Biomarkers

Ttrimetyllysine and risk of new-onset atrial fibrillation in two large norwegian cohorts

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Background/Aim

Increased plasma trimetyllysine (TML), a methylated amino acid, has recently been linked to higher risk of acute myocardial infarction (AMI). TML is also a precursor of trimethylamine-N oxide (TMAO), which has been linked to increased cardiovascular risk, including that of atrial fibrillation (AF). We investigated the association between TML and new-onset AF in two large Norwegian cohorts.

Methods: The primary cohort consisted of 6396 participants in the community-based Hordaland Health Study (HUSK). The validation cohort consited of 2027 patients who underwent coronary angiography due to suspected stable angina pectoris in the Western Norway Coronary Angiography Cohort (WECAC). Information on new-onset AF was obtained by linking patient data to Norwegian public health registries. Risk associations were explored by Cox regression.

Results: During median (25th-75th percentile) follow-up of 10.9 (10.6-11.3) and 7.0 (6.3-8.6) years, 560 (8.8%) patients in the HUSK and 210 (10.4%) in the WECAC was diagnosed with AF.

In the HUSK, the age and gender adjusted HR (95 % CI) for the 4th vs. 1st plasma TML quartiles 1.84 (1.37-2.48) $p < 0.001$. In multivariable models the association was only slightly attenuated. Correspondingsly, the age and gender adjusted HR (95% CI) for the 4th vs. 1st TML quartiles in the WECAC was 1.48 (0.96-2.27) $p = 0.07$.

Testing for collinearity between TMAO and TML revealed variance inflation factors between 1.0-1.1 in HUSK and WECAC, thus ruling out collinearity.

Conclusion: Plasma TML was associated with new-onset AF among subjects from the general population, and the relationship was independent from established AF risk factors. A similar trend was also seen in patients with suspected stable angina pectoris, strengthening our findings, which motivate further studies to explore potential pathophysiological relationships between one-carbon metabolism and cardiac arrhythmias