Developing a Marker of Ischemia

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INTRODUCTION

Assessment of the patient with suspected acute coronary syndrome (ACS) has remained challenging despite the growing armamentarium of both diagnostic and prognostic tests. Inadvertent discharge of patients thought to be at low risk of ischemia but later found to have an ACS remains unacceptably high. Present tools (history, clinical examination, electrocardiogram, and biomarkers of necrosis) are not optimally sensitive for the identification of patients with unstable angina. Technetium-based myocardial perfusion imaging is sensitive and specific and provides proof of principle that myocardial ischemia is both detectable and actionable. However, this technology is expensive and requires significant technical expertise. Biochemical tests have historically proven to be fast, accurate, simple to perform, relatively easy to interpret, and inexpensive. All of these characteristics provide a strong argument toward development of biochemical markers of myocardial ischemia. Nevertheless, there are many challenges to this effort. The physiology is complex, and it is complicated by the issues of chronicity, timing, and severity. The absence of a “gold standard” for diagnosis of unstable angina makes comparative analyses difficult to interpret. However, if successful, the potential payback is tremendous in terms of improved clinical management and outcomes.

Key Words: Unstable angina; ischemia; biomarkers; diagnosis.

INTRODUCTION

Assessing patients with suspected acute coronary syndrome (ACS) remains problematic even though there is a growing armamentarium of diagnostic and prognostic tests as well as continued improvement in the sensitivity and specificity of existing methods. The
percentage of inadvertent discharges of patients thought to be at low risk of ischemia but later found to have an ACS remains unacceptably high, at 4 to 5%, of whom about half have an acute myocardial infarction (AMI) and the remainder unstable angina (1). This limitation adversely impacts clinical outcomes, as well as the cost of health care (2) and underlies the need for exploration of new strategies aimed at rapidly identifying those patients who present with ACS but lack traditional diagnostic findings, including definitive electrocardiogram (ECG) findings, and/or biochemical evidence of necrosis. Biomarkers hold promise to be valuable in this regard. This chapter presents the rationale behind the quest for biochemical markers of myocardial ischemia, including the physiological basis, the clinical imperatives, and the challenges inherent in both.

FRAMING THE CLINICAL NEED FOR BIOMARKERS OF ISCHEMIA

**Risk Stratification Among Patients With Nontraumatic Chest Pain**

Given the current level of diagnostic uncertainty, risk stratification of every patient with possible ACS has become the foundation of virtually all chest pain evaluation strategies. An effective strategy to reduce the probability of inadvertently discharging a patient with ACS is to admit every patient who presents with chest pain or related symptoms. The correlation between increased admissions and reduced missed AMI rates is well described (Fig. 1) (3). Unfortunately, admitting large numbers of patients unnecessarily is not economically viable and is increasingly difficult to justify in the face of current constraints on hospital bed capacity. Utilization of standardized risk-based strategies that avoid admission for lower-risk patients is now well established as both clinically sound and cost-effective.