Interanalyzer Analytical Variation of a High-Sensitivity Cardiac Troponin T Assay Can Exceed the Cutoff of the European Society of Cardiology 1-Hour Algorithm for Ruling Out Non–ST-Segment Elevated Myocardial Infarction

To the Editor:

The European Society of Cardiology (ESC) guidelines (1) recommend that patients presenting with chest pain can be ruled out for non–ST-segment elevation myocardial infarction (NSTEMI) if their baseline Roche Diagnostics high-sensitivity cardiac troponin T (hs-cTnT) result is either <5 ng/L (if chest pain started at least 3 h earlier) or <12 ng/L and the change 1 h later is <3 ng/L. Because of the rounding of results, the analytical variation of the Roche hs-cTnT assay should not exceed 2 ng/L at concentrations <12 ng/L for use in the 0- to 1-h algorithm.

A serum pool with a hs-cTnT concentration of approximately 6 ng/L was made from anonymous and previously separated redundant serum obtained from the blood sciences department at St George’s Hospital. Intra- and interanalyzer precision was assessed on the Roche Cobas modules in use in the central laboratory (2 Cobas e602 and 1 Cobas e801) and the emergency department stat laboratory (1 Cobas e411) at St George’s Hospital. The serum pool was not recentrifuged before analysis on any of the Cobas modules.

Intra- and interanalyzer repeatability (short-term precision) was assessed by analysis of the serum pool 25 times on each analytical cell on each Cobas module within 1 h (n = 150 on 1 Cobas e411, 2 Cobas e801, and 3 Cobas e602 cells).

Interanalyzer analytical variation over an 8-h period was assessed by replicating realistic sample flow. Ten aliquots of the serum pool were analyzed in the stat laboratory on the Cobas e411 to represent a hs-cTnT baseline at 0 h. Five aliquots were then processed on our preanalytical modular Roche Cobas 8000 in the central laboratory at each 2-h interval; the samples were sent for analysis on a Cobas e602 or e801 (depending on system demand). The mean, SD, and 95% CIs were calculated using the Analyse-it software (3) for each Cobas module and time point.

The Cobas e411 module demonstrated the poorest intra-analyzer repeatability, with a CV of 9.6% and a range of 3 ng/L (n = 25). The Cobas e602 and e801 modules demonstrated improved intra-analyzer repeatability, with CVs <5.7% and ranges ≤2 ng/L. After exclusion of the Cobas e411, the interanalyzer repeatability within 1 h gave a CV of 7.7% and a range of 2 ng/L (n = 125).

<table>
<thead>
<tr>
<th>Table 1. Interanalyzer analytical variation of the Roche high-sensitivity cardiac troponin assay over an 8-h period.</th>
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<tbody>
<tr>
<td>Hours (Cobas module)</td>
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<tr>
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<tr>
<td>0 (e411) (n = 10)</td>
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<tr>
<td>2 (e601/e802) (n = 5)</td>
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<td>4 (e601/e802) (n = 5)</td>
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<td>6 (e601/e802) (n = 5)</td>
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<td>8 (e601/e802) (n = 5)</td>
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<td>Mean (n = 30)</td>
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<td>Mean excluding 0-h baseline (n = 20)</td>
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Results of the 8-h interanalyzer analytical variation experiment are shown in Table 1. When 0-h baseline samples were processed on the Cobas e411 and subsequent samples were analyzed on the Cobas e602/e801 (n = 30), results increased by up to 3 ng/L. After exclusion of the 0-h measurements on the Cobas e411, no 2 results over the 2-, 4-, 6-, and 8-h periods on the Cobas e602/e801 modules (n = 20) differed by >1 ng/L.

A previous study reported that Roche hs-cTnT assay lot variations between 2013 to 2018 were large (2). This finding could potentially render the use of the 0- to 1-h algorithm inappropriate if the lot numbers between the different Cobas modules vary. If hospitals adopt these ESC rule-out algorithms, it is important that laboratories monitor the performance of the Roche hs-cTnT assay by using third-party internal quality control material with appropriate concentrations at the clinical cutoff levels (5 and 12 ng/L).

In conclusion, the interanalyzer analytical variation between separate Cobas e601 and e802 modules is satisfactory for the implementation of the ESC 0- to 1-h NSTEMI rule-out algorithm. However, the independent Cobas e411 module should not be used to provide the baseline or repeat hs-cTnT measurement for use in this algorithm because the imprecision might lead to reporting a false increase of >2 ng/L, failing to correctly rule out NSTEMI. Therefore, we recommend that all hs-cTnT requests intended for the use in the ESC 0- to 1-h algorithm be processed on the more precise Cobas e602 and e801 modules. This recommendation is still subject to the monitoring of significant reagent lot-to-lot variation and the appropriate use of low-concentration internal quality control.

Nonstandard abbreviations: ESC, European Society of Cardiology; NSTEMI, non-ST-segment elevation myocardial infarction; hs-cTnT, high-sensitivity cardiac troponin T.

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References


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