

**Article:**

Rami Aalto, Akseli Lahtinen, K E Juhani Airaksinen, Tuija Vasankari, Tapio Hellman, Laura Koskimäki, Saara Wittfooth.

Design and Analytical Evaluation of an Immunoassay for Long Forms of Cardiac Troponin T.

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Guest: Dr. Saara Wittfooth is an Associate Professor of Biotechnology and Vice Department Head at the Department of Life Technologies of the University of Turku in Finland.

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 I and T are protein biomarkers useful in the diagnosis of myocardial infarction, or MI. Current high-sensitivity assays can detect much lower concentrations of these biomarkers than previous conventional assays. However, lower measured concentrations of cardiac troponins come with lower specificity for MI and some elevations can have non-MI related etiologies like myocarditis or even chronic kidney disease.

Current high-sensitivity assays measure the totality of cardiac troponin protein and cannot differentiate between different troponin fragments. Differentiation between different fragments may offer more specificity for elevations seen in non-MI related diseases. For example, it has been shown that in chronic kidney disease, the small central fragments of cardiac troponin T are predominant.

The January 2006 issue of *JALM* features an article that outlines the design of a cardiac troponin T assay for only the intact or mildly fragmented form of the protein. When compared to a commercial troponin T assay that measures the total amount of cardiac troponin T protein, the ratio between the intact and total troponin T was able to differentiate patients with MI and end stage renal disease etiologies.

Today, we're joined by the article's corresponding author, Dr. Saara Wittfooth. Dr. Wittfooth is an Associate Professor of Biotechnology and Vice Department Head at the Department of Life Technologies at the University of Turku in Finland. Her research focus is in the development of highly sensitive laboratory tests, especially for novel cardiac biomarkers such as long forms of cardiac troponin T and anti-troponin autoantibodies. Welcome, Dr. Wittfooth.

Cardiac troponins are routinely measured in patients suspected of having myocardial infarction, or MI. How is the measurement of long or intact forms of cardiac troponin T different?

Saara Wittfooth: All the cardiac troponin assays that are used in the hospitals measure either cardiac troponin I or cardiac troponin T. The cardiac troponin T assays that are being used at hospitals measure all major circulating cardiac troponin T forms, the long forms but also the small, highly fragmented forms. So that is why we often call such assays as total cardiac troponin T assays.

Our own assay for long cardiac troponin T forms measures only the intact and mildly fragmented forms of cardiac troponin T. More specifically, our assays target the troponin T forms that are not cleaved at the C-terminal cleavage area of troponin T.

Randye Kaye: All right. Thank you. Now you focus on cardiac troponin T in this study. Are similar patterns of fragmentation seen in cardiac troponin I?

Saara Wittfooth: Yes. Cardiac troponin I also undergoes fragmentation that seems to progress in time after the onset of myocardial infarction symptoms, which is similar to cardiac troponin T.

Randye Kaye: Okay. So should long forms of cardiac troponin T always be measured in patient samples or are there specific instances where this has more utility? Like how do you see this testing entering routine practice?

Saara Wittfooth: Our investigations with large patient cohorts are still ongoing but it seems that long cardiac troponin T could be especially useful in identifying mild cardiac infarction and the settings where the current assays are showing elevated results.

For example, when the patient has reduced renal function, when the patient has atrial fibrillation, or if the patient has been doing heavy exercise. In these settings, the current cardiac troponin tests can give a significantly elevated results but the long cardiac troponin T forms are low. But it remains to be confirmed whether the long cardiac troponin T forms should be measured in all patients and could the test for a long cardiac troponin T even completely replace the current cardiac troponin tests.

So we are working on this in our ongoing studies. Our assay for the long forms of cardiac troponin T is currently an investigational in-house test that requires a lot of manual work for the test to enter routine practice.

It should be applied into an automated system such as the systems being currently used at hospital laboratories. And the test is an immunoassay, like the current cardiac troponin tests, this should be possible. What is needed is that a test manufacturer would adopt the assay in their system.

Randye Kaye: All right, thank you. Now, your team previously published another assay for long cardiac troponin T forms. How do these assays differ?

Saara Wittfooth: The assay that we report in the article was our first generation assay that was used to produce our first remarkable results showing the clear discrimination between myocardial infarction patients and renal disease patients. But we have developed the assay further by implementing a more sophisticated label technology. And with this, we have achieved remarkably better sensitivity. That assay has already been published and it has been used in our new studies.

Randye Kaye: Finally, you also reported in the article on the stability of long cardiac troponin T forms. So why is that important?

Saara Wittfooth: So, what is very important for a new biomarker such as the long forms of cardiac troponin T is to show its performance in various patient cohorts. At the early stage, that can be most efficiently achieved with previously collected frozen sample panels of thoroughly characterized patients. But then it's very important to know that the analyte is stable in repeated freezing and thawing and in sample processing and storage. So that is why it was very important to study and report on the stability of long cardiac troponin T forms.

Randye Kaye: All right. Thank you, and thank you for joining us today.

Saara Wittfooth: Thank you.

Randye Kaye: That was Dr. Saara Wittfooth, from the University of Turku in Finland, describing the *JALM* article "Design and Analytical Evaluation of an Immunoassay for Long Forms of Cardiac Troponin T."

Thanks for tuning in to this episode of *JALM* Talk. See you next time. And don't forget to submit something for us to talk about.