SMARTT use of cardiac biomarkers

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Emergency physicians' ongoing quest for the perfect biochemical marker is understandable, if quixotic. After all, we constantly balance the increasing pressures of emergency department (ED) overcrowding with the desire to provide optimum care to each patient. This dilemma is especially critical in the assessment of chest pain. Studies repeatedly show that 2%–6% of patients with acute myocardial infarction (AMI) are inadvertently discharged from the ED,[1–4] yet only 10% of patients with chest pain are evolving a myocardial infarction when they present to the ED. Because chest pain is the second most common ED presenting complaint, representing 4%–5% of all emergency visits,[5,6] there is an ongoing need to be selective in whom we admit, and any universal admission policy would rapidly overwhelm available health care resources. But if we admit too few, we discharge people to have an infarction and, in many cases, die at home.

The ED chest pain dilemma has fuelled the search for a sensitive, specific marker of AMI that is rapidly released following the onset of cardiac ischemia. Unfortunately, no single test exhibits all of these properties. While CK–MB and troponins are sensitive and specific, they perform poorly during the first 6 hours of symptoms.[7,8] Myoglobin becomes detectable earlier after the onset of muscle damage; however, it is a nonspecific marker and its sensitivity for myocardial damage is suboptimal.[7] Repeating assays in serial fashion, using them in combination, or both, are strategies that have been proposed to improve the diagnostic accuracy for AMI.[9,10]

In this issue (see page 322), Innes and colleagues[11] examine the value of early serial testing, as well as the diagnostic performance of combined CK–MB and myoglobin assays in a well defined population of patients with ongoing chest pain. Of note, this study sample is large enough to allow for meaningful subgroup analysis based on the duration of chest pain. Their findings underline the lack of utility of a single CK–MB or myoglobin result for excluding the diagnosis of AMI. Even among patients with greater than 12 hours of chest pain, the sensitivity of a CK–MB assay at presentation was only 73%. And although myoglobin has been advocated as a sensitive test in patients with 3 to 6 hours of symptoms, these authors found that the combination of myoglobin and CK–MB was only 45% sensitive in patients with less than 4 hours of pain.

Serial testing clearly improves sensitivity, and other investigators have advocated repeated testing at increasingly short (i.e., 1- to 2-hour) intervals, to improve the identification of candidates appropriate for thrombolysis[12] and to shorten the "rule-out" period. While there may yet be a role for protocols using serial tests over longer periods (e.g., 3 to 6 hours apart), this study found no diagnostic advantage in repeating CK–MB and myoglobin assays after 1 hour.

Many emergency physicians are experienced with applying Bayesian principles to the investigation of pulmonary embolism. The same, however, cannot be said about the investigation of suspected AMI. This is in part due to the lack of published data describing likelihood ratios (LRs) for cardiac markers in patients with different durations of chest pain. Although it is known that a normal ventilation–perfusion scan reduces the probability of pulmonary embolism approximately 10-fold (negative LR [LR–] = 0.1),[13] we have not previously had corresponding data describing the diagnostic impact of a negative 3-hour CK–MB or myoglobin assay on the probability of AMI. Innes and colleagues are the first to report LRs for CK-MB and myoglobin, stratified according to symptom duration.

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Their cautionary data suggest that, even in patients with relatively prolonged symptoms, neither marker reduced the probability of AMI more than 4-fold (LR– = 0.25); therefore that these tests can only alter disposition and management decisions in patients at very low risk to begin with.

LRs, probably the most useful and least understood of diagnostic test parameters, are under-represented in the diagnostic testing literature. Future studies should highlight LRs, since these, more than sensitivity or predictive values, help physicians interpret test results in patients with different clinical risk profiles. A similar, and adequately powered analysis of the diagnostic performance of troponins, stratified by pain duration, will be an important contribution to the literature.

High-quality negative studies have more potential to change clinical practice than poorly executed positive trials, although they are rarely greeted with the same enthusiasm. The results of this study suggest that smart physicians cannot rely on early, negative CK–MB or myoglobin results, alone or in combination, to exclude myocardial infarction in the ED.

The search for the perfect cardiac marker continues.

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