Quantitative Point-of-Care Troponin I in Emergency Department in Comparison With Troponin I in Central Laboratory

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Abstract: Many patients may present simultaneously in emergency departments. We must ensure that patients are treated in the order of their clinical urgency and that the treatment is appropriate and timely. Rapid cardiac marker testing may aid in early detection of acute coronary syndromes. It is almost impossible for laboratories to deliver cardiac biomarker results in less than 30 minutes, using serum- or plasma-based assays. Use of plasma for measurement of cardiac biomarkers eliminates the clotting process involved in producing serum and therefore reduces the overall turnaround time for biomarker testing. Point-of-care devices allow cardiac troponin I testing using anticoagulated whole blood specimens at the site of patient care delivery. Elimination of transport and centrifugation can reduce the overall turnaround time to less than 30 minutes.

We compared the performance of a critical point-of-care device PathFast (Mitsubishi, Kagaku Iatron, Inc, Chiba, Japan) with a core laboratory Liaison analyzer (DiaSorin, Saluggia, Italy) for troponin I determination. Both methods are chemiluminiscent immunoassays. Thirty-one consecutive patients from the emergency department presenting with chest pain were included in this study. The results obtained with PathFast correlated very well with those obtained in the core laboratory. Optimum sensitivity and specificity of the PathFast cardiac troponin I were demonstrated at a cutoff of 0.1 μg/L (100% sensitivity and 100% specificity). A significant decrease in overall turnaround time was achieved with the PathFast (20 ± 5 vs 104 ± 33 minutes, $P < 0.001$).

Key Words: emergency department, acute coronary syndrome, cardiac troponin I (cTnI), point-of-care device, overall turnaround time

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Many patients may present simultaneously in emergency departments (EDs), and excessive waiting is the most common cause of complaints in the ED. We must ensure that patients are treated in the order of their clinical urgency and that the treatment is appropriate and timely. Chest pain is the second most common presenting symptom in the ED.[1] Clinicians focus on the immediate recognition and exclusion of life-threatening causes of chest pain including acute coronary syndrome (ACS). Less than 30% of patients, who present to the ED with non-traumatic chest pain, have ACS, including myocardial infarction and unstable angina.[2] Differentiating ACSs from noncardiac chest pain is a diagnostic challenge. The initial assessment requires a focused history (including risk factor analysis), a physical examination, an electrocardiogram, and, frequently, serum cardiac marker determinations.[3] Cardiac troponins are the most sensitive biomarker of acute myocardial injury. Rapid cardiac marker testing may lead to earlier detection and use of appropriate therapies and may improve patient flow in the ED.

It is almost impossible for central laboratories to deliver cardiac biomarker results in less than 30 minutes, using serum- or plasma-based assays. At the time of this study, a serum-based Liaison cardiac troponin I (cTnI) assay was used in our core (central) laboratory. Use of plasma for measurement of cardiac biomarkers eliminates the extra time necessary for the clotting process involved in producing serum and therefore reduces the overall turnaround time (TAT) for biomarker testing. In our hospital, the EDs, ICUs, and outpatient clinics are now implementing critical point-of-care (POC) devices that allow cardiac marker testing using anticoagulated whole blood specimens at the site of patient care delivery.[4,5] Elimination of the transport and centrifugation steps reduces the TATs to less than 30 minutes.[6] The Pathfast cTnI assay is representative of the POC group.

The Liaison troponin I is a 2-site immunoluminometric assay. A monoclonal antibody is used for the coating of the

TABLE 1. Characteristics of Liaison and Pathfast Methods

	Liaison	Pathfast
Characteristics		
Sample volume, μL	100	50
Sample material	Serum, plasma	Whole blood, plasma
Imprecision		
Intra-assay variation, %	1.2–4.5	2.8–3.7
Interassay variation, %	5.2–7.8	3.1–3.9
Analytical sensitivity, %	0.005	0.001
Limit of detection, μg/L	0.02	0.02
Functional sensitivity, μg/L	0.02	0.02
Linearity range (minimum), μg/L	Up to 100	Up to 50
Recovery, %	98–115	93.3–104.3
Cutoff, μg/L	0.06	0.06
Interferences		
Bilirubin	<10%	<10%
Hemoglobin (<10 g/L)	<10%	<10%
Triglyceride (<10 g/L)	<10%	<10%
Rheumatoid factor (<500 kU/L)	<10%	<10%

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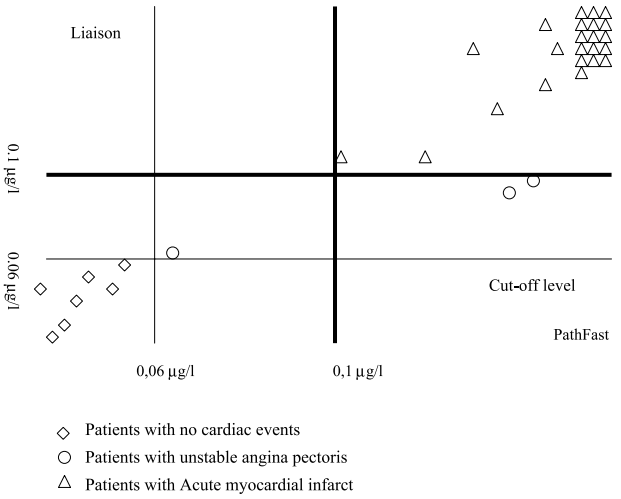

FIGURE 1. Distribution of the results obtained by both methods in relation to diagnosis.

solid phase (magnetic particles), and a polyclonal antibody is used for the tracer. During the incubation, cTnI in samples and calibrators are simultaneously bound to both the solid phase and the tracer antibodies. The unbound fraction is removed, a starter is added, and the generated chemiluminescence is measured as relative light units. Relative light unit is directly proportional to the amount of cTnI in the sample. The PathFast cTnI is an assay for measurement of cTnI in the format of a chemiluminescent enzyme immunoassay. All required components for performing the testing are packed in 1 reagent cartridge. The cTnI procedure is based on chemiluminescent enzyme immunoassay and Magtration (a technology of bound and free fraction separation where magnetic particles are washed in a pipette). In this procedure, alkaline phosphatase–labeled anti-cTnI monoclonal antibody and anti-cTnI monoclonal antibody–coated magnetic particles are mixed with the sample.

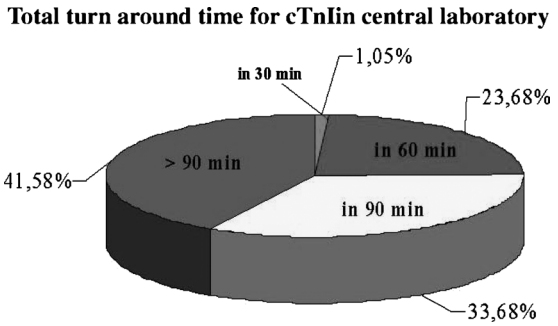

FIGURE 3. Total TAT for cTnI in the central laboratory. Most results required 90 minutes or longer.

Cardiac troponin I in the specimen binds to the anti-cTnI antibodies forming an immunocomplex. After removing the unbound antibody, a chemiluminiscent substrate is added. After a short incubation, the generated luminescence is detected. The intensity of the measured luminescence corresponds to the cTnI concentration. Characteristics of the Liaison and PathFast methods are summarized in Table 1.

The purpose of this study was to compare the diagnostic accuracy of the 2 methods, 1 classical laboratory method and 1 designed to determine cTnI in an ED. The second purpose was to establish the TAT for both methods used.

MATERIALS AND METHODS

After institutional review board approval, 31 consecutive patients who presented to the ED with chest pain were prospectively included in this study. Blood collection was performed as in other patients at time zero (t = 0, at admission in ED) in EDTA and thrombin tubes. Immediately, a few drops of blood from the EDTA tube were used to perform troponin I determinations on the PathFast (Mitsubishi, Kagaku Iatron, Inc, Chiba, Japan). The thrombin tube was sent to the central laboratory, centrifuged at 3000 rpm for 10 minutes, and the troponin I was

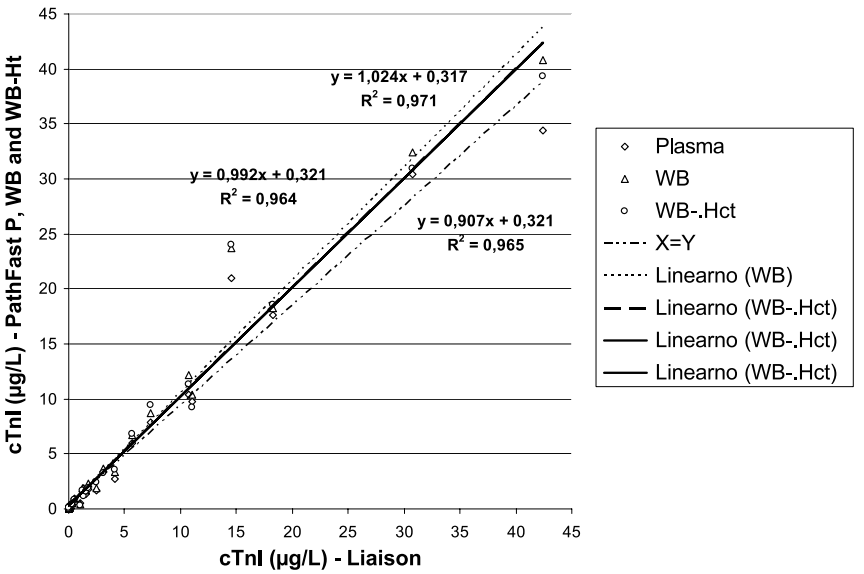

FIGURE 2. Correlation of the results obtained by the Pathfast and Liaison methods. Certain sets of results correspond to Pathfast plasma results, to Pathfast whole blood results, and to Pathfast whole blood results with hematocrit correction.

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TABLE 2. Total TAT for cTnI in the Central Laboratory

No. Samples	TAT, minutes	%
5	<30	1.05
114	>30 and <60	23.68
161	>60 and <90	33.68
200	>90	41.58
Total = 480		100.00

determined on the Liaison analyzer (DiaSorin, Saluggia, Italy). The effect of hematocrit in whole blood samples on the PathFast cTnI assay results was studied using 100 leftover whole blood samples with a normal cTnI level. The time used in the process was carefully logged and used for the calculation of TAT. The TAT for the Liaison analyzer was measured in 380 determinations of troponin I sent to the central laboratory from the ED at the time of the study (1 month). Means, SD, coefficients of variation, linear regression, and range were calculated using Microsoft Excel software (Microsoft, Cambridge, United Kingdom). A *t* test was used to compare the TAT for the 2 methods.

RESULTS

For the purpose of this study, we included 31 ED patients. The results obtained with the PathFast correlated very well with those obtained in core laboratory. Maximum sensitivity and specificity of the PathFast troponin I were observed at a cutoff of 0.1 μg/L (100% sensitivity and 100% specificity), whereas the optimum cutoff level was 0.06 μg/L (96% sensitivity and 95% specificity; Fig. 1). Comparison of the PathFast cTnI with the Liaison showed a good correlation using whole blood ($R^2 = 0.964$, $y = 0.992x + 0.321$) and when plasma was assayed ($R^2 = 0.965$, $y = 0.907x + 0.321$). The use of a hematocrit correction only slightly influenced the final result ($R^2 = 0.971$, $y = 1.024x + 0.317$; Fig. 2). The effect of the hematocrit in the whole blood samples was studied using 50 whole blood samples under the cutoff value. The κ coefficient of an individual hematocrit correction with a uniform hematocrit correction (0.40) was found to be 0.971, and the regression line showed a *y*-intercept of 1.024 and a slope of 0.317. The use of hematocrit correction only slightly influenced the final result. Significant decrease in the overall TAT was observed with the POC PathFast in comparison with the core laboratory (mean [SD], 20 [5] vs 104 [33] minutes, $P < 0.001$). Only 24.73% of the cases using the core laboratory analyzer Liaison were 60 minutes or shorter (Fig. 3 and Table 2). The distribution of time required for the various steps using the central laboratory is summarized in Figure 4 and Table 3.

TABLE 3. Time Required for Different Tasks That Are Needed to Analyze Troponin I in the Central Laboratory

Different Jobs in Laboratory	Time, minute	% Total Time
Sampling in ED	5.25	7
Sending blood to central laboratory	24.75	33
Centrifugation of blood	15.00	20
Administrative work before analysis	2.25	3
Analysis	24.75	33
Confirmation of results	3.00	4

DISCUSSION

This study confirms the overall good correlation of the results obtained with the PathFast cTnI assay with those with a core laboratory assay. Similar results were reported in other studies.[7,8] This POC assay showed analytical reliability in concordance with the guidelines of the European Society of Cardiology/American College of Cardiology and National Academy of Clinical Biochemistry. Studies comparing POC testing with core laboratories have universally demonstrated a decrease in TAT.[4,6,7] Most physicians in emergency units believe that the results of testing for myocardial injury should be reported back within 45 minutes or less.[5] This goal is easily achieved with the PathFast system. On the other hand, our core laboratory provided only 24.73% of cTnI results in less than 60 minutes, which is not in line with guidelines.[9] The results obtained using the Pathfast system were less than 30 minutes. Rapid TAT for troponin I testing—within 60 minutes—is a goal. New National Academy of Clinical Biochemistry guidelines

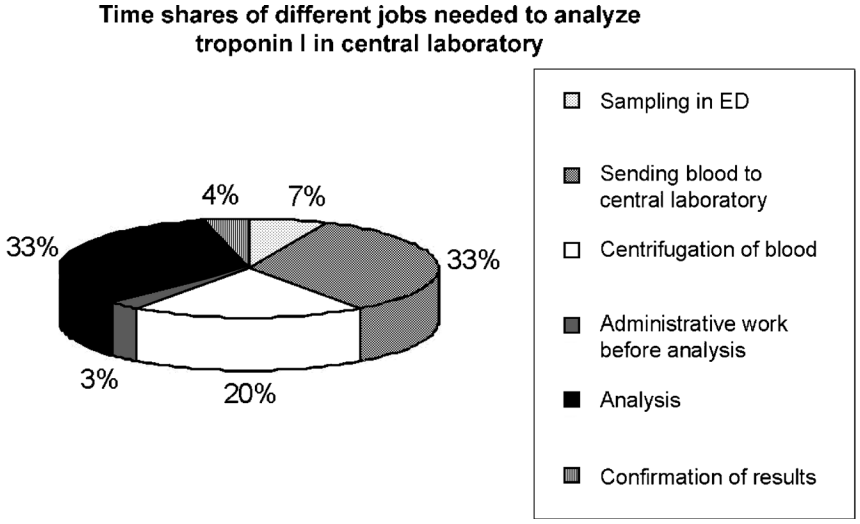

FIGURE 4. Time required for different tasks that are needed to analyze troponin I in the central laboratory.

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emphasize the need for rapid TAT and suggest consideration of POCT testing.[9] Another reason that laboratories should consider POCT is that these instruments have become more accurate in recent years. When considering POCT for troponin, laboratories must also take into account that central laboratory and POC troponin assays are not calibrated with the same reference materials. Therefore, results from different manufacturers may not correlate. In our case, we found a good correlation of the results and the same cutoff value.

As evident in Figure 4, there are some activities that are excessively time consuming and present as opportunities for improvement. We conclude that the PathFast POC system is rapid and easy to use without compromising analytical performance. These features may enable better outcomes, lower costs, and improved patient flow in EDs.

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