NORSKE ABSTRAKTER PRESENTERT PÅ ACC

1177-577. Insulin dependent AKT-phosphorylation in the porcine myocardium

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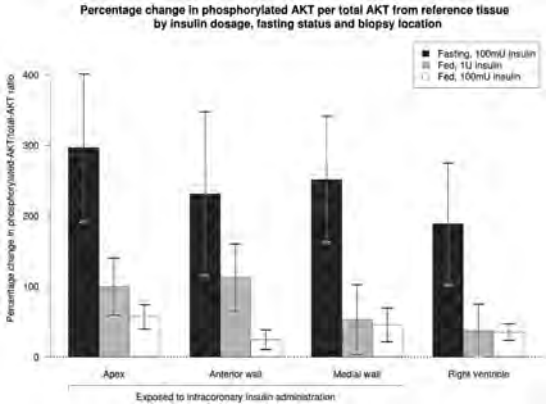
Background: Insulin promotes AKT-dependent pro-survival signalling and reduces reperfusion injury and infarct size in the ex vivo rat heart. We aimed to investigate: a) AKT-phosphorylation, b) impact of dose, and c) influence of fasting state on the AKT-response after intracoronary insulin administration in the in vivo pig myocardium.

Methods: Pigs fed 2 hours pre-procedure received 0.1U or 1U of insulin in the LAD, and fasting pigs 0.1U. Left auricle biopsies at baseline and left and right ventricle tissue 15 min post insulin administration were analysed for AKT-phosphorylation by densometric analysis of total AKT and phosphorylated AKT immunoblots expressed as a ratio. Relative AKT-phosphorylation compared to baseline was calculated.

Results: Mean relative AKT-phosphorylation was significantly increased in both fasting and fed animals after insulin infusion: 296.9% in the fasting group (p=0.012), 99.6% in the fed-1U-insulin group (p=0.031) and 56.8% in the fed-100mU group (p=0.005). The difference between fasting and fed groups was borderline significant (p= 0.059) and non-significant between the two fed groups (p=0.908).

Conclusions: Insulin phosphorylates AKT in the porcine myocardium. Feeding, with elevated serum glucose and insulin, attenuate the response, irrespective of insulin dose. The finding may help to explain the inconsistent results from clinical studies using insulin as reperfusion therapy in acute myocardial infarction.



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1178-22. Seven-year increase in exercise systolic blood pressure at 100w predicts long-term Risk of coronary heart disease in healthy middle-aged men

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Background: Exercise systolic blood pressure (SBP) predicts coronary heart disease (CHD) in the general population. We tested if changes (Δ) in exercise SBP through seven years predict CHD over 28 years.

Methods: Exercise SBP was measured among 1,392 men, apparently healthy in 1972-75 and at re-examination 1979-82. All completed the initial workload 100W during bicycle exercise-ECG test at both examinations. SBP was measured every second min, and SBP at the end of 100W (5.5METS) registered as SBP100. The men were divided into quartiles (Q1-Q4) according to the magnitude of ΔSBP100. Incidence of CHD events (angina pectoris, non-fatal myocardial infarction and CHD death) was provided from Norwegian Death Registry besides complete registration of all participants' hospital charts through 2008. Relative risks of CHD in the quartiles were calculated using Cox proportional hazard regression adjusting for baseline age, SBP 100, smoking status, resting SBP and cholesterol*.

Results: Mean ΔSBP100 was 3 mmHg. Q4 was associated with 54%, and Q3 with 30% increased CHD-risk using Q1 as reference, see table. Q4 was associated with a 1.40-fold (95% CI; 1.06-1.87) adjusted increased CHD risk using Q2 as reference.

Conclusions: Our results indicate that an increase in SBP100 of 5 mmHg or more over seven years is independently associated with significantly increased long-term risk of CHD. This suggests that high exercise sys-

	Q1 (-65 to -10 mmHg) n = 401	Q2 (-5 to - 0 mmHg) n = 300	Q3 (5 to 15 mmHg) n = 397	Q4 (20 to110 mmHg) n = 294
CHD-incidence, n (%)	116 (28.9)	89 (29.7)	137 (34.5)	110 (37.4)
Unadjusted	1.00	1.01 (0.77-1.34)	1.24 (0.97-1.59)	1.54 (1.18-1.99)
Multiple adjusted *	1.00	1.09 (0.83-1.45)	1.30 (1.01-1.69)	1.54 (1.17-2.02)

tolic blood pressure identifies underlying vascular changes in healthy men.

1202-222. Prognostic model of residual risk for major cardiovascular events in statin-treated coronary patients: a combined analysis of the ideal and tnt trials

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Background: Patients at high risk for a major cardiovascular event (MCVE) are treated with effective drugs that significantly reduce the risk of a future event. It is currently uncertain how much additional lowering of atherogenic lipoproteins (beyond that achieved with high-dose statins) would contribute to a further reduction in the risk of a future MCVE. Nor is it known whether measurements of atherogenic lipoprotein levels in statintreated patients adds significantly to risk prediction beyond the risk predicted by traditional non-lipid risk factors.

Methods: We addressed this issue using a prognostic (distinct from an etiological) analysis approach in high-risk stable coronary heart disease (CHD) patients from the Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL) and Treating to New Targets (TNT) trials.

Results: In a two-thirds training sample of the IDEAL trial, eleven baseline factors were significantly associated with subsequent MCVEs. When these factors were fitted to the remaining one-third test sample, only age, smoking, diabetes, history of cerebrovascular disease and uric acid remained as clearly significant. External calibration versus TNT data was generally good. On-treatment lipoprotein levels increased discrimination ability only to a minor degree.

Conclusions: This analysis suggests that among high-risk CHD patients on statin therapy, strategies for further risk reduction should include targeting other modifiable factors such as smoking, diabetes and blood pressure control. Formulas for calculation of individual 5-year probabilities of residual MCVEs for simvastatin- or atorvastatin-treated patients with CHD are now provided and can easily be used for individual risk calculations or risk stratification in planning future trials.

1128-320. Atrioventricular conduction delay predicts ventricular tachycardia in lamin A/C mutation carriers

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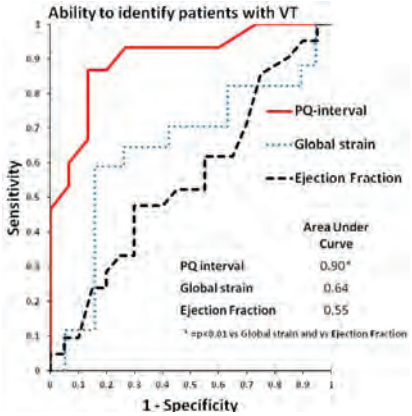
Background: Lamin A/C mutations commonly lead to atrioventricular block (AVB), ventricular tachycardia (VT) and dilated cardiomyopathy (DCM). Sudden cardiac death may occur before development of DCM. Prediction of VT in Lamin A/C mutation carriers is challenging.

Methods: We included 41 Lamin A/C mutation carriers from 2 centers. PQ interval was collected from resting ECG. Occurrence of VT was recorded from repeated Holter monitoring. Myocardial function was assessed by ejection fraction and global strain by echocardiography.

Results: Documented VT was found in 21 patients (51%). 13 patients without evident DCM had VT (62%). All patients with total AVB (n=6) had VT (p=0.01). Prolonged PQ interval (p<0.001), AVB (p<0.001) and reduced global strain (p=0.01) were markers of VT. By ROC analysis, PQ interval >230 ms showed the best ability to discriminate between those with and without VT with a sensitivity and specificity of



both 87% (Figure). Myocardial function in the intraventricular septum (IVS) was markedly reduced compared to the rest of the left ventricle (-16.7 vs -18.7%, p=0.001). Interestingly, prolonged PQ interval was correlated to reduced IVS function (R=0.41, p=0.03).

Conclusion: In Lamin A/C mutation carriers, PQ interval was the best marker of VT. PQ interval measurements may improve risk stratification of VT. Septal dysfunction was related to PQ interval and may play a role in ventricular arrhythmogenesis in these patients.

1192-600 Efficacy and safety of apixaban compared with warfarin for stroke prevention in atrial fibrillation in patients taking concomitant aspirin

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Background: Patients with atrial fibrillation (AF) frequently also have CAD or other indications for aspirin. We aim to define the efficacy and safety of apixaban in patients with AF who are taking and not taking aspirin.

Methods: ARISTOTLE included 18,201 patients randomized to apixaban 5 mg twice daily or warfarin. The use of concomitant aspirin (≤165 mg daily) was left to the discretion of the treating physician. We compared baseline characteristics and the efficacy and safety of apixaban compared with warfarin among patients taking and not taking aspirin at baseline.

Results: At baseline, 5632 (31%) patients were taking aspirin. Patients taking aspirin were more likely to have CAD (50% vs 31%), PAD (6% vs 4%), diabetes (28% vs 24%), and paroxysmal AF (17% vs 14%), equally likely to have prior stroke (12% vs 12%) and less likely to have used a VKA prior to randomization (39% vs 65%) or have AF of >2 year duration (45% vs 56%) compared with patients not taking aspirin. Outcomes by baseline aspirin use are shown in the table.

Conclusions: Use of concomitant aspirin therapy in patients with AF is common, particularly in patients with CAD, and tends to be associated with worse outcomes and increased bleeding. The significant reductions in stroke or systemic embolism and major bleeding with apixaban compared with warfarin are similar regardless of baseline aspirin use. Ongoing analyses will address switching off and on aspirin and other antiplatelet agents during the trial.

1162-644 Routine early eptifibatide, infarct size, and outcomes in non-st-segment elevation acute coronary syndrome patients with elevated troponin on admission

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Background: In the EARLY ACS trial, eptifibatide 12 hours or more before angiography was not superior to the provisional use of eptifibatide in patients with non-ST-segment elevation myocardial infarction (NSTE MI). This subanalysis examines the efficacy of early eptifibatide in patients with elevated troponin (Tn) on admission.

Methods: In EARLY ACS, 9406 high-risk NSTE acute coronary syndrome patients expected to undergo an invasive strategy were random-

Endpoint	Aspirin			No Aspirin			Interactionp-value
	Apixaban	Warfarin	HR (95% CI)	Apixaban	Warfarin	HR (95% CI)	
	Rate/yr (n)	Rate/yr (n)	Apixaban vs Warfarin	Rate/yr (n)	Rate/yr (n)	Apixaban vs Warfarin	
Stroke or Systemic Embolism	1.34 (70)	1.86 (94)	0.72(0.53 - 0.98)	1.23(142)	1.48(171)	0.83(0.67 - 1.04)	0.46
Ischemic Stroke or Systemic Embolism	1.09 (57)	1.28(65)	0.85(0.60 - 1.21)	1.02(118)	1.08(125)	0.946(0.74 - 1.21)	0.63
Myocardial Infarction	0.80(42)	0.77(39)	1.046(0.68 - 1.62)	0.41(48)	0.54(63)	0.76(0.52 - 1.11)	0.28
All Cause Death	4.02(216)	4.69(244)	0.86(0.71 - 1.03)	3.29(387)	3.61(425)	0.91(0.80 - 1.05)	0.60
Major Bleeding	2.73(129)	3.68(164)	0.75 (0.59 - 0.94)	1.87(198)	2.84(298)	0.66(0.55 - 0.79)	0.42
Major or Clinically Relevant Non-Major Bleeding	4.93(228)	6.86(298)	0.72 (0.61 - 0.86)	3.69(385)	5.65(579)	0.65(0.58 - 0.74)	0.38
Any Bleeding	21.10(826)	30.34(1030)	0.72 (0.65 - 0.79)	16.79(1530)	24.01(2030)	0.71(0.67 - 0.76)	0.96
Intracranial Hemorrhage	0.37 (18)	1.06(48)	0.36 (0.21 - 0.61)	0.32(34)	0.70(74)	0.46(0.30 - 0.69)	0.47

ized to early vs. delayed provisional eptifibatide. Of these, 7881 (84%) had an elevated Tn at baseline and were included in our analyses. We determined the median peak Tn level within 48 hours by treatment group using peak to upper limit of normal ratio and calculated area under the curve (AUC) for CK-MB at 48 hours using the trapezoidal rule method. We also determined the rates of the 30-day composite of death, MI, or recurrent ischemia requiring urgent revascularization (MACE) and in-hospital TIMI major bleeding (overall and non-CABG-related) by treatment group. Comparisons between groups were made using t-tests or Wilcoxon rank sum tests for continuous variables and chi-square or log-rank tests for event rates.

Results: Median 48-hour Tn level and CK-MB AUC were significantly lower in the group receiving eptifibatide compared with the early placebo group (median 48-hour Tn 13.2 [3.4-53.1] vs. 16.2 [4.2-58.2], p=0.02; median CK-MB AUC 83.2 [46.1-191.8] vs. 89.4 [47.9-199.6], p=0.04, respectively). MACE was significantly lower in Tn-positive patients who received early eptifibatide (13.2% vs. 14.7%, p=0.04), but overall TIMI major bleeding was significantly higher (2.7% vs. 1.9%, p=0.02) compared with the early placebo group.

Conclusion: Routine early eptifibatide in NSTE MI patients with an elevated Tn at baseline was associated with smaller infarct size at 48 hours and improved ischemic outcome, but at the cost of higher bleeding risk.

1184-285 Association of high serum glucose levels with low HDL cholesterol levels in non-diabetic hypertensive patients: implications for the development of new diabetes

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Background: Low HDL during treatment is strongly associated with development of new diabetes in hypertensive patients. Whether low HDL per se is associated with elevated serum glucose in the absence of diabetes is unclear.

Methods: Baseline and annual serum glucose levels were examined as a function of sex-specific quartiles of HDL in 6953 LIFE study patients with no history of diabetes who did not develop diabetes during the study. Patients were randomized to losartan vs atenolol-based treatment, with additional hydrochlorothiazide (HCTZ) therapy added as needed.

Results: Serum glucose was highest in the quartile with lowest HDL at baseline and throughout the study and decreased across quartiles of HDL (Table). The association between low HDL and elevated serum glucose was highly significant at baseline and each year of the study and was independent of randomized treatment allocation, in-study treatment with HCTZ and statins, body mass index, serum creatinine and uric acid, blood pressure and ECG left ventricular hypertrophy.

Conclusions: Low HDL levels are associated with elevated serum glucose levels during antihypertensive therapy, independent of the potential impact of treatment with losartan vs atenolol, HCTZ and statins, and of other potential factors that could influence glucose levels. These findings suggest that low HDL per se may be a stimulus to development of abnormal glucose tolerance and provide insights into the relationship between low HDL and development of diabetes.

1178-21 Low in-treatment HDL cholesterol levels strongly predict sudden cardiac death in hypertensive patients: the LIFE study

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Time	HDL Quartile 1 ≤1.22 men ≤1.30 women	HDL Quartile 2 1.08-1.29 men 1.31-1.58 women	HDL Quartile 3 1.30-1.55 men 1.59-1.89 women	HDL Quartile 4 >1.55 men >1.89 women	Overall p value	Adjusted p value*
Baseline (n=6953)	5.62±1.10	5.37±0.90	5.38±0.91	5.31±0.88	<0.001	<0.001
Year 1 (n=6846)	5.68±1.07	5.50±0.91	5.45±0.91	5.45±0.88	<0.001	0.001**
Year 2 (n=6557)	5.68±1.08	5.56±0.97	5.48±0.93	5.50±0.94	<0.001	0.009**
Year 3 (n=6355)	5.76±1.05	5.61±1.04	5.56±0.94	5.54±0.90	<0.001	0.006**
Year 4 (n=6134)	5.77±1.07	5.65±0.99	5.58±0.92	5.49±0.92	<0.001	0.003**

*adjusted for randomized treatment, race, prior antihypertensive therapy, body mass index, serum creatinine and uric acid, diastolic and systolic pressure, Cornell product left ventricular hypertrophy, hydrochlorothiazide and statin use at each time. **also adjusted for baseline serum glucose level

Background: Low HDL levels are associated with increased cardiac mortality and infusion of reconstituted HDL shortens cardiac repolarization in isolated rabbit cardiomyocytes, dyslipidemic patients and healthy volunteers. However, whether low HDL is associated with increased sudden cardiac death (SCD) risk in hypertensive patients is unclear.

Methods: SCD risk was examined in relation to in-treatment HDL levels in 8606 hypertensive patients randomly assigned to losartan- or atenololbased treatment. HDL at each year of testing was categorized into the lowest quartile vs upper 3 quartiles according to baseline HDL levels or examined as a continuous variable with hazard ratios calculated for each SD of the baseline mean lower HDL (0.44 mmol/l).

Results: During 4.8±0.9 years follow-up, there were 168 SCD (2.0%). In univariate Cox analyses, compared with HDL ≥1.21 mmol/l, in-treatment HDL <1.21 was associated with a 101% greater risk of SCD (95% CI 48-174%, p<0.001). In parallel analyses using in-treatment HDL as a continuous variable, each 1 SD lower HDL was associated with a 85% higher SCD risk (95% CI 50-177%, p<0.001). In multivariate Cox analyses adjusting for randomized treatment, age, sex, body mass index, prevalent and history of atrial fibrillation and diabetes, history of MI, ischemic heart disease, stroke, peripheral vascular disease, smoking status, baseline serum creatinine, glucose, urine albumin/creatinine ratio as standard risk factors and for statin use, incident MI, in-treatment diastolic and systolic pressure, heart rate, QRS duration, Cornell product criteria for left ventricular hypertrophy and non-HDL cholesterol levels as time-varying covariates, the lowest quartile of in-treatment HDL remained associated with a 49% greater risk of SCD (95% CI 6-109%, p=0.022) and, in alternative analyses, each 1 SD lower HDL treated as a continuous variable remained predictive of a 39% higher risk of SCD (95% CI 11-75%, p=0.004).

Conclusions: Lower in-treatment HDL is an independent predictor of SCD in hypertensive patients, even after adjusting for other potential risk factors and treatment effects. Whether increasing HDL levels can reduce the risk of SCD requires further evaluation.

916-5 Timing of angiography and clinical outcomes after fibrinolysis: a patient-level analysis of randomized early invasive clinical trials

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Background: The pharmacoinvasive strategy is ideal for ST elevation myocardial infarction patients (STEMI pts) arriving at hospitals unable to offer timely primary percutaneous coronary intervention (PCI). The optimal timing of coronary angiography (angio) after fibrinolysis and its impact on clinical outcomes is uncertain.

Methods: Patient level data from 6/7 trials (with median time to angio <12 hrs) of STEMI pts receiving fibrinolysis and randomized to early angio were included in a collaborative pt level analysis (SIAM III, GRACIA 1, CAPITAL AMI, WEST, CARESSinAMI, TRANSFER AMI, and NORDISTEMI). The primary endpoint was 30 day death or re-MI. A key secondary endpoint was in-hospital TIMI major bleeding. The relationship between treatment delay (time from lysis to angio) and outcomes was studied in multivariable models.

Results: Among 1238 pts (median age 59 years, 21% female, 82% Killip class I) randomized to early angio (87% had PCI), the median treatment delay was 165 (115, 228) min. Clinical outcomes were examined by treatment delay (Table). Age, presenting heart rate, and Killip class were significant independent predictors of 30 day death/re-MI; however, treatment delay per hour was not (HR=1.01, 95% CI=0.94-1.07, p=0.87).

Conclusions: Treatment delay was not predictive of 30 day death/re-MI among fibrinolytic-treated STEMI pts having early angio. Very early angio (< 2 hrs) did not appear to increase the risk of 30 day death/re-MI or in-hospital major bleeding and may reduce recurrent ischemia.

Outcome (%)	Overall n=1238	0-2 Hrs n=349	2-4 Hrs n=622	>4 Hrs n=267	p Value for trend
30 days					
Death/re-MI	5.2	4.9	5.8	6.4	0.41
Death	2.9	2.6	3.2	2.6	0.92
re-MI	3.0	2.3	2.9	4.1	0.19
Recurrent Ischemia	4.6	3.7	3.7	7.9	0.02
Stroke	1.0	0.9	1.0	1.1	0.74
In-Hospital					
TIMI major Bleeding	4.7	4.6	5.1	3.8	0.68