High-risk acute coronary syndrome patients and cardiac biomarkers in the emergency department: any role for new biomarkers of myocardial ischaemia?

In a recent editorial, Bagwe et al. discussed the role of cardiac biomarkers regarding treatment and outcomes of patients with evolving myocardial infarction (MI) in the context of the SYNERGY trial. High-risk acute coronary syndrome (ACS) patients with elevated cardiac troponin (cTnT) benefit from early invasive therapy, glycoprotein IIb/IIIa inhibitors, combined anti-platelet agent treatment, and the use of low molecular-weight heparins. However, while cTnT measurement has represented a useful tool for the management of acute chest pain in both the emergency department (ED) and the coronary care unit, it is known that a sizeable proportion of patients present with negative cTnT levels. Moreover, patients with unstable angina, i.e. acute chest pain, myocardial ischaemia, and negative TnT measurements, have been shown to have a high incidence (6-8%) of MI at 30 days, even with the use of state-of-the-art therapy.

Despite their ability to detect even minor degrees of myocardial necrosis, cTnTs exhibit a time-course for release and detection in the peripheral circulation that necessitates measurement at least 6 h after symptom onset to diagnose or exclude MI with high accuracy. Moreover, a proportion of patients with ACS may not develop necrosis despite severe coronary artery disease and myocardial ischaemia. These patients need further characterization and advice but can escape cardiology scrutiny due to the negative TnT results. Therefore, markers that could reliably detect myocardial ischaemia even in the absence of necrosis and/or before cTnT level increase are desirable.

The albumin cobalt binding test which measures the concentration of ischaemia-modified albumin (IMA) has been approved by the US FDA for use as a rule-out marker for acute myocardial ischaemia. The ACB test is a quantitative assay that measures IMA in human serum. Research from our unit has shown that IMA is an early marker of ischaemia in patients undergoing coronary angioplasty, and studies have also shown that IMA is a sensitive biomarker for the identification of ACS in patients presenting to the ED with typical chest pain at rest. We have shown that IMA has a higher sensitivity than the 12-lead ECG and initial cTnT levels for the diagnosis of ACS in chest pain patients attending the ED within 3 h of the onset of chest pain. A meta-analysis of current data has shown that the finding of a negative IMA result, negative cTnT measurements, and a normal or non-diagnostic ECG, has a high negative predictive value for excluding ACS in the ED.

IMA levels increase during myocardial ischaemia triggered by a primary reduction of blood flow, as seen in patients undergoing percutaneous coronary intervention. Several studies have shown a good correlation among objective markers of ischaemia such as lactate levels and isoprostane concentrations and IMA levels in this setting.

We have suggested that increased IMA levels may result from increased oxidative stress. Results from in vitro work support this hypothesis and suggest that the generation of reactive oxygen species can at least transiently modify the N-terminal region to yield increased levels of IMA.

Although the main limitation of IMA at present is its low specificity, it may be a useful test to rule out myocardial ischaemia in patients presenting with symptoms suggestive of ACS. For efficient provision of care in the ED, a high negative predictive value may be most critical, for while false negatives are undesirable, true negatives are of greater importance, because the correct exclusion of MI preserves limited and expensive resources. A test like IMA, with high sensitivity will have a high negative predictive value in a population with low prevalence of coronary artery disease, because of the relatively small number of false negatives in these subjects.

We suggest that in addition to the optimization of the use of cTnTs for management of ACS patients, as suggested by Bagwe et al., markers such as IMA should be tested objectively, as they may provide a useful adjunct to our diagnostic and prognostic armamentarium as well as helping to improve patient characterization and management.

References


