Point-of-care testing in the emergency department with emphasis on chest pain patients

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The management at the emergency department of patients presenting with symptoms of chest pain and/or acute dyspnea accounts for a substantial proportion of emergency care resources.

In the work-up of these patients the blood measurements of cardiac troponins and brain natriuretic peptides are recommended by current guidelines in addition to ECG, imaging and occasionally the measurements of D-dimer and blood gases.

The introduction of point-of-care testing for these biomarkers has the potential to change the work flow in the emergency department by providing rapid and accurate information.

However, in order to take advantage of point-of-care testing the brain-to-vein-to-brain time has to be adjusted with the elimination of unnecessary delays before any clinical decision and action are taken.

Thus, point-of-care testing at the emergency department has the potential to reduce length of stay at the emergency department, patient suffering and money.

The management at the emergency department of patients presenting with symptoms of cardiac disease such as chest pain and/or acute dyspnea accounts for a substantial proportion of emergency care resources.

Patients with symptoms of cardiac disease are high-risk patients and should be effectively identified by the emergency physician in order to initiate specific clinical actions.

Current recommendations identify the measurement of cardiac markers, i.e. cardiac troponins (cTn) and brain natriuretic peptides (BNP), as an important part of the diagnostic work-up, alongside other testing modalities such as ECG measurement and cardiac imaging.

Occasionally the measurement of D-dimer and blood gases may be indicated, e.g. in patients with suspected pulmonary embolism or patients suffering from cardiogenic shock.

The measurement at the point of care is a potential strategy for the reduction in turnaround time for cardiac marker testing in the emergency setting [1].

In this overview I have concentrated on the use of the cardiac biomarkers, BNP and cTn, in the diagnostic work-up in the emergency department.

However, the importance of cardiac troponins and natriuretic peptides for risk stratification is another very important aspect of these biomarkers, which is becoming increasingly important with the introduction of cardiac troponins with higher sensitivities.

In this respect many other biomarkers also seem to add to the outcome prediction of our patients with cardiac disease.

Thus, these aspects are outside the scope of this brief overview, which is a summary based on round-table discussions between experts in cardiology, emergency medicine and laboratory medicine and which were reported in two recent publications [1,3].

Cardiac troponins in the diagnosis of acute coronary syndrome

Increasing levels of cardiac troponins, either troponin I or troponin T, in blood signify damage to the myocardium.

The detection of circulating cardiac troponin is the most sensitive and specific biochemical marker of myocardial injury that is available to the physician in clinical settings, including the emergency department [4].

The early identification or ruling-out of the presence of an acute coronary syndrome relies on a combination of signs and symptoms, cardiac biomarker levels and findings in the ECG.

This is important, since signs and symptoms alone can be misleading, and since a substantial proportion of patients present with non-specific symptoms. Cardiac biomarkers can be elevated also in other conditions than acute coronary syndromes and findings in ECG are quite often unspecific [5,6].

Recent recommendations have noted that currently available cardiac troponin assays can contribute to rule-out protocols for myocardial infarction within 3 hours of arrival at the emergency department [7,8].

However, such protocols require the use of high-sensitive cardiac troponin assays currently only available at the clinical laboratory.

Contemporary studies using sensitive cardiac troponin assays show no added value of adding other markers of myocardial damages such as CKMB, myoglobin or Fatty-Acid Binding Protein [9,10].

The core principle underlying point-of-care measurement is the reduction in turnaround time without compromising the quality of information on which clinical decisions for patients are based [11].

A turnaround time of less than 1 hour should be achieved, and the availability of POCT could reduce the turnaround time to less than 30 minutes.

The 2011 guideline for management of non-ST-elevation acute coronary syndromes noted that a rapid (2-hour) rule-out protocol for acute coronary syndromes using POC testing of cardiac troponins, ECG and risk scoring was found to be safe [8,12].

Point-of-care systems should provide quantitative and not merely semiquantitative or qualitative measurement of cardiac troponin to support or rule out a diagnosis of acute myocardial infarction, given the importance of detecting changes in cardiac troponin levels for a correct diagnosis [13].

In addition, the sensitivity of the assay system should ideally not differ from that provided by central laboratory

assays. The imprecision of the measurement at the 99th-percentile concentrations of cardiac troponins of healthy subjects has been highlighted as important in current management recommendations [14].

Specifically, imprecision of 10 % CV (coefficient of variation) or less at the 99th-percentile limit is desirable, and routine use of cardiac troponin assays with imprecision greater than 20 % at this limit is not recommended [15].

In order to be implemented successfully, a POCT for cardiac troponins should significantly reduce turnaround time without jeopardizing the diagnostic performance.

In particular, emergency physicians would tolerate neither a significant increase in false negative results which might lead to discharge of patients with a persistent risk of cardiac adverse events nor a substantial increase in "false positives" with the risk of unjustified and potentially hazardous therapeutic interventions.

The safety of an accelerated 90-minute protocol to exclude a diagnosis of acute myocardial infarction has been demonstrated in the emergency department setting, using serial multimarker POCTs (cardiac troponin, CKMB, myoglobin) [16].

All cases of acute myocardial infarction were diagnosed within 90 minutes, and admissions to the coronary care unit were decreased by 40 %. In addition, 90 % of patients with negative cardiac biomarkers and ECG findings were discharged, with only one returning with myocardial infarction within 1 month.

Another study focused on 817 consecutive emergency department admissions for suspected acute myocardial infarction [17].

The POCT strategy, which involved measurement of CKMB and cardiac troponin, provided a negative predictive value of 99.6 % for the diagnosis of myocardial infarction within 90 minutes, facilitating prompt and reliable rule-out of acute myocardial infarction.

The median turnaround time for the POCTs was 24 minutes, compared with 71 minutes for the central laboratory.

The Disposition Impacted by Serial Point of Care Markers in Acute Coronary Syndromes (DISPO-ACS) trial set out to test the hypothesis that POCT for cardiac troponin I would reduce length of stay, relative to central laboratory testing, in a large sample of 2000 patients evaluated for suspected acute coronary syndromes [18].

There was no overall change in length of stay. The authors concluded that reduced assay turnaround time per se was insufficient to influence length of stay, and that POCT must impact on other aspects of patient management in order to translate reduced assay turnaround time to more rapid discharge.

Reducing "brain-to-brain time" (the time between a physician ordering a test and when he/she interprets its results) was considered key to reducing overall length of stay.

A previous study from the USA involved 545 patients admitted to a cardiology unit with chest pain in roughly equal proportions immediately before or after the introduction of POCT for cardiac troponin I [19].

Charges to patients dropped by 25 % after the introduction of POCT, due to reduced costs associated with boarding, other departments, pharmacy, laboratories, and cardiac or non-cardiac procedures.

Brain natriuretic peptides in the diagnosis of heart failure

Dyspnea has been observed in about half of patients who received a primary diagnosis of heart failure in the ED, though it is well known to the ED physician that a number of other conditions present with dyspnea, including asthma, pulmonary edema, chronic obstructive pulmonary disease, interstitial lung disease and myocardial ischemia.

Rapid and accurate assessment of acute heart failure

is therefore a priority when a patient presents with dyspnea in an emergency setting.

In recent years, the measurement of B-type natriuretic peptide (BNP) or NT-proBNP has become increasingly established for the management of patients presenting to an ED with dyspnea or other symptoms suggestive of heart failure in order to distinguish acute heart failure from these other conditions [20].

Point-of-care (POC) measurement of cardiac biomarkers has the potential for faster turnaround times and consequent increases in the speed of diagnosis and subsequent throughput of patients within the ED.

Data from randomized or observational clinical studies [21] [22] have generally demonstrated that the measurement of natriuretic peptides in the ED adds diagnostic information to other clinical measurements within a panel of biomarker and clinical measurements for the rule-in or -out of heart failure.

Importantly, the measurement of natriuretic peptides plus clinical judgment has been found to be superior to either alone. Major guidelines in the area support the measurement of natriuretic peptides most strongly where the clinical diagnosis of heart failure in patients presenting with acute dyspnea is uncertain.

A recent update of the main European guideline recommends measurement of natriuretic peptides in all patients with suspected heart failure [20].

Thus, rule-out may be possible with this measurement alone, without echocardiography, in patients with a normal ECG.

The measurement of NT-proBNP has been shown to result in significant cost savings relating to inpatient time, staff time, and usage of X-rays, echocardiography and treatments in a study of patients presenting to an ED with symptoms suggestive of heart failure (dyspnea or peripheral edema) [23].

Randomized studies have generally demonstrated reduced time to discharge following measurement versus no measurement of NT-proBNP with a tendency to reduce costs, or reduced time in hospital with use versus non-use of BNP testing at up to 1 year.

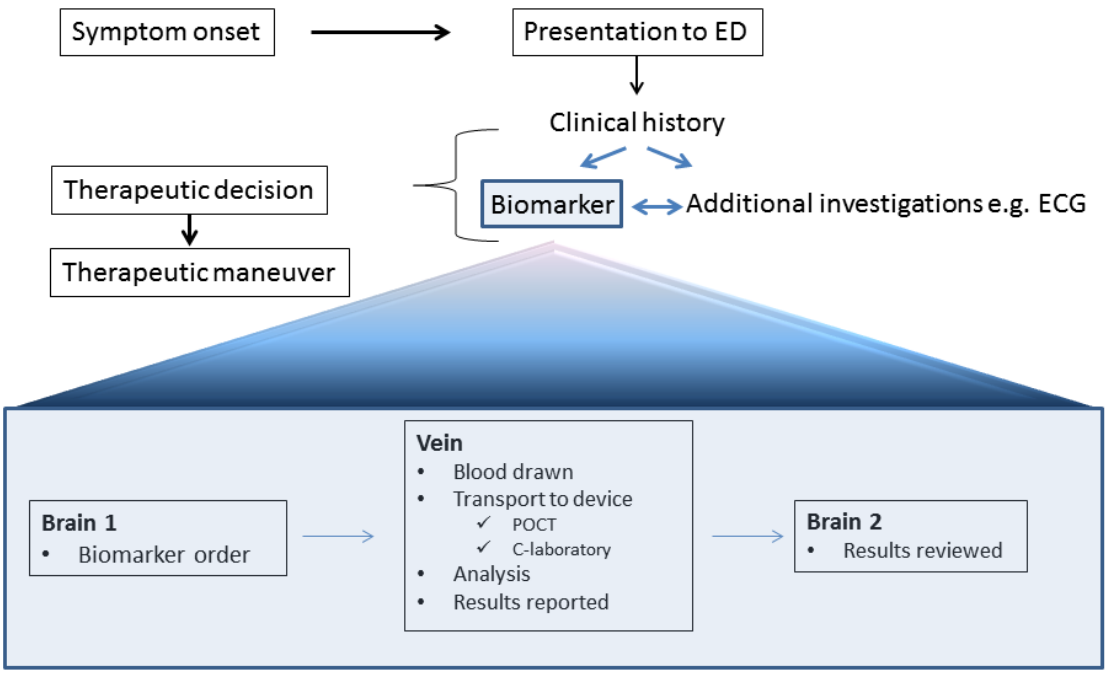

Fig.1

Point-of-care testing for cardiac biomarkers. Why?

As outlined above point-of-care testing of cardiac troponins and natriuretic peptides does not offer any advantages over laboratory testing as to quality or sensitivity. Moreover, no studies have as yet shown that point-of-care testing saves lives.

Why then is point-of-care testing in the emergency setting so attractive and how can we take advantage of this technology? In the figure the work flow of a patient coming to the emergency department is outlined.

The key issues in relation to biomarker testing are three. Brain 1 is the time when a decision is made to request a biomarker test, Vein is the time it takes to draw blood, perform the analysis and report the results, and Brain 2 the time when the results are reviewed and action taken.

The time of Brain 1 to Vein is considerably shorter when point-of-care testing is performed as compared to laboratory testing because of transport time and other logistic issues.

The Vein to Brain 2 is the weak link. A common scenario is that Brain 1 to Vein takes 20 minutes and Vein to Brain 2 1-2 hours. Thus, in order to take full advantage of point-of-care testing this latter time must be shortened.

By shortening the time to a therapeutic decision and therapeutic maneuver we reduce the suffering for our patients and can quickly refer them to settings outside the emergency department, much to the relief of the overcrowded emergency departments. In the end this will also save money.

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