BIOCHEMICAL ADVANCES IN DETECTION OF THE ACUTE CORONARY SYNDROMES: IMPLICATIONS FOR THERAPEUTIC DECISIONS

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ABSTRACT

In this paper, I have attempted to place the evolving insights of the pathophysiology of coronary atherosclerosis in the context of the conventional perspective of clinical medicine. We strive to prevent death and to relieve suffering. Our clinical tools are critical but limited. Troponin, a biomarker of unprecedented organ specificity, in the context of the appropriate setting of new chest pain (or its equivalent syndrome), is an extraordinary aid to clinical diagnosis. Highly effective therapy is evolving which reduces loss of myocardium, undoubtedly reducing not only acute death but progression to congestive heart failure. Even if the newer therapies of the GpIIb/IIIa platelet antagonists and anti-thrombins are not yet widely employed, or may not be available to some physicians, the convincing demonstration of myocardial injury by troponin presents objective evidence to both the patient and the attending physician that serious compliance with a program of risk reduction must be urgently considered. Hoeg has described the mosaic of risk factors beyond the conventional and often ignored basic ones (JAMA, 1997, 277, 1387-1390). He provides thoughtful hope and encouragement for both patient and physician to do more in prevention of the subsequent predictable progression. We should look on a troponin positive vague unstable angina event as similar to a tremor which precedes a subsequent earthquake. Although the mass of myocardium lost in such an episode may be small, it is a warning of the major acute myocardial infarction which can be predicted to follow at a later time if the course of the individual patient is not altered. Troponin is the objective evidence.

INTRODUCTION

Progress in the development of improved analytical procedures for the detection of markers of myocardial injury (1) have paralleled progress in the understanding of the underlying pathophysiology (2,3) of ischemic coronary artery disease. We are now poised for the era of successful treatment beyond thrombolysis of the patient presenting with Q-wave Acute Myocardial Infarction (AMI). We can more effectively treat the high risk Unstable Angina (UA) patient as well as the non-Q-wave AMI. The key to the successful application of these
advances is the reliable and confident documentation of the fundamental process of plaque rupture followed by sufficient impairment of physiologic function producing myocyte injury. This is manifest by the appearance of troponin in the blood of an appropriate candidate patient.

The New Troponin Rationale

If one considers the following six related points, the critical role of troponin to modern clinical medicine will be sustained.

1. Coronary artery disease is highly prevalent.
2. The diagnosis of the related acute coronary syndromes is difficult.
3. The pathophysiology is well-defined.
4. Troponin definitively rules in or rules out "AMI".
5. Troponin further defines "high risk" UA.
6. Troponin supports selection of candidates for therapy.

In this paper, I shall discuss each of these points. The first five are generally acknowledged, the final one is now coming to light and already supported by strong data.

Coronary artery disease is the leading cause of death in the United States and although progress has decreased fatality of AMI, the number of cases continues to rise (4). Estimates of chest pain presentations for emergency evaluation range from 5 to 10 million per year. Throughout the world, this is a highly significant disease.

The classic presentation of the AMI involves sudden onset of severe pre-cordial chest pain, radiation to the neck or arm and diaphoresis. While this is common, it occurs in fewer than 50% of AMI cases. In such cases, no physician requires a laboratory test, or for that matter, an electrocardiogram (ECG) to know that the patient is at risk and requires further evaluation including hospitalization. These cases comprise fewer than 10% of the cases presenting to the emergency department for evaluation. Distributed throughout the remaining 90% are presentations ranging from some variety of chest pain to those simulating biliary stones, or even simply a sense of weakness (5). It is for this reason that we continue to see reports of missed AMI in the 2-5% range, and high medical malpractice payments in the United States. Well documented studies confirm the difficulty of diagnosing this entity. As such, standardized protocols are advocated for the purpose of successfully documenting the absence as well as the presence of AMI (6,7).

Progress over several decades has confirmed that in the vast majority of patients experiencing AMI, atherosclerotic plaque rupture followed by localized platelet activation, with thrombin activation leads to localized clot formation with impedance of blood flow. In turn, this leads to impaired oxygenation, nutrient supply and removal of waste metabolites. Cardiac myocytes are injured or killed. Thrombolysis ensues endogenously and may be aided by therapeutic enhancement leading to successful or unsuccessful re-establishment of the flow. There may be microaggregates of platelet thrombi downstream leading to microinfarction of the distal vascular bed. Clinically, the imperfect correlates of these processes are the spectrum of UA to Q-wave AMI, with a common shared process of plaque rupture and activation of