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Evaluating Rapid Rule-out of Acute Myocardial Infarction Using a High-Sensitivity Cardiac Troponin I Assay at Presentation

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Guest: Dr. Jaimi Greenslade is biostatistician and research fellow in emergency medicine at the Royal Brisbane and Women's Hospital in Australia.

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

The assessment of patients with potential acute coronary syndrome usually includes the clinical history, electrocardiograms, and cardiac troponin testing.

The previous generations of troponin assays often showed low diagnostic sensitivity for acute myocardial infarction upon presentation, and the diagnosis of acute MI usually required serial sampling over six to twelve hours. This process is not consistent with the need to rapidly and safely assess patients in overcrowded emergency departments.

Cardiac troponin measured with newer generations of analytically highly sensitive assays have been investigated in accelerated discharge protocols on the assumption that they have an improved ability to detect and quantify cardiomyocyte injury more quickly than previous generation's assays.

In the May 2018 issue of *Clinical Chemistry*, Dr. Jaimi Greenslade from the Royal Brisbane and Women's Hospital in Herston, Australia, and her colleagues investigated a high sensitivity cardiac troponin I assay to see if a single test threshold can safely rule out acute MI.

Dr. Greenslade is our guest to this podcast. Doctor, using very low cutoff values of high sensitivity cardiac troponin assays has been reported earlier. What does your current paper in *Clinical Chemistry* add to our understanding of such testing?

Jaimi Greenslade: Yeah, so I guess you're correct. There's a growing body of literature that looked at this idea of whether a very low troponin value can rule out acute myocardial infarction early during the emergency department visits for these patients. I guess, what's different is, virtually all studies have used before have focused on either the Roche high sensitivity

troponin T assay or the other high sensitivity troponin I assay.

This study differs in that it's the first one to look at this new Beckman Coulter high sensitivity troponin I assay. I guess within the realm of troponin, that's actually a really important distinction, so troponin concentration measured using the different assays aren't interchangeable. They all have a different limit of detection. They have a different 99th percentile and slightly different analytical performance.

The work that we've done so far using those Roche T and Abbott I assays has kind of highlighted some of these differences, so we know that the T assay maybe a stronger predictor of death than the I assay, but the I assay seems to pick out injury slightly earlier and possibly less intense injury and hemolysis kind of seems to affect these concentrations different. I guess the point there is that there are distinct differences between these assays, and so we have to test new ones as they come out.

This study was the first to look at this particular assay in a clinical context; there has been some work done on its analytical performance. But until recently we really didn't know how well it would perform in ruling out AMI. Ultimately, our study found that they were also pretty consistent with the previous research on all those older assays, that using a low-level troponin does still appear safe for ruling out AMI on presentation.

Bob Barrett: Doctor, your group has previously published on sex-specific differences in troponin concentrations. But in this study, you seem to use a single cutoff value for both males and for females, why is that?

Jaimi Greenslade: Our work that we have done on the sex-specific differences is really irrelevant when we're using the 99th percentile as it cutoff for an abnormal test sort of to define myocardial infarction or injury.

The development of these highly sensitive troponin assays has shown us that that 99th percentile of the healthy male population is actually higher than the 99th percentile value for that female population. If we use that overall 99th percentile cutoff, that value is lower than the 99th percentile for males and it's higher than the 99th percentile for females.

In our previous work, we raised concerns that using this combined cutoff may miss the identification of some of those females with cardiac disease, who had a troponin value that was above the female 99th percentile but below the combined cutoff.

However, in this paper, we aren't referring to the 99th percentile at all. We're using a very low troponin concentration that is below that 99th percentile to try and rule out AMI. What we think is that this low-level value sseem to reflect patients who are cardiovascularly normal regardless of their sex.

So these differences really aren't coming out to be relevant. Certainly, in our study, we examined some of those, whether there was difference in sex in terms of how well the assay was performing in that low level and it didn't seem to make a difference.

Bob Barrett: In your paper, you mentioned the 2 nanogram per liter cutoff, how transferable is that cutoff to other institutions or even other high sensitivity cardiac troponin assays?

Jaimi Greenslade: Yes. Certainly, the cutoff is relevant to any institution that wants to apply this assay. It's certainly not transferable to other assays. We know that each troponin assay has a different limit of detection which was what the 2 nanograms that we chose reflects in this paper, but that is very different for different assays. We know, for example, that the Roche T has a cutoff of five. I believe the Abbott is somewhere around one to two. You would need to know which assay your institution was using before you try to apply this cutoff. But I guess across institutions, if you knew that you were using Beckman's assay, there is no reason necessarily why this wouldn't work.

I guess, the only thing is this is the first study, so we have quite a low disease prevalence in our cohort of patients. We perhaps need a little bit more data on how well the assay is performing before it could be rolled out across any institution. But certainly, that specific cutoff is probably able to be used.

Bob Barrett: Well, the sensitivity of the single cut point is very high. Your criteria rule out only 34% of patients without acute myocardial infarction. Is this protocol ready for clinical use?

Jaimi Greenslade: Yes, I guess there is -- in terms of using these low-level values to rule out AMI, there is a lot of data out there around the Abbott I and Roche T assays, and those have actually been included in the European Society for Cardiology guidelines as something that could potentially be used. We know that low-level cutoff values have been applied within standard care in some European hospitals.

With the Beckman's assay, it possibly needs a little bit more data as I mentioned. This was the first clinical study and we have quite low disease prevalence. Given that the data was

kind of reflects what we have seen with the other assays, it probably is safe to use but we really feel that sort of a perspective intervention trial would really be useful at this point to assess how well this would work within a clinical context if applied, particularly for clinicians willing to use this as a rule out, are patients are happy to be sent home after a single value.

I think that would really give way to some of this literature, and certainly that's something we would like to do with our intervention trial with this assay.

Bob Barrett: Well, finally doctor, let's look ahead. What is the next stage of your investigation and what do you see as its potential impact?

Jaimi Greenslade: Yeah, as I say I think we would really like to do a perspective trial where we implement this in standard care and we are working towards that.

In term of impact, this could really be fabulous for both the patients, clinicians, and the healthcare system. As you mentioned, there's about a third of patients who could be ruled out using a presentation value. That means that these patients don't have to sit around in hospital waiting to get an answer for whether their chest pain is serious or not.

We know in our institution, the medium length of stay for patients who present with chest pain is still over a day. If we could send these patients home earlier, that would be fabulous for them. Patients who are investigated for chest pain often are exposed to some risk associated with cardiovascular testing. If we could rule this out very early, we could avoid some of those risks associated with some of those tests.

Obviously, the big winner here would be the healthcare system. So we are very fortunate here that we have universal healthcare. But we know that emergency departments have -- they're becoming overcrowded, the healthcare costs in every country are rising, and we have to try and do something about that.

If we can safely move patients quickly through the system, that would have benefits in terms reducing that overcrowding, potentially reducing cost, but also letting clinicians sort of direct their attention towards other patients who need their care within the department.

We feel that this kind of protocol could help you rapidly move patients through the system, while allowing you maintain kind of a high-level of care for patients.

Bob Barrett: Dr. Jaimi Greenslade is biostatistician and research fellow in emergency medicine at the Royal Brisbane and Women's Hospital in Australia. She has been our guest in this podcast from *Clinical Chemistry* looking at high sensitivity cardiac troponin in order to rule out acute myocardial infarction. I'm Bob Barrett. Thanks for listening.