Abstrakter presentert på vårmøtet

1 Hypertension is associated with asymmetric septal hypertrophy in aortic stenosis (the SEAS study)

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Purpose: Some patients with aortic stenosis (AS) develop asymmetric septal hypertrophy (ASH) that may influence the surgical approach and also is associated with higher postoperative morbidity. Thus further characterisation of patients with AS and ASH is of clinical importance. Methods: Baseline clinic and echocardiographic data were recorded in 1719 patients (mean age 67±10, 39% women) with asymptomatic AS (average peak transaortic velocity 3.09 m/sec), participating in the Simvastatin Ezetimibe in Aortic Stenosis (SEAS) study evaluating the effect of randomized placebo controlled combined treatment with simvastatin and ezetimibe on progression of AS. The study population was divided according to presence of ASH (interventricular septal/posterior wall thickness ratio >1.5). LV hypertrophy was determined as LV mass/body surface area >104 g/m² in women and 116 g/m² in men. Hypertension was defined as history of hypertension reported by the patients attending physicians or baseline clinic systolic blood pressure ≥ 140mmHg or diastolic blood pressure ≥ 90mmHg.

Results: Compared to patients without ASH, patients with ASH (n=381, 22%) had higher left ventricular mass index (g/m²), total peripheral resistance (TPR) and peak transaortic velocity and included more patients with hypertension (all p<0.05), while there was no difference in age, gender distribution, blood pressure, LV ejection fraction or peak LV outflowtract velocity. In logistic regression analysis hypertension was the most important covariate of ASH (table). Combined ASH and LV hypertrophy (asymmetric LV hypertrophy) was present in 130 (34%) of patients with ASH. Asymmetric LV hypertrophy patients had higher systolic blood pressure and pulse pressure, lower LV ejection fraction and larger left atrial diameter, than patients with ASH without LV hypertrophy, but comparable cardiac output. There was no difference in aortic valve area index. In logistic regression analysis, hypertension was the most important predictor also of asymmetric LV hypertrophy [OR=2.66 (95% CI 1.40-5.07), p=0.03].

Conclusions: ASH in patients with asymptomatic AS is strongly associated with hypertension and increased TPR independently of severity of aortic stenosis.

Table

	Odds ratio	95% CI	p
Hypertension	1.37	1.04-1.81	0.027
Left ventricular mass index	1.23	1.09-1.38	0.001
Total peripheral resistance	1.21	1.07-1.35	0.002
Peak transaortic velocity	1.12	0.10-1.26	0.056

Variation in population-based levels of C-reactive protein, cardiovascular morbidity and all-cause mortality

2 An analysis of the relationship between CRP, Troponin-T, cardiovascular morbidity and deathrates in an unselected population in Southwest Norway.

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Background: Large population-based studies link inflammation to the prospective development of cardiovascular events. C-reactive protein (CRP) is the most widely used inflammatory marker and has also proinflammatory properties in the development of atherosclerosis. We hypothesized that the degree of inflammation in the general population assessed by CRP values correlates with the number of cardiovascular events and death rates in a time dependent manner.

Methods and results: We retrospectively studied 272,602 CRP- and 3,497 Troponin T values (TNT), the number of cardiovascular events and the death rates in the population of Southern Rogaland, Norway.

The mean, the median and the sum of CRP values per week were significantly correlated to the number of patients with a TNT≥0.03 µg/l in the same week (R=0.42, R=0.41, R=0.43, respectively, p<0.001 for all analysis). Furthermore, we found a significant correlation between the sum of CRP values per week and the number of patients admitted with a cardiovascular event 2 weeks later (R=0.21, p=0.035). The sum of CRP values per week was significantly correlated to the death rates in the following week (R=0.24, p=0.014).

Conclusions: These findings indicate that inflammation as assessed by CRP levels is linked to the prospective development of cardiovascular events and all cause mortality.

3 Har pulstrykket betydning for venstre ventrikkel struktur hos pasienter med asymptomatisk aortastenose?

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Bakgrunn: Det har vært vist at høyt pulstrykk er assosiert med øket risiko for hjertekarsykdom både i generell og i hypertensiv befolkning. Høyt pulstrykk er også assosiert med økt arteriestivhet og venstre ventrikkel (VV) hypertrofi. Hvordan pulstrykkpåvirker VV struktur hos pasienter med asymptomatisk aortastenose er ikke tidligere beskrevet.

Metode: Kliniske blodtrykk og ekkokardiografi fra baseline undersøkelsen av 1720 pasienter med asymptomatisk aortastenose (maksimal hastighet over klaffen mellom 2,5 og 4,0 m/s) i SEAS (Simvastatin and Ezetemibe in Aortis Stenosis) studien ble brukt til analysen. Pasientpopulasjonen ble delt inn i gruppene høyere (n=842, gjennomsnittlig pulstrykk=78 mmHg) eller lavere (n=931, gjennomsnittlig pulstrykk= 49 mmHg) enn median (60 mmHg) pulstrykk. VV geometri ble definert ut fra VV masse/høyde$^{2.7}$ og relativ veggtykkelse i kombinasjon. VV hypertrofi ble definert som VV masse/høyde$^{2.7}$ > 46,7 g/kg m$^{2.7}$ hos kvinner og > 49,2 g/kg m$^{2.7}$ hos menn. Konsentrisk geometri ble definert som relativ veggtykkelse >0,43.

Resultat: Grad av aortastenose var lik i de to pulstrykk-gruppene, men gruppen med høyt pulstrykk var eldre, kortere, hadde mer aortaklaffelekkasje og inkluderte flere kvinner og pasienter med kjent hypertensjon (alle p≤0.01). Denne gruppen hadde også større VV veggtykkelse, relativ veggtykkelse, VV masse og mer VV hypertrofi, særlig av eksentrisk type (p< 0,01) (Tabell1). I logistisk regresjon med en modell som inkluderte hypertensjon, kjønn, høyde, alder, alvorlighetsgrad av stenosen samt aortaklaffelekkasje var 10 mmHg høyere pulstrykk assosiert med en 14 % økt sannsynlighet for VV hypertrofi.

Konklusjon; Hos pasienter med asymptomatisk aortastenose er samtidig økt pulstrykk assosiert med endret VV struktur herunder økt masse, veggtykkelse, relativ veggtykkelse samt mer hypertrofi, særlig av eksentrisk type. Økt pulstrykk er en uavhengig risikofaktor for VV hypertrofi hos pasienter med asymomatisk aortastenose, selv etter justering for andre velkjente faktorer som påvirker VV struktur inkludert hypertensjon.

Tabell 1. Venstre ventrikkel geometri i relasjon til høyere og lavere pulstrykk

	Lavere pulstrykk (<60 mmHg)	Høyere pulstrykk (> 60 mmHg)
Normal geometri	60 %	51 %
Konsentrisk remodellering	8%	9 %
Eksentrisk hypertrofi	22 %	29 %
Konsentrisk hypertrofi	10 %	12 %

4 75-year old patients with permanent atrial fibrillation have impaired physical and mental quality of life compared to controls in sinus rhythm. A community-based study.

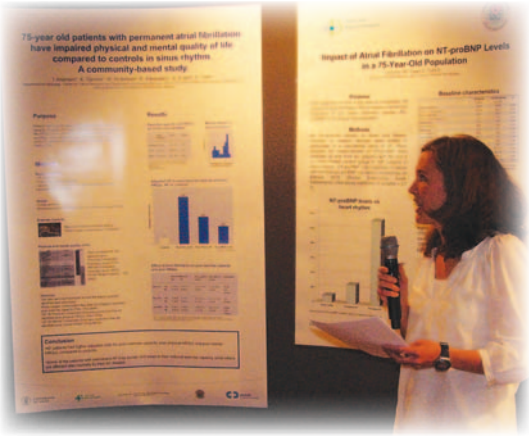
I. Ariansen, K. Gjesdal, M. Abdelnoor, E. Edvardsen, S. Enger, A. Tveit.

Objective: Patients with atrial fibrillation (AF) have reduced exercise capacity; however the impact of AF on health-related quality of life (HRQoL) in an out-of-hospital population is not well quantified. We compared exercise capacity and HRQoL in 75 years old patients with permanent AF to controls in sinus rhythm (SR).

Methods: All 75-year old citizens in a Norwegian municipality were invited to an ECG screening (Asker and Baerum Atrial Fibrillation study, ABAF). Patients with permanent AF and a gender-matched control group in SR underwent maximal treadmill exercise testing, measuring peak oxygen consumption (VO2peak). HRQoL was assessed by self-completed SF-36 questionnaires. Score results were pooled into a Physical Component Summary score (PCS) and a Mental Component Summary score (MCS). The data were dichotomized so that the lowest quartile identified poor outcomes. Odds ratios (OR) were adjusted for confounding comorbidity and gender.

Results: 25 subjects with permanent AF (median duration 5 years, range 0.6-25 years) and 70 subjects in sinus rhythm participated. AF patients had higher prevalence of compensated chronic heart failure (p=0.0001), coronary artery disease (CAD) (p=0.051) and hypertension (p=0.067) compared to controls. AF patients had lower mean VO2peak than the controls; 22.7±5.5 vs. 28.6 ± 6.3 ml/kg/min; p=0.0001, and more often poor VO2peak; crude OR 5.3 (95%CI 1.8, 15.3) and adjusted OR 7.4 (1.9, 29.6), adjusting for CAD, pulmonary disease, diabetes and gender. Median PCS (25th, 75th percentile) was 41 (31, 51) in the AF group vs. 52 (45, 55) in controls (p=0.0001). Furthermore, the AF group had higher odds for poor PCS; crude OR 5.0 (1.8, 13.7), adjusted OR 4.3 (1.5, 12.4), adjusting for CAD and diabetes. There was no difference in median MCS; 56 (42, 61) in the AF group vs. 57 (51, 60) in controls (p=0.565). However, the AF group had higher odds for poor MCS; crude OR 2.3 (0.8, 6.2), adjusted OR 2.8 (1.0, 8.4) adjusting for diabetes, pulmonary disease and gender. The distribution of MCS in the AF patients was bimodal; the subgroup with low MCS probably accounting for the increased OR for poor MCS in AF patients. The larger AF subgroup with normal MCS explains the similar median MCS for AF patients vs. controls.

Conclusion: AF patients had higher adjusted odds for poor exercise capacity, poor physical HRQoL and poor mental HRQoL compared to controls. Still, the median mental HRQoL score did not differ between the groups. Thus, some of the patients with permanent AF may accept and adapt to their reduced exercise capacity, while others are affected also mentally by their AF disease.



5 Stability over Time of Ventricular Rate and NT-proBNP Levels in Permanent Atrial Fibrillation

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Purpose: The aim of this study was to analyse the stability over time of average ventricular heart rate and circulating levels of the amino-terminal fragment of pro brain natriuretic peptide (NT-proBNP) in patients with permanent atrial fibrillation (AF).

Methods: We studied twelve patients (8 men and 4 women, age 71±8 years) with permanent AF (median duration 25 months, range 12-80) on stable treatment with a rate reducing drug (beta-blockers (n=2), calcium channel blockers (n=10, combined with digitoxin in one patient)). 24-hours Holter recordings were obtained at baseline and after 3 and

12 weeks, on weekdays with assumed normal physical activity level. Fasting blood samples were collected from all subjects at each visit, and NT-proBNP was measured in serum with the Elecsys proBNP sandwich immunoassay on Elecsys 2010 (Roche Diagnostics, Basel, Switzerland); intra-assay coefficient of variation < 1.5 %.

Results: There was a fair concordance between the mean ventricular heart rate at baseline (78±9 beats per minute - bpm) and 3 weeks (76±5 bpm), and between baseline and 12 weeks (79±9 bpm). The intraclass correlation coefficient (ICC) was 0.52 (95%CI -0.68, 0.86) between baseline and 3 weeks, p=0.122. Between baseline and 12 weeks ICC was 0.38 (95%CI -1.17, 0.82), p=0.224.

The NT-proBNP levels showed excellent concordance between baseline (932 pg/mL (interquartile range 722, 1237)) and 3 weeks (833 pg/mL (630, 1318)), and between baseline and 12 weeks (864 pg/mL (674, 1438)). The ICC values were >0.95 (95% CI 0.91, 0.99 and 0.87, 0.98, respectively), p=0.0001 for both, indicating very good reliability. No correlation between ventricular heart rate and NT-pro-BNP levels was found.

Conclusion: Only fair concordance was found for average ventricular heart rate assessed by repeated Holter recordings. Our findings question the use of single Holter recordings to evaluate rate control in patients with permanent AF. In contrast, NT-proBNP levels showed excellent concordance over time in this group of patients with permanent AF.

6 Stability of Atrial Fibrillatory Rate over Time in Permanent Human Atrial Fibrillation

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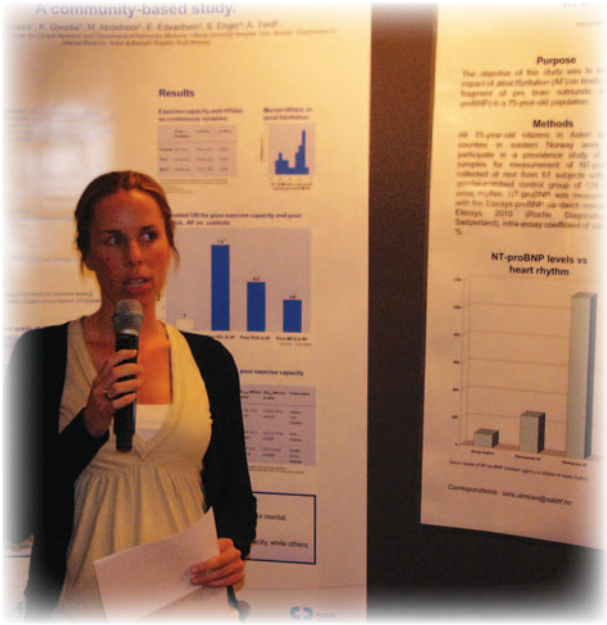
Purpose: The objective of this study was to investigate stability over time of atrial fibrillatory rate (AFR) in patients with permanent atrial fibrillation (AF), assessed by time-frequency analysis of surface ECG.



Methods: We studied twelve patients (8 men, 4 women) with permanent AF on stable treatment with a rate reducing drug (beta-blockers (n=2), calcium channel blockers (n=10, combined with digitoxin in one patient)). Mean age was 71±8 years, and median duration of AF was 25 months, range 12-80. Ten-second 12-lead ECG recordings were obtained in the morning after 10 minutes rest at baseline, after 3 weeks and after 12 weeks. Mean AFR was determined from lead V1 using spatiotemporal QRST cancellation and time-frequency analysis.

Results: The mean AFR in all recordings was 385 ±49 fibrillations per minute (fpm). The mean AFR was 369 ±58 fpm at baseline, 409 ±38 fpm at 3 weeks and 378 ±43 fpm at 12 weeks. There was good concordance between the three measurements, with intraclass correlation coefficients >0.65 (95% CI -0.20, 0.90 for baseline to 3 weeks; -0.22, 0.90 for baseline to 12 weeks), p <0.05 for both.

Conclusion: Atrial fibrillatory rate assessed by time-frequency analysis of surface ECG in patients with permanent atrial fibrillation was stable over time in the studied population.

7 Impact of Atrial Fibrillation on NT-proBNP levels in a 75-year-old population.

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Purpose: The objective of this study was to investigate the impact of atrial fibrillation (AF) on levels of N-terminal fragment of pro brain natriuretic peptide (NT-proBNP) in a 75-year-old population.

Methods: All 75-year-old citizens in Asker and Baerum counties in eastern Norway were invited to participate in a prevalence study of AF. Blood samples for measurement of NT-proBNP were collected at rest from 61 subjects with AF and a gender-matched control group of 126 subjects in sinus rhythm. NT-proBNP was measured in serum with the Elecsys proBNP sandwich immunoassay on Elecsys 2010 (Roche Diagnostics, Basel, Switzerland); intra-assay coefficient of variation < 3.7 %.

Results: Individuals with permanent AF had higher levels of NT-proBNP (median 1119 pg/mL (interquartile range 701, 1643)) than patients with paroxysmal AF (median 257 pg/mL (169, 382)) and the control group (median 95 pg/mL (60, 171)), $p<0.001$ for both. In univariate analysis, NT-proBNP levels were higher in subjects with heart failure: 1643 pg/mL (701, 2085) vs. 142 pg/mL(73, 346), $p<0.001$; coronary heart disease: 715 pg/mL(140, 1578) vs 128 pg/mL(69, 281), $p<0.001$ and hypertension: 204 pg/mL(83, 755) vs 119 pg/mL(68, 281), $p=0.008$. There was no significant association between NT-proBNP levels and creatinine clearance, body mass index or gender. Adjusting for the presence of heart failure, coronary heart disease and hypertension in a linear regression model, AF was still significantly associated with log NT-proBNP ($B=0.61$, $p<0.001$).

Conclusion: In this stable out-of-hospital population of 75-year-old subjects, AF was independently associated with increased levels of NT-proBNP, and related to AF burden.

8 D-dimer ved akutt aortadisseksjon

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Bakgrunn. Akutt aortadisseksjon (AAD) er en sjelden, men livstruende differensialdiagnose til akutt koronarsyndrom. Mortaliteten er høy, og diagnosen er vanskelig å stille uten ressurskrevende bildediagnostikk i form av CT, MR eller transøsofageal ekkokardiografi.

D-dimer, et nedbrytningsprodukt av fibrin, kan måles i en enkel blodprøve, og denne har i noen små studier vist seg å være forhøyet ved aortadisseksjon. Vi ønsket å undersøke nytten av D-dimer ved akutt aortadisseksjon ved vårt sykehus.

Metode. Vi gjorde en retrospektiv gjennomgang av sykehusets journal- og obduksjonsregister for perioden 2001 – 2007. Diagnosen AAD ble verifisert ved CT, operasjon eller obduksjon hos totalt 69 pasienter. D-dimer var blitt målt hos 45 pasienter, og disse utgjorde studiepopulasjonen. Det var ingen kjønns- eller aldersforskjell mellom studiepopulasjonen og gruppen som ikke fikk målt D-dimer. Det var 29 menn og 16 kvinner, gjennomsnittsalderen var 71 år (standardavvik 13), og 26 pasienter (58 %) hadde Stanford A disseksjon. Fem pasienter hadde intramuralt hematom (IMH). D-dimer ble i hele studieperioden målt vha. STA Liatest D-Di (Diagnostica Stago, Frankrike). Referanseområdet er ≤ 0,4 mg/l, og måleområdet er 0,1 til 20 mg/l.

Resultater. D-dimer var over referanseverdien hos alle 45 pasientene (diagnostisk sensitivitet 100 %) med medianverdi 6,7 mg/l, kvartilavstand (IQR) 3,3 – 20 mg/l og variasjon fra 0,5 til >20 mg/l. Pasienter med IMH hadde grensesignifikant lavere D-dimer verdi (median 1,8 mg/l) enn pasienter med klassisk disseksjon (median 7,7 mg/l), $p=0,056$. D-dimer viste en positiv, men ikke-signifikant korrelasjon med disseksjonslengde. Vi fant ingen assosiasjon mellom D-dimer verdi og hhv. disseksjonstype eller overlevelse, og ingen korrelasjon mellom D-dimer og tid fra symptomdebut til prøvetaking.

Konklusjon. Basert på vårt materiale kan diagnosen akutt aortadisseksjon ekskluderes ved en D-dimer måling innenfor referanseområdet (≤ 0,4 mg/l). Selv om studien er liten, er resultatene i overensstemmelse med tidligere studier, og vi vil anbefale rutinemessig måling av D-dimer for å utelukke AAD. D-dimer må ikke brukes for å bekrefte aortadisseksjon da prøven er forhøyet ved en rekke tilstander. Dens lave spesifisitet kombinert med den lave prevalensen av aortadisseksjon i en uselektert brystsmertepopulasjon, gjør at positiv prediktiv verdi vil være meget lav.

9 The Effect of Ischemic and Insulin Postconditioning on the mRNA levels of BAD

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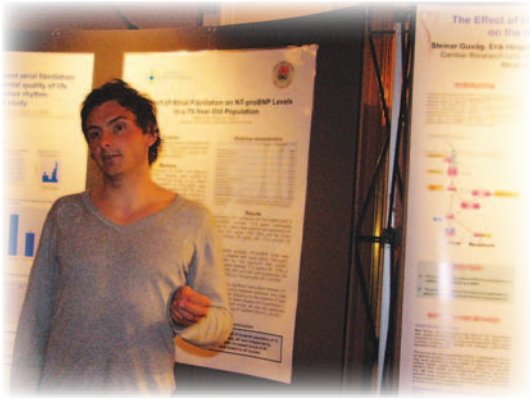
Ischemic postconditioning by transient cycles of alternating ischemia and reperfusion immediately after a sustained ischemic episode leads to reduced myocardial injury. We have already explored the cytoprotective effects of insulin administrated at ischemic reperfusion and insulin's ability to mimic ischemic postconditioning. However, in order to explore the underlying factors affording myocardial protection, the aim of this study was to investigate the effect of ischemic or insulin postconditioning on molecular markers of ischemia (BNP, c-Fos and Interleukin-6) and the pro-apoptotic protein BAD. The Langendorff perfused rat heart subjected to 30 min of regional ischemia (I) and 120 min of reperfusion (R) were exposed to Ischemic postconditioning (IPost) as 3 x 30 s of global ischemia and insulin induced postconditioning (InsPost) by 3 x 30 s infusion of insulin (0.3 mU/ml). The Akt/PKB inhibitor SH-6 (10uM) and mTOR/p70s6k inhibitor rapamycin (0.5 nM) was employed in order to explore the signaling pathway whereby insulin might induce its cardioprotection. Myocardial tissue samples for quantitative RT-PCR analysis were isolated at 15 and 120 min of ischemic-reperfusion. Both ischemic and insulin induced postconditioning increased the level of BAD mRNA, whereas the level of BNP mRNA remained unchanged in the ischemic area. Interestingly, the use of the Akt/PKB blocker SH-6 and the mTOR/p70s6k inhibitor Rapamycin repressed the mRNA expression of both BAD and BNP. These data suggest that Akt/PKB and mTOR/p70s6k is not only involved in the regulation of BAD, but also could be involved in the regulation of mRNA levels of BNP in the setting of ischemic and insulin postconditioning.



10 Elektrodeekstraksjon med enhylseteknikk. Erfaring etter ekstraksjon av 500 pacemaker/ICD-elektroder.

Eivind S Platou, Thomas Knutsen og Magnus Heldal, Arytmiseksjonen, Hjertemedisinsk avdeling, Ullevål universitetssykehus

Vi betjener det meste av Norge samt Island for elektrodeekstraksjoner. Vi bruker en enhylseteknikk, en variant av ekstraksjonsteknikken som ble beskrevet av Byrd et al. 1992 og videreutviklet av Bongiorni (Pisa).

Metode og materiell: Siden vi startet ekstraksjonsaktiviteten 1997 til utgangen av 2007 har vi behandlet 307 pasienter, median alder 65,5 år, (7 - 97 år) med 499 elektroder. 66 % av elektrodene ble fjernet pga. infeksjoner, resten elektive ekstraksjoner. Median alder av alle elektrodene var 5 år, (3 mnd – 27 år). Median alder for elektroder som kunne fjernes ved forsiktig traksjon var ett år (2 mnd - 16 år). Enhylseteknikken ble benyttet i 74 % av ekstraksjonene, traksjon alene i 22 %, iv. "fisking" med spesialredskap eller slynger i 2 %. Vi starter med lett traksjon med mandreng i elektroden, og går så videre med sikring av elektroden med låsewire (Cook/Spectranetics/VascoMed) og holdesutur. En enkel Cook polypropylenhylse med påmontert "håndtak" (Cook Pin Vise) blir så ført nedover elektroden med rask rotasjon. Hvis vi møter sterk motstand mot hylsen, blir hylsestørrelsen øket. I noen tilfeller (hvor for eksempel elektrodene er grodd fast i clavicula) må vi benytte stålhylse for å komme inn i subclavia.

Resultater: Klinisk suksess er oppnådd i 99 % av ekstraksjonene. For ICD elektroder (55 ekstraksjoner) er det 100 % suksess. Median hylsetid (tiden hylsen brukes på elektroden) er 6 min (1 – 600 min).

Komplikasjoner: Større komplikasjoner (tamponade): 2,2 %, hvorav 1 fatal. De andre ble behandlet uten sequelae. Mindre komplikasjoner 1 %.

Konklusjon: Enhylseteknikken vi benytter er rask og effektiv og like effektiv som laserteknikk som benyttes mest ellers. Enhylseteknikken er vesentlig rimeligere enn laserteknikk, og våre resultater er på høyde med de største sentra i verden hva gjelder suksessrate og sikkerhet.

11 Percutaneous Left Ventricular Assist Device in Cardiac Arrest

Tuseth V. Pettersen R, Salem M, Rotevatn S, Grong K, Nordrehaug JE

Background Ischemic cardiac arrest represents a challenge for optimal emergency revascularization. A percutaneous left ventricular assist device (LVAD) may help support circulation during percutaneous coronary intervention (PCI) and could improve clinical outcomes. Such a device could help maintain systemic blood delivery during cardiopulmonary resuscitation (CPR) and may also facilitate PCI by allowing short-term interruption of chest compression with less detrimental consequences.

We investigated the ability of a percutaneous transfemoral left ventricular assist device (Recover LP 2,5®) Abiomed, Aachen, Germany) to deliver blood to the systemic circulation during cardiac arrest. We randomized two groups to receive either conventional or intensive fluid infusion to evaluate the effect of increased right side filling upon pump function

Methods and Results The study was an acute experimental trial with pigs under general anaesthesia. Farm pigs (n=16) of both sexes had LVAD support during ventricular fibrillation (VF) and were randomized to conventional or intensive fluid.

After randomisation for fluid infusion VF was induced by balloon occlusion of the proximal left anterior descending artery. LVAD and fluid was started after VF had been induced.

Brain, kidney and myocardial tissue perfusion, and cardiac index, were measured with microsphere injection technique at baseline, 3 and 15 minutes. Additional hemodynamic monitoring continued for at most 30 minutes.

Mean cardiac index at 3 minutes of VF was 1.2 L·min/m^2 (28% of baseline). Compared to baseline; mean perfusion at 3 minutes was 65% ($P<0.05$) in the brain and 74% ($P<0.01$)in the epicardial myocardium supplied by the open left circumflex artery suggesting possible autoregulation augmenting the proportion of flow to these organs. Further, a moderate but non- significant decline was seen at 15 minutes. At 30 minutes LVAD function above 30% of the initial value after induction of VF was sustained in 11 animals (8/8 intensified fluid vs 3/8 conventional fluid) and was associated with intensified fluid loading ($P<0.001$).

Conclusions During VF a percutaneous LVAD may assist systemic circulation with potential preferential flow to vital organs. Intensified fluid loading may be beneficial for LVAD performance. This approach may improve clinical and technical results in PCI during cardiac arrest. Further investigation is needed to establish a potential clinical benefit.

12 Sustained non-ischemic cerebral metabolism during cardiac arrest with percutaneous Left Ventricular Assist Device

Tuseth v, Pettersen R, Husby P, Rotevatn S, Grong K, Nordrehaug JE

Objectives: Perfusion to vital organs with a percutaneous left ventricular assist device (LVAD) during ventricular fibrillation (VF) using microsphere injection has previously indicated in an experimental model. The significance of these findings requires evaluation. Microdialysis of intracerebral fluid can detect cerebral ischemia.

Methods: In 12 subjects (pigs) cerebral microdialysis and pressure catheters were implanted via a cranial burr hole. An LVAD was deployed percutaneously into the left ventricle. VF was induced by angioplasty-balloon occlusion of the left anterior descending artery. Microdialysis vials were sampled for 20 minutes per vial for 60 minutes after VF. Tissue perfusion was measured with microsphere injections.

Results: In 6 subjects cerebral microdialysis showed no significant ischemic changes in the metabolic markers glycerol, glucose and pyruvate

(all vials NS from baseline) during 60 minutes, lactate was significantly increased in the last vial (P=0.002). Mean cerebral perfusion pressure (96.0 to 32.2 mmHg, P=0.002) and et-CO_2 levels (5.2 to 2.3, P=0.001) dropped 10 minutes after VF but were subsequently maintained. Microspheres at 15 minutes showed mean blood flow to the brain at 57% (NS) and myocardium 73 % (NS) compared to baseline, with a further insignificant decline at 45 minutes. In the remaining 6 pigs microdialysis showed severe ischemia (all P<0.01). This group was identified by lower end tidal CO_2 (<1.0 after 20 minutes) and further characterized by fall in arterial Hgb levels (<8.0 at 45 minutes) and absent circulation by microspheres. Figure1 shows microdialysis results for intracerebral glucose in the two groups.

Conclusions: Intracerebral microdialysis indicate that ischemic metabolism in the brain during VF may be avoided for a limited time using a percutaneous LVAD. Further studies may resolve the issue of predictable efficacy.

13 B-Type Natriuretic peptide is a predictor of all cause mortality at long-term follow-up after hospitalization with acute chest pain

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Background: B-type Natriuretic peptide (BNP) is a marker of left ventricular dysfunction and heart failure. The aim of this study was to evaluate if elevated BNP levels are associated with increased risk of death within 24 months following hospitalization with acute chest pain.

Methods: BNP concentration in EDTA plasma harvested immediately following admission in 828 patients hospitalized with acute chest pain were analysed using the Abbott AxSYM® BNP assay. Data were analysed by grouping the patients into quartiles according to BNP concentrations; Quartile 1 (Q1) <35 pg/ml, Quartile 2 (Q2) 35 to 97 pg/ml, Quartile 3 (Q3) 98 to 300 pg/ml and Quartile 4 (Q4) > 300 pg/ml.

Results: At 24 months follow-up 123 patients had died. Univariate all cause mortality grouped according to BNP at admittance, are given in Table I. The odds ratio for death was 33.27 (p<0.0001) for participants with BNP concentrations in Q4 as compared to those with concentrations in Q1.

Conclusion: BNP strongly predicts the risk of all cause mortality at long-term follow-up after hospitalization with acute chest pain.

Table 1. All cause mortality during a follow-up period of 2 years.

BNP quartile	Q1(<35 pg/ml)	Q2(35-97 pg/ml)	Q3(98-300 pg/ml)	Q4(> 300 pg/ml)
Events	3	9	43	68
Odds ratio	1.00	3.09	17.83	33.27
p-value		0,047	<0,0001	<0,0001

14 The prognostic value of NT-proBNP versus PAPP-A, MPO and CD40L following an acute myocardial infarction

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Aims: We assessed the long-term prognostic value of plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) and various inflammatory markers in 300 patients (238 men) admitted for an acute myocardial infarction (AMI) from 1995 until 1996.

Methods: We compared the recurrence of Troponin T (TnT) positive coronary events in the upper quartile of NT-proBNP (>261.8 pmol/l) to the event rate below the 75% percentile during a median follow-up period of 18 and 45 months. Pregnancy-associated plasma protein A (PAPP-A), myeloperoxidase (MPO) and CD40 ligand (CD40L) were also evaluated.

The blood samples were drawn 4-6 days post-MI. The analyses of PAPP-A, MPO and CD40L were performed by ELISA-methodology, and NT-proBNP was analysed using the Abbott immunoassay.

Results: During the first 18 months, 33.3 % in the upper quartile (Q4) of NT-proBNP experienced an acute coronary syndrome (ACS), as compared to 16.1 % (p= 0.002) in the three lower quartiles (Q1-Q3). After 45 months, 40% versus 23.3% (p= 0.008) sustained an ACS event. The relative risks (RR) for Q4 versus Q1-Q3 were 2.61 (p<0.001) and 2.20 (p<0.001) after 18 and 45 months, respectively.

During the first 18 months, revascularization, defined as a secondary end point, was

Outcomes at 18 and 45 months follow-up

NT-proBNP quartile (pmol/l)	First recurrent ACS (median follow-up 18 months)	First recurrent ACS (median follow-up 45 months)	First revascularization (median follow-up 18 months)	First revascularization (median follow-up 45 months)
Q4(>261.8)*	25 (33.3)	30 (40.0)	14 (18.7)	15 (20.0)
Q3(134.0-261.8)	10 (13.7)	14 (19.2)	22 (30.1)	26 (35.6)
Q2(54.0-134.0)	15 (20.0)	21 (34.4)	29 (38.7)	33 (44.0)
Q1(< 54.0)	11 (14.5)	17 (22.7)	30 (40.0)	35 (46.7)
Q1-Q3	36 (16.1)	52 (23.3)	81 (36.3)	94 (42.2)

**For first recurrent ACS p=0.002 and p=0.008 for Q4 compared to Q1-Q3 for NT-proBNP after 18 and 45 months, respectively. For revascularizations p=0.001 and p<0.01 for Q4 compared to Q1-Q3 for NT-proBNP after 18 and 45 months, respectively.*

performed in 18.7 % in Q4 as compared to 36.3% in Q1-Q3 (p= 0.001). After 45 months, 20.0 % versus 42.2% (p<0.01) were revascularized. The RR after 18 months and 45 months for Q4 versus Q1-Q3 were 0.42 (p<0.001) and 0.29 (p<0.01), respectively. (Table)

Conclusion: Increased NT-proBNP predicts recurrent ACS in survivors of an AMI, whereas revascularizations were offered to patients in the lower NT-proBNP range. The inflammatory markers rendered no prognostic information.

15 Activated Factor XII and B-type natriuretic peptide, but not C-reactive protein, are independent predictors of mortality following admission with suspected myocardial infarction.

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Background: The study aim was to assess the utility of activated Factor XII type A (XIIaA), B-type natriuretic peptide (BNP) and highly sensitive C-reactive protein (hsCRP) in multivariate analysis models predicting all-cause mortality in patients admitted with chest pain.

Methods: Multivariate analysis of all cause mortality in 871 patients admitted with suspected MI was performed using the Cox Proportional Hazard Ratio. Data input into the model included XIIaA, BNP and CRP as well conventional risk factors for mortality such as age, smoking, previous history of coronary heart disease (CHD), hypertension, diabetes mellitus, left ventricular function (EF), troponin T (TnT) and se-creatinine.

Results: Of 871 patients, 386 had a TnT concentration [TnT]>0.05 ng/mL at admission whilst 485 had a [TnT]≤0.05ng/mL. 66 % of the latter group had known pre-existing CHD. 138 patients died within 24 months. Hazard ratios associated with XIIaA, BNP and CRP are shown in the table. Both XIIaA and BNP are independent predictors for all-cause mortality in the group containing all patients, BNP is an independent predictor for all cause mortality in patients who had confirmed MI (TnT>0.05ng/mL) at admission, whereas XIIaA

		All patients	TnT >0.05 ng/mL at admission	TnT ≤0.05 ng/mL at admission
Cox Proportional Hazard Ratio (95% CI)	XIIaA	2.30** (1.37-3.86)	N.S.	3.75** (1.63-8.63)
	BNP	5.47** (2.11-14.19)	4.34* (1.36-13.83)	N.S.
	hs-CRP	N.S.	N.S.	N.S.

**: p<0.05; **: p<0.01; N.S. = Not significant.*

is an independent predictor for all cause mortality in patients with low or absent TnT release at admission. In contrast, hsCRP was not an independent predictor of all-cause mortality in the studied population.

Conclusion: XIIaA and BNP provide independent and complementary information on all-cause mortality risk following admission with suspected MI. XIIaA is particularly useful in predicting mortality in patients who did not have MI at admission, whereas BNP is effective in predicting mortality in patients with confirmed MI.

16 Activated Factor XII type A is an independent predictor of cardiovascular outcome in coronary patients admitted with troponin T negative chest pain

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Background: Activated Factor XII (XIIa) is a predictor of recurrent coronary ischemic events in patients following a myocardial infarction (MI). Recently, novel in-vivo types of XIIa have been described. We assessed the relation between admission levels of activated factor XII type A (XIIaA) and a combined endpoint of recurrent troponin T (TnT) positive events (TnT >0.05 ng/mL and an MI typical pattern of gradual rise and fall in TnT) and cardiac mortality in a large, consecutive cohort of patients admitted with chest pain.

Methods: Blood samples for XIIaA determination were obtained immediately following admission in 871 patients admitted with chest pain and suspected acute coronary syndrome (ACS). Plasma XIIaA concentrations were determined by ELISA at admission. Cardiovascular outcome within each quartile of XIIaA was compared at 6 months follow-up.

Results: At index hospitalization, 386 (44.3%) patients had a peak TnT concentration exceeding 0.05 ng/mL and 485 (55.6%) had a peak TnT concentration of 0.05ng/mL or below. Of the latter group, 66% had known pre-existing coronary heart disease (CHD). After a follow-up period of 6 months, 67 patients had suffered from a recurrent TnT positive event and 52 patients had died from a cardiac reason. Whilst XIIaA levels were not related to increased risk for cardiovascular outcome in the group of patients with TnT>0.05ng/mL at admission, XIIaA predicted 6 months cardiovascular outcome for patients with absent or low TnT at admission. This risk prediction was particularly pronounced in the subgroup of patients with pre-existing CHD. The unadjusted odds ratios (OR) for quartile 4 versus quartile 1 for the combined endpoint of cardiac death or TnT positive events for the different subgroups are displayed in table 1. In a multivariate logistic regression model, XIIaA added prognostic information for cardiovascular outcome after adjustment for age, sex, peak TnT, BNP, CRP, creatinine, history of CHD or heart failure, NYHA class, hypertension, diabetes mellitus, smoking history, ejection fraction (EF), administration of clopidogrel, thrombolysis or statin prior to admission and angiography following admission.(table 1).

Conclusion: XIIaA is a powerful and independent indicator of 6 months cardiovascular outcome in CHD patients admitted with chest pain with low or absent TnT release and provides prognostic information above and beyond conventional risk factors.

Table 1: ORs comparing patients with XIIaA in Q4 with patients in Q1 for the combined endpoint of cardiac death or a recurrent TnT positive event 6 months following admission for chest pain.

	Univariate analysis, OR (95% CI; p)	Multivariate analysis, logistic regression; OR (95% CI; p)
TnT >0.05ng/mL) (n=386)	1.03 (0.47-2.24; ns)	--
TnT ≤0.05 ng/mL (n=485)	5.85 (1.65-20.79; p<0.01)	5.44 (1.43-20.67; p<0.05)
TnT≤0.05 ng/mL pre existing CHD (n=318)	4.00 (1.24-12.88; p<0.05)	3.76 (1.06-13.28; p<0.05)

CI: confidence interval; ns: not significant

17 Left ventricular size determines tissue Doppler derived longitudinal strain and strain rate

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Background: Tissue Doppler derived indices of strain (ε) and strain-rate (SR) have been developed to assess regional cardiac function. However, the effect of left ventricular size on ε and SR has not been studied in depth. Our objective was to assess to what extent heart size and loading influence ε or SR.

Methods and Results: In 21 anesthetized pigs ranging from 12.5 to 70 kg, tissue Doppler derived ε and SR, and a set of hemodynamic parameters, were assessed during controlled heart rates and different loading conditions. dP/dt did not correlate to pig weight, suggesting constant contractility during growth. Longitudinal ε and SR were significantly higher in smaller compared to larger hearts. The inverse hyperbolic correlation between pigs weight and longitudinal ε and SR were r^2=0.621 and 0.372 respectively, both p<0.0001. Radial ε and SR were not significantly altered by weight changes. Afterload elevation induced a reduction in longitudinal ε (from -24.2 ±3.2 % to -12.1 ±5.5 %, p=0.001) and SR (from -2.3 ±0.8s^{-1} to -1.3 ±2.4s^{-1}, p=0.034), while increasing preload increased longitudinal ε (from-26.4 ±10.3% to -38.1 ±14.3%, p=0.006) and SR (from -2.3 ±0.9s^{-1} to -4.22 ±1.8s^{-1}, p=0.002). Radial ε and SR were influenced by load in principally the same manner.

Conclusions: Longitudinal ε and SR decrease with increasing left ventricular dimensions in spite of an unaltered contractility. These results show that heart size influences TDI of ε and SR and that ε and SR are highly load dependent parameters.