RISK STRATIFICATION IN ACUTE MYOCARDIAL ISCHAEMIA: POTENTIAL USE OF A RAPID BEDSIDE TROPONIN T ASSAY

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ABSTRACT: This study is to examine the use of a Rapid Troponin T test in patients attending the Emergency Room with complaints of chest pain. The results show a strong correlation between time to positive development of the Rapid Troponin T test to ELISA Troponin T. These results indicate the use of a simple to perform bedside assay of Rapid Troponin T may be used in early risk stratification of patients presenting with acute coronary syndromes. *(JUMMEC 2002; 2:132-134)*

KEYWORDS: Rapid Troponin T, acute coronary syndromes, risk stratification.

Introduction

Acute chest pain is a common presenting complaint to the Emergency Room. Patients with acute coronary syndromes represent a continuum of disease with unstable angina at one end of the spectrum to acute myocardial infarction and death at the other. Approximately 5% of patients with acute myocardial infarction are released from the Emergency Room which places them at a high risk of morbidity and mortality (1,2,3,4).

Admission of patients with acute myocardial infarction with atypical presentation to the general medical wards may result in adverse patient outcomes should complications such as arrhythmias and heart failure occur (5). It is important therefore to risk stratify and triage patients at an early stage.

Methods of risk stratification have included the duration, frequency and timing of the chest pain (6), but these are not predictive of serious in hospital events (7). The electrocardiogram is found to be non diagnostic in as high as 50% (8-11). Single admission electrocardiogram foe the diagnosis of acute myocardial infarction is overall low with an accuracy of 75% (12) which increases to 94% with serial electrocardiograms (13). Electrocardiogram findings are misleading in 8% of all cases of myocardial infarction and indeterminate in an additional 12% due to the presence of left bundle branch block or non specific ST and T wave abnormalities (9).

The use of serum cardiac markers were first reported in 1954 (14) and have been traditionally used in the retrospective diagnosis of acute myocardial infarction. The gold standard is creatinine kinase MB (CK MB) (15). The lack of specificity of CKMB which can be elevated with skeletal muscle injury or physical exercise (16) remains a problem. Only few patients have early elevation of CKMB that would indicate a poor prognosis (3,4).

Cardiac Toponin T is a tropomyosin binding protein which is sensitive and specific for myocardial necrosis. Elevated peak Troponin T levels can occur even in those patients without elevated CKMB levels (17-19). The GUSTO IIa substudy reported 46.5% admission Troponin T in their ST elevation group with a 30 day mortality of 13% in Troponin T positive versus 4.7% in the Troponin T negative group ($p<0.001$). Admission Troponin T was found to be most strongly correlated to the 30 day mortality and was a powerful and independent risk marker for patients with acute ischaemic syndromes (20).

Cardiac Troponin T is measured by two methods: by an enzyme linked immunosorbent assay (ELISA) method and a rapid bedside qualitative assay. (Rapid Trop T) (Boehringer Manheim) The ELISA assay requires a biochemical laboratory with results available in about 90 minutes. This may not be available in all hospital settings or emergency situations. A rapid assay of Troponin T can be performed and read at the bedside within 20 minutes.

Method

We looked at patients in a prospective blind study presenting to the Emergency Room of the University Hospital, Kuala Lumpur, with chest pain of less than 12 hours of duration. All patients had blood drawn for Rapid Tropo-

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nin T (positive cut off value 0.2ng/l), ELISA Troponin T (Boehringer Manheim) and CKMB catalytic assay (Merck, Damstadt) at zero, two and four hours after admission. Acute myocardial infarction was determined by WHO criteria. Exclusion criteria included recent thoracic trauma, muscular dystrophy, severe distress. Patient disposition to the cardiac or medical wards was based on clinical impression of the Emergency Physician.

Results

A total of 80 patients were collected, 28 with the diagnosis of acute myocardial infarction, 28 with unstable angina and 24 with non ischaemic pain. 26 patients had a positive Rapid Troponin T test and a positive ELISA Troponin T test at 4 hours. The mean ELISA Troponin T level was 7.87 ng/ml (range 0.93 to 18.7ng/ml). The mean time to positive development of the Rapid Troponin T test was 9.3 min (range 3 - 20 min).

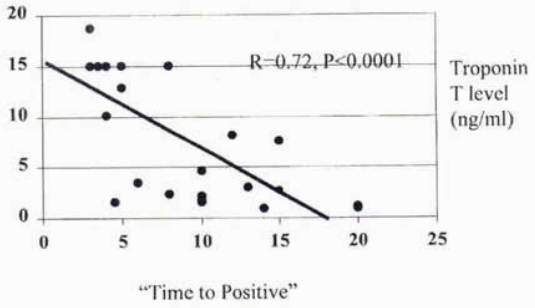
We found a strong correlation between the time to positive development of the Rapid Troponin T test to the ELISA Troponin T values (R - 0.72, $p < 0.001$) see figure 1.

The conclusion from our findings indicate a strong correlation with time to positive development of the Rapid Troponin T test with ELISA Troponin T. These results suggest that a simple to perform bedside assay of Rapid Troponin T may be used in the early risk stratification of patients presenting with acute coronary syndromes.

Discussion

There has recently been focus on the risk stratification of patients with acute coronary syndromes. The findings of the GUSTO IIa substudy (20) looking at 755 patients reported an increase in mortality at 30 days of those patients who have ST segment elevation and are Troponin T positive on admission (> 0.1ng/ml). Troponin T was much more predictive than CKMB or ECG at 30 day outcome. Another finding was the increased likelihood of death with increasing Troponin T levels. Data from this trial indicates Troponin T should be measured to identify high risk subgroups. The FRISC (21-23) trial is a randomised blinded placebo controlled trial of 976 patients in which fragmin was tested in patients with coronary artery disease. Troponin T was measured on admission and at 24 hours. The focus of this trial was on patients with minor myocardial damage and angina and not definite myocardial infarction. The results indicated that high Troponin T levels without definite evidence of acute myocardial infarction was also highly predictive of acute coronary events in the first five months. The higher the Troponin T level the higher the risk of death acutely and also at five months independent of ECG findings.

Troponin T level vs "Time to Positive"



The GUSTO and FRISC trials highlight Troponin T in the identification of minor myocardial damage and is critically important in risk stratifying patients and identifying high risk subgroups. These patients are not identified by ECG/ CKMB/ Exercise stress testing but only by Troponin T.

The qualitative Rapid Troponin T immunoassay allows simple and specific method of detection of pathologically elevated cardiac specific Troponin T in whole blood. It is easily performed at the patient's bedside without the need of a full laboratory service which may not be available in all hospital settings.

The test is based on a dual cardiac specific anti Troponin T monoclonal antibody "sandwich" principle using a poly (streptavidin) biotin capture system. It is a gold linked optical read immunoassay (GLORIA).

It is initiated by addition of 150 microlitres of whole blood in a sample to a hand held device, which separates the red cells from the plasma. Cardiac Troponin T in plasma combined with both biotinylated anti Troponin T antibody and gold labelled antibody to form a 'sandwich". The biotin adheres to streptavidin which immobilizes in a line across the read zone of the device. If Cardiac Troponin T is present in the patient's blood, gold particles in the sandwich produce a red or purple line which is read visually. The intensity and speed with which the colour forms is related to the concentration of Troponin T in the blood. The test is read within 20 minutes and considered positive even if the signal is only faintly detected. A positive result is obtained in patients with 0.2ng/ml or more cardiac Troponin T in the blood.

An internal control for the test is also provided where flow of plasma through the device carries unreacted gold labelled anti cardiac Troponin T antibody through the read zone where they combine with cardiac Troponin T immobilized in a line across the read zone, producing a red/ purple line. This control line provides an indication of proper test performance as well as viability of cardiac specific anti Troponin T antibody conjugated with gold particles (Boehringer Manheim, Germany).

The results of our study show a strong correlation with time to positive development of the line (Rapid Troponin T test) to the actual level of cardiac Troponin T measured in the patient's blood.

The limitations and potential problems of using this test were the inaccuracy of observer reading for the appearance of the line or the presence of a faint line. The test used was also semiqualitative with no numerical values.

Conclusion

The potential role with the new development of a Rapid Troponin T test which cuts out inter observer variation and can quantify the level of Troponin T in the blood would play a key role in the rapid, easy to use method of early risk stratification of patients with acute coronary syndromes.

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