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Trimethylamine N-oxide and Risk Stratification after Acute Myocardial Infarction.
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Guest: Dr. Toru Suzuki is professor and chair of cardiovascular medicine at the University of Leicester, United Kingdom.

Bob Barrett: This is a podcast from *Clinical Chemistry* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I'm Bob Barrett.

Risk stratification in acute myocardial infarction remains a clinical challenge. Trimethylamine N-oxide, also known as TMAO, is a metabolite produced by intestinal bacteria based on our diet and the composition of our gut bacteria, or microbiome. It has gained interest in understanding the role foods rich in choline and I-carnitine, such as eggs and red meat play in heart and kidney disease. However, elevated TMAO has also recently been shown to increase thrombotic risk, potentially leading to myocardial infarction and stroke.

The January 2017 issue of *Clinical Chemistry* includes the results of a study investigating TMAO for risk stratification in patients hospitalized due to acute myocardial infarction. Dr. Toru Suzuki, the primary author, joins us for this podcast. Dr. Suzuki is professor and chair of cardiovascular medicine at the University of Leicester, United Kingdom. And doctor, research in TMAO and cardiovascular disease has had an invested interest in recent years, talk about the factors that were present that influenced you in deciding to perform this study.

Dr. Toru Suzuki: Sure. So Trimethylamine N-oxide, abbreviated TMAO, is basically an oxidized phospholipid, basically a part of phosphatidylcholine. And there's always been interest in how oxidized phospholipid such as oxidized LDL cholesterol, low density lipoprotein cholesterol, which is a part of the bad component of what we call cholesterol, is involved in heart disease, especially coronary artery disease.

So as an analogy to that, when -- I've been doing studies on oxidized LDL for about 20 years now, and when you're looking at biomarkers, then -- when you find that there's another one that's smaller than that called TMAO, you sort of pursue that. And it make sense that this is elevated in acute myocardial infarction, which is the representative disease for coronary artery disease.

Bob Barrett: So doctor, as this is the first study to look at TMAO in myocardial infarction, what are the main findings of the work presented in the manuscript? Did you see what you expected to see?

Dr. Toru Suzuki: Well, yes. What we found was that high levels of TMAO are associated with poor prognosis, which means death or reinfarction in two years' time, because we only looked at two years' time. One that was unexpected is that we didn't find an association with death or reinfarction at six months' time. But we did find that using TMAO levels with a clinical risk score called "GRACE," improves the accuracy of risk stratification at six months.

So to summarize again, yes, we found an association between TMAO and poor prognosis in long-term, and we found that in the short-term, use with the clinical risk score, adds to that.

Bob Barrett: Readers of your manuscript maybe aware of your previous work in trimethylamine N-oxide and cardiovascular disease. How does this compare to your previously published work?

Dr. Toru Suzuki: Sure. So previously, we published on TMAO and its association with prognosis and acute heart failure. This now looks at prognosis in acute myocardial infarction. Since heart failure and myocardial infarction are the two major cardiovascular diseases, this shows the TMAO when it's high in levels with acute patients with either disease have poor outcomes, and I think that's very important to get across as a message.

Bob Barrett: You mentioned the clinical utility of measuring TMAO for risk stratification. Can you explain if and how your analytical methods can translate into the clinical setting?

Dr. Toru Suzuki: Sure. So we use what are called "liquid chromatography based mass spectrometry" methods, so these are used in chemical pathology labs throughout the world. And throughput for the substance that we're looking at, TMAO, we can do probably about 150 samples a night if necessary. So if there were a demand to measure TMAO clinically, this would definitely be possible.

But importantly, because measuring TMAO allows us to better risk stratify patients with acute heart failure and acute myocardial infarction, measuring this in those patients will let us further define what their outcomes might be and tailor medication and treatment accordingly as well.

Bob Barrett: Well, finally, doctor, now that the initial experiment showing that trimethylamine N-oxide in acute myocardial infarction has been performed, are there any follow up experiments

that have been highlighted as important from the results described in your study?

Dr. Toru Suzuki: Well, sure. These are basically observational studies which mean that we looked at what's happening.

We don't know what happens over time, do increases in TMAO levels after an acute event, basically meaning after a heart attack, myocardial infarction, or heart failure affect the outcome, or do lower levels improve outcome, does intervention against TMAO, perhaps using drugs and other types of medications affect that as well? These are questions which remain unanswered right now and need to be answered in the future.

Bob Barrett: Dr. Toru Suzuki is professor and chair of cardiovascular medicine at the University of Leicester, United Kingdom. He's been our guest in this podcast from *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.