The perfect biomarker in acute coronary syndrome: a challenge for diagnosis, prognosis, and treatment

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This editorial refers to ‘Novel biomarkers in early diagnosis of acute myocardial infarction compared with cardiac troponin T’ by C.J. McCann et al., on page 2843

The use of biomarkers is one of the most important strategies for risk stratification among the increasing number of patients admitting to hospitals for acute coronary syndrome (ACS). The revolutionary benefit of using cardiac-specific troponins in this setting is the excellent specificity and sensitivity for myocardial injury, and several studies have confirmed the superiority of troponins as compared with creatine kinase-MB (CK-MB) for this purpose. The discovery of troponins as valuable markers for predicting mortality in unstable angina led to ‘The Joint European Society of Cardiology/American College of Cardiology Committee Consensus for the redefinition of myocardial infarction’ from 2000 which included elevated troponins as an obligatory criterion in the diagnostics of acute myocardial infarction (AMI). These changes in the guidelines have increased the incidence of diagnosed AMI and expanded the groups of patients with a high risk for coronary events.

Increasing numbers of patients in need of percutaneous coronary intervention (PCI) are a challenge for the capacity of invasive centres. Those at high risk need to be identified at an early time point in order to optimize treatment for ACS patients. Biomarkers are important tools in this setting and provide potential information regarding early detection of subclinical disease, risk stratification, selection of therapy and monitoring disease progression or treatment efficacy. Elevated troponins are today the most important tool for selection of non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) for coronary angiography and PCI. However, the golden moment for optimal outcome of coronary revascularization is within 4 h after the onset of occlusive coronary thrombosis. Troponins are not necessarily elevated in serum before 12 h after onset of symptoms and are not optimal for identification of patients without ST-segment elevation on ECG that would benefit from early revascularization. Data from the OPERA registry have demonstrated similar 1 year mortality among ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI) patients from 36 centres in France in 2002 and 2003, despite different management and guidelines. This suggests that NSTEMI patients at high risk would obviously benefit from earlier revascularization than stated in today’s guidelines. Thus, increasing interest in early detection markers of myocardial injury has evolved over the last few years. In this respect, we are still searching for the perfect biomarker or set of biomarkers that would identify patients with increased risk at the earliest time point, and allow a better selection for early PCI, which in turn may increase survival among NSTEMI patients.

McCann et al. report a prospective study on early biomarkers of AMI that addresses this very important issue. The authors included 415 patients from a single centre during 3 years from August 2003 with acute ischaemic-type chest pain of <24 h duration. AMI was defined according to the guidelines using cardiac troponin T (cTnT) and ECG. The study demonstrates that assessment of heart fatty acid-binding protein (H-FABP) identifies AMI <4 h after onset of symptoms, with a sensitivity superior to cTnT. However, the lack of specificity in detecting AMI is obviously a major disadvantage of using H-FABP in this setting. H-FABP is also compared with several other biomarkers such as N-terminal pro-brain natriuretic peptide (NT-proBNP), d-dimer, high sensitivity C-reactive protein (hsCRP), myeloperoxidase (MPO), and matrix metalloproteinase-9 (MMP-9), which gave no additional information to cTnT regarding early sensitivity. The traditional marker of early myocardial injury, myoglobin, is not compared with H-FABP in the study, but was reported as less reliable than H-FABP in a previous study.

H-FABP is a 15 kDa protein thought to be involved in myocardial lipid homeostasis, and is present in substantial amounts in the
cytoplasam of myocardial tissue, but is also expressed in tissues outside the heart. Early release of H-FABP into the bloodstream during ischaemia has been known for many years. Glatz and collaborators reported as early as in 1994 that H-FABP is detectable earlier than CK-MB and demonstrated a good correlation to infarct size.6 H-FABP can be detected as early as 1 h and peaks at 6–8 h after an acute coronary occlusion. Myoglobin is a slightly larger molecule, 17.2 kDa, which may explain why H-FABP appears earlier than myoglobin. The role of H-FABP in early diagnosis of AMI is also supported by other previous, comparable studies.7–9 Although the prognostic utility of H-FABP in long-term follow-up is not clarified in this prospective report, an analysis of plasma from 2287 patients in the OPUS-TIMI 16 trial disputed H-FABP as a marker of death and major cardiac events among ACS patients.10 Among these patients, H-FABP was an independent predictor of adverse outcome and gave additional prognostic information to that provided by cTnl and BNP. The main importance of H-FABP is in the time window before 12 h, as demonstrated by McCann et al.4

Despite the variety of possible biomarkers in ACS, further studies are needed to clarify the optimal candidate for decision-making in clinical practice. There are several good candidates, and H-FABP is definitely one of them. Recent studies indicate growth differentiation factor 15 (GDF15) as another promising marker for early risk stratification among these patients.11 A ‘multimarker strategy’ is a possible scenario for prioritizing ACS patients to invasive treatment with PCI in the future. A panel of different biomarkers could give specific information regarding different aspects of the pathophysiology of ACS, i.e. myocyte ischaemia, hibernation, necrosis, inflammatory state, thrombosis, and haemodynamic profile. The ultimate goal is to improve an individualized diagnosis and management of these patients.

There is still a way to go to reach the goal of a precise and early identification of ACS patients with the highest risk for a detrimental outcome. When possible, the right patients will receive the right treatment at the right time.

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References