Sixth Generation High-Sensitivity Cardiac Troponin T: Will a Better Assay Make a Better Biomarker?

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Guest: Dr. Freddy Thurston is a Clinical Research Fellow in Cardiology at the Institute for Neuroscience and Cardiovascular Research at the University of Edinburgh.

Randye Kaye: Hello and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host, Randye Kaye.

Cardiac troponins are the most sensitive and specific biomarkers for myocardial infarction. The two specific subunits of the cardiac troponin complex used for clinical assays are troponin I and troponin T. Over the past three decades, assays for these cardiac troponins have been improving their analytical performance. Recently, the fifth generation cardiac troponin T assay was updated to its sixth generation.

The September 2026 issue of *JALM* features an editorial that reviews two articles published in the issue that evaluate the new sixth generation high-sensitivity cardiac troponin T assay. Today, we're joined by Dr. Freddy Thurston, one of the authors of the editorial. Dr. Thurston is a clinical research fellow in cardiology at The Institute for Neuroscience and Cardiovascular Research at the University of Edinburgh.

As part of the world class research teams at Edinburgh, Dr. Thurston has been involved in high-impact research focusing on clinical decision pathways utilizing cardiac troponins. His recent research has examined the clinical applications of the new sixth generation high-sensitivity cardiac troponin T assay and more widely, the use of machine learning to optimize the value of biomarkers in emergency settings.

Welcome Dr. Thurston, what makes a cardiac troponin assay high-sensitivity and where did this designation originate?

Freddy Thurston: Well, thank you. Thanks so much having me on the podcast. So, when we talk about high-sensitivity troponin assays, what we're talking about is assay that can measure cardiac troponin accurately at very low levels, kind of the amounts that you might find in the circulation of healthy people who don't have heart disease. So the International Federation of Clinical Chemistry gave us two criteria for an assay to be called high-sensitivity. It's important to know that it's not

anything about the thing it's measuring, its analytical properties of the assay that make an assay high-sensitivity.

So the criteria that IFCC defined for high-sensitivity assay is that it has to be able to detect troponin in more than half of healthy males, half of heathy females, and also that in these healthy males and healthy females, the upper reference of what we call the sort of 99th percentile of this healthy population, a high-sensitivity assay has to be very precise around that marker, variability less than 10% around the upper 99th percentile, and if an assay meets both of those criteria, then we'd refer to it has high-sensitivity assay.

Randye Kaye: I see. Well, your article summarized two studies reporting on the analytical characteristics of a new sixth generation high-sensitivity troponin T assay. What are the key differences to the previous version of the assay and how has it been improved?

Freddy Thurston: Yes. The fifth generation of the cardiac troponin T assay is one of the most widely used around the world in practice today and sixth generation builds on the same technology that is used in that assay. They're both what we call sandwich immunoassays, so that's where you've got a capture antibody and a detection antibody. They bind to the protein, and that's how your signal to detect the protein is generated. But for the sixth generation assay, then one of the antibodies that's used, the capture antibody's been improved.

So it binds at the same site through a process called affinity maturation, now has a higher binding affinity for cardiac troponin T molecule. Some further modifications we made to the reagents that use of a buffer and also in the components that allow separation of the troponin from the solution, also help to generate the chemiluminescence signal that's read out to measure concentrations. And the main improvement is now that the sixth-generation assay is much more precise at very low concentrations compared to the fifth-generation assay.

So the sixth-generation assay can now reliably detect cardiac troponin T down at concentrations of 1.5 milligrams per liter. Whereas the previous assay, that limited detection was up at 5 nanograms per liter and also what we call the limit of quantitation, so that limit at which there's a less than or equal to 10% variability, has also come down significantly. It's now well below the female reference limits. Other improvements that have been made in the assay include increased resistance to a fellow called hemolysis.

So quite often medical practice if you're in the emergency department, taking a blood sample can be sometimes handling areas and so I mean or just patient factors mean

that blood cells in the sample breakdown as it's being transported and it before it gets on to be analyzer, and that breakdown can affect the read out of different assays, and for the sixth generation assay in the article, we discuss showing that actually be resistance to hemolysis is much higher than the fifth generation assay. It might mean that fewer samples need to be repeated in clinical practice.

Randye Kaye: So, are there any other aspects that will be important for clinicians using the new assay to be aware of?

Freddy Thurston: So, the most important thing is to know that the assays aren't standardized to the same numbers. If you measure a sample with the sixth-generation assay, it'll give you a different number than if you'd measured it with a fifth-generation assay. That's because different reagents have been used for the calibration of the assays. Initially we got a large new study run by Professor Daniels from San Diego called REF-TSIX, that's derived new 99th percentile reference limits for men and women for this assay. It's important though--they're not the same as the old fifth generation assay, which means that clinicians who are switching from the old one to the new one will see different numbers and have to be aware that you generally expect to see a higher number with the sixth-generation assay as compared to the fifth-generation assay.

Randye Kaye: And how will these analytical improvements influence the clinical utility of the assay?

Freddy Thurston: This is a really interesting question and I know it's something we've been doing a bit of work looking at. So the main improvement being that now we can measure concentrations that are lower than before in the kinds we've seen in healthy people more precisely. That can be really helpful in the emergency department of sorting out patients who might actually had a problem like a myocardial infarction from people who have a healthy heart and might be able to be safely discharged.

So now we can systematically look at a range of decision thresholds below the upper reference limit that we can use to determine who might be, we could rule a heart attack out and we've seen that compared to the threshold that's used in the fifth-generation assay, we can now confidently say that a lot more patients, we can tell them that they haven't had a heart attack after just one sample because of the increased precision in the very low range means that we been able to systematically see how sensitive and how effectively these thresholds can rule out heart attacks in a way that wasn't possible with the fifth-generation assay.

And that's really promising, you know, we can identify patients who haven't had a heart attack at an early point in the patient journey and (a) that's very reassuring for the patient and not requiring serial blood tests, but also it means potentially, they can be reassured and sent home early if no other disease is found and given the number of patients who present with possible heart attacks to A&E departments around the world, anything we can do to speed up their assessment, help them get home, will help us tackle problems such as crowding in the emergency department, which is a real problem in a lot of healthcare systems.

Randye Kaye: Thank you. Last question, are there potentially any new clinical applications for the new assay?

Freddy Thurston: Typically think of using high sensitivity troponin assays in hospital for working out patients who may or may not have had a heart attack but there's been a lot of research over the past few years looking at whether we can get any information from measuring people's troponin when they're healthy, when they're not coming to the hospital but out and about in the community, and whether that can tell us anything about their longer-term risk of developing heart disease, might help identify patients who will identify most from starting preventative treatments or modifying their lifestyle and hope to help prevent heart disease at all.

At the recent European Society of Cardiology Congress actually, there's a excellent presentation from Professor Raphael Twerenbold who runs the Hamburg City Health study. They measured the sixth generation troponin assay in I think it's over 15,000 healthy residents of Hamburg City and they found that compared indeed to some of the other assays that have maybe slightly lower precision in the ranges you'd expect to see in healthy people. The sixth generation troponin T assay is actually able to more accurately predict which patients would go on to have cardiovascular disease, such as a heart attack or stroke, at a future date compared to older assays. So that's a very encouraging potential avenue for the future in identifying the people who're going to benefit from preventative treatment.

Randye Kaye: Well, that does sound promising and quite helpful. Thank you for joining us, Dr. Thurston.

Freddy Thurston: Well, thank you so much for having me.

Randye Kaye: That was Dr. Freddy Thurston discussing the *JALM* editorial, "Sixth Generation High-Sensitivity Cardiac Troponin T: Will a Better Assay Make a Better Biomarker?" which reviewed two articles in the September 2026 edition of *JALM* evaluating this assay? Thanks for tuning into this episode of *JALM* Talk. See

you next time and don't forget to submit something for us to talk about.