ABSTRAKTER PRESENTERT PÅ HØSTMØTET

Reduction in time to coronary angiography among patients with NSTEMI: Results from a quality improvement project at Haukeland University Hospital (HUS)

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Background: European guidelines recommend that coronary angiography is performed within 24 h after presentation among patients with non-ST-elevation myocardial infarction (NSTEMI). Results from Norwegian Registry for Invasive Cardiology (NORIC) have shown that median time to angiography at HUS were 1.8 days among patients admitted directly to HUS and 3.1 days among patients referred from other hospitals in 2015.

Methods: In order to reduce waiting time, a quality improvement project was started. Major changes were:

- Next day transfer from local hospital without referral
- Encourage local hospitals to call, rather than fax referral
- No compulsory echo before transfer
- V-scan upon arrival
- Increased focus and strict NSTEMI priority in cath lab
- Same day angio for all patients with NSTEMI in HUS identified before 11 am
- Time to angiography was studied through data registered in NORIC.

Results: Median time to angiography for patients admitted directly to HUS was reduced from 1.8 days in 2015 to 1.1 days 2016 and among patients referred from other hospitals from 3.1 days in 2015 to 1.9 days in 2016.

Further analyses showed that there were marked differences in waiting time depending on which weekday the patients were admitted to hospital. Patients admitted to referring hospitals on Fridays had the longest time to angiography of all groups.

Conclusion: Time from admission to coronary angiography was significantly reduced from 2015 to 2016 among patients with NSTEMI as a result of a quality improvement project at HUS. Further reduction would require earlier referral from local hospital, more efficient transport and increased capacity for angiography on weekends.

Randomised comparison of left ventricular assist device versus bi-ventricular assist devices in cardiac arrest

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Aim: To assess whether a percutaneous right ventricular impella assist device (RVAD) in adjunct to a percutaneous left ventricular impella assist device (LVAD) could be beneficial in cardiac arrest.

Methods: Twenty anesthetised pigs were randomised to receive maximised support by percutaneously implanted uni- or biventricular assist device(s) during 30 minutes of electrically induced ventricular fibrillation followed by 3 attempts of cardioversion. Continuous haemodynamic variables were recorded. Cardiac output, myocardial, cerebral, renal and ileum mucosa tissue perfusion were measured with fluorescent microspheres, and repeated blood gas analyses were performed.

Results: Higher LVAD output, mean aortic pressure, and end-tidal CO_2 could be maintained with biventricular support but at the cost of an increased left ventricular pressure. Tissue blood flow rates were higher for most organs with BIVAD, and blood gas analyses showed better oxygenation with lower s-lactate values and normal pH. Myocardial perfusion was significantly better in the LVAD group, and return of spontaneous circulation more frequent (10/10 vs. 5/10, p = 0.033). Univentricular support was associated with lower mean left ventricular pressure and

higher perfusion pressure, which correlated significantly with flow rates in the three layers of the left ventricular wall. A transmural gradient was observed for both support modes, with better maintained sub-epicardial than mid-myocardial and sub-endocardial circulation.

Conclusion: During ventricular fibrillation, biventricular support provides better systemic circulation with improved vital organ blood flow compared to univentricular support. However, myocardial perfusion was low and related to increased interventricular pressure and reduced rates of successful resuscitation.

Grading of aortic stenosis: Can three-dimensional transthoracic echocardiography be the preferred method?

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Background: Establishing the true severity of aortic stenosis (AS) is challenging in cases with discordant grading/low-gradient aortic stenosis. Calculation of the aortic valve area (AVA) with the continuity equation includes measurement of the left ventricular outflow tract (LVOT) diameter with two-dimensional transthoracic echocardiography (2DTTE). The LVOT is often elliptical, and the diameter obtained in 2DTTE is the shortest, which results in imprecise calculations of the LVOT area and AVA. We investigated whether 3DTTE measurements of the LVOT could provide a more accurate calculation of the AVA, and thereby potentially a more reliable grading of AS. We used computer tomography (CT) as reference.

Method and results: 41 patients referred for intervention of severe AS underwent 2DTTE, 3DTTE and CT measurements of LVOT area and maximum and minimum diameters. An acceptable LVOT evaluation was obtained in 73% of patients with 3DTTE and 100% with 2DTTE and CT, leaving 30 patients for comparison of the three methods. Correlations between CT and 3DTTE were r = 0.47 ($p<0.004$) for minimum diameter, r = 0.30 (n.s.) for maximum diameter, and r =0.51 ($p<0.008$) for LVOT area. Correlations between CT and 2DTTE were r= 0.50 ($p<0.005$) for minimum diameter and, r = 0.62, ($p<0.000$) for LVOT area. In 20 patients 3DTTE Interclass correlation coefficients (ICC) for interobserver variability were 0.63 for LVOT area, 0.56 for maximum diameter and 0.55 for minimum diameter. ICC for 2DTTE was 0.86 for minimum diameter.

Conclusions: 3DTTE measurements of LVOT dimensions were only feasible in a subset of patients and did not correlate better with CT than 2DTTE. ICC was higher in 2DTTE.

Effect of strenuous exercise on mediators of inflammation in patients with coronary artery disease

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Background: Acute strenuous exercise is an acknowledged trigger of acute coronary events. Coronary artery disease (CAD), being considered a low-grade inflammatory disease, makes underlying pathophysiological mechanisms of great interest. We aimed to identify effects of short-term strenuous exercise on mediators of systemic inflammation, endothelial and platelet activation in patients with angiographically verified CAD. We hypothesized that a more pronounced inflammatory response would be present in patients with CAD than in those without CAD.

Methods: In subjects with symptoms indicative of CAD, an exercise stress test on a bicycle ergometer was performed. Venous blood samples, taken at rest and within 5 min after termination of exercise, were analysed for the following markers by ELISAs: IL-6, MCP-1, TNF-α, ICAM-1, VCAM-1, E-selectin, P-selectin, CD40L and RANTES. All participants underwent conventional coronary angiography. CAD was defined as having any degree of atherosclerosis.

Results: A total of 110 patients were included, of whom 74 were found to have CAD. Mean exercise duration was 10:06 ± 3:56 min with no significant difference between the two groups. All measured markers increased during exercise ($p \leq 0.012$). A significantly less pronounced increase in CD40L in the CAD group than in the no CAD group, was observed ($p = 0.05$), however, after

adjustment for hematocrit this difference was no longer significant. P-selectin increased to a higher extent in patients without CAD after hematocrit adjustment, results where however of borderline significance (p = 0.074).

Conclusion: An instant inflammatory response was observed during short-term strenuous exercise in patients with symptoms of CAD. However, the exercise mediated response was not more pronounced in patients with angiographically verified coronary atherosclerosis.

Mechanical dispersion: a sensitive marker of left ventricular dysfunction in stable coronary artery disease

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Background: Both cardiac biomarkers and traditional echocardiographic measurements are important in the early identification of subclinical left ventricular (LV) dysfunction. However, it is largely unknown whether LV mechanical dispersion is relevant in this context.

Purpose: We wanted to elucidate the role of LV mechanical dispersion in the identification of subclinical LV dysfunction, as assessed by sensitive cardiac biomarkers and all-cause mortality, in patients with stable coronary artery disease (CAD).

Methods: We included 160 patients with stable CAD, one year after successful coronary revascularization. LV systolic function was assessed through measurement of ejection fraction (EF), global longitudinal strain (GLS) and mechanical dispersion. Serum levels of high-sensitivity cardiac troponin I (hs-cTnI, Abbott) and amino-terminal pro B-type natriuretic peptide (NT-proBNP, Roche) were quantified and used as established markers of LV dysfunction. An end point of time to first event of all-cause mortality was generated.

Results: Baseline mean LV mechanical dispersion was 46±14 ms. LV mechanical dispersion correlated with both hs-cTnI (R=0.450, $p<0.001$) and NT-proBNP (R=0.379, $p<0.001$). During a mean follow up period of 3102±128 days, 14 events were registered. Overall, LV mechanical dispersion was significantly increased in nonsurvivors, and was significantly associated with mortality (hazard ratio 1.05; 95% CI, 1.00-1.09; $P<0.05$) in a Cox model adjusted for both LV EF and GLS. Continuous net reclassification improvement (NRI) showed that LV mechanical dispersion did not add incremental value when LV GLS was known.

Conclusion: LV mechanical dispersion may give additional information of LV dysfunction to traditional echocardiographic measurements in patients with stable CAD.

Markers of neutrophil extracellular traps are associated with new cardiovascular events in patients with stable coronary artery disease

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Background/aims: Neutrophil extracellular traps (NETs), comprising nuclear content and granule proteins, are expelled from neutrophil granulocytes in a process termed NETosis, and are thought to play a central role in atherothrombosis. We investigated whether the circulating NETs markers, double-stranded DNA (dsDNA) and myeloperoxidase-DNA (MPO-DNA), are associated with future clinical outcome in patients with stable coronary artery disease (CAD).

Material/methods: Patients with angiographically verified stable CAD (n=1001) enrolled in the ASpirin non-responsiveness and Clinical Endpoints Trial (ASCET)* were included. Follow-up

was ≥2 years, recording 106 clinical endpoints (unstable angina, non-hemorrhagic stroke, myocardial infarction, or death). Blood samples collected at baseline were used to measure serum dsDNA and MPO-DNA using Quant-iT PicoGreen® and ELISA, respectively.

Results: Significantly higher dsDNA levels (median (25^{th},75^{th} percentile)) were observed in the group reaching clinical endpoint as compared to those without (402 ng/ml (372,447) vs. 393 ng/ml (359,433), p=0.019). Patients with dsDNA in the upper three quartiles versus the lowest quartile were more likely to suffer the clinical endpoint, also after adjusting for relevant covariates (OR 1.87, 95% CI [1.07,3.30], p=0.029). Levels of dsDNA correlated with neutrophil count, body mass index, LDL-cholesterol, and triglycerides (r=0.11-0.26, p≤0.001 for all). Males, smokers, and patients with metabolic syndrome had significantly higher levels of dsDNA (p≤0.002 for all). The highest quartile of dsDNA was associated with elevated markers of hypercoagulability (prothrombin fragment 1+2, D-dimer, free and total TFPI (p<0.001 for all)). The two NETs markers were only weakly inter-correlated (r=0.103, p=0.001), and no significant associations to clinical endpoints, cardiovascular risk factors or hypercoagulability were encountered for MPO-DNA levels.

Conclusions: DsDNA levels were related to adverse clinical outcome, as well as several cardiovascular risk factors. DsDNA levels associated significantly, although weakly with a prothrombotic state, suggesting that other detrimental NETs effects also may be important in atherothrombosis.

Systematic screening for atrial fibrillation in a 65-year-old population with risk factors for stroke – data from the Akershus Cardiac Examination (ACE) 1950 Study

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Background: The prevalence of undiagnosed or subclinical atrial fibrillation (SCAF) has been estimated to a third of the total atrial fibrillation (AF) population. Systematic screening has been suggested to diagnose subjects with SCAF above the age of 65 years, in order to identify candidates for anticoagulation treatment to prevent stroke.

Aim: To investigate the yield of screening for AF in a cohort of 65-year-old individuals from the general population with additional risk factors for stroke.

Methods: We invited participants with additional risk factors for stroke (CHA_2DS_2-VASc score ≥2 for men or ≥3 for women) without previously known AF from the population-based *Akershus Cardiac Examination (ACE) 1950 Study* to participate in a two-week screening for AF. Screening was performed by 1-lead "thumb-ECG" recordings of 30 seconds twice daily or when the participants experienced symptoms.

Results: In total, 1742 (47.0%) of the ACE 1950 study participants had at least one additional risk factor for stroke. Out of these, 123 reported a history of AF, and 101 (5.8%) cases were ECG-validated. Eight (0.5%; 95% confidence interval [CI], 0.2–0.9) new AF cases were diagnosed by 12-lead ECG at baseline, and 10 additional participants were diagnosed with AF before screening commenced. We invited all 1601 participants who met the inclusion criteria for screening, of which 1510 (94.3%) were included (44% women, 56% men). The screening revealed AF in 13 (0.9%; 95% CI, 0.5–1.5) participants. The total prevalence of ECG-validated AF after screening among 65-year-olds with risk factors for stroke was 7.6% (95% CI, 6.4–8.9); in men 10.0% (95% CI, 8.2–12.0) and in women 4.3% (95% CI, 3.0–6.1); p<0.001.

Conclusion: In a group of 1510 well-characterized 65-year-olds with risk factors for stroke, two-week intermittent ECG screening identified undiagnosed AF in 0.9%. The total prevalence of AF was 7.6%.

Prolonged release of cardiac troponin I after endurance exercise could indicate silent coronary artery disease in recreational athletes, cut-off values proposed: the NEEDED study 2014

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Background: Sudden cardiac death (SCD) among recreational athletes is predominantly due to coronary artery disease (CAD). It's unclear whether the magnitude of the exercise-induced cTn increase can be used to identify recreational athletes at risk of cardiac events. The aim of this study was to assess whether the magnitude of the exercise-induced cTn increase is associated with presence of obstructive CAD.

Methods: 1002 healthy subjects (45.6 (39.7-50.9)) years (median (IQR)), 78.1 % males) who participated in a 91-km mountain bike race were included. Clinical status, blood samples, ECGs, blood pressure and demographics were obtained 24 h prior to the race, and 3 and 24 h after the race. Coronary Computed Tomography Angiography (CCTA) was performed in the 80 subjects with highest post-exercise cTnI, and in a control group of 40 subjects with moderately elevated cTnI concentrations matched for age, sex and race performance.

Results: 84.1 % exceeded the 99th percentile of the assay (26 ng/L). In the CCTA cohort 11 (9.2 %) participants were found to have obstructive CAD, and these had higher cTnI values than the rest of the participants, particularly at 24h after the race (p=0.001). ROC-AUC for identifying obstructive CAD for cTnI 24h after the race was calculated to 0.80. A cut-off value of 101 ng/L had a sensitivity of 81.8 % and a specificity of 80.7 % in predicting obstructive CAD, and numbers needed to screen to find one subject with obstructive CAD was 4.7.

Conclusion: A prolonged post-exercise cTn response is associated with increased incident of obstructive CAD. Having a cTnI value above 101 ng/l 24h after exercise should be considered a potential pathological finding and further investigation are warranted.

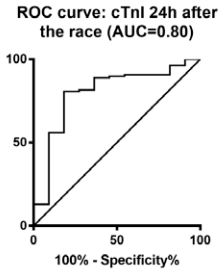

Figure: cTnI 24h after the race, ROC-curve (total n=120, obstructive CAD n=11). AUC=0.80.