P4661 Low levels of IgM antibodies against phosphorylcholine predict development of coronary artery disease in a population based cohort

J. Frostegard[1], H. Gronlund[1], G. Hallmans[2], J.H. Jansson[2], K. Boman[2], M. Wikstrom[1], I. Dahlbom[3], H. Lettesjo[4], U. De Faire[1]. *[1]Karolinska Institutet, Stockholm, Sweden; [2]Umea University, Umea, Sweden; [3]Uppsala University, Uppsala, Sweden; [4]Athera Biotechnologies AB, Stockholm, Sweden*

Purpose: Phosphorylcholine (PC) is an epitope on oxidized low density lipoprotein (oxLDL) that may contribute to the atherogenicity of oxLDL. IgM antibodies against PC (anti-PC) are natural antibodies present ubiquitously in the population. The association between anti-PC and the incidence of myocardial infarction (MI) was investigated.
Methods: Included were 462 incident cases of first MI events and 888 age- and sex-matched controls identified through 13 years of follow-up (1987-1999) of subjects included in the FIA-2 study from northern Sweden. Serum levels of anti-PC were measured by ELISA (CVDefine). Relative risks (RR) with 95% confidence intervals (CI) of incident MI with adjustments for age, gender, geographical region, hypertension, diabetes, BMI, smoking habits, s-cholesterol and hsCRP were determined.
Results: Low anti-PC values were associated with increased risk of MI. Significant associations were found for values below 26.8 U/ml, corresponding to the lowest 25th percentile, and the highest association was seen below 16.9 U/ml, These results remained almost unaltered after adjustment for confounding factors (RR crude: 1.56, CI: 1.07-2.28 and RR adjusted, 1.69, CI: 1.09-2.54).
Conclusions: Our results suggest that IgM anti-PC assessment adds independent information to the more traditional risk factors for MI. Low levels of natural IgM antibodies against PC could be an important risk marker for the development of MI development.

P4662 N-terminal pro B-type natriuretic peptide, C- reactive protein and gamma glutamyltransferase are independent risk markers in patients with stable coronary heart disease

E. Bode, T. Bode, T. Wuppinger, H. Alber, H. Ulmer, O. Pachinger, J. Mair. *Innsbruck Medical University, Innsbruck, Austria*

Biomarkers are gaining interest for risk stratification in patients with stable coronary artery disease (CAD). The aim of the present study was to determine the importance of novel recently proposed markers in the context of multimarker testing and classical risk factors.
Methods: We enrolled 525 patients with stable CAD from March 2004 until end of February 2005 in whom CAD was verified by coronary angiography (CAG). N-terminal pro B-type natriuretic peptide (NT-proBNP), high sensitivity C-reactive protein (hs-CRP), and gamma-glutamyltransferase (γGT) were measured as part of the routine laboratory testing before CAG. The severity of CAD was assessed by angiographic criteria and ventricular function was quantified by ventriculography or echocardiography. Mortality and the combined endpoint (mortality, coronary revascularization, myocardial infarction, rehospitalization for cardiac causes or stroke) were evaluated with the help of death registry data, chart review, or telephone interviews. From these 525 patients 394 had a complete follow-up, the remaining patients could not be reached or declined an interview. The T-test, Mann Whitney U test and the Chi square test were used for group comparisons and did not show significantly differing results. The prognostic value of each variable was assessed univariately by means of Kaplan Meyer survival rate analysis and by the multivariate Cox regression analysis. P-values <0.05 were considered as statistically significant.
Results: The average follow-up period was 1177 days. The mortality rate was 10.2% and the combined endpoint rate was 31%. The univariate analysis showed that the standard risk factors apart from diabetes mellitus and impaired renal function at the time of CAG were of no prognostic relevance for prediction of outcome defined as mortality or combined endpoint. The severity of CAD and a status post coronary bypass surgery or coronary intervention and the ventricular function were of prognostic relevance. NT-proBNP, hs-CRP and γGT were significant predicators of mortality, however only NT-proBNP was a significant predictor of the combined endpoint. In an age- and gender adjusted multivariate analysis, NT-proBNP was the strongest independent predictor of the combined endpoint (odds ratio 2.92). All three laboratory parameters remained independent risk markers for mortality in the multivariate analysis. NT-proBNP, however, revealed the highest odds ratio (5.23).
Conclusion: In comparison with other tested novel biomarkers and classical risk factors, NT-proBNP was the most predicitve prognostic marker in patients with stable CAD.

P4663 Urinary albumin excretion, even within the normal range, predicts increase in left ventricular mass over the following five years

T. Reffelmann, M. Doerr, H. Voelzke, S.B. Felix. *Universitaetsklinikum Greifswald, Greifswald, Germany*

Purpose: Cardiac left ventricular hypertrophy is a significant predictor of cardiovascular events, heart failure, stroke and overall cardiovascular mortality. We investigated whether urinary albumin excretion, as a cardiovascular risk marker, could prospectively predict the development of left ventricular mass (LVM).
Methods: Subjects, aged 45 – 79 years, from the population-based, longitudinal "Study of Health in Pomerania" with complete echocardiographic data at baseline and after five years of follow-up were grouped into four quartiles according to the urinary albumin-to-creatinine ratio (ACR) at baseline (n=1086). The relation of ACR and LVM (M-mode-derived formula) was analysed by various models including multivariate analysis by general linear model.
Results: Baseline LVM in quartile IV differed significantly from quartile I – III ($p<0.004$) and further increased by 13.9±3.2 g over five years (table). In quartile I, LVM did not significantly change over five years (+0.2±2.7 g, $p<0.001$ versus II-IV). In quartile II and III (ACR: 0.902-1.804), both with ACR values well below the threshold for definition of microalbuminuria, LVM increased by more than 10 g. The difference in LVM (Δ LVM) correlated significantly with ACR in the entire population ($p<0.001$), and also in the female ($p<0.016$) and the male subgroup ($p<0.016$). Unlike age, gender, prevalent hypertension and diabetes mellitus, body mass index, estimated glomerular filtration rate and use of various antihypertensive drugs, ACR, pulse pressure, and glycated hemoglobin at baseline were identified as significant predictors of increase in LVM by multivariate analysis.

LVM in relation to urinary ACR

Quartiles	I	II	III	IV
ACR (mg/mmol)	ACR $\leq$ 0.532 (n=272)	ACR $\leq$ 0.902 (n=271)	ACR $\leq$ 1.804 (n=271)	ACR $>$ 1.804 (n=271)
LVM baseline (g)	182.8±3.3	186.8±3.4	182.9±3.3	198.1±3.6
LVM after 5 years (g)	183.0±3.3	198.3±3.5	197.2±3.5	211.9±3.9
Δ LVM (g)	+0.2±2.7	11.5±2.6	14.3±2.9	13.9±3.2

Conclusions: Urinary ACR, even below the threshold for definition of microalbuminuria, predicts increase in LVM over the following five years. Elevated urinary albumin excretion should initiate decisive preventive measures in subjects prone to developing left ventricular hypertrophy.

P4664 Low serum testosterone and increased mortality in men with coronary disease

C.J. Malkin[1], P. Morris[1], T.H. Jones[2], K.S. Channer[1]. *[1]Sheffield Teaching Hospitals, Sheffield, United Kingdom; [2]Centre for Diabetes and Endocrinology, Barnsley Hospital, Barnsley. S75 2EP, UK, Barnsley, United Kingdom*

Background: Male sex is a risk factor for coronary disease and testosterone is widely believed to be the cause. We examined the effect of serum testosterone levels on survival in a consecutive series of men with proven coronary disease and calculated the prevalence of testosterone deficiency.
Methods: A total of 930 men with coronary disease (age 32-85 years) were recruited and followed up for a mean of 6.9±2.1 years. Baseline total (TT) and bio-available (Bio-T) testosterone levels were taken and co-morbidities recorded. Mortality was recorded by the office of National Statistics. Analysis was by Cox proportional hazard regression with adjustment for baseline covariates, giving an odds ratio for survival.
Results: The overall prevalence of biochemical testosterone deficiency in the coronary disease cohort using (Bio-T$<$2.6nmol/L) was 20.9%, using (TT$<$8.1nmol/L) was 16.9% and using either 24%. Excess mortality was noted in the androgen deficient group compared to normal (41[21%] v 88[12%], p=0.002). The only parameters found to influence time to all cause and vascular mortality (OR survival±95% confidence) in multivariate analyses were presence and severity of left ventricular dysfunction (OR=0.26[0.12–0.58]), aspirin therapy (OR=1.6[1.0–2.6]), beta-blocker therapy (OR=2.2[1.5–3.2]), low serum Bio-T (OR=0.44[0.28–0.69]) and TT (OR =1.04[1.0–1.1]). In addition baseline TT level ($<$15nmol/L) was associated with reduced survival (OR=0.54[0.3–0.9]) [figure 1].

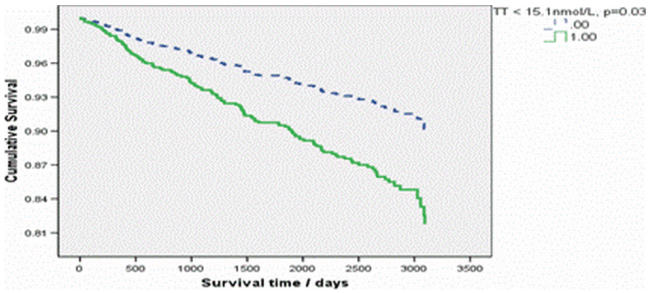

Figure 1. Survival by TT level

Conclusions: In patients with coronary disease testosterone deficiency is common and significantly negatively impacts on survival. Prospective trials of testosterone replacement are urgently needed to assess the affect of treatment on survival.