Cardiac Troponin Scorecard

To the Editor:

The recent opinion paper by Apple (1) on a cardiac troponin assay scorecard has enhanced the conundrum on whether cardiac troponin assays are clinically usable or not. Apple has proposed a scorecard that evaluates cardiac troponin assays according to the total imprecision at the 99th percentile. The cited data include the concentrations at the 10% CV and whether the value is greater or less than the cited 99th-percentile value. No data for the 20% CV are presented, however, and all of the cited values are derived from separate independent studies.

Values for the 99th percentile of a healthy population have been reported to show considerable variation between assays and even within an assay (2), due to such factors as the reference population chosen, the skewness of the distribution, specimen type, exclusion criteria, and sample size. In addition, the selection of the zero-concentration calibrator can skew values for the 99th percentile by 3-fold (3). All of the variables used to define a healthy population remain nonstandardized among manufacturers, making comparisons difficult.

Likewise, the determination of the 10% or 20% CV value can be inconsistent, given the potential differences with respect to multiple variables, such as the number of days tested, the total number of replicates, the number of calibrations, and the number of reagent batches. Plotting the CV values thus yields a curve with multiple options for fitting the data, the choice of which could affect the estimated CV at specific concentrations.

We also note an inconsistency between the criteria used in the scorecard opinion paper (1) and those previously published by Apple et al. (4) and included in the recent National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines on biomarkers of acute coronary syndromes (5). In these publications (4, 5), CV values as high as 25% at the 99th percentile do not lead to clinically important patient misclassification over serial measurements. The scorecard uses a 20% CV decision point.

Therefore, discussions and comparisons regarding the variables affecting 99th-percentile and CV values can be complex. Until uniform methods can be used to evaluate these variables, comparisons should be made with caution and be based on studies that use the same materials and testing procedures.

Historical data based on functional-sensitivity studies for the Abbott AxSYM Troponin-I ADV assay indicate that the 20% CV aligns with a concentration between 0.04 ng/mL and 0.05 ng/mL (95% confidence limits), which is in agreement with the reported value for 99th percentile of a healthy population, 0.04 ng/mL. More recently, Tate et al. (2) independently reported that the AxSYM Troponin-I ADV assay has a 20% CV at a concentration of 0.025 ng/mL. This concentration is less than the 99th-percentile value of 0.04 ng/mL, a finding that meets Apple’s criteria (1) for a clinically usable assay. Furthermore, this study used the same samples and procedure to compare 6 troponin-I assays and found that the performance of the AxSYM analyzer at the 20% CV (0.025 ng/mL) was comparable to the performance results for the Beckman Coulter Access (0.043 ng/mL), the Abbott Architect (0.023 ng/mL), the Siemens ADVIA Centaur (0.022 ng/mL), the Siemens Dimension (0.03 ng/mL), and the Johnson & Johnson Vitros (0.019 ng/mL) assays, all of which were considered acceptable or clinically usable according to the proposed criteria (1). These findings indicate that the AxSYM Troponin-I ADV assay is clinically useful and that the results are comparable to those of other available assays.

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References
4. Apple FS, Parvin CA, Buechler KF, Christenson RH, Wu AHB, Jaffe AS. Validation of the 99th percentile value of 0.04 ng/mL, a finding that meets Apple’s criteria (1) for a clinically usable assay. Furthermore, this study used the same samples and procedure to compare 6 troponin-I assays and found that the performance of the AxSYM analyzer at the 20% CV (0.025 ng/mL) was comparable to the performance results for the Beckman Coulter Access (0.043 ng/mL), the Abbott Architect (0.023 ng/mL), the Siemens ADVIA Centaur (0.022 ng/mL),


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