Editorials

The promise of high-sensitivity troponin testing

The benefits of diagnostic innovation rely on appropriate clinical practice reforms

Derek P B Chew
MB BS, MPH, FRACP
Professor of Cardiology[1]

Louise Cullen
MB BS, FACEM
Emergency Physician[2]

1 Department of Cardiovascular Medicine, Flinders Medical Centre, Adelaide, SA.

2 Department of Emergency Medicine, Royal Brisbane and Women's Hospital, Brisbane, QLD.

Derek.Chew@flinders.edu.au

doi: 10.5694/mja14.00858

The development of troponin T and I assays for assessing and managing patients with chest pain has revolutionised care for those with suspected or confirmed acute coronary syndromes.[1] The availability of these assays has led to more patients who are at increased risk of recurrent cardiac events being identified, plus improvements in selecting patients who might benefit from early invasive management and revascularisation and more potent antithrombotic therapy. Development of point-of-care testing has extended the reach of these assays to inform the care of patients presenting in rural and remote areas of Australia.[2]

However, incremental improvements in analytical precision, with the emergence of assays that enable detection of serum troponin in up to half the apparently normal population, threaten to undo some of the initial gains offered by troponin testing.[3] While increased sensitivity ensures that the problem of missed myocardial infarction (MI) is far less likely, it also creates the problem of reduced specificity. The consequence is a test with a lower positive predictive value for MI.

In this issue of the Journal, two articles highlight the practical implications of using assays with improved precision. One describes a large single-centre observational study comparing emergency department flow and cardiac investigations before and after the implementation of a troponin I assay with improved analytical precision. It shows moderate reductions in time spent in the emergency department with no significant changes in rates of admission to hospital or discharge with a diagnosis of acute coronary syndrome.[4,5] Hence, it appears that the availability of a troponin assay with improved analytical precision offered the opportunity to arrive at a clinical decision to admit or discharge earlier, but did not change the proportions of patients for whom each of those decisions were made.[6] Of note, there was a significant eight percentage point increase in coronary angiography rate without a commensurate increase in the rate of coronary revascularisation, suggesting a greater rate of invasive investigation that did not lead to coronary lesion-specific therapy. No difference in inhospital mortality due to acute coronary syndrome was observed, and differences in late outcomes would be of great interest but are not currently available.

The other article contemplates the utility of extending troponin testing to primary care to assess patients who present with chest pain. It underscores the challenges of interpreting troponin test results when faced with a single elevated value in a clinical setting where serial testing within hours is impractical because of long turnaround times for results.[7] Thus, troponin testing may be useful for reassuring general practitioners in the context of intermediate or low clinical suspicion of MI, but only when sufficient time has passed since the resolution of symptoms to allow for evidence of myonecrosis (elevated troponin levels) to emerge if it was destined to do so. The pragmatic issue of receiving results in a timely manner to enable an appropriate clinical response remains problematic.

Both of these articles highlight the challenges in translating this diagnostic innovation into effective health care and improved outcomes. Merely improving test precision without an adaptive response in clinical decision making and test interpretation may be a possible driver for increased costs and inefficiencies.[8] While troponin assays with higher analytical precision might offer improved patient outcomes through lower rates of missed MI, they could also increase the investigative burden borne by patients with abnormal test results because of the many non-coronary causes of detectable troponin. Complicating this further is the knowledge that troponin elevation deemed not to be due to unstable coronary plaque is still a marker of increased risk for late mortality, although the current evidence base cannot provide advice on appropriate investigation and management in this common situation.[9]

To reap the returns of improved patient outcomes by providing more efficient clinical care through widespread adoption of innovation in diagnostic testing, such as high-sensitivity troponin assays and point-of-care testing, clinical decision making will need to evolve. Diagnostic innovation will need be used in conjunction with more effective clinical practice, and be used by clinicians who have a clear understanding of the utility of the innovation and are able to appropriately harness the diagnostic information.[10] This will require more robust protocols for risk quantification before troponin tests are requested, coupled with pathways for very early discharge and possibly investigations in ambulatory care settings.[11-13] Similarly, we urgently need a more sophisticated evidence base for assessing and managing patients who have elevated troponin levels that are deemed not due to an acute coronary syndrome. Only through further clinical and health service research, combined with clinical practice reforms focused on maximising the rule-out decision of a negative result

For debate p 155
Research p 158

and the risk information provided by a positive result, will we realise the promise of high-sensitivity troponin testing.

Competing interests: No relevant disclosures.

Provenance: Commissioned; externally peer reviewed.

1 Morrow DA, Cannon CP, Rifai N, et al. Ability of minor elevations of troponins I and T to predict benefit from an early invasive strategy in patients with unstable angina and non-ST elevation myocardial infarction: results from a randomized trial. *JAMA* 2001; 286: 2405-2412.

2 Tideman PA, Tirimacco R, Senior DP, et al. Impact of a regionalised clinical cardiac support network on mortality among rural patients with myocardial infarction. *Med J Aust* 2014; 200: 157-160.

3 Reichlin T, Hochholzer W, Bassetti S, et al. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. *N Engl J Med* 2009; 361: 858-867.

4 Apple FS. A new season for cardiac troponin assays: it's time to keep a scorecard. *Clin Chem* 2009; 55: 1303-1306.

5 Wu AHB, Christenson RH. Analytical and assay issues for use of cardiac troponin testing for risk stratification in primary care. *Clin Biochem* 2013; 46: 969-978.

6 Yip TPY, Pascoe HM, Lane SE. Impact of high-sensitivity cardiac troponin I assays on patients presenting to an emergency department with suspected acute coronary syndrome. *Med J Aust* 2014; 201: 158-161.

7 Marshall GA, Wijeratne NG, Thomas D. Should general practitioners order troponin tests? *Med J Aust* 2014; 201: 155-157.

8 Diamond GA, Kaul S. How would the Reverend Bayes interpret high-sensitivity troponin? *Circulation* 2010; 121: 1172-1175.

9 Petrie CJ, Weir RAP, Anwar MS, et al. High sensitivity troponin T in acute medicine; more questions than answers? *QJM* 2014; 107: 193-200.

10 Bandstein N, Ljung R, Johansson M, Holzmann MJ. Undetectable high-sensitivity cardiac troponin t level in the emergency department and risk of myocardial infarction. *J Am Coll Cardiol* 2014; 63: 2569-2578.

11 Cullen L, Mueller C, Parsonage WA, et al. Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. *J Am Coll Cardiol* 2013; 62: 1242-1249.

12 Than M, Cullen L, Reid CM, et al. A 2-h diagnostic protocol to assess patients with chest pain symptoms in the Asia-Pacific region (ASPECT): a prospective observational validation study. *Lancet* 2011; 377: 1077-1084.

13 Aldous SJ, Richards MA, Cullen L, et al. A new improved accelerated diagnostic protocol safely identifies low-risk patients with chest pain in the emergency department. *Acad Emerg Med* 2012; 19: 510-516. ❑