ABSTRAKTER PÅ NCS' VÅRMØTE 2014

Diastolic function during exercise: effects of a 12 week high-intensity exercise program in patients with a recent myocardial infarction

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Purpose: Reduced left ventricular (LV) diastolic function is a negative prognostic marker after acute myocardial infarction. High-intensity interval training can improve functional capacity in myocardial infarction patients, but it is not known whether it can improve diastolic function. Our aim was to study whether a twelve-week high-intensity interval training program could improve diastolic function in patients with a relatively recent myocardial infarction.

Methods: Twenty-eight patients (24 males, 3 females, mean age = 56 (8) years, mean time from infarction = 74 (32) days) performed high-intensity interval training twice a week for 12 weeks. Each training session consisted of four 4-minute intervals at 85-95% of peak heart rate, separated by 4-minute active breaks at 70%. A cardiopulmonary exercise test was performed to determine peak oxygen uptake (VO2peak). Echocardiography, including color tissue Doppler of the LV, was performed during supine rest and during an upright bicycle exercise test (peak load 75 Watt).

Results: There was a significant increase in VO2peak from baseline to follow-up (35 (7) vs. 39 (7) ml/ (kg*min), $p < 0.001$). The only echo variable that correlated with VO2peak both at baseline and follow-up was mitral annulus early diastolic velocity (e') at peak exercise (75 Watt) ($r = 0.50$, $p = 0.007$, and $r = 0.41$, $p = 0.032$, respectively). There was a significant increase in e' at peak exercise from baseline to follow-up (7.9 (1.5) vs. 8.4 (1.7) cm/s, $p = 0.012$), but no differences in e' at rest (7.1 (1.9) vs. 7.3 (1.7) cm/s, $p = 0.42$). There was a significant increase in early diastolic inflow velocity (E) at 25 Watt (67 (11) vs. 73 (13) cm/s, $p = 0.007$), but not at rest (69 (17) vs. 71 (15) cm/s, $p = 0.54$) or peak exercise (87 (15) vs. 90 (15) cm/s, $p = 0.26$). There were no changes in other variables describing left ventricular diastolic function: E/A ratio at rest (1.2 (0.3) vs. 1.1 (0.3), $p = 0.45$), E/e' at rest (10 (3) vs. 10 (2), $p = 0.84$) or E/e' at peak exercise (11 (3) vs. 11 (3), $p= 0.70$). There were no changes in variables describing left ventricular systolic function: mitral annulus systolic velocity (s') at rest (6.0 (1.0) vs. 5.9 (0.8) cm/s, $p = 0.68$), s' at peak exercise (7.7 (1.0) vs. 7.9 (1.3) cm/s, $p = 0.41$), or mitral annular plane systolic excursion at rest (13 (3) vs. 13 (2) mm, $p = 0.32$). Heart rate was unchanged at rest (59 (7) vs. 58 (8), $p = 0.17$) and at peak exercise (95 (13) vs. 92 (11), $p = 0.14$).

Conclusion: The present study shows that left ventricular diastolic function during exercise is related to VO2peak. We also found an improvement of diastolic function after exercise training, even in a population with a relatively well preserved systolic and diastolic function. The results demonstrate the importance of obtaining measurements during exercise when evaluating the effects of an exercise training intervention.

Elevated plasma dimethylglycine is a risk marker of mortality in patients with coronary heart disease

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Aim To investigate whether plasma dimethylglycine levels were associated with and improved risk prediction of mortality among patients with coronary heart disease (CHD).

Methods By Cox modelling, we explored the association between plasma dimethylglycine and mortality in two independent cohorts of patients with suspected stable angina pectoris (SAP) (n = 4156) and acute myocardial infarction (AMI) (n = 3733). We also assessed any improvement in risk prediction by adding plasma dimethylglycine to established CHD risk factors.

Results Median follow-up time was 4.7 and 7.0 years among patients with SAP and AMI, respectively. Across both cohorts, elevated plasma dimethylglycine levels were linearly associated with increased risk of all-cause mortality (age and gender adjusted hazard ratios (95% confidence interval, CI) were 1.72 (1.21–2.46) and 1.76 (1.42–2.18) when comparing the fourth versus the first plasma dimethylglycine quartile in patients with SAP and AMI, respectively). There was a particularly strong risk association between plasma dimethylglycine and cardiovascular, as compared with non-cardiovascular, mortality (age and gender adjusted hazard ratios (95% CI) 1.94 (1.21–3.11) and 1.43 (0.83–2.47) among patients with SAP and 1.97 (1.50–2.59) and 1.44 (1.02–2.04) among patients with AMI, respectively). The relationship between dimethylglycine and all-cause and cardiovascular mortality was only slightly attenuated in analyses adjusted for established CHD risk factors. Among patients with SAP the adjustment for serum high sensitive cardiac troponin T levels did not influence the risk estimates. Plasma dimethylglycine also improved risk prediction for all-cause and cardiovascular mortality, and especially among patients with AMI.

Conclusions Elevated plasma dimethylglycine levels were associated with and improved risk prediction of mortality in patients with suspected or verified CHD. This relationship was stronger for death from cardiovascular, as compared with non-cardiovascular, causes, and seemed independent of traditional CHD risk factors.

β-blockade abolishes the augmented cardiac tPA release induced by transactivation of heterodimerized bradykinin receptor-2 and β2-adrenergic receptor in vivo

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Background: Both bradykinin (BK) infusion and cardiac sympathetic nerve stimulation (SS), induce cardiac tissue plasminogen activator (tPA) release. In transfected frog oocytes, BK-receptor 2 (BK2R) and β2-adrenergic receptors (β2AR) form heterodimers which may allow cross-talk between the receptors. However, clinical consequences of this receptor interaction have so far not been shown. Accordingly, in the present study, we investigated the interplay between BK and SS stimulation on cardiac tPA release, and furthermore, if β-blockade affected this potential interplay. Finally, we examined physical interaction between BK2R and β2AR in left ventricular myocardium (LVM).

Methods: Six pigs were subjected to 4 min of electrical SS1. Thirty min later, 9 min of coronary BK1 infusion was given, and the last 4 min with simultaneous SS2 (BK1/SS2). Subsequently, β-blocker (propranolol) was given and the stimulations repeated (BK2 and BK2/SS3). Blood was collected frequently from the coronary vein and the femoral artery to determine cardiac tPA release. Co-immunoprecipitation studies in lysates from pig LVM were performed using antibodies against β2AR and BK2R.

Results: SS1 induced a 6.3 ± 2.2-fold increase in tPA release compared to baseline, whereas BK1 induced a 13.2 ± 4.8-fold transient tPA response with return to baseline despite continuing BK infusion. At this point, BK1/SS2 induced 13.5 ± 4.7-fold increased tPA release, 2.3 ± 0.3-fold compared to SS1. β-blockade prevented increments in BK2 and BK2/SS3-induced tPA release. Co-immunoprecipitation studies demonstrated interaction between BK2R and β2AR in LVM.

Conclusions: We demonstrated physical interaction between BK2R and β2AR in pig LVM. Despite desensitized BK2R in vivo and abolished tPA release, BK still enhanced SS-induced cardiac tPA release indicating BK-transactivation of the β2AR. β-blocker inhibited both SS and combined BK/SS-induced tPA releases. Importantly, this is the first in vivo study demonstrating interplay between SS and BK stimulation through BK transactivation of BK2R-β2AR, leading to enhanced SS-induced cardiac tPA release..

Aerob intervalltrening reduserer mengde atrieflimmer

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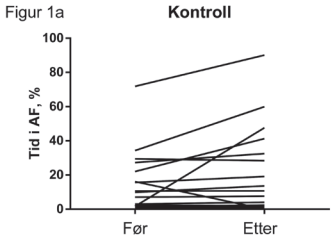
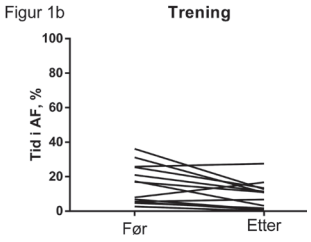
Bakgrunn: Utholdenhetstrening er en effektiv behandling av mange risikofaktorer og sykdommer assosiert med atrieflimmer (AF). Imidlertid tyder epidemiologiske data på at høye volum med utholdenhetstrening øker risikoen for AF. I denne studien vurderes effekten av aerob intervalltrening hos pasienter med AF.

Metoder: 51 pasienter med paroksysmal eller persisterende AF ble randomisert til aerob intervalltrening (n=26) bestående av 4 x 4 min med gange/løping på tredemølle, ved 85-95% av maksimal hjertefrekvens, 3 dager/uke i 12 uker, eller til en kontrollgruppe (n=25). En implanterbar loop recorder (ILR) målte tiden i AF kontinuerlig fra 4 uker før, til 4 uker etter intervensjonsperioden. Hjertefunksjon,





lipidstatus og livskvalitet ble målt før og etter intervensjonsperioden.

Resultater: Det var en økning av tid i AF i kontrollgruppen og en reduksjon i treningsgruppen (P=0.001 mellom gruppene). Trening reduserte odds for å ha AF på et vilkårlig tidspunkt i perioden etter trening med en observert faktor på 0,28 (Odds Ratio). Det ble registrert en nedgang av tid i AF hos 10 pasienter i treningsgruppen og 5 pasienter i kontrollgruppen, mens det var en økning av mengde AF hos 3 pasienter i treningsgruppen og 16 pasienter i kontrollgruppen. Det var en trend mot færre elektrokonverteringer (1 vs. 6, P=0.14) og sykehusinnleggelser (1 vs. 9, p=0.07) i treningsgruppen. Det var ingen signifikante endringer i bruk av antiarytmisk medikasjon mellom gruppene i studieperioden. I treningsgruppen var det en signifikant økning i maksimalt oksygenopptak (VO2Peak) (9.5% vs. -1.1%, p=0.002), venstre atriums ejeksjonsfraksjon under atrial systole (+1,7% vs. -5.0%, p=0,007) og venstre ventrikkels ejeksjonsfraksjon (+3.2% vs. -1.6%, p=0.03) målt ved MR. Livskvalitetsmål (SF-36) på generell helse og vitalitet økte, mens det var en signifikant nedgang i total kolesterol (-0.38 mmol/L vs. +0.13mmol/L, p=0.009) og triglyseridnivå (-0.23 mmol/L vs. +0.18 mmol/L, p=0.008) sammenlignet med kontrollgruppen. Konklusjon: Aerob intervalltrening i 12 uker reduserer mengde AF og forbedrer VO2Peak, venstre atrie- og ventrikkelfunksjon, lipidverdier og livskvalitet hos pasienter med anfallsvis AF. Det trengs ytterligere studier for å vurdere underliggende mekanismer og effekt av utholdenhetstrening over en lengre tidsperiode.

Delay in treatment of patients with NSTEMI at the Department of Heart Disease, Haukeland University Hospital

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Background: Patients with acute coronary syndrome (ACS) without persistent ST-segment elevation constitute a large group of patients treated for cardiac disease. If myocardial markers (troponin) are elevated (rise and fall), it is considered as non-ST-elevation myocardial infarction (NSTEMI). According to guidelines from ESC from 2011(1), an early invasive strategy, within 2-72 hours from symptom onset, is recommended in NSTEMI. A meta analysis (2) further shows that early coronary angiography and intervention reduce new ischemic episodes and shorten the hospital stay in NSTEMI patients.

The Norwegian registry for invasive cardiology (NORIC) is a national quality registry which from January 2014 includes all invasive coronary procedures performed at hospitals in Norway. The local database at Haukeland University Hospital (HUS) has data from January 2013.

Aim of the study: To use NORIC in order to study the time from hospital admission to coronary angiography for NSTEMI patients, and evaluate our practice according to current guidelines. We also wanted to examine if there is a delay in treatment of patients referred to HUS from other hospitals compared to those admitted directly to HUS (primary PCI unit), and examine if differences in age, ejection fraction (EF) and biochemical data, available before angiography, could be related to any delay.

Methods: Data is collected from NORIC local database at HUS; all patients with NSTEMI admitted at HUS who had performed coronary angiography during 2013.

Results: From hospital admission to coronary angiography, there is mean 5.2 days (median 4 days) for all patients (n=768) with NSTEMI. For patients primarily admitted to HUS (n=286), this period is mean 3.9 days (median 3 days), as compared to patients referred from other hospitals (n=429) (6 days, median 5 days).

Analyses in different age groups reveal a trend towards an increasing delay with age, with a mean of 3.6 days among patients < 50 years (median 3 days) to mean 6.2 days in patients > 80 years (median 5 days). High CRP and low Hb in blood test available before angiography seems to be related to delay. Also patients with reduced EF experience more delay: EF<50% mean >7.5 days (median days) EF >50% mean 4.8 days (median days).

Conclusion: The time from hospital admission to performed coronary angiography is too long in NSTEMI patients, and not according to current guidelines. The discrepancy between patients who are admitted directly to HUS versus referred patients is a cause of concern. In our analysis the blood works do not explain this difference. According to guidelines, reduced EF is a risk factor promoting early invasive examination, but our data suggest that these patients are delayed for coronary angiography. We have to look further

into factors explaining why patients with increasing age get a lower priority.

ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent St-segment elevation, Eur Heart J 2011; 32: 2999-3054

Metaanalyse i EHJ 2011(32,32-40 doi:10.1093/eurheart/ehq276)

Incidence of atrial fibrillation requiring ablation after elective cavotricuspid isthmus ablation for atrial flutter. Can flecainide complicate the clinical evaluation?

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Introduction: Previous studies showed that a large proportion of patients develops atrial fibrillation (AF) following cavotricuspid isthmus (CTI) ablation for CTI-dependent atrial flutter (AFL). In a significant proportion of these, symptomatic AF will require an additional dedicated ablation procedure exposing to higher economic burden and enhanced risk of complications. It is of importance to investigate parameters that may predict occurrence of symptomatic AF and rather recommend a combined AF and AFL ablation in these patients.

Methods: 133 patients (109 male, age 60±10 years) treated between 2006 and 2012 with elective CTI ablation (index procedure) for AFL at our institution, were included in this study. Patients were referred with a clinical history of recurrent, symptomatic AFL and typical electrocardiographic documentation. Although AF was previously documented in 59 patients, AFL was deemed to be the major clinical problem. Radiofrequency ablation (irrigated ablation catheter, power limited to 40W) was performed in the CTI with the endpoint of bidirectional conduction block. Demographic data was retrieved together with information on further hospital admissions. All patients were additionally followed-up on an ambulatory basis and with telephonic questionnaires.

Results: During a mean follow-up of 41±26 months from the index procedure, 74 patients (55.6%) experienced manifest paroxysmal or persistent AF. Among these, 49 symptomatic patients (36.8% of total) underwent AF ablation after a mean of 23±14 months from the index procedure. Documentation of AF (OR 4.03, $p<0.01$) and multiple DC cardioversions (56 patients) preceding the index procedure (OR 2.40, $p<0.05$) were predictors for later occurrence of AF. Documentation of AF (OR 3.12, $p<0.01$) and long-term treatment with flecainide (33 patients) (OR 2.26, $p<0.05$) preceding the index procedure were predictors of additional AF ablation in logistic regression analysis.

Conclusions: Symptomatic AF requiring additional ablation occurs in over one third of patients following elective CTI ablation. Presence of coexisting AF should be carefully evaluated when referring for AFL ablation. Flecainide promotes conversion of AF to AFL and its long-term treatment may conceal AF under recurrent AFL.