Creation of a Universal Sample Bank for Determining the 99th Percentile for Cardiac Troponin Assays

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Guest: Dr. Alan Wu is Professor of Laboratory Medicine at the University of California, San Francisco and co-core laboratory chief at Zuckerberg San Francisco General Hospital.

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

Cardiac troponins T and I are the preferred biomarkers for detection of myocardial injury. However, they are also elevated in a number of other chronic diseases, such as kidney disease, diabetes, and vascular disease. In order to diagnose acute myocardial infarction, AMI, professional organizations including cardiology, emergency medicine, and laboratory medicine practitioners agree that laboratories should use elevations in troponin above the 99th percentile of a healthy population as the cutoff concentration. However, this 99th percentile cutoff is assay- and sample population- dependent and is therefore inconsistent between assays.

An initiative responded by a research grant from the American Association for Clinical Chemistry, and it was carried out by the Biomarkers of Acute Cardiovascular Disease Division. This led to an article published in the May 2017 issue of JALM. It's entitled "Creation of a Universal Sample Bank for Determining the 99th Percentile for Cardiac Troponin Assays." This article aimed to help streamline the determination of the 99th percentile for troponin assay manufacturers. The first author of this article is Dr. Alan Wu, Professor of Laboratory Medicine at the University of California, San Francisco and co-core laboratory chief at Zuckerberg San Francisco General Hospital. He's our guest for today's podcast. Welcome, Dr. Wu.

Dr. Alan Wu: Thank you, Randye.

Randye Kaye: So my first question is, let's just ask, why did the AACC create this sample bank?

Dr. Alan Wu: Well, there are a number of manufacturers of troponin I assays and the bad thing is that none of them are standardized to each other. So when you get a result from one assay, you have to compare it against either the

manufacturer's stated 99th percentile cutoff, or the hospital has to establish their own. While that's okay when you're just looking at one assay at one institution, when you want to try to compare results against another institution, or if you want to compare how one assay is rated against another, then we felt that it was necessary to establish the 99th percentile on a single population, because who you select as being "normal" will determine the actual 99th percentile value.

Randye Kaye: All right. So what did you do next?

Dr. Alan Wu: So we submitted a proposal to the AACC to fund a project whereby we would enroll apparently healthy subjects attending the AACC Annual Meeting that was held in 2015 in Atlanta, Georgia. So we got a grant. It was approved by the AACC Board of Directors, and we spent many months planning a blood collection protocol. It was done in conjunction with the AACC Meetings Management Group.

Randye Kaye: Great! So how many people signed up to participate?

Dr. Alan Wu: On the week of the AACC meeting, we had over 800 individuals who participated in the program. They were each given a gift card for participating at the AACC bookstore. They were also asked to fill out a case report form which told us who they were and whether or not they had any comorbidities that might affect the 99th percentile for troponin.

Randye Kaye: Great! Is there anything else I should know about how they were processed through this procedure?

Dr. Alan Wu: That's a great question. What we had were a number of phlebotomists that we had on hand. We also had processors. Once an individual had consented to participate in the study, blood was collected. They were centrifuged onsite, aliquoted into small freezer vials, about 250 microliters into each and about 100 different aliquots were stored, aliquots that were collected in blood that were preserved with either EDTA, heparin, or no preservatives, in which case, we froze serum samples.

Randye Kaye: Okay. So now you've got all these samples, so what are you going to do with the samples?

Dr. Alan Wu: So these samples then were put into boxed sets, whereby all of the sets would contain at least one sample from each individual. We also did some screening tests to rule diseases that we knew were going to affect the troponin values. So we ran NT-proBNP which is a marker of left ventricular dysfunction. We measured hemoglobin A1c to determine if there was any diabetes or pre-diabetes or

uncontrolled glucose. And we also ran a creatinine and from that calculated the eGFR, the estimated glomerular filtration rate, to determine whether or not any of these individuals had any renal insufficiency.

Randye Kaye: And so there's testing for troponin. Now, what's going to be the impact of that testing?

Dr. Alan Wu: So these individual boxed sets then were made available to different companies who purchased them and are running troponins now. In addition, the Biomarkers of Acute Cardiovascular Disease Division of the AACC has also obtained boxed sets and are running troponin independently of the manufacturers to determine the 99th percentile in our labs.

Randye Kaye: Terrific! So, if there's another researcher or manufacturer that would like to purchase a set, is there a way that they can do that?

Dr. Alan Wu: Yes. So the sets were originally designed for measuring the 99th percentile of troponin. But we have enough leftover samples that we haven't sold that now are going to be made available to other manufacturers or researchers who are interested in determining the normal range for other clinical chemistry analytes. They would be made available for sale in the same manner.

Randye Kaye: And who would they contact to purchase one, if they wanted to?

Dr. Alan Wu: So they should contact the AACC office, Stephanie Kleinman or Loretta Doan. These individuals are going to be the custodians of the sample bank, and communications through them directly would allow anybody to make a purchase.

Randye Kaye: All right. Thank you! Just last question, is there anything else you'd like to say or add to what you've already shared with us that you haven't had a chance to say?

Dr. Alan Wu: Well, the publication in *The Journal of Applied Laboratory Medicine* details the methodology that we used, the screening data that we imposed, and the final number of subjects which is a smaller subset of individuals than the total amount. We took out people with some of these comorbidities, but if you are interested in purchasing this set, you can then determine if you want to exclude these individuals. If not, because you may not need to be concerned about renal function, then the entire set can be made available.

Randye Kaye: All right. Very interesting! Thank you so much for joining us today, Dr. Wu.

Dr. Alan Wu: You're welcome.

Randye Kaye: That was Dr. Alan Wu from the University of California, San Francisco, talking about the JALM article, "Creation of a Universal Sample Bank for Determining the 99th Percentile for Cardiac Troponin Assays" for this podcast. Thanks for tuning in for "JALM Talk." See you next time and don't forget to submit something for us to talk about.