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Alan H.B. Wu and Robert Christenson.
The Era for High-Sensitivity Cardiac Troponin Has Begun in the US (Finally).
J Appl Lab Med 2017;2:1-3.
http://jalm.aaccjnls.org/content/2/1/1

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 troponin is the preferred biomarker for detection of myocardial injury, and in the United States, laboratories are currently using fourth generation immunoassays. In January 2017, a new fifth generation assay that measures cardiac troponin T was approved by the US Food and Drug Administration, which has been termed a high-sensitivity troponin assay. 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 cut-off concentration, in order to diagnose acute myocardial infarction.

There is concern that there could be confusion in interpreting the new cut-off concentrations and change in units. And editorial titled, "The Era for High-Sensitivity Cardiac Troponin Has Begun in the US (Finally)," published in the July 2017 issue of JALM, discusses the advantages and challenges of implementing the high sensitivity assay, which will result in a higher number of patients with an elevated troponin. The first author of this editorial 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, and he is our guest for today's podcast.

Welcome, Dr. Wu. First question, what is the medical advantage of high-sensitivity troponin assays?

Dr. Alan Wu: Well, being able to detect a lower concentration of troponin in blood will allow us to detect minor myocardial damage and earlier acute myocardial infarctions, and this may have a significant advantage to medical care of these patients.

Randye Kaye: Okay, great! So, how do we proceed to educate emergency department physicians and cardiologists?

Dr. Alan Wu: I think the key is to have them recognize that cardiac troponin is not just a marker of acute myocardial infarction, but that it can detect any type of cardiac injury that can be caused by a number of other diseases besides AMI. These includes renal disease, congestive heart failure, pulmonary emboli, sepsis, and a host of other things that can increase troponin in the blood.

Radye Kaye: When we go about educating these physicians and cardiologists, is that a big process or is it just perhaps, reading your editorial? What is the process for really educating them?

Dr. Alan Wu: Well, I think everybody knows what troponin is, and feel like they have an understanding of how to use it. What is needed is to understand why high sensitivity provides additional information that the troponin that they were using before does not. And perhaps, the key is the fact that there will be many more cases of minor myocardial damage that will have to be adjudicated than they may be used to. So, it's incumbent on the clinical laboratory to tell them that we have an assay that has lower detection limits, and that they need to think more carefully as to what a result might mean in a particular patient.

Randye Kaye: So, will there be high-sensitivity troponin I assays approved soon?

Dr. Alan Wu: That is certainly our hope. There have been a number of companies who have submitted data to the FDA for approval of their high-sensitivity assays. They have not yet achieved approval. We're hoping that with the release of the fifth-gen troponin T assay by Roche that these other troponin I assays, which should show very similar performance, will also be approved.

Randye Kaye: So, will we be needing to change units, and will there be sex-specific reference ranges?

Dr. Alan Wu: So, currently, the approval units of the older generation troponin assays have been in nanograms per milliliter and that results into values that are below 1. So a cut-off might be .01 or .04 nanograms per milliliter. With the use of high-sensitivity assays, manufacturers are changing their units from nanograms per mL to nanograms per liter which is a multiplication of the results by 1,000.

So, a .04 becomes 40, a .01 becomes 10. Most clinicians, emergency department, and cardiologists, are more comfortable with using whole numbers than trying to find numbers that have decimal points and zero values before the numbers. And I think that in the long run, this will reduce the confusion as to what a result might mean.

Randye Kaye: That sounds like a good change. What about the sex-specific reference ranges?

Dr. Alan Wu: So, the FDA has recommended that manufacturers list in their package inserts sex-specific cut-off concentrations, because it has been known for many years that men typically have higher troponin values than in women. And therefore, the use of sex-specific cut-offs may enable a better differentiation of abnormality than if a single cut-off applicable to both sexes is used.

We have known for a long time that women tend to have more under-diagnoses of AMI than men, and it may be because of the application of a single cut-off. By using a lower cut-off for females it is hoped that we will be able to detect more women who have myocardial injury and perhaps, myocardial infarction that would have been missed using the higher cut-off for men or the combined cut-off.

Now, not everybody agrees with that, so there's still some debate as to whether or not it is applicable. Some investigators feel that perhaps, the lowest cut-off, the female cut-off should be used for everybody. So this is going to be a debate that will continue as we begin to implement high-sensitivity assays.

Randye Kaye: I see that it will continue. So with that in mind, is there anything you'd like to add that you haven't said before we close out this interview?

Dr. Alan Wu: I think that clinical laboratories that are preparing themselves to implement high-sensitivity assays whether it be troponin T now, or troponin I in the future, must really establish a good dialogue between themselves and both the emergency department and cardiologist, that this cannot just be done in a vacuum by changing the units, by changing the cut-offs, by using the sex-specific reference ranges. It's going to cause a lot of confusion. There's a lot of confusion already today because not everybody uses the 99th percentile cut-off. Some of them continue to use a higher cut-off that is derived from receiver-operator characteristic curves. Those labs will have the most difficulty in converting to high sensitivity. The advantages of high sensitivity definitely supersede the current generation of conventional assays, so it is well worth implementing, but it needs to be done very carefully.

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

Dr. Alan Wu: Well, you're very welcome.

Randye Kaye: That was Dr. Alan Wu from the University of California San Francisco talking about the JALM article, “The Era for High-Sensitivity Cardiac Troponin has Begun in the US (Finally)” 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.