Clinical Value Of Troponin T In Patients With Unstable Angina

Thesis

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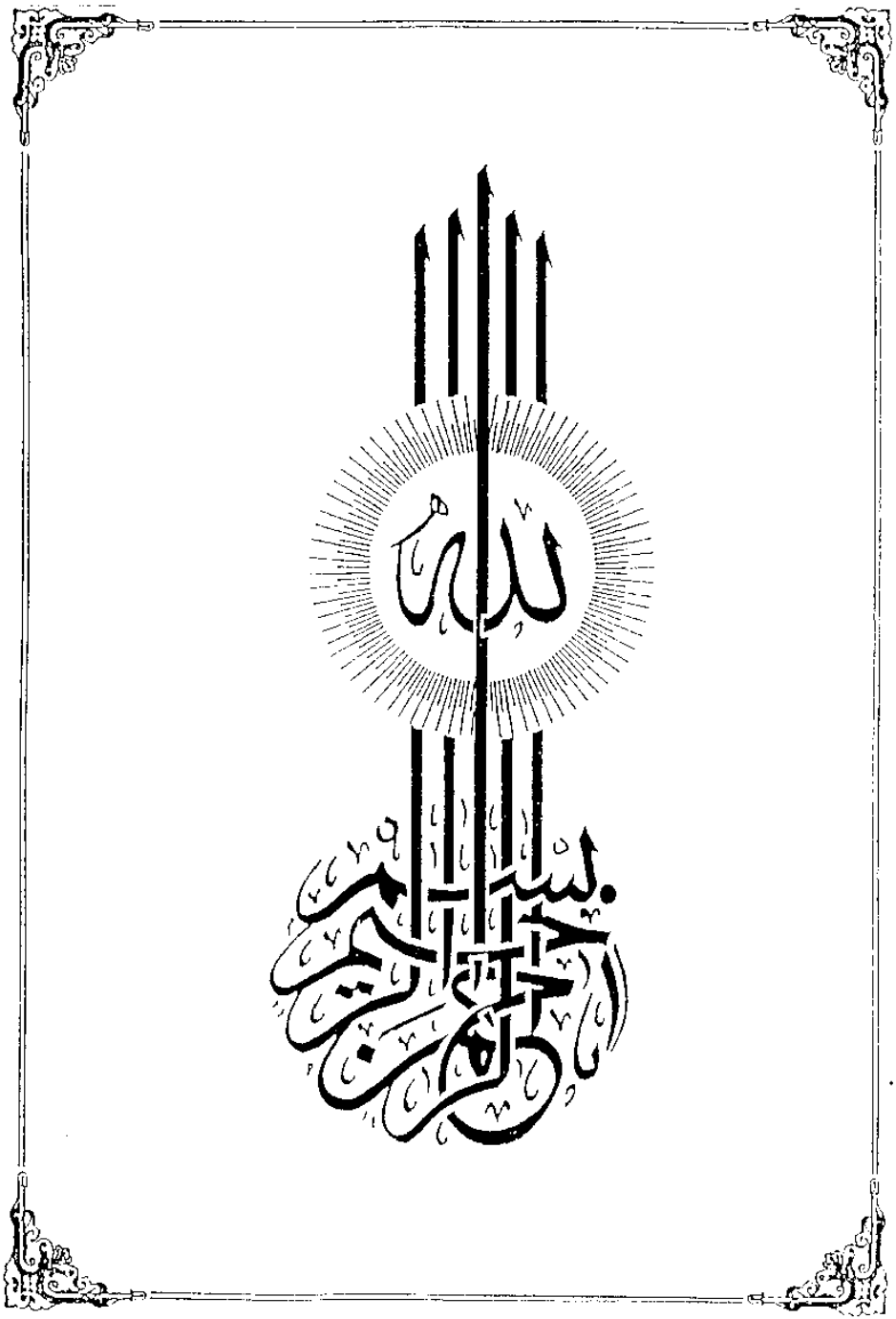

To

My Family

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List of Abbreviations

AMI	Acute myocardial infarction
CAD	Coronary artery disease
CK	Creatine kinase
ECG	Electrocardiogram
LAD	Left anterior descending
LCX	Left circumflex artery
MI	Myocardial infarction
MLC	Myosin light chain
RCA	Right coronary artery
SWMA	Segmental wall motion abnormality
TnT	Troponin T

Introduction

Unstable angina is a critical phase of coronary heart disease that bridges the gap between stable angina and acute myocardial infarction. Patient may have stable angina for many years with no increase in the risk of acute myocardial infarction. However, if their angina becomes unstable with an increased frequency of episodes and greater severity, the risk becomes much greater.

Acute myocardial infarction is rarely unpredictable. Before its onset, about 20% of patients have unstable angina for at least 4 weeks and about 30% have it for at least 2 weeks and 70% have at least 1 week of unstable angina ***(Hamm et al., 1992)***.

So the aim of therapy for unstable angina is to relief pain and to identify high risk patients and to improve the prognosis. In unstable angina, the pathophysiology is as in acute myocardial infarction i.e. thrombus formation as a result of activation of platelets and coagulation cascade. After a thrombus has been formed, acute myocardial infarction and sudden cardiac death may occur in some patients. However, it is more likely that the initial thrombus will not occlude the vessel but rather that microinfarcts will occur and produce - from the clinical standpoint - unstable angina.

It has been suggested that Troponin T as a specific and sensitive indicator of cell injury may be of value in trying to predict which patient may have microinfarcts and therefore likely to experience a negative outcome ***(Seino et al., 1993)***.

The minor myocardial damage (cell death) is associated also with intra-normal rise in CK-MB values observed in some high risk patients. The extended life-time may be responsible for the superior ability of troponin T assay to elucidate patient risk compared to test for other markers. Although microinfarction causes the release of CK-MB, myoglobin, MB subtypes and troponin I as well as troponin T, clearance of the first four markers occurs within few hours or days. In contrast, troponin T release can result in an accumulation of troponin T in blood after repeated ischemic events. This accumulation of troponin T will result in values exceeding the cutoff, while the other markers are still within normal limits ***(Mair et al., 1992)***.

Aim Of Work

The aim of this study is to correlate the presence of an elevated serum troponin T in patients admitted with unstable angina with the patient's prognosis and cardiac events during hospital stay (7-10 days) and in-hospital mortality and severity of coronary artery lesion.

Unstable Angina; Pathophysiologic Considerations

Unstable angina is diagnosed clinically as angina pectoris in an accelerating pattern. Because of its uncertain etiology, the understanding and treatment of unstable angina have lagged be hind other aspects of coronary disease. New insights, however, suggest that unstable angina represents the change of coronary artery disease from a chronic to an acute stage. Recognizing unstable angina before the occurrence of myocardial necrosis permits therapeutic intervenion that may profoundly modify the natural course of coronary disease.

Unstable angina : Relationship to the Biology of Atherosclerosis.

Unstable angina and acute myocardial infarction are considered together because, from a biological point of view, it is likely that the underlying cellular mechanisms in the atheroscierotic plaque are similar,if not identical. The presence of mural thrombus is the common pathological feature uniting the two syndromes (**Mizuno K, et al . 1992**). It may be partially or transiently occlusive in unstable angina and totally occlusive for an extended period in myocardial infarction. The syndromes also share the underlying cellular mechanisms asso

ciated with conversion of the lesion from the stable state to one that has a propensity to fracture or rupture.

Thrombosis superimposed on a fissured or ruptured complex plaque is present in a high proportion of patients with advanced stages of unstable angina (**Mizuno K. et . al. 1992**). The development of mural thrombus with the associated decrease in lumen diameter probably accounts for the decrease in exertional threshold for angina or rest pain. In this context, the only fundamental difference between an atherosclerotic plaque causing either unstable angina or myocardial infarction is wheter or not the thrombus is occlusive for a suffcient time to cause tissue death downstream . The thrombus most commonly occurs with disruption of the plaque or desquamation of endothelial cells(**Sherman CT. et . at . 1986**) to expose thrombogenic surfaces and tissue thromboplastins. Clot could theoretically occur with intact endothelium since inflammatory mediators, such as interleukin -1 and tumor necrosis factor, which are expressed in active, inflammatory lesions, can stimulate epression of the procoagulant tissue factor in human endothelial cells in culture (**Bevilacqua MP. et . at . 1987**) Such a mechanism has not been demonstrated definitively in diseased artiries. Other products of inflammatory cells may contribute to the breakdown of the connective tissue skeleton of the plaque, compromising its structural integrity and predis

posinng it to fracture and fissuring.

Vasospasm also plays an important role in unstable angina, (**Maseri A. et . at . 1978**) . The constrictor predominance present in stable angina may be enhanced further in the unstab state by increased sensitivity to vasoconstrictors. Furthermore, the presence of clot with thrombin and platelet products such as 5- HT and thromboxane A_2 also may provide increased vasoconstrictor stimuli.(**Willerson et . at . 1991**)

Pathophysiology of vasospasm.

The general appreciation of the widespread importance of vasospasm in contributing to angina in many,if not most, patients coincided with the discovery by Furchgott and Zawadzki. they demonstrated the existence of an endothelialderived humoral factor, which they termed endothelialderived rilaxing factor (EDRF) , that caused the dilatation of blood vessels by diffusing to the underlying smooth muscle cells and increasing c GMP. (**Furchgott et . at . 1980**)

Early work characterizing endothelialderived relaxing factor suggested similarities to nitric oxide (NO) (**Palmer RM. et . at . 1987**) Nitric oxide has proven to be the most important of the endothelial - derived vasodila tor substances. One of the characteristics of endothelialderived relaxing factor that wasknown to be shared with NO was its ease of degradation by

oxygen - free radicals. (**Gryglewski RJ. et at 1986**).

Endothelial dysfunction was generally assumed by experimentalists to contribute to the pathogenesis of atherosclerosis, it was thought that this dysfunction might extend broadly and encompass the endothelial dependent vasodilator functions. **(Luvmer PL. et . at. 1986)** In other words, atherosclerosis might compromise this dilator system and Provide the substrate for abnormal control of vasomotor tone. Thus, vasospasm might result from loss of endothelial - dependent dilator function.

This hypothesis has been tested and found to be true in a variety of clinical studies. Initially, acetylcholine, an endothelial- dependent vasodilator, was shown angiographically to dilate normal coronary arteries and to constrict both minimal and advanced stenoses. (**Ludmer PL. et . at . 1986**) The pathophysiological importance of these obsrvations was emphasized by the findings that exercise (**Gordon JB. et . at . 1980**) and cold pressor testing (**Nabel EG. et . at . 1988**) dilated normal coronary arteries but constricted both minimally and advanced stenotic lesions . Endothelial abnormaliies were inferred in the exercise studies since acetylcholine and exercise had qualitatively identcal effects on segments that dilated or constricted. Furthermore, endothelialdepindent relaxation of coronary arteries becomes defective with the presence of increasing num