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Objectives: Non-alcoholic fatty liver disease is an important feature of the metabolic syndrome and is characterized by an elevated alanine aminotransferase / aspartate aminotransferase (ALT/AST) ratio. The association of the ALT/AST ratio with cardiovascular events in insulin-resistant patients with established coronary artery disease (CAD) is unclear and is addressed in the present study.

Methods: The ALT/AST ratio was measured in a high-risk cohort of 1063 patients with angiographically proven CAD. Patients with a homeostatic model assessment index of insulin resistance >2.5 were considered insulin resistant. Prospectively, vascular events were recorded over 10 years.
Results: At baseline, the ALT/AST ratio was significantly higher in insulin resistant patients than in subjects who were not insulin resistant (HOMA-IR 1.1±0.4 vs. 0.9±0.4;p<0.001). Prospectively, cardiovascular events occurred in 34.7% of our patients. The ALT/AST ratio after multivariate adjustment strongly and significantly predicted vascular events among insulin-resistant patients (standardized adjusted hazard ratio (HR) 1.37 [1.10-1.70]; p=0.004) but not among subjects without insulin resistance (HR 1.10 [0.95-1.39]; p=0.158).
Conclusions: We conclude that the ALT/AST ratio in insulin-resistant CAD patients is elevated and is significantly predictive of cardiovascular events.

EAS16-0125, GENETICS, NUTRITION, BIOMARKERS: BIOMARKERS. IMPACT OF AGE ON THE CARDIOVASCULAR EVENT RISK CONFERRED BY HBA1C IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

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Objectives: In the present study we tested the hypothesis that age modulates the impact of HbA1c on cardiovascular event risk in patients with sonographically proven peripheral arterial disease (PAD).

Methods: We prospectively recorded cardiovascular events over a mean follow-up period of 4.9±1.7 years in a consecutive series of 319 patients with sonographically proven PAD, including 78 subjects <65 years and 241 subjects ≥65 years.
Results: During follow-up, the incidence of cardiovascular events was 48.1% among subjects <65 years and 49.4% among subjects ≥65 years (p=0.473). Among the older patients, HbA1c strongly and significantly predicted cardiovascular events (adjusted HR for a 1% increase 1.24 [1.07-1.44]; p=0.004), but not among younger patients (adjusted HR for a 1% increase HR 1.01 [0.83-1.21]; p=0.963). An interaction term age x HbA1c was statistically significant (p=0.048), indicating that HbA1c was a significantly stronger predictor of cardiovascular events among older than among younger PAD patients.
Conclusions: We conclude that HbA1c is a significantly stronger predictor of cardiovascular events in older than in younger PAD patients.

EAS16-0135, GENETICS, NUTRITION, BIOMARKERS: BIOMARKERS. PROBNP STRONGLY PREDICTS FUTURE MACROVASCULAR EVENTS IN ANGIOGRAPHIED CORONARY PATIENTS WITH AS WELL AS IN THOSE WITHOUT TYPE 2 DIABETES

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Objectives: Pro-B-type natriuretic peptide (proBNP) is a prognostic biomarker in various patient populations including those with congestive heart failure. The power of proBNP to predict cardiovascular events in patients with type 2 diabetes (T2DM) undergoing coronary angiography is unclear and addressed in the present study.

Methods: We measured serum-proBNP in 737 patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD). Significant CAD was diagnosed in the presence of coronary stenoses with lumen narrowing ≥50%. T2DM was diagnosed according to ADA criteria. Prospectively, we recorded vascular events over 5.6±2.1 years.
Results: ProBNP was significantly higher in patients with (n=391) than without significant CAD at baseline (720±1358 vs. 674±1606 pg/ml;p=0.001). Prospectively, we recorded 183 cardiovascular events. The incidence of vascular events significantly increased over tertiles of proBNP in patients with T2DM (21.3%, 30.2%, and 43.5% respectively;p=0.028) as well as without T2DM (16.9%, 21.2%, and 29.3%, respectively;p=0.015). Concordantly, serum-proBNP significantly predicted the incidence of major cardiovascular events after adjustment for age, gender, BMI, smoking, systolic and diastolic blood pressure, LDL-cholesterol, HDL-cholesterol and the eGFR in patients with T2DM (standardized adjusted HR 1.50 [1.25-1.78];p <0.001) and in subjects without T2DM (HR 1.15 [1.03-1.29];p=0.015). These results were not attenuated after further adjustment for the angiographically determined baseline CAD state (HRs 1.49 [1.24-1.79];p <0.001 and 1.27 [1.13-1.43];p <0.001 in patients with T2DM and in subjects without T2DM,respectively).
Conclusions: We conclude that serum-proBNP predicts cardiovascular events independently of established cardiovascular risk factors and of the baseline CAD state, in patients with and without T2DM.

EAS16-0316, GENETICS, NUTRITION, BIOMARKERS: BIOMARKERS. THE LEVEL OF EOSINOPHIL CATIONIC PROTEIN IS CORRELATE WITH SEVERITY OF CORONARY ATEROSCLEROSIS

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Objectives: Atherosclerosis is a chronic inflammatory disease and it is important to study various inflammatory markers as possible predictors of atherosclerosis. In particular, the evaluation of the eosinophils' activity, determined by the level of eosinophil cationic protein (ECP). The aim of our study to compare the level of eosinophil cationic protein in patients with different degrees of severity of coronary atherosclerosis.

Methods: The study included 168 patients (119 males) aged from 54 to 67 years (mean age 60 years), undergoing coronary angiography. The ECP level in all the patients had been measured before the procedure.
Results: According to the results of the coronary angiography, the patients were divided into several groups: the patients with normal coronary arteries (NCA) (n=17); the patients with primary coronary atherosclerosis (n=11); the low (n=109), intermediate (n=16) and high (n=11) risk patients according to the Syntax scale. The ECP level in the patients with NCA was significantly lower than the groups of middle and high risk according to the Syntax scale and amounted to 8.7 ng / ml (6.5 ng / ml - 11.5 ng / ml), 11.9 ng / ml (11.2 ng / ml - 15.9 ng / ml) and 15.6 ng / ml (8.9 ng / ml -18.8 ng / ml) respectively (p <0.05).
Conclusions: In the groups with severe coronary atherosclerosis (the groups of medium and high risk according to the Syntax scale) ECP rate was significantly higher than in patients with NCA, suggesting increasing activity of eosinophils during the progression of coronary atherosclerosis.

EAS16-0324, GENETICS, NUTRITION, BIOMARKERS: BIOMARKERS. SIMPLE MORTALITY PROGNOSTIC RISK CALCULATOR FOR PATIENTS WITH ACUTE CORONARY SYNDROME

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Objectives: The high prevalence of coronary artery disease (CAD) and acute coronary syndrome (ACS) needs mortality risk assessment also on the outhospital level to stratify the mortality risk of patients.

Aim: To create a simple risk-scale calculator for patients with ACS.
Methods: In the retrospective register, 1000 medical records of patients with ACS were analyzed. Patients were divided into the group 1 (survivors) and group 2 (nonsurvivors). Firstly, the risk factor were evaluated using the binary model, secondly the multifactor (9 factors) mathematical model and computer program "Kardiorisk" of mortality risk prediction was constructed and thirdly the computer risk assessment model was tested on 50 patients with ACS.
Results: The following risk factors were analyzed: heart rate (HR), age, gender, myocardial infarction (MI) in the past, arrhythmias. The highest impact on mortality had ventricular tachycardia, atrial fibrillation, age, HR and MI. The multifactor regression model based the was created and showed high likehood ratio and accuracy. Then the computer program based on 9 risk factors was constructed in which the output data was the mortality risk ranging from 0 to 1 (min-max). The program was tested in 50 patients with ACS (25 non- and 25 survivors) and 14 survivors showed low mortality risk, 5 – moderate and 6 – high. All nonsurvivors had the highest risk. Thus, the simple risk stratification model showed 80% sensitivity and 100% specificity.
Conclusions: The simple mortality prediction risk model of ACS was highly effective.

EAS16-0337, GENETICS, NUTRITION, BIOMARKERS: BIOMARKERS. THE INVERSE ASSOCIATION BETWEEN PLASMA ENDOGLIN LEVELS AND THE SEVERITY OF CORONARY ATHEROSCLEROSIS IN PATIENTS WITH STABLE CAD

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Objectives: Transforming growth factor-β1 is a inhibitor of endothelial cell growth and migration. Endoglin is a transmembrane glycoprotein highly expressed on endothelial cells and has been identified as an accessory receptor for TGF-β, thereby modulating TGF-β1 signaling. Endoglin is released from cell membrane into blood as a soluble form, but blood endoglin levels in patients with coronary artery disease (CAD) has not been elucidated.

Methods: We investigated the association between plasma endoglin levels and the severity of coronary atherosclerosis in 244 consecutive patients undergoing coronary angiography. Patients with acute coronary syndromes were excluded. On angiograms, the severity of coronary atherosclerosis was represented as the numbers of >50% stenotic vessels and segments. Endoglin levels were measured using a commerciably available ELISA kit.
Results: Of the 244 patients, CAD (>50% stenosis) was found in 148 patients, of whom 62 had 1-vessel, 41 had 2-vessel, and 45 had 3-vessel disease. Compared with patients without CAD, those with CAD had lower endoglin levels (median 4.06 vs 4.32 ng/mL, P<0.02). A stepwise decrease in endoglin levels was found depending on the number of stenotic vessels: 4.32 in CAD(-), 4.19 in 1-vessel, 4.16 in 2-vessel, and 3.77 ng/mL in 3-vessel (P<0.02). Endoglin levels correlated with the number of stenotic segment (r=-0.22, P<0.001). In multivariate analysis, endoglin levels were an independent factor for 3-vessel disease. Odds ratio for 3-vessel disease was 0.96 (95%CI=0.93-0.99) for 0.1 ng/mL increase in endoglin levels.
Conclusions: Plasma endoglin levels were found to be inversely associated with the severity of coronary atherosclerosis in patients with stable CAD.

EAS16-0458, GENETICS, NUTRITION, BIOMARKERS: BIOMARKERS. NITRIC OXIDE-RELATED CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH MAJOR DEPRESSION

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Objectives: Major depression is a well-known risk factor for cardiovascular diseases and increased mortality following myocardial infarction. Nevertheless, biomarkers of depression and increased cardiovascular risk are still missing. The aim of this prospective study was to evaluate, whether nitric oxide (NO) related factors for endothelial dysfunction, such as global arginine bioavailability, arginase activity, L-arginine/ADMA ratio and the arginine metabolites asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) might be useful biomarkers for depression-induced cardiovascular risk.

Methods: In 71 in-patients with major depression and 48 healthy controls the Global Arginine Bioavailability (GAB) ratio, arginase activity (arginine/ornithine ratio), the L-arginine/ADMA ratio, ADMA, and SDMA were determined. Psychiatric and laboratory assessments were obtained at baseline (i.e. in-patient admittance), and at the time of hospital discharge.
Results: The ADMA concentrations in patients with major depression were significantly elevated and the SDMA concentrations were significantly decreased in comparison with the healthy controls. Even after a first improvement of the depression symptoms at the time of discharge, ADMA and SDMA levels remained unchanged. However, we observed a significant decrease in arginase activity, and an increased L-arginine/ADMA ratio as well as an increased GABR.
Conclusions: Herein we show in patients with major depression that ADMA and SDMA might be useful biomarkers to indicate an increased cardiovascular risk based on depression-triggered NO reduction. Arginase activity and the ratios of L-arginine/ADMA and GAB might be indicators of anti-depressive therapy success associated with an increased NO production.

EAS16-0518, GENETICS, NUTRITION, BIOMARKERS: BIOMARKERS. BRANCHED-CHAIN AMINO ACID PROFILES INDICATE CARDIO METABOLIC RISK INDEPENDENT OF BODY MASS INDEX

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Objectives: Cardiovascular risk is increased in obese subjects. Nevertheless, some overweight and obese individuals are cardio-metabolically healthy. Conversely, cardio metabolic abnormalities are found among normal-weight individuals. Hence, there is a need to identify persons at risk for cardio metabolic disease independent of BMI. Herein, we investigate the potential of branched-chain amino acids (BCAAs) to identify such individuals.

Methods: High pressure lipid chromatography (HPLC) was used to measure BCAAs in a cross-sectional study of 666 adults and juveniles (age 25.3 ± 12.8 years). Individuals were classified as lean, overweight or obese. Cardio metabolic groups were established based on cut offs of systolic blood pressure (BP) <130 mmHg, diastolic BP <85, glucose <125 mg/dl, triglycerides <150 mg/dl, HDL-C >40 mg/dl males, >50 females, and HOMA-IR<5. Cardio-metabolically healthy (CMH) were defined as <1 cut off, and cardio-metabolically abnormal (CMA) as > 2 cut offs.
Results: 224 lean, 220 overweight, and 222 obese were classified with regard to BMI and investigated. CMA subjects were found among the obese (42%) and overweight (58%) subjects but also among the lean (50%). Valine correlated with 5, leucine with 3, and isoleucine with 5 of the cardio metabolic risk classification factors. Serum levels of valine and leucine were significantly higher in the obese (p<0.001, p=0.015, respectively), overweight (p<0.001, p=0.015, respectively) and lean (p=0.024, p=0.012, respectively) CMA compared to CMH subjects. Isoleucine showed, except of the lean group, the same results.