Increasing Cardiac Troponin Changes Measured by a Research High-Sensitivity Troponin I Assay: Absolute vs Percentage Changes and Long-Term Outcomes in a Chest Pain Cohort

To the Editor:

With novel high-sensitivity cardiac troponin assays, there is great interest in determining the change needed between successive cardiac troponin measurements to inform the diagnosis of acute myocardial infarction (MI)1 (1). Recent publications have reported both short- and long-term reference change values (RCVs) in healthy populations for both high-sensitivity cardiac troponin I (hs-cTnI) and high-sensitivity cardiac troponin T (hs-cTnT); thus, the RCV perhaps could be the metric used for determining the optimal clinical change value (2, 3). The RCVs for the hs-cTnT and hs-cTnI assays, however, are markedly different, possibly because of assay characteristics, differences in the biology of the 2 isoforms, or the healthy populations studied (1). The optimal clinical change for detecting patients with acute MI might be greater than the published RCVs. Two recent studies that used ROC curve analyses suggest exactly that. Giannitis et al. (4) determined the optimal δ to be \(243\%\) for hs-cTnT, whereas we identified an optimal \(\delta\) of \(235\%\) on the basis of MI or death at 30 days for a research hs-cTnI assay (5). Percentages may work well when values are low but may become impractical when more substantial increases occur. The 2 studies neither reported δ in terms of absolute concentration nor defined its role in long-term risk stratification. In this report, we calculate \(\delta\) for hs-cTnI, both in absolute concentration and as a percentage, and we relate these values to long-term outcomes.

The study population has previously been described (5). In brief, individuals presenting with chest pain to the emergency department had blood collected into heparinized tubes hourly until 6 h after symptom onset and then at 9, 12, 24, and 48 h, or until the patient was discharged, declined participation, or was removed from the study by those responsible for care. The present study included only the individuals (n = 223) with \(\geq 2\) hs-cTnI measurements (research assay, Beckman Coulter) and with peak hs-cTnI concentrations occurring after the earliest-collected sample. The absolute \(\delta\) was obtained by subtracting the earliest hs-cTnI concentration from the peak concentration, and the percentage value for \(\delta\) was obtained by dividing the absolute \(\delta\) by the earliest hs-cTnI concentration and multiplying by 100.

Health outcomes (death or MI) were obtained via linkage to the Registered Persons Database for mortality outcomes and with the Canadian Institute for Health Information Discharge Abstract Database for Ontario hospital discharges associated with MI over a 10-year period after study presentation. Kaplan–Meier and Cox proportional hazard analyses were performed with tertiles for both the absolute \(\delta\) and the \(\delta\) percentage, with tertile 1 (i.e., the group with the smallest changes) used as the referent for the Cox models (adjusted for age and sex). ROC curve analysis and logistic models for death or MI at 1 year were also performed to find the optimal \(\delta\) (5). The statistical analyses were performed with SAS software (SAS Institute). P values < 0.05 were considered statistically significant. The study received prior ethics approval.

Of the 223 study participants, 60% were male, and female participants were older (mean, 67 years, vs 62 years for males; \(P = 0.006\)), with 136 events (i.e., death or MI) occurring within the 10-year period. The median number of hs-cTnI measurements per individual was 5 (interquartile range, 3–6), and the median time to the peak hs-cTnI value was 9 h from symptom onset (interquartile range, 6–13 h). The Kaplan–Meier analysis indicated different probabilities of survival among the tertiles of change, with both the absolute \(\delta\) group and the \(\delta\) percentage group manifesting significant differences at 1 year [\(P < 0.001\), and \(P = 0.032\) (log-rank tests), respectively]. Only the absolute \(\delta\) value was statistically predictive at 10 years [\(P < 0.001\), and \(P = 0.070\) (log-rank tests), respectively] (Fig. 1). Individuals in the highest \(\delta\) tertile (>104 ng/L for absolute \(\delta\) and

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1 Nonstandard abbreviations: MI, myocardial infarction; RCV, reference change value; hs-cTnI, high-sensitivity cardiac troponin I; hs-cTnT, high-sensitivity cardiac troponin T.
>728% for the δ percentage) had significantly higher risks for death or MI than those in the lowest δ tertile (<5.4 ng/L and <43%). The 1-year hazard ratio for absolute δ was 2.95 (95% CI, 1.43–6.10; P = 0.004), compared with 1.89 (95% CI, 1.002–3.573; P = 0.049) for the δ percentage. The area under the curve for death or MI at 1 year was 0.697 (95% CI, 0.613–0.781) for the absolute δ and 0.626 (95% CI, 0.532–0.720) for the δ percentage, with the optimal change being 33 ng/L and 77%–79%, respectively. For earlier outcomes (30 days and 6 months), only individuals in the highest absolute δ tertile (>104 ng/L) had significantly higher risks for death or MI [30-day hazard ratio, 4.73 (95% CI, 1.36–16.48); 6-month hazard ratio, 3.41 (95% CI, 1.46–7.99)].

These data describe how both absolute and percentage changes in hs-cTnI within the emergency department setting may help to identify patients at risk for long-term adverse events. The results are consistent with data demonstrating worsening outcomes with increasing cardiac troponin concentrations; however, these changes are different from the RCVs that have been reported. Prospective studies that evaluate the published RCVs and ROC δ values as well as define the minimum δ or high-sensitivity cardiac troponin velocity will be useful.

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