The use of troponin testing in primary care

Stewart Mann, Lynn McBain

The triage and diagnosis of patients with acute or recent chest pain is a common worldwide challenge that is met in various healthcare settings. A majority of patients with this complaint will not have cardiac pain, some will have identifiable non-cardiac causes and a considerable number end up with a diagnosis of non-specific chest or chest wall pain. A few will have an acute coronary syndrome (ACS) and the consequences of missing such a patient can be severe. However, the pathophysiology of an acute coronary event may mean that even the best professionals equipped with the most sophisticated tests will not always be able to dismiss this diagnosis with complete accuracy.

Much relies on the usual pillars of history and examination which can take into account the background risk of coronary disease, nature of the pain, other accompanying symptoms and signs. An electrocardiogram (ECG) can help define particular ACS syndromes but many patients with ACS will have a normal ECG (or non-specific abnormalities) at initial presentation. Recent studies (ironically evaluating biomarkers) do show how identification of a low risk group can be made with confidence even at this point.

Over recent decades we have come to rely increasingly on biochemical markers in the blood released by damaged myocardium to help define the condition. Initially, such biomarkers were not particularly specific and could be released from skeletal muscle or liver but the increasing use of cardiac troponins has made a step change in both sensitivity and specificity. Their high performance here has tended to bring about a clinical dependence on them as final arbiters of appropriate triage decisions.

Two important lessons have emerged here which apply to all laboratory and other tests: (1) widespread use of even a highly specific test can mislead when used in a population with low risks of the condition in question and (2) increasing sensitivity leads to a trade-off in lower specificity and decisions made as a result can result in adverse consequences for both patient and health service.

Over the last 15 years or so, the measurement of cardiac troponin levels in the blood has become the dominant arbiter of whether there has been damage to cardiac muscle cells. These proteins are highly specific to myocardium and generally have very low circulating levels. Indeed, until recently, these ‘normal’ levels and even small abnormal elevations were below the limits of analytical sensitivity. Thus, at the higher thresholds used, a single raised troponin test would indicate a high probability of a cardiac problem and, in the right context, a likely ACS. Traps in this attractively simple interpretation do exist; a sample taken too early in the course may yield a ‘false negative’ result and there is an ever-growing list of other conditions likely to produce a ‘false positive result’.

To try to help navigate this diagnostic swamp, the European and American Cardiac bodies convened panels (on which New Zealand has been directly represented) to
produce a consensus definition of myocardial infarction with reports being promulgated in 2000\(^2\) and 2007\(^3\). The definitions do depend heavily on biomarkers, especially troponin, and have set a high bar for diagnostic companies to produce accurate assays at low levels of troponin, a standard that several are now capable of achieving. A feature of the definitions that does not appear to have been widely adopted despite being specified on both occasions has been the requirement to demonstrate a ‘typical rise and/or fall’ in the biomarker.

Those assessing patients for a possible ACS face particular timing pressures. In Primary Care, provision for obtaining the first test result can be challenging, let alone awaiting a second test result. Physicians in a hospital Emergency Department are constrained by targets of patient discharge within 6 hours or less which again do not fit well with an ideal troponin testing protocol.

There are of course situations where decisions could or should be made without recourse to a biomarker level; acute ST elevation on ECG is an emergency requiring urgent revascularisation and any patient with a clinically probable ACS appropriate for hospital admission should proceed there directly by ambulance without awaiting a biochemical result. Given the false negative trap, perhaps the best use of troponin testing in General Practice is for the patient who had chest pain possibly representing an ACS some hours or even a few days ago. Practitioners should also guard against the false positive trap by minimising the use of the test in those with a low likelihood of an ACS.

Aldous et al report in this issue\(^4\) on an audit of troponin testing in Primary Care and conclude that management appears to have been appropriate, although without detailed clinical information about the duration of chest pain prior to testing, confirmation of this is lacking. It should also be noted that the survey was performed with a Troponin I assay which would not have been fully compliant with international guidelines\(^5\). Nevertheless, the paper is a useful snapshot of recent usage of this test in that environment. Some patients had serial troponin measurements although the rate was low. Clinical pre-test probabilities were not recorded. Of those with positive tests referred to hospital only around half ended with an ACS diagnosis but the prognostic significance of a raised troponin level was confirmed by the presence of other conditions, not all cardiac.

One recent development has been the introduction of troponin T and I tests with higher degrees of sensitivity\(^6,7\), so much so that levels can be registered in a reasonable proportion of the ‘normal’ population. With high-sensitivity tests, an arbitrary cut-off point has to be used, defined by the international consensus\(^3\) as the 99\(^{th}\) percentile of the local ‘normal’ population. By definition then, 1% of ‘normal’ people will have an abnormal result and there are now many other non-ACS conditions where raised levels will be found. This gives greater weight also to the need for the use of serial testing to improve specificity.

The International consensus panel did not specify the degree of a necessary rise or fall in troponin level but various schemes have been proposed. An algorithm we have developed after local research\(^8,9\) has been implemented successfully locally and is given below, with units referring to a high sensitivity assay for troponin T. Another major current issue is that the adoption of the newer sensitive tests (and with them—for Troponin T—a 1000-fold shift in expression of units from ng/mL or mcg/L to
ng/L) is not universal across New Zealand resulting in a potential source of clinical error and confusion.

Perhaps one advantage of the adoption of tests with higher sensitivity is that clinicians will have to apply a little more qualitative thoughtfulness to referral decisions that can no longer be predicated on a single test result.

Figure 1. Algorithm to aid diagnosis of myocardial infarction using high sensitivity troponin T in patients with a clinical presentation suggestive of an acute coronary syndrome

Adapted with the author’s permission from White and see http://journal.nzma.org.nz/journal/125-1357/5245/content.pdf

Competing interests: None known.

Author information: Stewart Mann, Cardiologist, Capital and Coast District Health Board and Associate Professor, University of Otago Wellington; Lynn McBain, General Practitioner and Senior Lecturer, University of Otago Wellington

Acknowledgements: We thank Dr Michael Crooke for helpful comments on the manuscript. The research leading to development of the algorithm proceeded with valuable contributions and collaboration from Prof Harvey White who also provided comments on the manuscript.

Correspondence: Assoc Prof Stewart Mann, Head, Department of Medicine, University of Otago Wellington, PO Box 7343, Wellington South 6242, New Zealand. Fax: +64 (0)4 3895427; email: stewart.mann@otago.ac.nz
References:


