Cardiac troponin by Point of Care testing - the once and future king?

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The measurement of cardiac troponin as either cardiac troponin T (cTnT) or cardiac troponin I (cTnI) is the gold standard biochemical test for the detection of clinically significant myocardial injury and the definitive test to confirm the diagnosis of acute myocardial infarction (AMI) (1).

The technology to measure cTnT and cTnI was initially laboratory based (2, 3). However, measurement using point of care testing was developed. Visually read semi-quantative assays were progressively replaced by compact analysers which read test strips or cartridges to produce quantitative results. The analytical performance of these systems was equivalent to central laboratory testing (4-6). Interestingly, the cTnT POCT device was to some extent introduced to bridge the lack of a stat laboratory cTnT analyser. Clinical studies demonstrated the diagnostic efficiency of POCT (7). However, while POCT for cTnT and cTnI is used, the majority of troponin testing is still performed in the central laboratory. POCT is seen as a useful test when laboratory testing is not readily available due to geographic factors but laboratory testing is preferred. The reasons for this are not very well defined but probably include pressure on emergency department staff, who do not see POCT as part of their role, and the relatively high cost of POCT compared to central laboratory testing (CLT). An additional complication may be the shift in diagnostic “gold standard” arising from the redefinition of myocardial infarction to the 99th percentile of cardiac troponin. Early POCT studies utilised the diagnosis based on much higher troponin cut-offs. POCT troponin measurement has always had a relatively lower analytical sensitivity compared to CLT. POCT is useful for ruling in but less so for ruling out. The final step has been the development of high sensitivity (hs) troponin assays. There have been two consequences of this. First, the differences in analytical sensitivity between POCT and CLT have become very large. Second has been the development of rapid diagnostic protocols based on admission and 1-2 hour serial testing based on hs Troponin assays.

These algorithms use very low levels of troponin measured on an admission sample for immediate rule out, usually combined with a formal risk score, a rule in threshold typically above the 99th percentile of the assay and serial measurement over a 0-1 or 0-2 hour time period. Using a laboratory based high sensitivity assay, although the turnaround time (TAT) is typically 60 minutes, compared to 15-20 minutes for POCT, a definitive management decision can be made from 60 minutes from admission or if serial sampling is used,120-180 minutes from admission. POCT can adequately rule in if the admission troponin value is sufficiently high. However, admission with AMI occurs in the minority of cases and rapid rule out is the goal. Rule out AMI, based on the current analytical sensitivity of those systems suitable for use by Emergency Department (ED) staff, will require repeat blood sampling up to 6 hours from admission. Admission measurement or measurement at 1-2 hours even with a 60 minute TAT trumps measurement at 3-6 hours with a 10 minute TAT if the goal is rapid decision making.

Should we therefore abandon POCT entirely leaving analysis in the hands of the laboratory experts and concentrate on process improvement to reduce CLT TAT. This can be achieved with the use of primary sample tubes that allow immediate centrifugation, vacuum delivery systems and dedicated stat lines or laboratories. All of the problems of analytical quality and staff resistance are immediately removed. This however excludes the significant and often overlooked impact of the immediacy of results on clinical decision making. In an early randomised controlled trial of cTnT measurement comparing POCT with CLT where the decision limit used for diagnosis of AMI was equivalent (0.2 µg/L) there was a significant reduction of length of stay between the POCT and CLT arms (8). Retrospective discussion with the participating CCU staff ascribed this to immediacy of the cTnT results empowering decision making. It has been a feature of RCT’s of POCT that direct impact on length of stay (LOS) or treatment decision has depended critically on process and not speed of result provision (9). The conclusion would therefore be that POCT has the potential to deliver significant impact on LOS and therefore ED throughput if it is integrated within the clinical decision making process and analytical sensitivity is comparable with that required for rapid rule out algorithms.

The study by Boeddinghaus et al (10) reported in this issue of JACC is therefore of of great clinical interest and may transform troponin measurement in the ED. They report the results of a clinical study using the well characterised Advantageous Predictors of Acute Coronary Syndromes Evaluation (APACE) cohort to evaluate a novel high sensitivity (hs) cTnI method. The special feature of this hs cTnI method is that it is delivered using a POCT analyser that is compact and utilises application of whole blood to a disposable cartridge. This format is very familiar to cardiologists and ED physicians alike. Such a technology is compact and ideally suited to use in the ED and less sensitive assays of this type have been in use for some time. To date, the only high sensitivity cTnI assay delivered in a compact analytical format has only really been suitable for use by laboratory trained personnel. The 99th percentile was 14.4 ng/L (female) and 25.7 ng/L (male). The assay detected 72% of individuals in the reference population. Analytical imprecision at the 99th percentile was 5.9% (female) and 5.4% (male) with a 10% CV of 4 ng/L. These analytical characteristics mean that this assay definitely meet the criteria for a high sensitivity cTnI assay, and, as such, is first in class.

The authors demonstrate clearly that this assay has entirely comparable clinical diagnostic performance to CLT when compared with two comparable well validated CLT state-of-the-art cTnT and cTnI assays. Comparing assay performance by receiver operating characteristic curve analysis showed that this POCT assay showed equivalent diagnostic efficiency. In addition, using a validation and then verification cohort they were able to demonstrate the potential use of cTnI measurements by POCT for single measurement on admission to rule out AMI and for use in the European Society of Cardiology rapid rule out algorithm. There is therefore now the opportunity, which did not exist before, to combine the benefits of high sensitivity troponin measurement with the benefits of POCT.

Does this mean we should immediately shift over to POCT for troponin measurement? These findings are extremely encouraging and highlight the potential pathway for troponin measurement in the future. However, independent validation of the analytical and clinical performance of the assay is required. This study demonstrates the clinical validity of this POCT device but does not represent an “in use” prospective validation. Further studies where the POCT method is used in real time are required, either comparative or, ideally, in a clinical trial format (direct randomisation or cluster randomisation) to confirm these exciting findings. Finally, it must be remembered that measurement by POCT is not the whole solution to improvement in ED workflow. There must be appropriate infrastructure to support POCT in general. Incorporation of appropriate testing within a decision-making framework is essential. The importance of process to achieve benefit cannot be underestimated.

So, in the spirit of Saint Augustine, give me POCT troponin, but not yet. But, hopefully, soon.

There are no conflicts of interest

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