Evaluation of a Novel Rule-Out Myocardial Infarction Protocol Incorporating High-Sensitivity Troponin T in a US Hospital

The US Food and Drug Administration recently approved a high-sensitivity (hs) troponin T (cTnT) assay that has greater sensitivity and precision than the conventional fourth-generation cTnT assay currently in use in the United States.\(^1\) Using this assay, European Society of Cardiology (ESC) guidelines endorse a 0/1-hour “rule-out” of myocardial infarction (MI) in low-risk individuals,\(^2\) as well as a more traditional 3-hour algorithm.\(^3\) However, the safety and effectiveness of rapid MI rule-out algorithms using hs-cTnT in US practice have not been established.

A multidisciplinary team at Parkland Health and Hospital System developed a novel hs-cTnT protocol modified from published data.\(^2-4\) An important difference from previous protocols was the addition of a 3-hour hs-cTnT measurement for patients classified into the indeterminate zone at 1 hour (Figure [A]). An observational study of unselected patients undergoing MI rule-out was performed to evaluate the safety of the protocol and its potential impact on patient disposition. The proportion of patients who would have been eligible for early rule-out with the new protocol incorporating hs-cTnT was compared with existing practice in which the conventional fourth-generation cTnT assay was tested at baseline and ≥3 hours after presentation. The negative predictive value was calculated to assess safety. Both cTnT and hs-cTnT were measured at 0, 1, and 3 hours after presentation to the Parkland Health and Hospital System emergency department in 536 patients with symptoms warranting MI rule-out (60% chest pain, 16% shortness of breath, 24% other complaints), but no ST elevations on ECG, between August and October of 2017. Individuals were classified into 2 mutually exclusive categories, “ruled out” or “abnormal,” based on hs-cTnT levels and change values (Figure [A]). Individuals were classified as ruled out with the conventional assay if cTnT was <0.01 ng/mL at all time points and abnormal if any value was ≥0.01 ng/mL. The final diagnosis was adjudicated by 3 cardiologists based on all available clinical information, including the conventional cTnT assay, using the Third Universal Definition of MI. A second adjudication was performed as a sensitivity analysis using the hs-cTnT assay instead of the conventional assay.\(^2,5\) Finally, we compared our new hs-cTnT algorithm with the 0/1 hour ESC algorithm.\(^3\)

In this cohort (N=536, mean age 55 years, 44% women), the final adjudicated diagnosis was MI in 2.1%, unstable angina in 0.4%, and nonischemic myocardial injury in 17.0%. With the conventional assay, 80.4% of patients ruled out for MI at 3 hours. With the new hs-cTnT protocol, 83.8% ruled out by 3 hours, including 30.0% at baseline, 24.8% at 1 hour, and 28.9% at 3 hours. Compared with 19.6% of patients considered abnormal by the conventional assay, 16.2% of patients were abnormal under the new protocol (P=0.03; McNemar’s test; Figure [B]). The new protocol had a sensitivity and negative predictive value of 100%, specificity of 86%, and positive predictive value of 13% for a final adjudicated di-
agnosis of MI. After readjudication using hs-cTnT as the gold standard, operating characteristics were identical except for a slightly lower positive predictive value of 12%. Of the patients who ruled out, no recurrent MI events were detected over 30 days of follow-up. When compared with the ESC 0/1 hour algorithm, a higher proportion ruled out with our new algorithm (83.8 versus 55.4%, \( P < 0.0001 \)), resulting from movement of 152/154 patients assigned to observation status with the ESC 0/1 hour algorithm to the rule-out group with the new protocol (Figure [C]).

In summary, a new protocol for rapid rule-out of MI using the hs-cTnT assay, applied to a contemporary US emergency department population, ruled out more patients than the existing protocol using the conventional assay, and did so sooner, with more than half of all patients ruled out by 1 hour after presentation. This protocol also appropriately ruled out a much higher proportion than the ESC 0/1 hour algorithm. This early rule-out protocol appears safe, with a sensitivity and negative predictive value of 100%. The positive predictive value of an abnormal hs-cTnT value was notably lower in this population than in prior studies,\(^1\) reflecting similar specificity applied to a population with much lower MI prevalence. Thus, clinical judgment remains essential in the interpretation of abnormal troponin values as the hs-cTnT assay becomes adopted in the United States, where troponin is measured more indiscriminately than in many other countries. A subtle but important distinction of our protocol from the ESC 0/1 protocol is the classification

![Figure. High-sensitivity (hs) troponin T (cTnT) algorithm and comparisons with conventional cTnT algorithm and European Society of Cardiology (ESC) 0/1 algorithm.](http://ahajournals.org)
of individuals as “abnormal” rather than “rule-in.” We recommend a similar approach in other centers with an anticipated low MI prevalence among those undergoing troponin measurement. This study is limited by its small size and lack of external validation; thus, future studies are needed to externally validate this novel algorithm and determine its resource implications.

ARTICLE INFORMATION

Data sharing: The data and study materials will not be made available to other researchers.

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