P4661 | BEDSIDE
Asymmetric dimethylarginine (ADMA) - intermediate phenotypes and atrial fibrillation in the general population

M. Ramuschkat[1], S. Appelbaum[1], D. Atzler[2], T. Zeller[1], R.H. Boeger[2], P.S. Wild[3], T. Muenzel[3], S. Blankenberg[1], E. Schwedhelm[2], R.B. Schnabel[1] on behalf of Gutenberg Health Study. *[1]University Heart Center Hamburg, Hamburg, Germany; [2]University Medical Center Hamburg Eppendorf, Hamburg, Germany; [3]Johannes Gutenberg University Mainz (JGU), Mainz, Germany*

Background: The pathophysiological background of common atrial fibrillation (AF) is not well established despite its increasing prevalence in the general population and significant public health burden. Pathways of oxidative stress, nitric oxide bioavailability and L-arginine derivatives are hypothesized to be related to AF. Circulating methylated L-arginine metabolites can be assessed in the general population and may show an association with AF.
Purpose: This study investigates correlations of methylated L-arginine metabolites and other diagnostic variables in the general population with AF.
Methods: We determined L-arginine and its metabolites asymmetric dimethylarginine (ADMA), L-N-monomethylarginine (NMMA) and symmetric dimethylarginine (SDMA) in a large population-based study (n=5000), mean age 55±11 years, 51% men, in association with intermediate phenotypes of AF such as electrocardiographic and echocardiographic measures and manifest AF.
Results: Individuals with AF (N=161), 71% men, were older, mean age 64.9± 8.3 years. In Bonferroni-corrected multivariable-adjusted regression analyses we observed moderate inverse associations for L-arginine, SDMA, and L-arginine/ADMA ratio with ventricular heart rate, and for L-arginine and L-arginine/ADMA ratio with QTc interval. L-arginine was correlated with QRS duration. In echocardiographic analyses, SDMA was related to left atrial diameter, deceleration time and left ventricular ejection fraction, ADMA and NMMA were correlated with left ventricular mass. ADMA (odds ratio [OR] 1.21, 95% confidence interval [CI] 1.04–1-41; P=0.01) and NMMA (OR 1.16, 95% CI 1.03–1.32, P=0.02) were related to prevalent AF. L-arginine/ADMA ratio was inversely associated (OR 0.8, 95% CI 0.65–0.98, P=0.03). Results were similar after adjustment for creatinine.
Conclusions: In our large, population-based cohort, we observed moderate associations of L-arginine metabolites and intermediate electrocardiographic and echocardiographic variables and AF. Our findings support further investigations to define the role of L-arginine derivatives in AF and their clinical utility.
Acknowledgement/Funding: Stiftung Rheinland Pfalz für Innovation, "Wissen schafft Zukunft", CTVB, Stiftung Pathobiochemie

P4662 | BEDSIDE
Neutrophil/lymphocyte ratio predicts cardiovascular risk. The PREDIMED trial

J. Rodriguez Capitan[1], E. Gomez-Gracia[2], M. Jimenez-Navarro[3], M.A. Martinez-Gonzalez[4], J. Salas-Salvado[5], M. Fito[6], F. Aros[7], L. Serra-Majem[8], J.R. Alvero-Cruz[9], J. Warnberg[10]. *[1]Hospital De Poniente, El Ejido, Spain; [2]Health Institute Carlos III, CIBER Fisiopatología de la Obesidad y Nutrición, Madrid, Spain; [3]Hospital Universitario Virgen de la Victoria, Málaga, Spain; [4]University of Navarra, Department of Preventive Medicine and Public Health, Navarra, Spain; [5]Universitat Rovira i Virgili, Human Nutrition Unit, Reus, Spain; [6]Hospital del Mar Medical Research Institute (IMIM), Cardiovascular Risk and Nutrition Research Group, Barcelona, Spain; [7]Txagorritxu Hospital, Department of Cardiology, Vitoria, Spain; [8]University of Las Palmas de Gran Canaria, Research Institute of Biomedical and Health Sciences, Las Palmas de Gran Canaria, Spain; [9]University of Malaga, School of Sports Medicine, Malaga, Spain; [10]University of Malaga, Department of Preventive Medicine and Public Health, Malaga, Spain*

Background: Increasing evidence support that neutrophil/lymphocyte ratio (N/L) is a good predictor of future adverse cardiovascular outcomes, but most of the previous studies have been conducted in patients with symptomatic cardiovascular disease. We sought to evaluate the predictive ability of N/L for risk of cardiovascular disease (CVD) in an asymptomatic population sample at high cardiovascular risk.
Methods: Participants were recruited from seven PREDIMED study centers, where information about white blood cells count was collected. Our primary end point was a composite of myocardial infarction, stroke, and death from cardiovascular causes. The predictive ability for our end point in the highest quintile versus lowest quintile N/L, and total leucocyte, lymphocyte, neutrophil, monocyte, basophil and eosinophil counts were assessed using Cox regressions.
Results: A total of 4336 participants were included. The median of follow-up was 4.3 years. According to Cox regression, N/L and percentage of neutrophils were related with our primary end point, both of them in an unadjusted model (HR for N/L: 1.62; HR for percentage of neutrophils: 1.62) and in a model adjusted for sex, age and baseline risk factors (HR for N/L: 1.67; HR for percentage of neutrophils: 1.69). Similarly, N/L was related with cardiovascular death in the unadjusted (HR: 4.67) and the adjusted model (HR: 5.67), absolute number of neutrophils was related with cardiovascular death in the unadjusted model (HR: 3.24), and percentage of lymphocyte was inversely related with cardiovascular death in the unadjusted (HR: 0.25) and the adjusted model (HR: 0.23).
Conclusions: N/L was a strong predictor of cardiovascular disease in a selected population sample free of symptomatic cardiovascular disease at baseline, but at high cardiovascular risk.

P4663 | BEDSIDE
Relationships of QTc interval with cardiac biomarkers in young adults

T. Kofler[1], M. Bossard[2], S. Aeschbacher[1], A. Maseli[1], S. Blum[1], J. Todd[3], J. Estis[3], M. Risch[4], L. Risch[4], D. Conen[1]. *[1]University Hospital Basel, Internal Medicine, Basel, Switzerland; [2]University Hospital Basel, Cardiology Division, Basel, Switzerland; [3]Singulex, Inc., Alameda, United States of America; [4]Labormedizinisches Zentrum Dr. Risch, Schaan, Liechtenstein*

Background: Prolonged QT interval is a predictor of sudden cardiac death and other adverse cardiovascular outcomes. It is currently unclear whether subclinical cardiac alterations are involved in QT interval determination among young and healthy adults.
Methods: Healthy adults aged 25–41 years were enrolled in a prospective population based cohort study in the Principality of Liechtenstein. Main exclusion criteria were prevalent diabetes, overt cardiovascular disease or a body mass index $\geq$35 kg/m^2. Corrected QT (QTc) interval was automatically measured from a standard 12-lead electrocardiogram and validated by a trained physician. N-terminal prohormone brain natriuretic peptide (NT-proBNP) and high–sensitivity cardiac troponin I (hs-cTnI) were analyzed using a Roche analyzer and a Singulex assay, respectively. NT-proBNP and hs-cTnI were log transformed because of a non-normal distribution pattern. Multivariable regression models adjusting for potential confounders were constructed to assess the relationships of QTc interval with NT-proBNP and hs-cTnI.
Results: Our sample consisted of 2102 participants (53.6% females) with a median age of 36.7 years. The median hs-cTnI and NT-proBNP levels were 0.69pg/ml and 34pg/ml, respectively. The median (interquartile range) QTc interval was 402msec (387msec; 416msec). Results of NT-proBNP and hs-cTnI levels across quartiles of QTc interval are shown in the table. In multivariable analyses using NT-proBNP and hs-cTnI as log-transformed continuous parameters, the beta coefficients (95% confidence interval) were 2.48 (1.34, 3.62), p<0.0001 per 1pg/ml increase in NT-proBNP and –0.08 (–1.15; 1.00), p=0.89 per 1pg/ml increase in hs-cTnI.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4
QT_c (msec) – Linear regression, β (95% confidence interval)				
NT-proBNP†	ref.	0.64 (–1.67; 2.96)	1.77 (–0.54; 4.08)	4.25 (1.90; 6.59)
hs-cTnI†	ref.	–2.06 (–4.38; 0.27)	–3.56 (–5.90; –1.21)	–2.38 (–4.75; –0.01)

†n=2095. Coefficients were adjusted for sex, age, BMI, systolic blood pressure, diastolic blood pressure, HbA1c, GFR, education level, alcohol consumption, vegetable/fruit consumption, high density lipoprotein, low density protein, physical activity, smoking status (current or past), potassium, calcium and sodium.

Conclusion: There is a strong continuous relationship between NT-proBNP and QTc interval in young and healthy adults, an association that was not evident for hs-cTnI levels. These results may suggest that intravascular volume but not subclinical myocardial injury are related to QTc prolongation
Acknowledgement/Funding: Schweizerischer Nationalfonds, Schweizerische Herzstiftung, Singulex

P4664 | BEDSIDE
Correlation between plasma pentraxin-3, endothelial function and arterial stiffness in hemodialysis patients

M.M. Ciccone[1], M. Gesualdo[1], G. Ricci[1], S. Carbonara[1], R. Carbonara[1], F. Giardinelli[1], A. Zito[1], G. Pertosa[2], G. Loreto[2], P. Scicchitano[2]. *[1]University of Bari, Department of Cardiology, Bari, Italy; [2]University of Bari, Bari, Italy*

Objective: The pentraxin-3 (PTX3), produced by endothelium and mononuclear cells,is considered a new marker of vascular inflammation.The aim of the study was to evaluate the association between fluid overload, endothelial dysfunction and production of PTX3 and reactive oxygen species (ROS) in a population of subjects permanently (>12 months) in hemodialysis (ED).
Materials and methods: We enrolled 60 patients in ED 3 times/week with synthetic membranes (mean age 62.5 aa; dialysis average age: 44.3 months) and 10 healthy subjects. The plasma levels of PTX3 were measured by ELISA. The gene and protein expression of PTX3 on neutrophils was analyzed by flow cytometry and Real-Time PCR. The fluid overload was assessed by estimation of pulmonary artery systolic pressure (PAPS) measured during transthoracic echocardiography, impaired blood pressure was assessed by heart-ankle index (CABLES, expression of arterial stiffness) and ankle-brachial index (ABI), endothelial dysfunction through the flow-mediated vasodilation (FMD) of the brachial artery with ultrasound B-mode method.
Results: PTX3 levels observed at the beginning of the dialysis session (pre-ED) were significantly higher than in controls (2.43±0.63 ng/ml vs. 1.05±0.21 ng/ml; p=0.003) and tended to decrease at the end of the treatment itself. The high values were associated with a significant increase in gene and protein expression of PTX3 in neutrophils in pre-ED. The values of FMD were low in pre-ED compared to controls (4.7±1.8 vs 7.5±2.1; p<0.01), it normalized after 4 hours of ED (7.03±0,7; p<0.001) and tended to decline after 24 hours (5.59±0.4). The values of FMD pre- and post-ED inversely correlated (p<0.002) with those of the PAPS pre- (27.7±2.4 mmHg) and post-ED (18.1±1.6 mmHg).Furthermore, in the pre- ED patients high values of CABLES (9.7±0.3; p=0.003 vs controls) and a reduction of the values of ABI (0.9±0.2; p=0.004 vs controls) were observed. The plasma levels of PTX3 directly correlated with the CABLES (p=0.0001) and inversely with the values of FMD (p=0.02) and ABI (p=0.03). The reduction of FMD