Multicenter Evaluation of a High-Sensitivity Troponin I Assay and Verification of an Early Rule-Out Algorithm

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Background: The objectives of this study were to independently evaluate the analytical performance of the STAT high-sensitivity troponin I (hs-cTnI) assay on a recently launched and CE-marked integrated chemistry and immunoassay system, confirm acceptable performance of the assay in line with The Third Global MI Task Force recommendations, and confirm suitability of the assay for continued use of an early rule-out algorithm for acute coronary syndrome at our Trust.
Methods: A multicenter evaluation of the analytical performance characteristics of the hs-cTnI assay on the Abbott Alinity ci series was performed in 5 clinical laboratories across Europe. Comparison studies were performed vs the existing Abbott ARCHITECT hs-cTnI assay.
Results: Passing and Bablok regression analysis revealed a slope of 0.99 [95% confidence interval (CI), 0.98–1.00] and an intercept of −0.09 ng/L (95% CI, −0.21–0.11). Intermediate imprecision ranged from 3.7% to 5.4%, 2.6% to 4.5%, and 2.0% to 6.1% at concentrations of 19.1–21.1 ng/L, 196.6–205.5 ng/L, and 15 229–16 265 ng/L, respectively. There was good concordance between the 2 assays at the early rule-out cutoff.
Conclusion: Comparable analytical performance of the hs-cTnI assay on new Abbott Alinity ci series supports the continued use of the early rule out algorithm for patients with suspected ACS at our Trust.

IMPACT STATEMENT

This evaluation of the new Abbott Alinity ci series STAT high sensitivity cardiac troponin I assay confirms acceptable analytical performance within independent clinical laboratories, and acceptable rule out of myocardial infarction in a single Trust. This work may be of value to other laboratories considering this assay for use in an early rule out algorithm for patients with suspected acute coronary syndrome.

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[2] **Nonstandard abbreviations:** ED, emergency department; hs-cTnI, high-sensitivity cardiac troponin I; RWT, Royal Wolverhampton National Health Service Trust; ACS, acute coronary syndrome; NPV, negative predictive value; MI, myocardial infarction.

Chest pain is one of the most common reasons for presentation at the emergency department (ED).[2] Following the introduction of the Abbott ARCHITECT high-sensitivity cardiac troponin I (hs-cTnI) immunoassay in April 2013, a novel pathway was implemented at the Royal Wolverhampton National Health Service Trust (RWT) that facilitates the early discharge of patients with suspected acute coronary syndrome (ACS). An hs-cTnI concentration of ≤1.9 ng/L on admission, which is the manufacturer's stated limit of detection for the assay, is used to discharge patients with suspected ACS. The high negative predictive value (NPV) of an undetectable hs-cTnI at presentation in suspected ACS had been supported before the commercial release of the assay (*1*). Patients at our Trust deemed to be at high risk of ACS are not discharged and are instead admitted to the acute medical unit. Low-risk patients with an hs-cTnI >1.9 ng/L require a repeat sample taken 3 h post admission (*2*, *3*). These patients are transferred to a CDU (clinical decision unit) within the ED while they await a second sample. The full algorithm currently in use is shown in Fig. 1.

A study post introduction of this algorithm confirmed an NPV of an undetectable hs-cTnI on admission of 99.6% and successfully reduced the number of patients admitted to the hospital from 60.9% to 38.4%, and the mean length of stay was reduced from 23 h and 2 min to 9 h and 36 min (*2*). Similar rapid rule-out protocols have been supported in larger prospective cohort studies and have also since been endorsed by the ESC (European Society of Cardiology) (*4*, *5*).

The Third Global Myocardial Infarction (MI) Task Force for the redefinition of MI recommends use of assays that demonstrate a total CV of ≤10% at the 99th percentile of the reference population (*6*).

Abbott Diagnostics have recently launched a CE-marked, integrated chemistry and immunoassay system for use in clinical laboratories. The Alinity ci system, Abbott's next-generation immunoassay and clinical chemistry system, uses CMIA (chemiluminescence microparticle immunoassay) technology or photometric/potentiometric technology for the quantitative determination of analytes in human serum, plasma, urine, and cerebrospinal fluid. The benefits include smaller footprints, improved workflow, and greater throughput for the chemistry laboratory.

The objectives of this study were to independently evaluate the analytical performance of the STAT hs-cTnI assay on the recently launched Abbott Alinity ci series in routine clinical laboratories and confirm acceptable performance of the assay in line with the Third Global MI Task Force for the redefinition of MI recommendations, to support the continued use of the early rule-out algorithm at our Trust.

METHODS

A multicenter evaluation of the analytical performance characteristics of the hs-cTnI assay on the Abbott Alinity ci series was performed in 5 clinical laboratories across Europe (Labor Krone-Germany, RWT, Nicolaus Copernicus University Collegium Medicum-Bydgoszcz Poland, Ospedale Civile, Guastalla Italy, and Clinique St. Pierre, Belgium). The method comparison was performed across the 5 sites in accordance with CLSI guideline EP9-A2 (*7*). A total of 261 deidentified residual human serum samples from a population of patients presenting with suspected MI were analyzed. The local ethics committee reviewed the study and determined that it did not require specific research ethics review because it is laboratory method evaluation, using anonymized acellular patient samples, and no new clinical procedure was performed.

The samples had already been analyzed using the hs-cTnI assay on the Abbott ARCHITECT as part of the initial request. Passing and Bablok regression analysis was performed in Analyse-it®. The 94 samples analyzed at a single site, RWT, were classified as positive or negative by each assay

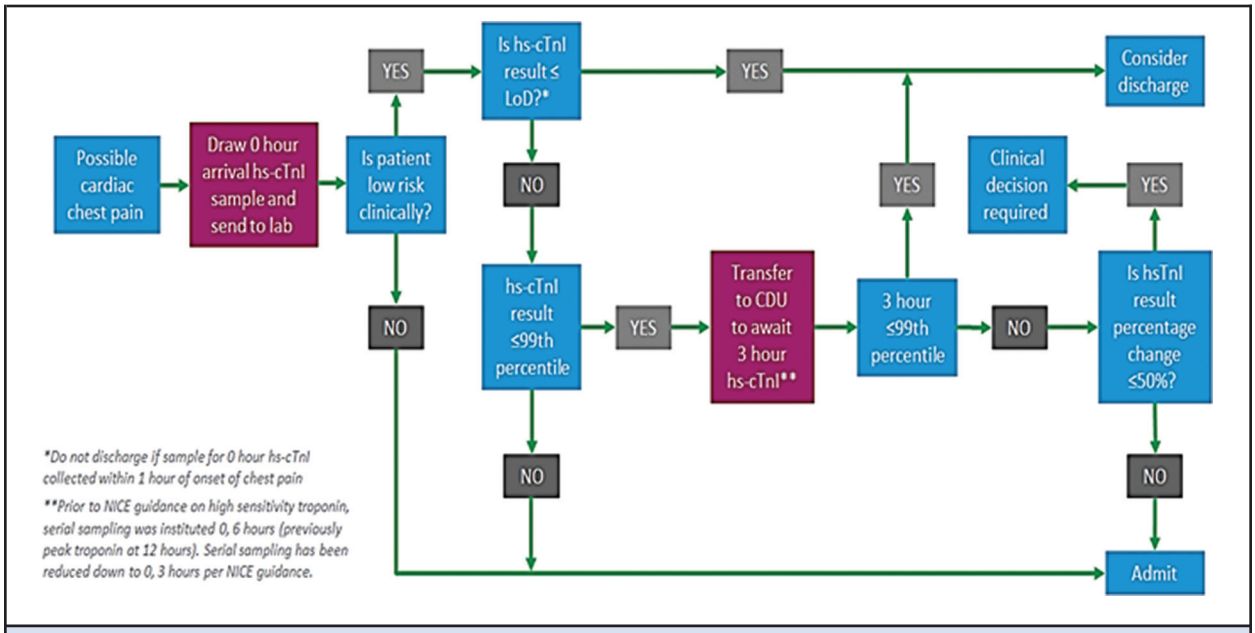

Fig. 1. RWT hs-cTnI early rule-out algorithm.

using the cutoff in use of ≤1.9 ng/L. Cohen's κ analysis was then performed in Analyse-it® to determine the theoretical agreement between the 2 instruments at the early rule-out cutoff.

Intermediate imprecision was assessed at the 5 sites in accordance with CLSI guideline EP15-A2 using each laboratory's internal quality control material (*8*). Materials tested included Abbott Troponin control materials as well as third-party control materials at 3 clinically relevant concentrations. Intermediate imprecision was also assessed at a single site, RWT, using pooled patient sera at a value 10-fold higher than the overall 99th percentile for the assay (≥260 ng/L), male and female 99th percentiles (34 ng/L and 15 ng/L, respectively), and the early rule-out cutoff (≤1.9 ng/L) currently in use at RWT. Patient samples were pooled and stored at −20 °C. Each aliquot was subjected to a single freeze thaw cycle before analysis.

In accordance with schedule 1, part 2 of the Human Tissue Act (2004), and following advice from the local research ethics committee, ethical approval was not required for the use of anonymized residual patient samples in the assessment of the analytical performance of this assay.

RESULTS

Fourteen samples yielded undetectable results on both instruments and were excluded from the final data analysis. The results ranged from 1.1 to 49955 ng/L (an improved LOD on both the ARCHITECT and Alinity assays permitted measurement of hs-cTnI concentrations as low as 1.1 ng/L). Passing and Bablok regression analysis of the remaining 247 results revealed a slope of 0.99 (95% CI, 0.98–1.00) and an intercept of −0.09 ng/L (95% CI, −0.21–0.11). The samples were distributed across a clinically relevant range with no outliers identified. R = 0.998 (Fig. 2).

A κ statistic of 0.85 (95% CI, 0.73–0.98) indicated good to very good agreement between hs-cTnI results on the 2 instruments using an early rule-out cutoff of ≤1.9 ng/L. Altman–Bland analysis showed a mean agreement of 0.13 ng/L at concentrations less than the male 99th percentile (Fig. 3).

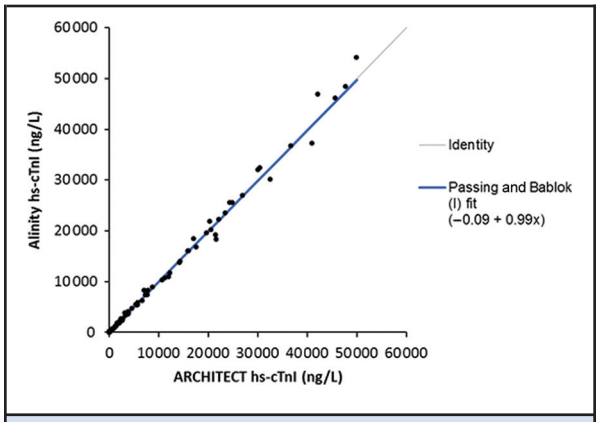

Fig. 2. Passing and Bablok regression analysis of hs-cTnI on the Abbott ARCHITECT vs Abbott Alinity ci series.

Intermediate imprecision ranged from 3.7% to 5.4%, 2.6% to 4.5%, and 2.0% to 6.1% at concentrations of 19.1–21.1 ng/L, 196.6–205.5 ng/L, and 15 229–16 265 ng/L, respectively. Precision profile analysis using patient sample pools revealed CVs of 16.1%, 12.5%, 6.0%, 5.8%, and 4.3% at concentrations of 2.1 ng/L, 2.9 ng/L, 15.6 ng/L, 31.8 ng/L, and 253.1 ng/L, respectively (Fig. 4).

DISCUSSION AND CONCLUSIONS

The STAT hs-cTnI assay on the recently launched Abbott Alinity ci series analyzer offers comparable analytical performance to the existing Abbott ARCHITECT hs-cTnI assay in routine use in 5 independent clinical laboratories.

In addition to excellent analytical comparability, this study showed very good concordance between the assays on the 2 instruments at the early rule-out cutoff currently in use in our Trust. Further, the imprecision at male and female 99th percentiles was confirmed to be ≤10%, which demonstrates acceptable performance in accordance with the Third Global MI Task Force recommendations.

Imprecision at the early rule-out cutoff in use at RWT is acceptable. Furthermore, according to CLSI guideline EP28-A3C, if an appropriately established reference interval for an analyte already exists for the population of subjects being tested using the clinical laboratory's current system, then transference and validation of the reference interval within the same laboratory to an alternate

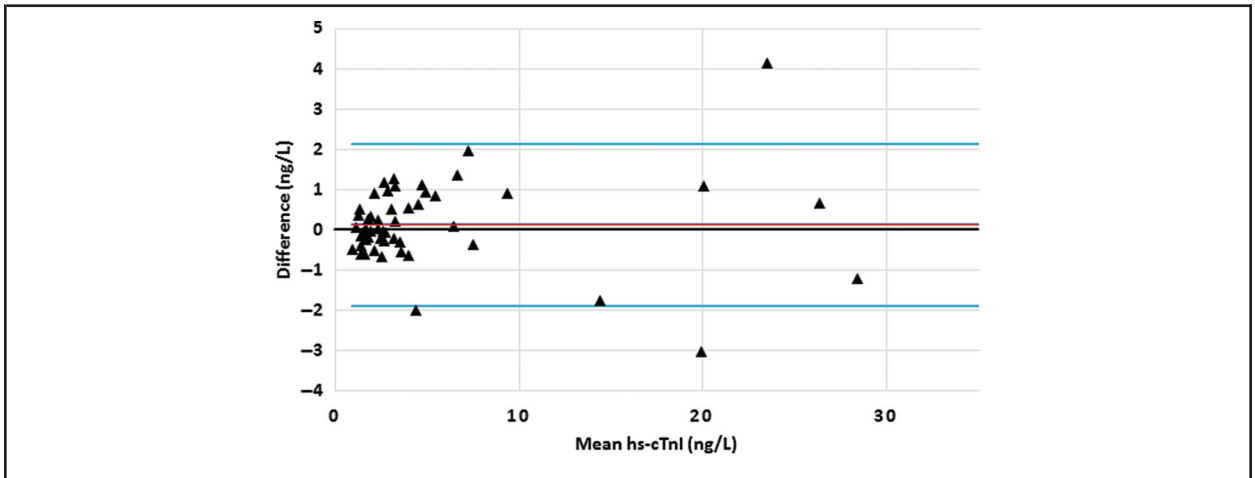

Fig. 3. Altman–Bland plot of ARCHITECT hs-cTnI versus Alinity hs-cTnI at concentrations below the male 99th centile.
The blue solid lines indicate the 95% limits of agreement. The red line indicates the mean agreement of 0.13 ng/L (n = 53).

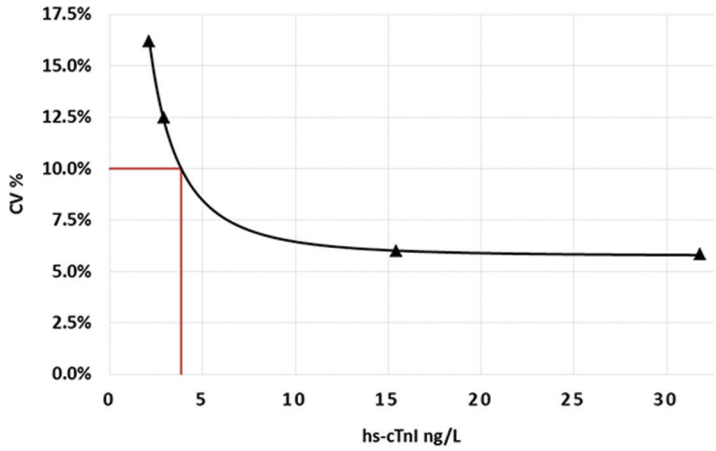

Fig. 4. Precision profile of hs-cTnI on the Abbott Alinity ci series.
The red line shows a 10% CV at 3.8 ng/L, which is below the male and female 99th centiles.

method/instrument largely becomes a question of the comparability of the analytical systems (*9*). With this in mind, we believe that the comparable analytical performance of the hs-cTnI assay on the new Abbott Alinity ci series supports the continued use of the early rule-out algorithm for patients with suspected ACS at our Trust. It must, however, be highlighted that these cutoffs are assay-specific and are not transferrable to alternative hs-TnI assays.

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H.J. Sharrod-Cole, statistical analysis.

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