The value of troponin T in the coronary care unit

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ABSTRACT

Objective: To assess the value of troponin T (TpT) in the coronary care unit (CCU) setting compared to creatinine phosphokinase (CK-MB) in patients admitted with acute coronary syndrome.

Methods: This was a prospective study conducted over a period of 2 months between May 2003 and June 2003. All patients who were admitted to the CCU at Queen Alia Heart Institute, Amman, Jordan with acute coronary syndrome were included. Troponin T and CK-MB were performed simultaneously on all patients upon admission and serially every 4 hours for 24 hours. The times of the serial measurements from the onset of chest pain and the results were recorded. The result of coronary angiography was recorded in those patients who underwent this procedure during the index hospitalization. Patients with chest pain more than 48 hours prior to admission and those with renal impairment were excluded.

Results: One hundred and ninety-seven patients were enrolled in our study. Sixty-one percent were males. The mean age was 60 years with a range of 28-90 years. The total number of patients with a positive biomarker (TpT or CK-MB) was 136. Forty-nine patients (36%) had a positive TpT without an accompanying CK-MB leak. Only 2 patients (1.4%) had a CK-MB without a positive TpT. The positive predictive value of TpT was 94%, with a negative predictive value of 96%, giving 98.5% sensitivity and 97% specificity. The earliest time from the onset of pain to having a positive TpT was one hour. Out of the 197 patients 173 (87.8%) had cardiac catheterization and it did not seem to have been affected by a negative TpT or CK-MB. There were 5 deaths, and their TpT results were well above the average positive value.

Conclusion: Troponin T is a more sensitive and specific biomarker than CK-MB in detecting myocardial injury. It can become positive as early as one hour from the onset of chest pain. The decision whether to do coronary angiography remains based on clinical assessment rather than laboratory data.

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Assessment of patients presenting with chest pain remains one of the most challenging tasks, as the consequences of missing a diagnosis of myocardial infarction (MI) or unstable angina can have a detrimental outcome. The electrocardiogram (ECG) which is the most common initial investigation carried out for patients presenting with chest pain is only 50% sensitive in diagnosing myocardial injury[1-4] and even less in unstable angina.[5] Thus, many patients are unnecessarily hospitalized to expensive coronary care units (CCU) while awaiting investigations. This has a considerable impact on the health care expenditure and hospital budgets worldwide. The availability of new biochemical markers has permitted new strategies to be used for evaluating patients with acute chest pain. Our study was set out to assess the value of quantitative troponin T (TpT) assay as compared to creatine kinase (CK-MB) in patients admitted to our CCU with acute coronary syndrome.

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To see how sensitive and specific TpT is, and its predictive value in patients with myocardial injury as compared with CK-MB. We also looked at how early it can give a positive result in patients with myocardial injury, and to assess if it affects our decision on sending the patient for coronary angiography. We also looked at the prognostic value of a raised TpT.

Methods. It was a prospective study carried out over a period of 2 months between May 2003 and June 2003. All patients who were admitted to the CCU at Queen Alia Heart Institute (QAHI), Amman, Jordan with acute coronary syndrome had serial TpT and CK-MB every 4 hours for the first 24 hours of their hospital stay. The time and results of these measurements were noted. The result of coronary angiography was recorded in those patients who underwent this procedure during the index hospitalization. A positive biomarker result was defined as a value of 0.10 µg/L for TpT and CK-MB ratio of 6.5%.

Exclusion criteria were patients with impaired renal function, defined as a creatinine >2.0 g/dl or if they had chest pain more than 48 hours prior to admission (as it would have been after CK had normalized).

Results. There were 197 patients who had serial TpT and CK-MB carried out during our study period. Their age ranged from 28-90 years with a mean of 60 years (**Figure 1**). There were 121 males and 76 females. There were 140 patients who had a positive biochemical marker (either TpT or CK-MB isoenzyme). Four patients had a positive TpT and chest pain more than 48 hours prior to admission, and were not included when comparing 2 biochemical markers. The reason for this exclusion is due to the fact that the TpT remains elevated for around 2 weeks as compared to CK, which returns to normal value within 72 hours. Forty-nine patients (36%) had a positive TpT without an accompanying CK leak on serial testing of the cardiac biomarkers. On the other hand, only 2 patients (1.4%) had a positive CK-MB with a negative TpT. Of the 197 patients studied, 173 patients (87.8%) had cardiac catheterization. Of those, only 22 had normal coronaries. Thirty patients were sent for aorto-coronay bypass surgery, 71 had coronary intervention for a single vessel, 22 for 2 vessels and 2 for 3 vessels (**Figure 2**). There was no correlation between the value of TpT and the number of diseased coronary vessels. There were 5 deaths in our study population and their TpT value were 4 times that of the mean positive troponin of 0.39 mg/L. The earliest positive TpT from onset of pain was as early as one hour from the reported onset of chest pain.

Discussion. Levels of CK-MB usually rise above the normal range within 4 hours of the onset of MI. But, it can be due to other causes than myocardial injury. In comparison, cardiac troponins are encoded by different genes from those for slow and fast skeletal muscles, yielding proteins that are immunologically distinct. Hence, these markers are more specific than CK-MB for myocardial injury. The troponin complex regulates the contraction of striated muscle and consists of 3 subunits (**Figure 3**). 1) Troponin C, which binds to calcium ions. 2) Troponin I, which binds to actin and inhibits actin myosin interactions. 3) Troponin T, which binds to tropomyosin and attaching the troponin complex to the filament.

The loss of integrity of cardiomyocyte membrane in myocardial injury leads to the release of intracellular macromolecules into the interstitium, lymphatics and microvascular bed and eventually into the peripheral circulation. Normally, cardiac troponins T and I are not detectable in the blood of healthy persons. Thus, microinfarcts can produce detectable elevations of cardiac troponins T and I.[6,7] Nowadays, bedside assays are available for quantitative assessment of cardiac troponins T and I.

Our study of consecutive patients admitted to the CCU with suspected acute coronary syndrome showed that the diagnosis of myocardial injury made on the increased serum TpT concentration increases the total number of patients with the diagnosis of acute MI by 36% as compared with CK-MB. Other studies have reported figures between 15 and 33%.[8,9] This becomes more significant when taking into account that the ECG is approximately 50% sensitive in myocardial injury. The borderline between what is labeled as MI or acute coronary syndrome without MI is moving and comprising an increasing proportion of patients who formerly got a diagnosis of unstable angina. This development will have important clinical, psychological and social as well as epidemiologic implications. This also means that TpT is useful in ruling out a MI in patients whose symptoms are relieved within the first 6-12 hours, thus reducing unnecessary hospitalization and costs of hospital care. Also, the adoption of new biochemical markers in the routine diagnosis of MI has 2 important epidemiologic implications. The increase in the number of MIs detected will have an impact on studies and programs for monitoring cardiovascular disease in populations and on the assessment of coronary end points in clinical trials. The Consensus Document of the Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction[10] has emphasized that some of the monitoring projects should retain the established definition of MI but at the same time should have the new biochemical marker based on

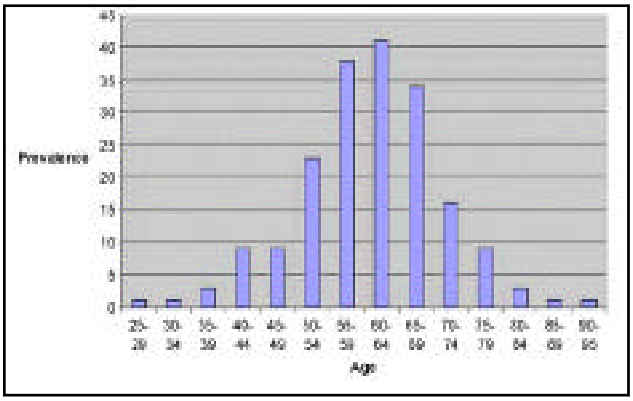

Figure 1

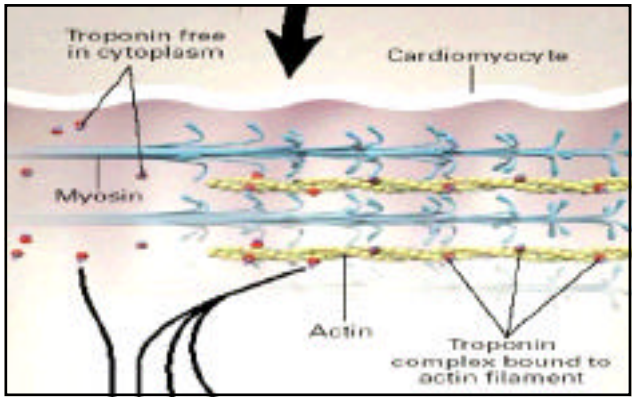

Figure 3

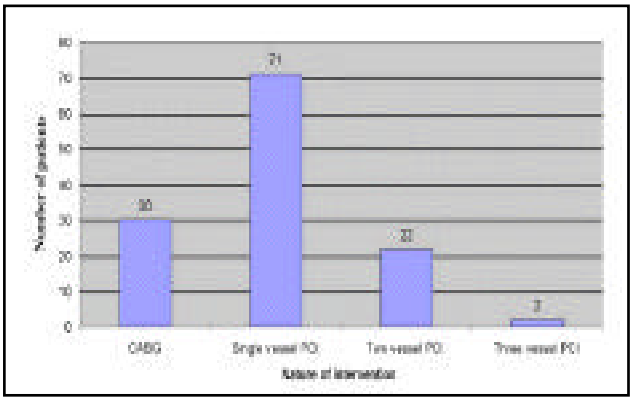

Figure 2

Figure 1 - Shows the age distribution of the study sample.

Figure 2 - Shows the various types of intervention after coronary angiography.

Figure 3 - Shows the structure of the cardiac myocyte and the presence of troponin.

the definition of MI to be able to compare the diagnostic classification. Troponin T was found to have a sensitivity of 98.5%, with a specificity of 97%. Its positive predictive value was 94% and a negative predictive value of 96%. With these high specificity and sensitivity TpT comes close to being an ideal biochemical marker. The reason for this is that the assays that are available now are based on high affinity antibodies and are specific for cardiac troponins T and I. Previously, studies have shown that these tests for detecting myocardial injury have a sensitivity ranging from 33-86% and a specificity from 86-100%. The higher figures we reported here may be due to previous studies having been carried out on the earlier generations of troponin detection assays.

The earliest positive TpT was as early as one hour from onset of reported chest pain. This is earlier than has been reported in the literature. This may have been due to miss reporting by patients, and it would be difficult to prove one way or another. The concentration of TpT is a predictor of mortality as shown in our study. The original Fragmin During Instability in Coronary Artery Disease Study already showed continuous relation between marker concentration and the risk of clinical events.[11,12] More recently, the second Fragmin During Instability in Coronary Artery Disease Study confirmed that optimal risk stratification in patients with acute coronary syndrome can be achieved with use of a cut-off concentration around the detection limit of the TpT assay (such as 0.03 mg/L) instead of the suggested higher cut-off of the manufacturer (such as 0.10 mg/L).

In conclusion, TpT is a highly specific and sensitive biomarker in picking up myocardial injury with a high predictive value. As a biomarker it comes close to a novel marker for myocardial injury. Troponin T can be detected as early as one hour from the onset of chest pain. Using CK-MB alone as a biomarker would miss an approximately 36% of patients with myocardial injury. The decision to cath a patient remains a clinical one, with no correlation between the level of TpT and the number of diseased coronary vessels.

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