Trimethylamine-N-oxide (TMAO) and cardiovascular outcome

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Swiss MedLab Bern, 15.06.2016
Dietary-associated and intestinal microbiota-dependent metabolite TMAO has emerged as independent cardiovascular risk factor.
TMAO Metabolism

Carnitine
- Transport of long-chain acyl groups into mitochondrial matrix

Choline
- Cell membranes
- Neurotransmission
- Synthesis of betaine

Betaine
- Methyl group donor to form methionine

Mouse Model

Mouse Model

Mouse Model

Food intake → Gut → Liver → Blood vessel

Choline → TMA → Microbiome

FMO3: TMA → TMAO → Atherosclerosis
Healthy Adults

- Increase after dietary choline Challenge
- Suppression through broad-spectrum antibiotics

Patients undergoing Elective Coronary Angiography

- TMAO
- Stroke
- Heart attack
- Death

- Low-risk subgroups
- Adjusted for age and cardiorenal indices

Graph showing myocardial infarction, stroke, or death over years with different quartiles of TMAO. P < 0.001 by log-rank test.

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
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</tbody>
</table>

n = 3903

Chronic Heart Failure

Risk of all-cause mortality according to quartiles of TMAO

Chronic Heart Failure

TMAO levels were significantly higher in:

- Diabetes mellitus (9.4 [4.9-13.2] vs. 4.8 [3.4-9.8] µmol/L)
- NYHA III or greater (7.0 [4.7-14.8] vs. 4.7 [3.4-11.3] µmol/L)
Chronic Kidney Disease

Prognostic Value of Plasma trimethylamine $N$-oxide (TMAO) Levels in the CKD Cohort

Chronic Kidney Disease

Dietary choline/TMAO Exposure Contributes to Progressive Renal Fibrosis in Murine Model

Objectives and Methods

- Our aim was to evaluate the predictive role of TMAO in CAP patients.
- Primary endpoint was all-cause mortality after a follow-up period of 6 years.

- 317 patients hospitalized with CAP (median 72 years).
- TMAO levels were measured by liquid chromatography coupled with tandem mass spectrometry.
Any Questions?

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List of References

Journal articles:

Pictures:
• URL: [http://edubily.de/2015/05/reizdarm-darmbakterien](http://edubily.de/2015/05/reizdarm-darmbakterien) (08.06.2016)
• URL: [http://www.surgery.usc.edu/hepatobiliary/liversurgery.html](http://www.surgery.usc.edu/hepatobiliary/liversurgery.html) (08.06.2016)
• URL: [http://www.klinikum-stuttgart.de/fileadmin/_processed_/csm_darstellung-nieren_dc45964833.jpg](http://www.klinikum-stuttgart.de/fileadmin/_processed_/csm_darstellung-nieren_dc45964833.jpg) (08.06.2016)
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