OBJECTIVES:
1. Understand the role of point-of-care (POC) testing in the efficient evaluation and management of ACS and AHF patients.
2. Review the diagnostic test characteristics for cardiac POC analytes.
3. Consider the issues related to POC testing versus an ED satellite laboratory.

INTRODUCTION
In the emergency department (ED), it is extremely important to rapidly identify patients with an acute coronary syndrome (ACS) or acute heart failure (AHF) to improve overall outcomes. In an environment strained by an increasing volume of patients, risk stratification must be performed making effective use of available resources. Many hospital-wide processes are required to optimize efforts toward this goal. Within the context of overall hospital and ED processes, the introduction of point-of-care (POC) testing for biomarkers of cardiac injury or dysfunction are available to help emergency physicians achieve these goals. In the evaluation of ED patients with symptoms suggestive of ACS or AHF, the utilization of POC tests is playing an increasingly important role in making decisions regarding treatments and disposition. Cardiac biomarkers of necrosis CK-MB, myoglobin, and both troponin I and troponin T, as well as markers of AHF including B-type natriuretic peptide (BNP) and its precursor N-terminal pro-BNP (NT-proBNP) have become incorporated into ED strategies for early identification of high risk patients.1-4

The primary goal of any POC testing strategy for ACS and AHF should be to enhance risk stratification for patients through shorter turn-around times for biomarkers. It is not always easy to demonstrate, even in the era of evidence-based practice, that POC testing accomplishes these goals. It seems intuitively obvious, however, more rapid test processing will lead to faster decisions, prompt and appropriate therapy, and thus improve patient outcomes. Clinicians must be confident that POC test results are as accurate as tests performed on larger laboratory-based instruments. Evidence is accumulating that some of these elements are enhanced by incorporating POC testing within the ED.2-7 While mortality and serious morbidity are the primary outcomes, studies have used surrogates for these outcomes and softer endpoints such as ED length of stay (LOS), time to symptom resolution, or time to treatment initiation. Renaud’s study7 of patients
with suspected ACS showed that POC testing was associated with decreased time to anti-ischemic therapy by approximately 45 minutes. This effect was attributed to shorter time to physician notification of a troponin level. This information did not translate into a mortality benefit for patients in this relatively small study of 113 patients with non ST-segment elevation ACS. In an analysis of the ADHERE registry of AHF patients, Maisel4 has shown that the time to BNP levels is directly related to the time required to initiate intravenous diuretic therapy and elevated BNP levels are associated with increased risk for mortality. Patients with the greatest in-hospital mortality were those with greatly elevated BNP levels which prolonged delay to initiating diuretic treatment.

A secondary goal of including POC testing within the ED are to enhance patient throughput, allowing more patients to be seen in the ED for a given period of time. If an ED has little control regarding the influx of an ever-increasing volume of patients, then a briefier LOS for certain patients within the ED should allow accommodation of a larger number of patients. In the recent multi-center DISPO-ACS trial,6 the effect of POC testing on ED LOS varied between institutions. One of the main conclusions of this study was that the potential effects of POC testing on patient throughput must be considered in the full context of ED operations. A portion of the justification for POC testing expenses should include the potential to reduce the number of patients who present to the ED but leave prior to evaluation. Potentially, in some situations a reduction in EMS diversion time can be realized.8,9 These patient care improvements have the potential to enhance revenue and offset the potentially more expensive strategy of POC testing.

Test Accuracy and Precision
For any laboratory testing, accurate results are the first and greatest requirement. Faster is clearly not better if accuracy is compromised. The National Academy of Clinical Biochemistry suggests performance specifications for POC and central laboratory platforms should not differ.10,11 Several recent publications have clarified the role of an accurate and precise definition of myocardial injury, a finding that marks patients for increased risk. The current definition of myocardial infarction is based on troponin testing, with abnormal results defined as those which exceed the 99th percentile of the reference population.12 This point on the analytical curve should also be precisely measurable with a coefficient of variation of no more than 10%, a requirement that may be difficult to achieve but still necessary to appropriately stratify risk.13,14 Currently available POC instruments show analytic test performance characteristics comparable to, or in some instances possibly even better than, central laboratory instruments.15

One consideration in POC and lab-based troponin testing is particularly vexing. Because quantification of troponin testing is not standardized, each assay instrument reports a specific range of normals and diagnostic cut-off points that vary by up to 10 - 100 fold between instruments. This is presumed to be due to the variations in antibodies employed within the specific devices as the basis for analysis. Troponin exists in various complexes and is broken down into multiple peptides within the blood, so a panel of antibodies will have varying degrees of binding to each of these particles. When both POC devices and laboratory-based devices are used to follow the course of a particular patient, this can be problematic. It is not uncommon for patients to be tested in the ED with a POC device, and then have subsequent testing performed using the laboratory’s platform. Caution must be exercised to ensure clinicians caring for these patients realize that the ranges for normal/ abnormal vary between such devices.

It has been notoriously difficult to standardize PT/INR results between POC devices and laboratory systems.16 This is due in part to the calibration system requirements for the devices. With a narrow window for therapeutic range, differences between tests of 0.5-1 INR unit can affect changes in medical management. In addition to the date and time the results are generated, laboratory test reports should clearly indicate the device which was used for the test, as well as the range of normal and diagnostic
abnormal values. A statement of caution may be included with the test result report if several devices are used within an institution to measure the same analyte, particularly if these devices show significantly different test performance characteristics.

Decision Making
Emergency physicians are decision makers. These clinicians work under time constraints and often without the luxury of access to all information which would make diagnosis and therapeutic decisions straight-forward. Often decisions can be made to initiate life-saving therapy when only a few key data pieces are known. In ST-segment elevation myocardial infarction (STEMI) cases, for example, emergency physicians activate the cardiac catheterization laboratory and staff when a symptomatic patient is found to have a diagnostic 12-lead electrocardiogram. Few, if any, laboratory tests will impact this decision. Alternatively, laboratory test results may be the key pieces of information required for the physician to make a diagnosis or be able to appropriately gauge the prognosis for a patient.

Risk stratification is a major aspect of the practice of emergency medicine. Deciding to initiate specific therapy as well as deciding on the appropriate disposition for patients – ICU or hospital admission, clinical decision unit, or home – is now the domain of emergency medicine in a growing number of disease processes often in collaboration with hospitalists. The appropriate level of care is provided to the seriously ill patients quickly, once they are identified; and those who are identified to have less severe issues may avoid unnecessary further testing and hospitalizations. Chest pain centers evaluate patients at low risk for adverse events using accelerated diagnostic pathways, and heart failure centers focus their evaluation and treatments on interventions targeted to patients’ specific presentations and risk factors. By incorporating POC testing to the ED evaluation of the undifferentiated patients who may have ACS or AHF, the appropriate therapy can be delivered to the patient at the earliest opportunity.4,7

Implementing a POC Program – Cardiac Injury and Heart Failure
Hospitals and EDs uniformly already utilize a number of POC tests everyday – from arterial blood gas determination to urinalysis and urine pregnancy testing. Perhaps the most ubiquitous POC testing is for blood glucose determination. The menu for POC testing available for use within the ED is expanding rapidly. Cartridge based devices and instruments which utilize small amounts of whole blood now allow cardiac biomarker testing with results available within 5 – 20 minutes. Is this timeliness absolutely required for new test analytes – such as troponin and BNP? Could central laboratory-based testing strategies provide test results within a reasonable time frame, one that meets the needs of the ED? Guidelines provided by both clinically oriented societies and laboratories suggest that timely test result availability is crucial.11,17 These guidelines direct that test results should be available to the clinician preferably within 30 minutes, and not greater than 1 hour defined as the time from blood sample acquisition until the result is received by the responsible physician. The common phrase ‘laboratory turn around time’ means different things at different hospitals. Most hospital laboratories provide quality assurance monitoring for time intervals related to reporting results, but definitions for these intervals are inconsistent. The real time interval which is important to the clinicians caring for patients begins when the clinician decides to order the test, and ends when that clinician knows the result and can act on it. This so called ‘brain to brain’ time includes many intervals which are outside the realm of influence of the central laboratory – such as the time to communicate the order once the test is decided upon, the time for order processing and sample acquisition, and the time from test result reporting until the clinician is aware that the result is available. Many POC devices have a time advantage over laboratory based instruments because they do not require a time-consuming step of sample centrifugation. Whole blood is easier to process quickly in POC devices. While the time required for test processing is important, focusing solely on this interval leaves the clinician vulnerable to the risk of ignoring overall system design that may have an even greater impact on the ‘brain to brain’ time.
Laboratorians have developed recommendations regarding the development of POC testing for cardiac biomarkers. An inter-departmental collaboration is mandatory involving emergency medicine, hospitalists, cardiology, and laboratory medicine for both the development of the appropriate protocols, as well as the ongoing quality assurance improvement and performance monitoring necessary to reduce the potential for medical errors. Selection of devices, training, maintenance, user competency, and regulatory compliance must involve laboratory medicine. In addition, having uniform POC instruments within an institution promote ease of use and training, program management, and connectivity with the laboratory information system.

**POC or ED Satellite Laboratory?**

As previously noted, rapid single test performance times will add little to a system which is not well organized to optimize the complex process of patient evaluation, treatment, and disposition. When viewed as an individual item, POC testing is often incorporated into the duties of a very busy ED nursing and technical staff. Each additional analyte or device brings with it a new set of training, technical procedures, and maintenance issues. Conversely, hospital laboratory staffs may not realistically be able to staff each unit, including EDs, where POC testing is performed. Perhaps the notion of ED satellite laboratories deserves consideration again. Efforts should focus on eliminating bottlenecks, and at making rate-limiting steps more timely and efficient. If CT scanning is incorporated into diagnostic algorithms, delaying that procedure for 90 minutes to obtain a creatinine result from the central laboratory is unacceptable. Point-of-care devices which return a creatinine result within 10 minutes may be an important aspect of the solution to such a significant delay.

A large proportion of patients in EDs have laboratory testing of one sort or another. At Massachusetts General Hospital, Johnson found that 66% of ED patients had POC tests performed. By adding a rapid chemistry analyzer and standard hematology cell counter to the menu of POC devices, they found that a satellite lab performed 75% of all ED testing, and provided complete testing for 62% of their patients. Development of a satellite laboratory within the ED may provide the best of each perspective – rapid and accurate test results provided within the customary laboratory professionals’ environment. Volume of testing in such a laboratory must offset the significant personnel costs associated with 24/7 availability.

**Future Directions**

Considerable advances have been made with POC testing within the past decade. Expedited patient care and efficient processing of laboratory tests have been the primary objectives. Momentum for these modalities continues to grow, and input on the direction to focus new efforts within the POC domain must come from all users. In the September 2008 issue of *Point of Care*, Lewandrowski compiled a wish list of items to advance the field. Among the nearly 50 items cited as areas of unmet need included a number of those applying directly to the topic of biomarker POC testing in a Chest Pain Center. Kroll calls attention to several items which will impact the evaluation and treatment of the emergency cardiac patient. Accuracy and precision of POC measurement of activated clotting time (ACT) remain problematic. This test helps guide appropriate dosing of heparin in patients with ACS. With the current focus on risk reduction and error prevention in dosing anticoagulants, clinicians absolutely rely on accurate test results. When ACT test imprecision may be up to 20%, it is clear why patients may be either under- or over-anticoagulated, thus either at risk for inadequate therapy or at increased risk for bleeding complications.

In the future, clinicians will see the introduction of *in vivo* testing for some of the analytes discussed above. This is the ultimate POC testing. Currently, indwelling electrodes are available which dwell within the central circulation, quantifying the delivery of oxygen and helping to guide resuscitation in sepsis and shock. In the future, proposed systems using even less invasive approaches could provide second to second or minute to minute quantification of markers of cardiac ischemia or decompensation in heart failure.
SUMMARY

In summary, current POC testing instruments can provide timely and accurate results. These rapid test results are best utilized when placed in the context of an efficient process for patient evaluation, treatment and disposition using inter-departmental care pathways. Critical decisions depend on the accuracy and timeliness of results. Physicians having Chest Pain Centers which focus on the safe and efficient evaluation of patients with symptoms of ACS and AHF can use these POC tests to favorably impact patient flow in the ED, and more importantly to enhance clinical outcomes.

REFERENCES


