ORIGINAL ARTICLE

Clinical Predictors of a Positive Troponin T Test in Patients Presenting With Probable Acute Coronary Syndromes

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Summary

Acute coronary syndrome (ACS) patients with positive troponin T (TnT) test are at higher risk for death and myocardial reinfarction. They would significantly benefit from early aggressive pharmacologic and invasive therapy. However, TnT test is not widely available. This retrospective study of 173 patients with ACS showed that prolonged or repetitive episodes of angina at rest in the previous 24 hours ($p=0.01$) and evidence of myocardial ischaemia on ECG ($p<0.001$) were associated with positive TnT tests ($\geq$ 0.1ng/mL). The two variables in combination showed 100% positive predictive value, facilitating early identification and streamlining of therapy.

Key Words: Acute Coronary Syndromes, Troponin T

Introduction

Acute coronary syndrome (ACS) without ST segment elevation includes unstable angina (UA) and non ST segment elevation myocardial infarction (NSTEMI). This is a heterogeneous group with wide spectrum of risk of death and recurrent cardiac ischemic events[1-4]. From previous studies, patients with ACS who are troponin T (TnT) positive at admission are known to be at higher risk for death and myocardial reinfarction [5-8] and are more likely to have an active plaque with thrombus in the culprit vessels [9-10]. Such patients would significantly benefit from glycoprotein IIb/IIIa receptor inhibitors [11-13] low molecular weight heparin[14] and early percutaneous coronary intervention [15]. However, TnT test is generally limited to tertiary care hospitals, and is still not widely available. This study aims to look at the possible clinical factors [2,4,7,16] that may predict a positive TnT test in patients who present with ACS.

Materials and Methods

The study population consisted of patients who were admitted to the Coronary Care Unit of the National University Hospital, Singapore, from December 1999 to June 2001 for acute ischemic chest pain in whom the diagnosis of probable acute coronary syndrome [17] was made clinically by the attending clinician. This population included a wide spectrum of patients from those who presented with unstable angina to those with non ST-segment elevation myocardial infarction.

TnT measurements were performed with the third generation assay (TropT®, Roche Diagnostic Germany). The minimum detectable concentration is 0.01ng/mL. The prespecified cut-off level used in this study was a TnT level $\geq$0.1ng/mL at 24 hours after admission. The cut off point of TnT level $\geq$0.1ng/mL was chosen, based upon an earlier study which identified it as optimal for risk stratification for 30 days mortality [5].

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Electrocardiogram (ECG) evidence of myocardial ischaemia was defined as ST segment deviation of >0.05mV and/or T wave inversion of ≥0.2mV [17].

Excluded were patients who presented with ST elevation myocardial infarction, those with chest pain deemed not to be of cardiac origin, and renal impairment (serum creatinine concentration > 221 mmol per liter)[5]. Based on previous studies [7,18-19], fourteen clinical factors were analysed in the troponin T positive and the troponin T negative patients as potential candidate predictor variables of risk of developing positive troponin T in ACS (Table I). The statistical significance of each comparison was assessed using chi-square contingency table methods for categorical data, and analysis of variance (T test) for continuous variables. Clinical factors that achieved stastical significance level were entered into a multivariate logistic regression analysis. A p value of less than 0.05 was considered to be statistically significant.

A validation study was performed using the significant clinical factors identified to a separate group of forty-one consecutive patients who presented with probable ACS.

Results

For the period between December 1999 to June 2001, 173 patients were admitted to the coronary care unit with ACS. One hundred and thirty-four of these patients were positive for TnT test. The TnT positive group had more patients with age > 65 years, prior history of myocardial infarction, previous coronary bypass surgery, prior history of heart failure and diabetes. Ischemic changes on electrocardiogram and a history of continuous chest pain (of more than 20 minutes) were more common in the TnT positive group (Table I). Previous studies[7,18-19] had identified clinical factors to predict or identify ACS patients with poor outcome. However, these factors were varied, and their findings not easily applied in daily clinical practice. Based on previous studies, we tested 14 easily available clinical factors in our cohort of patients. These factors include age, gender, history of prior myocardial infarction, prior coronary artery bypass graft surgery (CABG) or percutaneous coronary intervention (PCI), stroke, heart failure, hypertension, diabetes, smoking, chronic renal insufficiency, hyperlipidemia, family history of premature coronary artery disease, ECG evidence of myocardial ischemia and symptoms of prolonged chest pain or repetitive episodes of angina at rest in the last 24 hours. By univarate analysis we found statistically significant association of two of these factors; namely a prolonged (>20 minutes) or repetitive episodes of angina (≥ 2 episodes of chest pain) at rest in the previous 24 hours ($p = 0.008$) to correlate with a positive TnT test (Table I). In addition, those with ECG evidence of myocardial ischaemia (defined as ST segment deviation of ≥0.05mV and/or T wave inversion of >0.2mV) [17] were also associated with a positive TnT test result ($p < 0.001$). Using multivariate analysis these two clinical factors, a prolonged or repetitive episodes of angina at rest in the previous 24 hours ($p = 0.01$) and ECG evidence of myocardial ischaemia ($p < 0.001$) independently predict positive troponin T test in our patient cohort.

We validated these 2 clinical variable predictors on a group of forty-one patients who presented with probable ACS after the study was completed. Their clinical characteristics (Table II) were comparable to the derivation group. They were predominantly male above the mean age of sixty years with a significant proportion having electrocardiographic changes indicating myocardial ischaemia and presented with symptoms of prolonged chest pain or repetitive episodes of angina at rest in the last 24 hours. In this validation cohort, the presence of a prolonged (>20 minutes) episode, or repetitive episodes of angina at rest in the previous 24 hours were associated with a positive predictive value for TnT test results in 73 percents, and absence of ischaemic myocardial changes on electrocardiogram was associated with 100 percent negative TnT. When both the two clinical factors were present together in a patient with ACS, it is 100 percent predictive of a positive TnT test (Table III).

Discussion

Patients with ACS are a heterogeneous group. The syndrome comprises two distinct clinical sub-groups - Unstable Angina (UA) and non ST segment elevation myocardial infarction (NSTEMI). While they both share a common pathophysiology, namely plaque rupture with various degree of non-occlusive thrombus deposition, resulting in myocardial ischaemia with or without necrosis, their clinical course and prognosis are quite distinct[5-8]. Earlier studies had identified ACS patients with TnT positive having higher rate of death, reinfarction, and recurrent angina[1-8].

In our study, prolonged (>20 minutes) or repetitive episodes of angina (≥ 2 episodes of chest pain) at rest in the previous 24 hours, and evidence of myocardial ischaemia on ECG were associated with positive TnT value of ≥0.1ng/mL. These two statistically significant clinical factors had been shown to independently predict adverse outcomes [7,20-21]. The higher risk of mortality and morbidity in TnT positive patients highlights the need for rapid identification, triage and treatment of these patients.

Bedside assays in which whole blood is used for the qualitative assessment of cardiac troponins are currently available and being used in emergency department to obtain rapid information on whether these markers are elevated [22,23]. However, the interpretation of the results is not always straightforward. Interpretation of a positive troponin T must be in the correct context of the presence of ischaemic chest pain and/or evidence of ischaemic changes on ECG to avoid false positive diagnosis of myocardial infarction.

While TnT testing is not widely available, the two clinical factors identified in our study are easily obtained in patients presenting to primary care doctors. A prolonged episode, or repetitive episodes of rest angina could easily be obtained from the history. Resting 12-leads ECG is a standard evaluation test for patients presenting with chest pain. Our findings indicate that they could discriminate acute coronary syndrome patients with Non ST elevation myocardial infarction from the lower risk unstable angina group. The ability to differentiate these two groups of patients with the two clinical variations have important implications for triage at Emergency Room (i.e. disposition of patient to Coronary Care Unit versus general ward), and institution of acute medical therapy. This is especially useful in hospital or situation where TnT test is not available. Early identification of these higher risk patients helps in streamlining therapy. The recently published TACTICS-TIMI 18 study showed that upstream treatment with a Glycoprotein IIb/IIIa receptor inhibitor (Tirofiban) in ACS patients with positive TnT, coupled with early invasive strategy, is associated with superior outcome [24].

As mentioned earlier, we validated our results on a separate group of forty-one patients who presented with acute coronary syndrome ACS to our department after the study had concluded and the result was consistent and promising. However, this is a retrospective study with limited number of patients. The clinical parameters identified should be validated in bigger cohort of patients. While the results may be applicable to patients with demographics similar to our study group, they may not apply to sub-groups of patients, e.g. those who are older and long standing diabetics. Similarly, in patients with suspected renal failure (creatinine > 221 mmol per liter), troponin T marker may be spuriously elevated [25]. This study may also be of limited value in hospitals or health care facilities where TnT test is freely available.

Conclusion

In patients with ACS, a single prolonged episode, or repetitive episodes of angina at rest in the 24 hours prior to admission, and evidence of myocardial ischaemia on ECG predict a positive TnT test. These clinical factors may be useful in the early diagnosis of myocardial injury and infarction in ACS patients particularly when TnT test is not available. These easily obtainable clinical information help to identify a high risk sub-group who will benefit from aggressive pharmacological and percutaneous coronary intervention.

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