

Study shows gut bacteria byproduct impacts heart failure

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A chemical byproduct of intestinal bacteria-dependent digestion, TMAO (trimethylamine N-oxide) – already proven to contribute to heart disease and to be an accurate tool for predicting future heart attacks, stroke and death – has for the first time been linked to heart failure and worse long-term prognosis for those patients, according to Cleveland Clinic research published today in the *Journal of the American College of Cardiology*.

The research team was led by Stanley Hazen, M.D., Ph.D., Chair of the Department of Cellular and Molecular Medicine for the Lerner Research Institute and section head of Preventive Cardiology & Rehabilitation in the Miller Family Heart and Vascular Institute at Cleveland Clinic, and W.H. Wilson Tang, M.D., Department of Cardiovascular Medicine in the Miller Family Heart and Vascular Institute and Lerner Research Institute.

Drs. Hazen and Tang followed 720 heart failure patients over a five-year period and found that higher TMAO levels predicted higher future risk of death from heart failure, independent of other clinically used blood tests or risk factors. Interestingly, patients who had high levels of natriuretic peptides (an indicator of advanced heart failure) but low levels of TMAO had a much lower mortality rate than individuals with elevated levels in both markers. The researchers also found that when both TMAO and BNP (a peptide typically measured in heart failure patients) levels were raised, patients had more than a 50 percent mortality rate over 5 years.



TMAO, the researchers previously found, is produced when intestinal bacteria digest certain dietary components that are found in red meat, egg yolks, liver and some energy supplements. They found in a large clinical study that high levels of TMAO can predict future adverse outcomes like heart attack, stroke, and death.

"I am excited that these studies suggest TMAO testing may not only help identify those patients at greatest risk and for whom more aggressive monitoring is needed, but also that TMAO testing may help to tailor dietary efforts to the individual in the hopes of reducing future risks among those high-risk subjects," said Dr. Hazen.

"Our new results suggest that understanding why TMAO levels are elevated in the setting of heart failure may provide important insights into how intestinal bacteria contribute to disease progression in heart failure," said Dr. Tang.

According to the Centers for Disease Control and Prevention, heart failure occurs when weakened heart muscles do not pump blood effectively. More than 5 million patients in the United States are affected, costing the U.S. approximately \$32 billion each year.

The current study is an extension of Drs. Hazen and Tang's previous work, in which they found TMAO is linked to increased risk of <u>heart</u> <u>disease</u>, even in the absence of known cardiovascular risks, and is produced when intestinal bacteria digest carnitine, found in red meat and some energy drinks, and the nutrient phosphatidylcholine, commonly known as lecithin. The prior research showed that higher TMAO levels in the blood were associated with poorer outcomes in heart disease. Dr. Hazen and colleagues have now confirmed that gut flora are essential in forming TMAO in humans and demonstrated a relationship between TMAO levels and future cardiac events like <u>heart attack</u>, stroke, and death—even in those with no prior evidence of cardiac disease risk.



Provided by Cleveland Clinic

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