A special series on cardiac troponin: an analytical and clinical matter

Since the first redefinition of myocardial infarction (MI) in 2000, cardiac troponin (cTn) has been the biomarker of choice for the evaluation in patients with possible MI. Over the years, assay sensitivity has increased remarkably as has the precision of the assays. However, these advances have caused a marked increase in the frequency of 'elevated' values, which has brought additional complexities to the previously facile use and interpretation of cTn results. Accordingly, a special series evaluating some of the relevant analytical and clinical issues seemed apropos. We embarked on this initiative to elucidate some of the potential benefits and uses for these assays, as well as to indicate where the present gaps in our knowledge are present. This special series includes the following contributions:

(I) An erudite discussion of the changes in cTn assays and the need for quality analytics from one of those who has developed the field, Alan Wu (1). He discusses the evolution of the assays and provides practical guidance about how to implement and quality assure the high sensitivity cTn (hs-cTn) assays we now have. These assays facilitate more rapid evaluation of patients if used properly. He then provides information on the changes in assays, including the point-of-care assays we will see in the future.

(II) Paul Collinson whose work in monitoring the conversion and application of cTn assays over time then provides a perspective on this important aspect of cTn use (2). He describes the global uptake of hs-cTn assays and the utilization challenges in routine clinical practice. His information warns of continuing challenges in this area.

(III) Mair and Hammarsten address the potential analytical interferences in cTn immunoassays, highlighting the risk of obtaining false negative and false positive troponin results (3). The authors propose an algorithm for investigating troponin results that deviate from the clinical presentation. Additionally, they offer a comprehensive overview of laboratory tests that can be employed to detect and identify the most common analytical interferences in troponin assays.

(IV) Denessen and colleagues then discuss the different troponin forms present in the circulation as well as various methodologies to detect them (4). Interestingly, mainly larger cardiac troponin T (cTnT) forms are found in MI, as opposed to smaller forms in end-stage renal disease and after vigorous exercise. They note that an additional simultaneously performed test that would specifically target these larger cTnT forms may aid in specifying the cause of cTnT elevation. This may increase the positive predictive for MI rule-in for hs-cTnT, while retaining its negative predictive value.

(V) The narrative review by Lee and Aw looks across studies to assess the extent to which there is population variability related to the 99th percentile upper reference limit (URL) for hs-cTn assays, including issues related to sex and race (5). Although not a totally comprehensive evaluation of all studies, it does put the literature in appropriate context and indicates the need for a more standardized approach to harmonize the data that exist across various studies.

(VI) In their manuscript, Thulin and co-authors explore recent advancements in point-of-care hs-cTn assays, shedding light on their clinical applications and considerations for implementation (6). These assays, newly introduced to the market, have the potential to reshape workflows in diverse clinical environments, ranging from cardiac emergency departments (EDs) and pre-hospital investigations of acute coronary syndrome to ambulant settings where access to central laboratory facilities is restricted.

(VII) Joyce *et al.* discuss the use of the so-called single high sensitivity troponin measurement to rule out MI from the perspective of ED physicians (7). They point out that ED overcrowding is a major problem and that this may be one of the partial solutions to it. They review the approach for high sensitivity and negative predictive value from the unique perspective of the ED. They also focus on some of the data that exists in this area including tabulating the observational and meta-analysis studies.

(VIII) Finally, Taggart and Chapman review the role of cTn in the diagnosis of type 2 MI and acute non-ischemic myocardial injury, conditions accounting for a significant portion of cTn elevations (8). They describe that although some differences in hs-cTn concentrations exist between different conditions, hs-cTn alone cannot differentiate myocardial injury or MI subtypes. However, they explain that the ratio of hs-cTnI to hs-cTnT may have good performance distinguishing type 1 from type 2 MI and acute non-ischemic myocardial injury.

We trust that this information will be important to readers both from the laboratory community, the ED, and cardiology communities. Further education in the area of hs-cTn is desperately needed to adequately assess the benefits that can be achieved utilizing these assays but also to appreciate where the gaps and knowledge are so that clinicians can compensate for them when evaluating patients. That was our goal. We hope we have achieved it.

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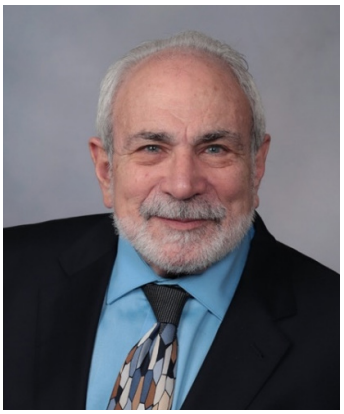

Allan S. Jaffe

Steven J. R. Meex

Amy K. Saenger

Xander M. R. van Wijk

Allan S. Jaffe[1,2], MD
[1]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, USA;
[2]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA.
(Email: jaffe.allan@mayo.edu)
Steven J. R. Meex[3,4], PhD
[3]Central Diagnostic Laboratory, Department of Clinical Chemistry, Maastricht University Medical Center, Maastricht, The Netherlands;
[4]CARIM School for Cardiovascular Diseases, Maastricht University, Maastricht, The Netherlands.
(Email: steven.meex@mumc.nl)
Amy K. Saenger[5,6], PhD
[5]Department of Laboratory Medicine and Pathology, Hennepin Healthcare/Hennepin County Medical Center, Minneapolis, MN, USA;
[6]Department of Laboratory Medicine and Pathology, University of Minnesota School of Medicine, Minneapolis, MN, USA.
(Email: amy.saenger@hcmed.org)
Xander M. R. van Wijk[7], PhD
[7]van Wijk Consulting LLC, Houston, TX, USA.
(Email: xandervanwijkphd@gmail.com)

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