Troponins in pericarditis: implications for diagnosis and management of chest pain patients

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Considerable research has investigated the use of cardiac troponins for diagnosis and risk stratification in patients who present to emergency departments with acute chest pain[1-4]. For many institutions and practitioners, use of troponins is rapidly supplanting creatine kinase MB for these purposes. The basis for use of troponins for diagnosis (to ‘rule-out’ myocardial infarction) or to identify high-risk patients among those presenting with chest pain is their specificity for cardiac muscle injury. Further, the assays for troponins are very sensitive and can detect even small amounts of circulating cardiac troponin that may be missed by a creatine kinase MB value within the normal background range.

Although cardiac troponin assays are highly specific for cardiac muscle and extremely sensitive indicators of myocardial injury, elevated or detectable levels of troponin I or T are not always reflective of myocardial injury related to acute ischaemic coronary artery disease. A number of other processes have been identified which may be associated with serum cardiac troponin elevation[5].

In this issue, Bonnefoy and colleagues examine the relationship of troponin I with one of these disease processes, pericarditis, in a retrospectively identified cohort of 69 patients[6]. The investigators show that troponin I measured on admission was elevated above threshold in 22% of this cohort which presented with a clinical syndrome of chest pain with features of pericarditis. Further, ST-segment elevation was more common in troponin I-positive (93%) compared with troponin I-negative (57%) patients.

The association of elevated troponin I in a subset of patients with the diagnosis of pericarditis with ST-segment elevation and recent infection suggests that these patients may have a more extensive or severe acute inflammatory process involving the myocardium, myopericarditis[6]. ST-segment elevation was common in this cohort, however, and was also seen in patients without troponin I elevation. This may reflect timing of the troponin testing relative to the onset of the disease process and symptoms. Since serial troponin I testing was not performed and time from symptom onset to testing is not reported, it is not possible to ascertain what proportion of patients would ultimately have been positive, or the relationship to these features. Since only patients with a final
clinical diagnosis of pericarditis were included in the evaluation, it is also difficult to extrapolate these results prospectively to the spectrum of chest pain patients evaluated in emergency departments who may have pericarditis or other diagnoses. Regardless, elevation of troponin I (or T) in this disorder raises two important questions: (1) what are the prognostic and treatment implications, if any, of a positive troponin in patients with pericarditis?, and (2) what are the diagnostic and management dilemmas created within our current paradigms of chest pain evaluation and management by this lack of specificity of the troponins for ischaemic heart disease?

It is clear that in acute ischaemic heart disease there is an association between troponin positivity and both short- and long-term outcome, and that the risk is proportional to the magnitude of the troponin elevation[1,2]. This is true independent of electrocardiographic or clinical features, and the information is additive to that in the electrocardiogram even within groups with low-risk presentations[3–5]. Knowing that troponins are elevated in some cases of pericarditis, but not others raises the possibility that they could also carry prognostic significance in this condition.

If, as has been postulated, troponin I elevation reflects more extensive acute myocardial inflammation and injury, then one might expect that a positive value would carry prognostic and therapeutic importance. However, the underlying pathophysiological process leading to troponin release in myopericarditis is distinctly different from that in patients with acute coronary syndromes, and it is uncertain whether a troponin elevation carries the same prognostic utility in this disease. Further, the aetiologies of pericarditis are diverse and prognosis may be related more to that for the underlying illness than to the presence or absence of troponin release itself. The current study was too small (69 patients) and follow-up too limited to explore the relationship between troponin levels and clinical outcomes, although there was a trend for more relapse in patients with elevated troponin[6]. Because idiopathic symptomatic pericarditis is much less common than acute coronary syndromes and the overall outcomes less severe, exploring this relationship may be difficult.

However, if a relationship between troponin positivity and outcome were established the next important question would be whether knowledge of a patient’s troponin status (positive or negative) or the troponin level could impact on medical care for that patient and thus alter outcome. In general, the management of pericarditis and myopericarditis is conservative and aimed at treating the symptoms and at identifying and treating the underlying illness[8]. In neither of these cases has it been shown that such therapy improves short- or long-term outcome. Thus, routine use of troponin testing for diagnosis and/or risk stratification in suspected or confirmed pericarditis is not currently justified.

Perhaps the greatest concern raised by the inevitability of positive troponins in cases of pericarditis is the potential diagnostic confusion that such results may create and the impact that they could have on management of chest pain patients — from erroneous treatment to delays in treatment caused by diagnostic uncertainty. Although the classical clinical and electrocardiographic presentations of pericarditis and acute ST-segment elevation myocardial infarction or acute non-ST-segment elevation coronary syndromes are distinct, only a minority of patients within each group present with classical distinguishing features. In many cases, only in retrospect is the distinction made, but in some cases the result of a troponin test may influence the decision to treat or how to treat.

This study highlights the importance of a stepwise approach to the evaluation of patients with chest discomfort that integrates first the history and physical examination followed by electrocardiographic findings, then the use of the very sensitive cardiac markers such as troponins as the last step, if indicated. For example, in a young patient with classical symptoms of positional chest discomfort, recent illness, and a pericardial friction rub on examination the diagnosis is virtually assured. ST-segment elevation or even less specific ST or T-wave changes are interpreted entirely differently with this background. Even if the history and physical examination findings are less classic, if the electrocardiogram reveals widespread ST-segment elevation without reciprocal depression and/or PR depression the diagnosis can be made with the electrocardiogram. With such a step-wise approach to the evaluation of chest discomfort, only in patients where the diagnosis remained unclear from the history, the physical examination and the electrocardiogram would troponin testing be invoked, avoiding unnecessary testing and potentially confusing results.

In patients with chest pain syndromes and electrocardiograms that are non-specific at presentation the results of serial troponin testing are often relied upon to guide triage and management. Troponin-positive patients such as these have now been shown in multiple studies to benefit the most from aggressive management strategies. In particular, more potent antithrombotic therapy with intravenous glycoprotein IIb/IIIa inhibitors (either alone or in combination with unfractionated heparin) or with low molecular weight heparins has shown the greatest benefit in troponin-positive patients[9–11]. Further,
early data show that these therapies, like thrombolytic therapy in ST-segment elevation myocardial infarction, may be particularly beneficial in acute coronary syndrome patients when given early after the onset of symptoms\textsuperscript{[12]}\textsuperscript{12}. Although early treatment may reduce the likelihood of subsequent adverse cardiac events in patients with true acute coronary syndromes, these agents do carry some increased risk of bleeding which might worsen or complicate myopericarditis. Small series suggest that in patients with ST-segment elevation who receive thrombolytic therapy but ultimately ‘rule-out’ for myocardial infarction there is no evidence of an increase in adverse consequences\textsuperscript{[13]}\textsuperscript{13}. For treatments such as intravenous glycoprotein IIb/IIIa antagonists in suspected acute coronary syndromes these considerations remain largely theoretical.

Given the clear benefits of prompt treatment of acute coronary syndrome patients and the lack of excessive risk, delay to sort out whether a positive troponin is due to pericarditis rather than ischaemic disease is probably not justified. Whether additional diagnostic testing (such as acute echocardiography to assess for wall motion abnormalities or effusions or sestamibi imaging) or other serum markers of active ischaemia that are in development for use in chest pain patients with unclear diagnosis would improve the accuracy of diagnosis or be timely or cost-effective in doing so remains to be proven. Of concern from the current work is that five patients (7\%) with a final diagnosis of pericarditis had wall motion abnormalities on acute echocardiography\textsuperscript{[6]}\textsuperscript{6}, suggesting that even these techniques may not be sufficient to improve diagnostic certainty.

In summary, the information presented by Bonnefoy and colleagues is intriguing and highlights an area where much future investigation is warranted to better understand the relationship between troponin status and outcome in pericarditis. At this point, however, there is not sufficient data on its diagnostic or prognostic utility to support routine troponin testing in patients with suspected or definite pericarditis. With this and other reports, a new dimension has been added to our understanding of the results of troponin testing in chest pain patients and should raise caution about how that information is used in making acute treatment decisions.

References