OBJECTIVES:
1. To describe recent point-of-care (POC) testing trials for cardiac markers in the ED
2. To describe the strengths and limitations of POC testing
3. To describe the stakeholders involved with implementation and regulation of a successful point-of-care testing program for cardiac markers in the ED

INTRODUCTION

Several factors in the medical care environment have influenced the growth of point-of-care (POC) testing. This is particularly true in the emergency department (ED), where there are now over 110 million visits each year and five million of these patients have potential acute coronary syndrome (ACS). EDs are now not only used for the treatment of the acute manifestations of illness, but have become in many ways diagnostic centers. What used to be routine inpatient evaluation for chest pain has become a standard evaluation in the ED or chest pain unit. Patient expectations of emergency evaluation include not only accurate and knowledgeable care, but also care that is efficient. Additionally, there has been a significant increase in time dependent therapies, particularly for patients with ACS. These accelerated demands and protocols have increased the need for rapid testing and reduction in laboratory result turn-around-time.

POC testing is a response to process challenges in the central laboratory. Central laboratory processing of blood samples includes the delivery of blood, clot extraction if serum is used, centrifugation, and up to 20 minutes of assay time for the large automated immunoassay analyzers. In the ED accelerated model with its combination of rapid diagnosis and treatment, demands for rapid laboratory information have clearly increased. These demands on the ED have translated to increased volume of testing and necessity of rapid turnaround. POC testing, often called “near patient testing,” occurs where patient care is rendered and has taken an increasingly larger role in most ED environments.

Recent consensus guidelines published by the American College of Cardiology and the American Heart Association for the diagnosis and treatment of ACS recommend that cardiac markers should be available within 30-60 minutes from the time of ED presentation. As many EDs and central laboratories are unable to meet this recommendation, POC testing has to be considered as an operational necessity in evaluating these patients.

Selected POC Cardiac Marker Assay Performance and Selected Trials

The most commonly used markers in cardiac risk stratification are CKMB, cardiac
troponin I or T (Tn), and variably myoglobin. Other markers such as brain natriuretic peptide (BNP), high-sensitivity CRP (hsCRP), and D-dimer are also available but beyond the scope of routine ED evaluation.4-9 There are many cardiac assays from which to choose (Table 1) hence initial trials evaluating POC testing assays generally focus on analytical performance and/or clinical utility.10,11 While there have been dozens of trials investigating POC assays in patients presenting with acute chest discomfort, the following paragraphs summarize some of the more noteworthy trials.

Table 1.

<table>
<thead>
<tr>
<th>Current Widely Available Cardiac Marker Assays</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Triage System (Biosite)</td>
</tr>
<tr>
<td>2) i-STAT®1 Analyzer (i-STAT)</td>
</tr>
<tr>
<td>3) Cardiac Reader (Roche)</td>
</tr>
<tr>
<td>4) RAMP System (Response Biomedical)</td>
</tr>
<tr>
<td>5) Stratus CS (Dade Behring)</td>
</tr>
</tbody>
</table>

It is clear that the accurate measurement of the cardiac troponins is a major focus for POC testing in patients presenting with potential ACS. As there is no value standardization between the many different assays, evaluation of analytical performance is complicated and requires laboratorian expertise. The analytical performance of the i-STAT whole blood TnI assay was evaluated in a recent trial of 248 total patients. Antibody specificity, detection limit, imprecision, linearity, assay specificity, sample type stability, interferences and reference limit determination were compared to the Stratus CS device. The detection limit was found to be 0.02 ng/L with a 99th percentile reference limit of 0.08 ng/L. This study showed that the i-STAT TnI assay was a sensitive and precise monitor of TnI and appropriate for use in the POC testing environment for the evaluation and risk assessment of patients with possible ACS.12

In the Chest Pain Evaluation by Creatine Kinase-MB, Myoglobin, and Troponin I (CHECKMATE) trial, “time to positivity” between POC testing and central laboratory were compared in the risk stratification of non-ST-segment elevation chest pain patients. The primary assessment of this trial was to relate marker status to 30-day death and myocardial infarction. Three markers strategies were compared: (1) POC myoglobin, CKMB, and TnI, (2) POC CKMB and TnI, and (3) local laboratory. The POC assay used in this trial was the Stratus CS instrument. This study found that time to positivity was decreased in both POC marker strategies (2.5 hours and 2.8 hours, respectively) when compared to the local laboratory (3.4 hours). Outcome data of 30-day death or infarction showed that the relation between the POC marker strategies was stronger than that of the local laboratory (positive 18.8% and 21.9% versus 13.6%). The authors concluded that POC multimarker determination provided faster and better risk stratification in this patient population.13

The RAMP® (Response Medical) CK-MB and TnI whole blood POC assays were evaluated in a multicenter trial in 185 patients suspected of acute coronary syndrome and 180 healthy subjects. The standard comparison assays were the Biosite Triage POC device and the Dade Behring Dimension RxL central laboratory system. Clinical sensitivity and specificity for AMI were determined using the redefined guidelines from the ESC/ACC.14 The authors concluded that for 39 AMI and 67 non-AMI patients, the clinical sensitivity, specificity, and diagnostic efficiency of the RAMP were similar to the predicate assays and this device was an acceptable alternative to automated central laboratory instruments. Total imprecision ranged from 7.2% to 11.4% for TnI over the range of 0.22 to 5 ng/mL and 4.8% to 8.6% for CKMB at 7, 14, and 25 ng/mL.15
In another trial conducted with 817 consecutive ED patients presenting with symptoms consistent with ACS, serial determinations of myoglobin, TnI, and CKMB at 0, 1.5, 3, and 9 hours were obtained using the Biosite Triage Cardiac Marker System. Sensitivity and negative predictive value were compared for both the multimarker POC approach and the central laboratory strategy. This study found that sensitivity and negative predictive value for myoglobin and TnI by 90 minutes was 96.9% and 99.6%, respectively. CKMB measurements did not add to this evaluation. Additionally, lab result reporting was on average 57 minutes faster with the POC assay.\textsuperscript{16}

Renal failure patients represent a particularly challenging population for cardiac marker assessment. False positive tests complicate the assessment and diagnosis in this high-risk group. POC testing has been successfully evaluated in these patients as well. Using the same patient population as the previously mentioned study by McCullough \textit{et al.}, patients were divided into five groups based on their renal function. Two independent cardiologists determined the diagnosis of AMI. TnI was found to be the most consistent across all patient groups without significant false positive results.\textsuperscript{16,17}

\textbf{Economic Assessment of Point of Care Testing}

As medicine is under constant scrutiny to provide quality medical care with reduced costs, implementation of additional laboratory services will be understandably called into question. Is POC testing cost effective? This question is central for all parties involved with implementation of such a program. Benefits of POC testing generally fall into the major categories of consumer demand, medical care, and time and resource management. The ultimate goal is clearly high quality, cost-effective, and efficient health care.

Both physicians and patients have a demand for POC testing. Physicians understandably want accessible and rapid results in the diagnosis and care of their patients. Patients and their insurers want rapid diagnosis and treatment for their conditions. In a world of internet, fast food, instant replay, e-mail, digital audio, cell phones, and pagers – does it not seem reasonable that lab results in acute care environments would return faster today than 10 years ago?

For time sensitive high morbidity medical conditions that are frequently encountered in the ED, rapid and improved turn-around time (TAT) for laboratory tests intuitively translates into improved medical care. If POC testing can improve the ability to diagnose efficiently, more effectively utilize medical treatment, improve pharmaceutical consumption, and decrease lengths of stay in the ED, the OR, the ICU, and the hospital, improve resource utilization, then certainly an economic benefit has to be realized. These inter-related parameters are extremely difficult to quantify. Just as in the implementation of any new intervention, the ultimate test for POC testing will be to determine its effect on these outcomes. Showing improvement of outcomes is difficult but will be imperative in the ultimate judgment of POC testing.
Most notably, the cost/benefit analysis is not as basic as simply comparing the cost of the lab result in the POC and central laboratory environments. This has traditionally been called, “cost-centered analysis.” Labor and reagent costs are not the only considerations. The focus of POC testing should be medical care and systems costs, not the very isolated cost of testing itself. The viewpoint of a global evaluation of the entire cost of a health care episode with an outcomes approach is imperative. Even with all the efforts of trying to find an answer to this question, we understand very little about what POC testing actually accomplishes in terms of benefits and outcomes.

The Time Issue
Decreased TAT is likely the central issue in POC testing. Lee-Lewandrowski et al. showed a 84.5% reduction in TAT using a qualitative POC TnI assay which translated to a length-of-stay reduction from 386 to 338 minutes.18 Likewise, Caragher et al. showed a TAT reduction of 55% compared to the central lab using the quantitative assay Stratus® CS Analyzer (Dade Behring) for TnI, CKMB, and myoglobin.19 POC assays can perform tests faster. While it is intuitive that a test performed at the bedside in 10 minutes would take less time than a test that has traditionally required 60 minutes, these studies illustrate that TAT can be decreased in the acute patient setting.

Does this decrease in laboratory TAT matter? The strength of POC testing is only as robust as the clinical assumption that fast diagnosis and treatment is better for patients. From numerous studies we know that early intervention and medical treatment is beneficial in patients with non-ST-segment elevation acute coronary syndrome.1,3,20 ED length of stay is also a critical factor for potential implementation of a POC system. Singer et al. demonstrated a reduced ED length of stay of 68 minutes for potential ACS patients after implementation of a POC cardiac marker system.21 The success and benefits of POC testing clearly require that action be taken on the results obtained (Figure 1).

Strengths and Limitations
It is important to note that POC testing supplements testing from the central laboratory. Some environments benefit more and are more conducive to POC testing. While the need for more rapid results is clear, the already burdened ED environment is challenging for non-laboratory personnel such as nurses or patient care assistants to perform rapid and high quality tests. Implementation of any POC system must start with clinical laboratory scientist’s direction. These individuals are specifically trained in quality control and assurance and can assist in the complex implementation of this kind of system (Table 2).

Figure 1. Model for Point-of-Care Testing

![Figure 1](image-url)
We know from previous studies that POC assays for cardiac markers are “good.” But, how “good” is “good enough?” The ACC and AHA recommend the cardiac specific troponins in the triage and treatment in patients with potential ACS. As even the most minor of elevations of troponin portend increased risk, how good does a POC test have to be? Trials such as TACTICS have shown that patients with troponin levels above the 99th percentile but below the 10% CV value are at increased risk. It is important for emergency medicine physicians to understand the limitations of POC testing and make informed decisions based on the qualities of the individual platforms.

**SUMMARY**

Studies demonstrating improvement in patient outcome and overall health care cost savings will determine the ultimate long-term success for POC testing. Additionally, success of ED POC cardiac marker testing will require standardization of the varied platforms. With nearly a dozen current manufacturers of TnI assays, correlation, particularly within the same clinical setting, is a significant concern. Physicians have to be able to communicate results to the patient and other physicians in a standardized format that can be interpreted from assay to assay. Evidence of improved outcomes, total cost savings, and assay standardization using POC testing will undoubtedly add to our ability as emergency physicians to provide the best care for our patients.
REFERENCES


