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 levels of 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: The determined L-arginine and its metabolites asymmetric dimethylarginine (ADMA), L-N-monomethyl-L-arginine (NNMA) 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 NNMA were correlated with left ventricular mass. ADMA (odds ratio [OR] 1.21, 95% confidence interval [CI] 1.04–1.42), SDMA (OR 1.01, 95% CI 1.00–1.02) 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