What Criteria Should Be Used to Assess Troponin Assays?

To the Editor:

Since the introduction of cardiac troponin testing in the 1990s, troponin measurement has become the main diagnostic criterion for the diagnosis of myocardial infarction. Multiple improvements have been made in the available commercial assays, with lower detection limits, improved imprecision at low concentrations, and improvements in standardization. Because troponin has been shown to be a powerful predictor of death and is required for revascularization in patients presenting with the acute coronary syndrome, the analytical performance of assays is very important. Frequently, clinical decisions are based on increased troponin concentrations, and the performance of different assays is difficult to assess objectively.

To allow better evaluation for the clinical and laboratory community, Apple suggested a scorecard for cardiac troponin assays (1), with the value of the troponin assay being based on 2 criteria. The main criterion is the imprecision of the assay at the 99th percentile of a reference population. A good assay was defined as one with a 10% CV at the population’s 99th percentile, a clinically usable assay was defined as one with a CV between 10% and 20% at that percentile, and a CV >20% at this cutpoint was deemed unacceptable. Apple further differentiated assays on their ability to detect troponin in healthy control individuals. We have concerns with some aspects of his scorecard.

Our major point of disagreement with Apple is that he uses the 99th percentile of a reference population and the imprecision of the assay for assessing assay quality but gives no consideration to the clinical value of that assay. This latter point is of particular importance. For example, Venge et al. used samples from the FRISC (Fast Revascularisation during Instability in Coronary Artery Disease) study to compare the performance of the Liaison cardiac troponin I assay (DiaSorin) in unstable coronary artery disease (2). The Liaison assay showed good imprecision, with a 10% CV at 0.027 µg/L and a 99th percentile reference population value of 0.041 µg/L. This assay would have been qualified as acceptable; however, comparison with another troponin assay, the Access AccuTnl from Beckman Coulter, showed that the Liaison assay missed about 10% of patients with unstable angina and an increased risk of death or acute myocardial infarction within 6 months. More recently, a large prospective cohort study of patients presenting with chest pain to the emergency department showed similar results (3). In this study, assays that were more sensitive for troponin I show an improved diagnostic performance for acute myocardial infarction compared with a so-called standard assay (Roche fourth-generation troponin T assay). Assays with superior diagnostic performance in the recent cohort study were the Abbot Architect, the Siemens Centaur Ultra, and the Roche Elecsys high-sensitivity troponin T assays. Assays that were less sensitive included the fourth-generation troponin T assay; however, according to Apple’s scorecard, the Abbott Architect assay is ranked as “clinically usable” at his level 1 designation, similar to the rank of the fourth-generation Roche Elecsys troponin T assay. The use of assay imprecision defined as a 10% CV and the 99th percentile of healthy individuals falls short in judging assay performance.

A better way forward to compare assay performance might be to use patient serum pools with different cardiac troponin concentrations, as was done in a 2004 study (4). In this study, the Abbott AxSYM assay was unable to measure troponin in the pool with the lowest concentration, as were other analyzers at the time: the Immuno 1 analyzer (Bayer Diagnostics), the Vidas analyzer (bioMerieux), the Dimension Rxl analyzer (Siemens), the Opus analyzer (Dade Behring), and the Vitros ECI analyzer (Ortho Clinical Diagnostics). In contrast, other analyzers measured detectable troponin down to the pool with the lowest concentration. Clearly, these findings illustrate the different analytical sensitivities of the different assays. This consideration translates into the recognition of additional patients at risk.

In his scorecard, Apple uses the 10% CV as an important point of assay differentiation. However, there is no evidence to support the use of the 10% CV; in fact, the opposite is true. There currently is a wealth of evidence showing that in the setting of acute coronary syndrome, troponin concentrations corresponding to assay CVs well above the 10% CV are informative for a worse prognosis (5).

What is the way forward? Although we agree that assays can and should be scored objectively on their technical characteristics, we also believe that assays can and should be compared for their clinical performance. Useful information for comparing troponin assays includes clinical cohort studies that use chest pain patients in the emergency department, patients with a high pretest probability for unstable angina, and patient populations from the glycoprotein IIb/IIIa inhibitor trials. Additional clinically relevant information can be obtained from the exchange of patient pools and measuring troponin in these pools with different analyzers and assays. This matter needs further debate.
References


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