GUT FLORA METABOLITE TRIMETHYLAMINE N-OXIDE PREDICTS INCIDENT CARDIOVASCULAR RISKS IN BOTH STABLE NON-DIABETICS AND DIABETIC SUBJECTS

Poster Contributions
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Background: Recent animal studies show a mechanistic link between intestinal microbial metabolism of dietary phosphatidylcholine and coronary artery disease (CAD) pathogenesis. Levels of the pro-atherosclerotic metabolite trimethylamine-N-oxide, TMAO, are elevated in patients with diabetes mellitus (DM), but their prognostic value remains unclear.

Methods: We examined the relationship between fasting plasma TMAO and incident major adverse cardiac events (MACE=death, myocardial infarction, stroke) over 3-year follow-up in 4,007 stable subjects undergoing elective coronary angiography.

Results: In our study cohort, median TMAO levels were higher in DM (4.4[IQR 2.8-7.7]) versus non-DM (3.5[2.3-5.6], p<0.001). Higher plasma TMAO level was associated with a 3-fold increased risk of MACE in DM and a 2.1-fold increased risk of MACE in non-DM. Following adjustments for traditional risk factors and hsCRP, elevated TMAO levels remained predictive of MACE risk in both DM (Quartiles 4 vs. 1: Hazard ratio [HR]2.53 [95%CI 1.66-3.84], p<0.001) and non-DM (HR 1.61 [95%CI 1.15-2.26], p<0.001). There was only modest correlation between TMAO and HbA1c (r=0.11; p<0.01).

Conclusion: High plasma TMAO levels, a pro-atherogenic compound formed by gut flora dependent metabolism of the choline group of phosphatidylcholine, portend stronger incident risk of MACE in both diabetics and non-diabetics alike, with modest relationship to glycemic control.