Point-of-Care: Roadmap for Analytical Characterization and Validation of a High Sensitivity Cardiac Troponin I Assay in Plasma and Whole Blood Matrices

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Robert H. Christenson, Lisa D.S. Frenk, Henk J. de Graaf, Trees S.Y. van Domburg, Frank P.G. Wijnands, Helma W. J. Foolen, Danielle W.M. Kemper, Anne L. Bruinen, Bernadet D.M. Meijering, Judith M. Fonville, and Femke K. de Theije.
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Guest: Dr. Rob Christenson is Professor of Pathology and Professor of Medical and Research Technology at the University of Maryland School of Medicine. He is also the medical director of the core laboratories and point-of-care services at the University of Maryland Medical Center.

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.

Approximately 10 million people present to emergency departments with signs and symptoms of acute myocardial infarction, or AMI, annually in the United States. For over 20 years, cardiac troponins T and I have been the premier blood biomarkers for AMI diagnosis and risk assessment. The analytical characteristics and clinical performance of cardiac troponin assays have evolved through several generations with the most recent generation of assays being referred to as high sensitivity.

The advent of high sensitivity troponin testing has allowed for rapid triage and rule-out protocols in the emergency room. However, most troponin testing occurs in the central clinical laboratory. Point-of-care troponin assays, if properly validated, could allow for faster result turnaround times. In order to be effective, these point-of-care tests would need to use whole blood rather than serum or plasma to eliminate sample processing and centrifugation steps. However, validation of whole blood point-of-care assays can be difficult due to possible sample interferences and limited sample stability.

In a special report in the July 2022 issue of *JALM*, the authors present a roadmap for the evidence-based analytical validation of point-of-care high sensitivity troponin assays. The article is intended to function as a template that other laboratories can use for the analytical evaluation of such tests.

Today, we are joined by the corresponding author of the article who also happens to be the editor-in-chief of *JALM*, Dr. Rob Christenson. Dr. Christenson is Professor of Pathology with tenure and Professor of Medical and Research

Technology at the University of Maryland School of Medicine. He is also the medical director of the Core Laboratories and Point-of-Care Services at the University of Maryland Medical Center.

Dr. Christenson, let's start here. What were the main objectives for your group in authoring this special report about evaluating point-of-care troponin assays?

Rob Christenson: We are clearly in an era of high-sensitivity cardiac troponin measurements. Implicit in the definition of high-sensitivity assays are analytical characteristics including the limit of detection and total imprecision at low cardiac troponin concentrations. Thus, practitioners, regulators, and manufacturers must understand how to define the limit of detection for determination of the proportion of healthy females and males that are detectable and also total imprecision at the lowest 99th percentile reference limit. That is, the one for females.

The other issue is that point-of-care assays generally are run with whole blood, plasma, and even some with serum. Stakeholders must understand that all matrices used clinically must be fully validated and results compared with each other.

Randye Kaye: All right, thank you. So now, what would you say is an unmet need in the area of cardiac biomarker testing that this report addresses?

Rob Christenson: The unmet need is the thoroughness with which validations are conducted. For example, understanding that numerous reagent lot numbers of cardiac troponin must be examined to fully validate the assay. Although either plasma or whole blood can be used at point-of-care, serial measurements must be run using only one matrix because there may be differences between the matrices. Also, understanding comparison studies and the relationship between high-sensitivity troponin assays is critical, particularly when patients are moved from one care environment, such as the emergency department, to an inpatient bed.

The point-of-care assay may show different results from the central lab cardiac troponin used at the institution. So there must be strategies to let users explicitly know which assays are being used when.

Randye Kaye: All right, thank you. What about benefits? Who benefits? What kinds of stakeholders will benefit from the information provided in the article, and how does that happen?

Rob Christenson: My view is that the information is critical for laboratory professionals, manufacturers, and particularly regulatory

stakeholders. However, clinicians should also be aware of the definition of high-sensitivity and what that means clinically.

So high-sensitivity really is an analytical term, and it means that we're using a better assay to make these measurements, not that we're measuring a different analyte. We're still measuring the same cardiac troponin that we were measuring before, just in a more stringent way. Stakeholders should also know the important analytic parameters that are used in the field: limit of blank, limit of detection, limit of quantification, 10% CV and how that's calculated, and what populations are used to determine 99 percentile upper reference limits.

Randye Kaye: So, any caveats or limitations within the article that readers should know about?

Rob Christenson: There are. The major caveat is that analytical studies indeed set the stage for important measurement parameters. However, once the test, in this case, cardiac troponin in whole blood or plasma, is developed and fully characterized, it is compulsory to run a properly designed clinical trial to guide patient use and clinical interpretation.

Randye Kaye: Thank you. So finally, what do you hope will be the key takeaway or impact of this report?

Rob Christenson: Technologies are available to deliver laboratory quality high-sensitivity cardiac troponin measurements at point-of-care in whole blood or plasma. However, point-of-care assays must not get a pass on meeting the quality metrics necessary for high-sensitivity designation.

Randye Kaye: That was Dr. Rob Christenson from the University of Maryland describing the *JALM* Special Report, "Point-of-Care: Roadmap for Analytical Characterization and Validation of a High Sensitivity Cardiac Troponin I Assay in Plasma and Whole Blood Matrices."

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.