

## Commentary

# Cardiac troponins in intensive care

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### Abstract

The cardiac troponins are integral components of the myofibrillary apparatus and they regulate muscle contraction. The measurement of cardiac troponins has replaced other biomarkers for the specific detection of myocardial necrosis and for the diagnosis of myocardial infarction. The tissue specificity plus sensitivity of the measurement technology has meant that cardiac damage can be detected in circumstances other than conventional acute coronary syndromes. The ability to specifically detect cardiac damage as part of multiple organ failure in intensive care patients has been shown to provide prognostic information, but it is unclear whether this is a dependent or an independent marker of outcome.

In the present issue of *Critical Care*, King and colleagues have examined the role of troponin as an outcome predictor [1]. The troponins, troponin T and troponin I, are part of the contractile apparatus of all striated muscles. Voltage changes across the sarcolemmal membrane alter the intracellular calcium concentrations that act as the coupling mechanism to alter the conformation of the troponin-tropomyosin complex. This complex acts as a molecular switch to regulate muscle contraction and relaxation via activation or inhibition of the actinomyosin ATPase.

There are tissue-specific isoforms of both troponin T and troponin I in cardiac muscle: cardiac troponin T (cTnT) and cardiac troponin I (cTnI). Rapid, sensitive immunoassays have been developed for both cTnT and cTnI [2]. This has produced a paradigm shift in the ability of the diagnostic laboratory to diagnose myocardial infarction. A series of landmark studies established that the measurement of cTnT and cTnI was superior to the existing methods of biochemical detection of myocardial infarction, the measurement of creatine kinase and its MB isoenzyme (creatine kinase-MB). Initial studies showed that cTnT and cTnI measurements identified a high-risk group in patients where creatine kinase-MB [3] or creatine kinase [4] measurement excluded

myocardial infarction. Subsequently, cTnT and cTnI measurements on admission were shown to identify high-risk groups [5,6] even in patients with ST-elevation myocardial infarction [7]. The ability of cTnT and cTnI measurements to diagnose myocardial infarction, to predict prognosis and to guide management in patients admitted with acute coronary syndromes (ACS) is now well documented. Measurement of cTnT and cTnI is now included in the current guidelines for diagnosis [8] and management [9] of ACS and myocardial infarction, and other biomarkers are no longer recommended.

In addition to sensitivity, cTnT and cTnI measurements offer absolute cardiospecificity. There is a misconception that creatine kinase-MB is cardiospecific. This is not the case. In situations where there is skeletal muscle damage, creatine kinase and creatine kinase-MB are both elevated but cTnT and cTnI are not [10,11]. The sensitivity and specificity of cTnT and cTnI measurements have demonstrated that elevations of both can be documented in a large range of non-ACS populations [12], including patients in intensive care. In such cases, the mechanism of troponin elevation was initially suggested to be due to problems in the measurement technology. This has been demonstrated not to be the case, and it is recognised that non-ACS troponin elevations are both true reflections of myocardial damage and associated with an adverse prognosis [2]. Non-ACS elevations of cardiac troponin may occur on a background of ischaemic heart disease (secondary ischaemic cardiac injury) or as non-ischaemic cardiac injury, although both situations may coexist. The actual mechanism of cardiac damage is unclear. It is possible that this might be previously unrecognised microinfarction. In cocaine-induced cardiac damage, magnetic resonance imaging demonstrates diffuse myocardial damage associated with troponin elevation but no specific coronary artery occlusion. Troponin elevation in this group is more commonly associated with diffuse coronary artery disease

[13]. It has also been suggested that under conditions of myocardial stress there may be ischaemia with intracellular degradation of troponin and release of troponin fragments [14].

Whatever the mechanism, the elevation of cardiac troponins in intensive care patients was described early [15]; this finding has been replicated subsequently [16,17], including by this study. All studies are consistent in acknowledging the fact that elevation of cardiac troponin carries prognostic significance. The disagreement within the literature concerns whether the troponin elevation is an independent risk predictor or whether it is an organ system failure marker. If the latter, it would be expected to be a dependant variable within an organ system failure score, and therefore a univariate predictor rather than a multivariate predictor. There are published data to support both arguments [18], as the authors point out.

Is there a way out of this impasse? In a study of septic patients who had troponin measurements and ventricular function assessment by trans-oesophageal echocardiography, although mortality was predicted by cTnT and cTnI elevation, multivariate analysis showed that the major predictor of troponin elevation was left ventricular dysfunction [19], consistent with previous reports [20]. It is therefore probable that, for a given population, cardiac troponin as the dominant predictor will be dictated by whether or not ventricular dysfunction is the major contributor to mortality. Given the different population mixes in different intensive care units, it will be expected that different conclusions will be drawn from different studies. The search for a single biomarker that will be the Holy Grail for prognosis on admission is seductive. The cardiac troponins are predictors of mortality. Differences in demographics and case mix across different intensive care units, as well as a lack of standardisation of cTnI methods, make it probable that this particular search for a Holy Grail will be similarly inconclusive – occasional glimpses of the truth but no certainty.

### Competing interests

The author(s) declare that they have no competing interests.

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