an effect on Alx (Central mean arterial pressure (CMAP), height, use of statins and antihypertensives) were adjusted for age and gender.

Variables with a p-value<0.2 were included in a multivariate model. Non-significant variables were removed stepwise until only significant variables remained.

Results: 85 AS patients participated. Baseline mean (SD) age was 47.3 (12.6) years, 59% male, 25% smokers. Median (IQR) CRP (mg/l) 4 (2-13). In the multivariate linear regression models CRP was independently associated with higher future Alx (table).

Conclusion: Elevated CRP but not NSAID-use predicted higher future Alx, indicating that inflammation is a risk factor of CVD in AS.

Uveitis is associated to hypertension and atherosclerotic cardiovascular disease in patients with ankylosing spondylitis.

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Background: Uveitis is a common feature of ankylosing spondylitis (AS) and may indicate a more widespread disease. AS patients

are at increased risk of cardiovascular disease (CVD) and the objective was to investigate if AS patients with a history of uveitis is associated to atherosclerosis.

Methods: A cross-sectional study of AS patients recruited from a hospital cohort. Atherosclerosis was defined as either having atherosclerotic CVD and/or carotid plaques (assessed by ultrasound examinations). Univariate analyses with atherosclerosis as dependent variable were adjusted for age and gender. Variables with a p-value ≤0.25 were included in a backwards multivariate logistic regression model.

Results: 159 AS patient participated and 84 (52.8%) had history of uveitis. The patients with uveitis were non-significantly older than patients without uveitis (uveitis vs. no uveitis): 52.1 years vs. 48.8 years, p=0.08 and more patients with uveitis were using TNF-inhibitors (25% vs. 11%, p=0.02). More patients with uveitis had atherosclerosis (43% vs. 21%, p=0.004) and hypertension (30% vs. 11%, p=0.003). There were no significant differences regarding other demographic data, traditional cardiovascular (CV) risk factors, acute phase reactants or use of NSAIDS. In the multivariate logistic regression model uveitis was independently associated to atherosclerosis with an odds ratio (95%CI) of 2.5 (1.1-5.8), p=0.04 (table).

Conclusion: We found a significant independent association between uveitis and atherosclerotic CVD. The clinical implication is that AS patient with a history of uveitis may represent a subset of special awareness regarding management of CV risk factors.

Focus on implementation of cardiovascular risk factor recording for patients with rheumatoid arthritis in a rheumatology outpatient clinic

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Objective: There is a need for clinical implementation of the knowledge of cardiovascular (CV) risk in patients with rheumatoid arthritis (RA). Our aim was to evaluate CV risk factor (CVRF) recording in a rheumatology outpatient clinic (ROC), where the standard was annual CVRF recording. We also evaluated the influence on CVRF recording, comparing a regular ROC (RegROC) to an arthritis clinic (AC), a structured, team-based model.

Methods: In 2012, 1142 RA patients visited the ROC at the Hospital of Southern Norway. Of these 612 attended RegROC and 530 attended AC. We conducted a search in the patient journals to ascertain how many patients had their CVRFs recorded.

Results: CVRFs were recorded in 38.2% of the patients. In only 26.9% all the CVRFs included in the European CV risk calculator, Systematic Coronary Risk Evaluation (SCORE) were recorded. Overall, the rate of CVRF recording was for: blood pressure: 50.4%, total cholesterol: 47.0%, fasting blood glucose: 30.7%, HbA1c: 33.7%, smoking: 66.2%, CV medication: 22.0%

and CV co-morbidities: 20.2%. When comparing AC versus RegROC, odds ratios for CVRFs being recorded in the patient journal was for: BP: 12.4, the various lipids: 5.0-6.0, fasting blood glucose: 9.1, HbA1c: 6.1, smoking: 1.4, CV medication: 6.3 and CV co-morbidities: 6.4.

Conclusion: The overall CVRF recordings were low in a ROC, although a systematic team-based model increased CVRF recording significantly; it was still suboptimal compared to what is shown for other high CV risk patients. There is an unmet need

	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	1.11 (1.07-1.15)	<0.001	1.10 (1.05-1.15)	<0.001
Gender, male	0.88 (0.45-1.74)	0.72	0.52 (0.20-1.36)	0.18
Uveitis	2.57 (1.15-5.72)*	0.02	2.46 (1.05-5.76)	0.04
Education>12 years	0.59 (0.26-1.32)*	0.20		
Current smoking	1.62 (0.64-4.09)*	0.31		
BMI (kg/m ²)	1.10 (0.97-1.23)*	0.13		
Hypertension	2.59 (1.03-6.50)*	0.04		
Diabetes	0.62 (0.12-3.30)*	0.60		
Total cholesterol (mmol/l)	1.09 (0.77-1.55)*	0.65		
LDL (mmol/l)	1.18 (0.79-1.75)*	0.42		
HDL (mmol/l)	0.29 (0.11-0.81)*	0.02	0.29 (0.10-0.83)	0.02
Systolic BP (mmHg)	1.03 (1.00-1.05)*	0.03	1.03 (1.01-1.06)	0.02
Diastolic BP (mmHg)	1.04 (1.00-1.08)*	0.09		
CRP (mg/l)	1.00 (0.96-1.04)*	0.97		
TNF-inhibitor	1.46 (0.52-4.11)*	0.47		
NSAID	1.28 (0.56-2.90)*	0.56		

for systems improving CVRF recording in RA patients.

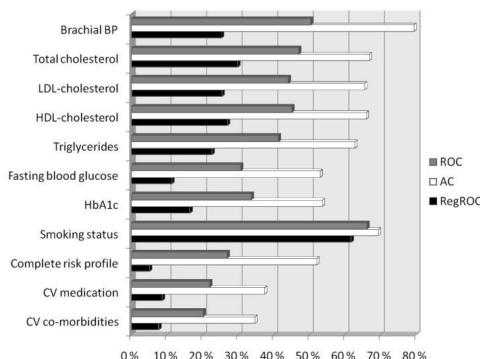


Figure. BP: Blood pressure, Complete risk profile: total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides, smoking and blood pressure, CV medication: Anti-hypertensives and statins, CV co-morbidities: Hypertension, angina pectoris, acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery, cerebrovascular accident, premature familiar cardiovascular disease

Health-related quality of life in ST-elevation myocardial infarction- a comparison of the utilities of 15D and SF-36/6D

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Background: Cardiovascular trials often use a primary composite endpoint for comparing efficacy, analysis focuses on time to first event, whichever that is. There are limitations in this approach, only noticing first event and handling all endpoints as if of equal importance. New methods have been introduced. An alternative might be health-related quality of life (HRQoL) as an endpoint measuring health benefits as quality adjusted life years (QALYs).

The aim of this study was to compare the utility scores obtained from the instrument SF- 36/6D, and from Sintonen's 15D in patients with ST-elevation myocardial infarction (STEMI). Finally, the aim was to evaluate the consequences in estimation of QALYs.

Methods: 266 patients with STEMI treated with tenecteplase were randomised to immediate transfer for angioplasty or standard management. At baseline and all follow-up visits (1, 3, 7, and 12 months) HRQoL data were collected. Those with complete data were included in this

substudy. Agreement between the instruments was assessed by Bland-Altman plots. The incremental QALYs were adjusted for baseline score.

Results: 248 patients were included. The mean utility scores of 15D were higher compared to 6D and distribution differed. Bland-Altman plots indicated moderate agreement between the utilities from SF-6D and 15D. The differences diminished with increasing utility score. Mean QALY for the whole group was higher using 15D than SF-6D (0.89 vs. 0.77). The adjusted incremental number of QALYs were 0.005 (95% CI -0.018 to 0.028) using SF-6D and 0.004 (95% CI -0.010 to 0.018) using the 15D instrument.

Conclusions: SF-6D and 15D generated different HRQoL scores and QALYs in this population. The disagreement is more pronounced in poor health. Even though there was no difference in QALY gains between the two instruments that may not be the case in other trials.

Pregnancy outcome in women with repaired tetralogy of Fallot

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Objectives: The aim of the study was to describe the pregnancy outcome in women with repaired tetralogy of Fallot (TOF) referred to Oslo University Hospital in the period 2006- 2012.

Background: Pregnancy outcome in patients with TOF is incompletely defined. Published studies have reported adverse maternal events during pregnancy related to severe pulmonary regurgitation (PR), right and left ventricular (RV, LV) dysfunction and increased risk of fetal congenital abnormalities (CA) and fetal loss.

Material and methods: Since 2006 a multidisciplinary team has been responsible for pregnancy- and birth healthcare for TOF patients at a Norwegian tertiary center. All pregnant women with TOF referred from 2006 were eligible for the study. Baseline data were registered prospectively, and a retrospective chart review was performed.

Results: Twenty-one women with repaired TOF (mean age 30±5 years), underwent 30 successful pregnancies with live-born offspring. 19 (37%) suffered from mild PR, 11 (22%) moderate PR, and 4 (13%) had severe PR. Twenty-nine (57%) women had mild PS and 4 (8%) developed moderate PS. RV dysfunction occurred in 10 (33%) of the pregnancies and 2 had severe RV dysfunction. One woman had LV dysfunction. Postpartum, two patients developed increasing heart failure due to pulmonary insufficiency, and

underwent pulmonary valve replacement before their second pregnancy. 50% had vaginal delivery. Gestational age at delivery was 39 ± 3 weeks vs. national reference data (NRD) 403. Mean birth weight was 3239 ± 640 g vs. NRD 3500 g. None of the infants had CA.

Conclusions: In this cohort of women with repaired TOF, there were no adverse events related to pregnancy or delivery. All patients had a degree of PR and PS, and 33% had some degree of RV dysfunction. Two patients had a pulmonary valve replacement postpartum. There were no CA, however birth weight and gestational age were slightly lower than NRD.

Impaired RV systolic function in lymphoma survivors after mediastinal radiotherapy.

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Purpose: Lymphoma survivors (LS) have increased cardiovascular disease burden, because of cardiotoxic treatment, in particular anthracyclines (AC) and mediastinal radiotherapy (MRT). Our aim in the present study was to assess RV systolic function after MRT in this patient group.

Methods: We studied 20 LS (median age 46 yr, range 30-70) with MRT (median 30 Gy, range 20-40) and AC-treatment (mean cumulative dose $321 \text{mg/m}^2 \pm 116 \text{mg/m}^2$). Median time since primary treatment was 10 years (range 5-29). These patients are included in a Norwegian national follow up study of LS after high dose chemotherapy with autologous stem cell transplantation (HDT). In total 22 AC-treated patients (mean cumulative dose $308 \text{mg/m}^2 \pm 65 \text{mg/m}^2$, $p=0.67$) from the same follow-up study without MRT were matched for age, gender and body mass index, and used as controls. Conventional echocardiograms were obtained by a Vivid 7 or E9 (GE Vingmed, Norway). RV global longitudinal strain (GLS) by two-dimensional speckle tracking and fractional area change (FAC) of the RV were both measured from the apical four chamber view.

Results: We found a significantly impaired RV systolic function in the MRT-group, as judged from a lower RV GLS and FAC. Conventional echocardiographic measures of RV function did not differ (Table 1).

Conclusions: RV systolic function is impaired in LS after HDT when MRT are added to AC. RV GLS and FAC are more sensitive than conventional parameters for right heart systolic function in this setting.

Table 1:

Variable	+MRT n=20	-MRT n=22	P
RV GLS (%)	-19.5 ± 3.4	-22.8 ± 2.6	0.004
FAC (%)	41 ± 5	46 ± 4	0.005
TAPSE (cm)	2.1 ± 0.5	2.3 ± 0.5	0.14
Displacement RV (mm)	19.2 ± 5.7	21.1 ± 3.9	0.23
s' RV (cm/s)	12.2 ± 2.7	13.5 ± 2.0	0.10
TRV (m/s)	2.3 ± 0.4	2.3 ± 0.3	0.75
RA area (cm ²)	14.2 ± 3.5	15.0 ± 3.9	0.56

Pretest characteristics of elective patients below 60 years with chest pain and no known coronary heart disease referred to angiography.

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Background: The yield of stenosis when examining patients with suspected coronary heart disease is below 30-40% in industrialized countries. Cardiovascular risk scoring is a better selection criterion than non-invasive testing, but still with a low positive predictive value. The aim of the present study was to detect significant pretest predictors of patients with need of revascularization.

Methods: All 1893 patients below 60 years of age without previous known coronary heart disease referred to invasive angiography in the period 2005-2010 were selected from the clinical database at the University Hospital North Norway. The angiograms were characterized as normal (lumen <25% atherosclerosis), Nonobstructive atherosclerosis (lumen 25-50%) or stenosis when lumen was less than 50%. A random sample of 150 subjects with normal, 150 with nonobstructive lesions and 150 with stenosis were selected half from women and half from men.

Results: 46% of men and 18% of women had stenosis. As significant predictors of stenosis we found presence of typical retrosternal angina symptoms, lack of relation to exercise predicted normal coronaries as well as only second degree relatives with coronary heart disease. A positive stress ECG and NORRISK score was only significant in men and diabetes only in women. Canadian Cardiovascular Society angina score was not significant, but became significant in men if chest pain without relation to exertion was excluded. In multivariable models Stress ECG, NORRISK score and classification of symptoms were significant in men with a ROC of 80% and classification of

symptoms and a history of diabetes in women with a ROC of 70%. Extrapolated to the total sample the model had a negative predictive value >90% in 11% of men and 24% of women.

Conclusion: A better pretest selection of patients in need of referral to angiography is possible based on co-morbidity, symptoms, cardiovascular risk score and stress ECG.

Septal hypofunction and excessive load on the right ventricular free wall in patients with transposition of the great arteries and atrial switch.

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Purpose: A non-invasive regional work analysis of the systemic right ventricle (RV) in patients with transposition of the great arteries (TGA), in order to characterise differences in work which may contribute to ventricular dysfunction.

Methods: Ten patients (33 ± 6 (mean \pm SD) years) were studied 32 ± 5 years after operation with atrial switch (Senning: 7 and Mustard: 3). ProBNP (n=8) was 30 ± 13 pmol/L. Arterial blood pressure was $116 \pm 13 / 72 \pm 12$ mmHg and QRS duration 107 ± 28 ms. Longitudinal strains were measured by speckle tracking echocardiography (GE Vivid E9) from apical 4 chamber views. RV pressure was estimated non-invasively using a standard pressure waveform fitted to

the specific patient. Pressure-strain loop areas were used to represent regional myocardial work (Figure). In four patients we also obtained parasternal short axis views and calculated circumferential strains and pressure-strain loops. Additionally, circumferential wall stress was computed by taking into account regional RV curvature.

Results: There was increased regional contraction in RV free wall compared to septum, as confirmed by peak longitudinal (-19 ± 3 vs. $-14 \pm 2\%$, $P < 0.01$) and circumferential (-18 ± 5 vs. $10 \pm 3\%$, $P < 0.05$) systolic strain. Correspondingly, longitudinal and circumferential work in RV free wall was also increased compared to septum (1848 ± 344 vs. 1128 ± 252 mmHg·%, $P < 0.01$ and 1691 ± 634 vs. 747 ± 265 mmHg·%, $P < 0.05$). Similar findings were seen in work using wall stress (64 ± 31 vs. 34 ± 23 J/m², $P < 0.01$).

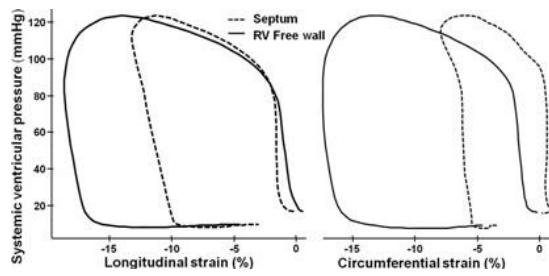


Figure. Average pressure-strain loops from all patients

Conclusions: In TGA patients there was septal hypofunction as demonstrated by strain and work measurements. This was compensated by increased contraction and high workload in the RV free wall. Consequently, this imbalance may be related to a greater risk of developing heart failure in these patients.



Rune Wiseth takkes for sin innsats for høstmøtet.