Background: Cardiac troponins are specific biochemical markers of myocardial injury used in the diagnosis of acute myocardial disease and cardiac risk stratification. To avoid misclassification of patients, troponin assays must demonstrate precision at the low end of the measuring range. We report our evaluation of the Architect STAT Troponin-I assay (Abbott Diagnostics), comparison of low-positive results with 2 other assays, and occurrence of heterophile antibody interference in the assay.

Methods: We assessed analytical performance on the c8200 according to CLSI protocols, using quality-control and patient samples. Our healthy reference population included 480 blood donors. For correlation studies against the AxSYM first-generation cTnI (Abbott Diagnostics) and Access second-generation AccuTnI (Beckman Coulter) assays, we used 339 samples from hospital patients.

Results: The CV of the Architect STAT Troponin-I assay was 10% near the 99th percentile for the reference population (0.03 µg/L). Comparison with the AxSYM first-generation cTnI assay showed good correlation at higher concentrations, but better sensitivity of the Architect cTnI assay at low concentrations, which were clinically relevant as shown by review of patient histories. Correlation was good at the low end of the measuring range with the Access second-generation AccuTnI. Over the last 12 months we have identified 6 patients with heterophile antibodies causing positive interference.

Conclusions: The Architect STAT Troponin-I assay provides highly sensitive measurement of cTnI with a CV of 10% near the upper limit of a reference population; however, heterophile antibodies can interfere with this assay.

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Cardiac troponins are specific biochemical markers of myocardial injury with clinical applications in the diagnosis of acute myocardial disease and cardiac risk stratification. In their consensus redefinition of myocardial infarction (1), the European Society of Cardiology and the American College of Cardiology defined an increased troponin value as one greater than the 99th percentile of a healthy reference population with the added recommendation that assay imprecision (CV) at this concentration be ≤10%. This emphasizes the importance of performance at the low end of the measuring range if one is to avoid misclassification of patients. Currently available troponin assays fail to achieve such precision at their 99th percentile reference values (2), and laboratories using these assays quote higher decision limits. Accuracy is another issue, with past concerns regarding antibody specificity and standardization now partially addressed (3). However, reports of interference from rheumatoid factor, heterophile antibodies, autoantibodies, and hemolysis (4–11) emphasize the potential for both false-positive and false-negative results to influence therapeutic decisions and the importance of the serial rise and fall of troponin concentrations in the circulation after myocardial infarction.

The Architect STAT Troponin-I assay (Abbott Diagnostics) is a 2-step chemiluminescent microparticle immunoassay designed to detect cardiac troponin I (cTnI) in serum and plasma. We assessed the assay on the c8200, particularly evaluating the performance at the low end of measurement and in response to interfering substances. We also report on the reference limit for a healthy population, the correlation with the Access second-generation AccuTnI (Beckman Coulter) and the AxSYM 1st-generation cTnI (Abbott Diagnostics) assay, and the detection of interference in the assay. The Architect STAT Troponin-I assay uses 3 murine monoclonal antibodies to the cTnI molecule. Two act as capture antibodies coating the paramagnetic microparticles, and the third is acridinium-labeled. The assay is traceable to the AACC candidate reference material for cTnI (human ICT tertiary complex; NIST SRM 2921) with a calibrator range of 0–50.00 µg/L (as reported by the manufacturer).

Analytical evaluation was performed to Clinical and Laboratory Standards Institute (CLS; formerly NCCLS) protocols. The analytical detection limit was defined as the mean value ± 2 SD above the mean of 10 replicates of calibrator A (0 µg/L). Functional sensitivity was determined by measuring 10 samples between 0.01 and 0.10 µg/L, assayed in duplicate daily for 10 days. For total imprecision, 3 concentrations of the manufacturer’s quality-control material were measured in duplicate in 2 runs each day for 5 days. Reference intervals were determined on freshly collected serum and plasma from 480 consenting donors from the Australian Red Cross Blood Bank. The 99th percentile reference limits were calculated by a simple nonparametric approach.

Correlation experiments with the AxSYM cTnI assay were performed on 296 consecutive hospital plasma samples with cTnI requests, of which the Emergency and Cardiology Departments accounted for ~70%. When testing was not possible within 4 h, plasma was stored (~30 °C) for later analysis. For correlation with the Access AccuTnI assay, we compared plasma samples from 43 patients with cTnI concentrations =0.10 µg/L. In addition, 25 stored samples from 7 patients with false-positive AXSYM cTnI results (negative clinical history and undetectable cTnI in 2 other assays) were analyzed with the
Architect assay to study immunoassay interference. During the study, lithium heparin was the anticoagulant used for all plasma samples, and heterophile blocking tubes (Scantibodies Clinical Laboratories) were used to investigate the presence of heterophile antibody interference. This study was approved by the Alfred Hospital ethics committee.

The Architect STAT Troponin-I assay had a limit of detection of 0.004 μg/L and a CV of 10% at concentrations approaching 0.03 μg/L (Fig. 1A). The total CV did not exceed 6% at concentrations of 0.12, 0.45, and 12.04 μg/L. The healthy reference population had a 2:1 male preponderance (age range, 16–82 years; mean, 47 years for males and 41 years for females). Distribution of cTnI results was slightly lower in serum than for plasma ( detection limit, 90th percentile for serum, 75th percentile for plasma; Wilcoxon rank test, P <0.01) with the 99th percentiles in serum (n = 475) and in plasma (n = 480) both at 0.03 μg/L. Matched patient serum and plasma samples across a wide range of cTnI results (0.1–85 μg/L) were in excellent agreement [Deming regression: serum cTnI = 1.03(plasma cTnI) − 0.065 μg/L; correlation coefficient (r) = 0.999, n = 32].

The correlation of the Architect TnI assay with the AxSYM cTnI assay was good across the clinical measurement range [Deming regression: Architect = 0.11(AxSYM) + 0.28 μg/L; correlation coefficient (r) = 0.98] but weaker at concentrations below the AxSYM cutoff (2 μg/L) for acute myocardial infarction [Architect = 0.18(AxSYM) + 0.02 μg/L; r = 0.65]. Of 296 consecutive patient samples, 245 (82.8%) were either positive or negative on both assays. In 51 discrepant samples (17.2%), the AxSYM assay measured increased cTnI in 3 samples (≥0.6 μg/L), whereas the Architect assay was below the 99th percentile value of the reference population. Conversely, the Architect assay results were increased (i.e., ≥0.03 μg/L) for 48 samples that were negative by the AxSYM method.

At the time of evaluation, clinical decisions were based on the results of the AxSYM assays. Two of the 3 increased AxSYM samples were taken 7–10 days after myocardial infarction. Time course data obtained with serial samples from patients with myocardial infarctions did not show any time difference between AxSYM and Architect results (data not shown). The other positive AxSYM result was likely a false positive (no evidence of cardiac ischemia on nuclear medicine imaging). Of the 48 samples with increased cTnI by the Architect assay only, clinical files were available for 28 samples (25 patients) and were reviewed by 2 physicians. The Architect assay identified 6 patients with a new acute coronary syndrome/acute myocardial infarction, and an additional 7 samples were obtained from patients with acute pulmonary edema, arrhythmia, or chest trauma or after cardiac procedures. In 3 samples, other AxSYM results from the same clinical episode showed increased troponin. One sample was taken from a patient with severe illness who subsequently died, and 2 samples were collected from patients with renal impairment. Six of the 48 samples (in 4 patients) were likely to be true AxSYM negatives because there were no detected cardiac events during follow-up. The Architect values in these 6 samples ranged from 0.04 to 0.09 μg/L. These findings highlight the potential of the Architect assay to reclassify patients previously labeled as "normal". Of the 25 specimens with known AxSYM cTnI assay interference, all had Architect STAT cTnI concentrations below the reference population.

Deming regression for sample comparison with the AccuTnI assay at plasma concentrations <0.10 μg/L showed good agreement [Architect = 1.06(Beckman) − 0.01 μg/L; r = 0.83; Fig. 1B]. The published limit of detection for the AccuTnI assay is <0.01 μg/L, with the concentration giving a CV of 10% reported as 0.06 μg/L (12). No clinical information was obtained regarding the outcome of these patients.

The Architect STAT Troponin-I assay has now been in routine clinical use in our hospital for almost 12 months with wide acceptance of the new assay and the change to a reference interval in line with the European Society of Cardiology and American College of Cardiology guidelines. Using a commercial control serum (Abacus MAS) at
a concentration of 0.05 μg/L, we obtained long-term CVs between 12% and 20% over 12 months. As expected, long-term CVs have been higher than that obtained in our initial evaluation. During this time, we have identified 6 patients with suspected false-positive results (range, 0.1–0.6 μg/L) based on discrepancies between results and clinical information and persistently increased TnI concentrations. Normal TnI concentrations were obtained in these samples after preincubation with heterophile blocking tubes and in other troponin assays. The theoretical incidence of these heterophile antibodies in our population is 1 in 5000.

The Architect STAT Troponin-I assay provides measurement of cTnI in plasma with a CV of 10% near the 99th percentile of a reference group of healthy blood bank donors (0.03 μg/L). Our 99th percentile value is higher than that reported by the manufacturer (0.012 μg/L) and may be attributable to our use of freshly collected blood bank specimens.

Comparison with the clinically evaluated AxSYM cTnI assay (13–15) showed that the Architect STAT Troponin-I assay identified additional patients who had clinical evidence of cardiac damage. This is in keeping with studies showing that the AxSYM assay may miss patients who later developed poor cardiac outcomes (16). Furthermore, the Architect TnI showed good agreement with the Access AccuTnI at the lower end of the measurement range. Similar data comparing the Architect assay with the Advia Centaur assay were reported recently (17). Identification of such patients is important given the likely benefit from early intervention.

Although the Architect STAT Troponin-I assay was not affected by any of the substances that cause interference in the AxSYM cTnI assay, our 6 cases of heterophile antibody interference are reminders that interference from these and like substances remains an issue. Consistently increased troponin concentrations without a pattern of increase and decrease should be questioned by laboratory staff. Laboratories should have documented procedures to investigate suspicious results such as access to different troponin methodologies in real time.

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References

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Atorvastatin Reduces the Expression of COX-2 mRNA in Peripheral Blood Monocytes from Patients with Acute Myocardial Infarction and Modulates the Early Inflammatory Response, Ping Deng,1* Shui-ping Zhao,3 Hai-yung Dai,2 Xian-song Guan,2 and Hong-jiang Huang2 (1 Department of Cardiology, the Second XiangYa Hospital, Central South University, Hunan, People’s Republic of China; 2 Department of Cardiology, Changsha Central Hospital, Hunan, People’s Republic of China; 3 address correspondence to this author at: Department of Cardiology, Changsha Central Hospital, E-410014 Hunan, People’s Republic of China; fax 86-731-5590171, e-mail dengping2115@yahoo.com.cn)

Background: We examined the effect of atorvastatin on the expression of COX-2 in peripheral blood monocytes from patients with early stage of acute myocardial infarction (AMI), and the plasma C-reactive protein (CRP) concentrations were also examined.

Methods: Patients with AMI (n = 40) and with stable coronary heart disease (CHD; n = 18) were registered,