ASSOCIATION BETWEEN QUANTITATIVE TROPONIN T LEVELS AND ANGIOGRAPHIC FINDINGS IN UNSTABLE ANGINA AND NON ST ELEVATION MYOCARDIAL INFARCTION

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ABSTRACT

Background: Patients with elevated Troponin T levels had more complex lesion characteristics in baseline coronary angiogram. Cardiac troponin T positive patients had predominantly multi vessel disease, greater coronary narrowing and frequently complex lesion morphology. Objective: To determine the association between quantitative Troponin T levels and angiographic findings in unstable angina/non ST elevation MI. Patient and Methods: The study population was composed of 210 consecutive patients with clinical diagnosis of unstable angina, admitted at Punjab Institute of Cardiology, Lahore. Samples for troponin T levels were obtained 6-12 hours after the onset of chest pain. Patients were grouped into quartiles according to the level of troponin T measured. Coronary angiography was performed in every patients before discharge. All coronary angiograms were evaluated without knowledge of clinical or Troponin T status. Results: The mean age was $53.3 \pm 10.49$. 165(76%) were males. Left main disease (LMD) was present in 13.3% (n=28). Three vessels, two vessels and single vessel disease was present as 41.4%, 27.1% and 26.7% respectively. Normal coronary angiogram was noted in 4.8%. More than 70% luminal narrowing at least in 1 vessel was present in 95.2% of the patients, 3.3% has calcification, 67.6% has occlusion and 6.2% had visible thrombus as well. Conclusion: Our study has demonstrated that there was a significant association between elevated quantitative Troponin T levels and number of diseased vessels. Therefore, Troponin T positive patients should be evaluated by coronary angiography to know the severity of the disease.

Keywords: Unstable angina, Troponin T, Coronary angiography, Coronary artery disease.

INTRODUCTION

Coronary artery disease is now a leading cause of death, not only in the Western countries but also in Asian countries like Pakistan. Every 25 seconds, an American will suffer from ACS and every minute, one American will die from AMI. One out of every six deaths in the United States is attributable to ACS. In-hospital mortality is similar between STEMI and NSTEMI patients. One year mortality is higher for NSTEMI patients compared with STEMI Patients. Mortality from ACS has declined dramatically with the advent of evidence-based therapies, but up to 25% of patients do not receive optimal medical therapy for ACS, resulting in a significant increase in mortality in those patients. Unstable angina (UA) and non-ST elevation myocardial infarction (NSTEMI) differ primarily in whether the ischemia is severe enough to cause sufficient myocardial damage to release detectable quantities of a marker of myocardial injury. UA is considered to be present in patients with ischemic symptoms suggestive of an ACS and no elevation in troponin with or without ECG changes indicative of Ischemia. NSTEMI is diagnosed in an appropriate clinical setting by cardiac biomarker elevation. Troponin is the most sensitive and specific biomarker for myocardial cell death. Troponin is used to evaluate patients with ACS determines whether a similar between STEMI and NSTEMI patients.

PATIENTS AND METHODS

We conducted this cross sectional study of 210 consecutive patients admitted at Punjab Institute of Cardiology, Lahore, from 1st January 2007 to 31st August 2007, with the diagnosis of unstable angina/non ST elevation myocardial infarction.
Inclusion Criteria: Patients with following criteria were included in this study.
I. Chest pain occurs at rest (or with minimal exertion) usually lasting more than 20 minutes.
II. Chest pain was severe and described as frank pain and of new onset (i.e., within one month).
III. Chest pain occurs with the crescendo pattern (i.e., more severe, prolonged, or frequent).
IV. All patients with positive troponin T levels (>0.10 ng/ml).

Exclusion Criteria: The exclusion criteria included patients with ST elevation myocardial infarction, previous history of coronary artery disease, prior coronary revascularization procedure either CABG or angioplasty or coronary stenting, renal insufficiency (serum creatinine > 1.4 mg/dl), coagulopathy, (INR > 1.8), serious intercurrent disease and patients who refused to undergo coronary angiography during hospitalization.

Troponin T measurement: Cardiac troponin T was measured on the Elecsys 1010 and 2010 (Roche Diagnostics) immuno assay analyzers in the Central Pathological Laboratory at Punjab Institute of Cardiology, Lahore. Serum samples for Troponin T were obtained 6-12 hours after onset of chest pain. The sensitivity of Cardiac Troponin T (cTnT) measurement was 98% at 6 hours and 100% sensitivity was at 12 hours. However, a majority of the patients (more than 97%) had their cTnT samples drawn between 11-12 hours after symptom onset. The manufacturer had reported the minimal detectable concentration as ≤ 0.01 ng/ml. A diagnostic threshold value of 0.10 ng/ml was used to classify patients as Troponin T positive. Patients were grouped into five quartiles according to the level of troponin T measured (according to CAPTURE trial)

1). ≤ 0.01 ng/ml.
2). 0.02 to 0.04 ng/ml.
3). 0.05 to 0.12 ng/ml.
4). 0.13 to 0.32 ng/ml.
5). > 0.32 ng/ml.

In unstable angina patients with troponin T levels of 0.12 ng/ml or less, cardiac event rates were low, in contrast for patients with Troponin T levels above 0.12 ng/ml, the risk of cardiac events were higher.

Baseline characteristics and the electrocardiogram
The presence of a history of hypertension, diabetes mellitus, hypercholesterolemia, (from the patient's record verified by identification of actual treatment with anti hypertensive, antidiabetic, or antihyperlipidemic medication), and a pertinent family history and history of smoking were also noted. Routine standard 12-lead electrocardiograms were obtained at admission and in association with episodes of chest pain. All electrocardiograms were evaluated for the presence of ST-segment depression and or elevation and inverted T-waves. Patients who had ST-elevation > 0.1 mV in at least 2 contiguous leads at admission were diagnosed as STEMI and ruled out from the study.

Coronary Angiography
Coronary angiography was performed in every patient before discharge in the cardiac catheterization laboratory of Punjab Institute of Cardiology, Lahore, using the Bicore mode and Hicore mode (siemens's Germany) and INTEGRUS (Philips Netherlands) angiographic machines. Left sided cardiac catheterization, Coronary angiography and ventriculography were performed using the judkins technique. Coronary angiography was not performed acutely but after 3-4 days. All angiographic films were reviewed, blinded to the results of the serum Troponin T analysis. We noted that how many patients had triple vessel, double vessel and single vessel disease left main stem disease, number of coronary arteries >70% stenosis/per patient, visible thrombus, calcification and occlusion. Significant CAD was defined as ≥70% lumen narrowing of a major epicardial artery or its branches. Left main coronary artery stenosis > 50% was regarded as equivalent to two vessel disease.

The collected data was analyzed statistically. Nominal variables were reported as frequency and or percentages. Numerical variables were expressed as mean ± SD. The ANOVA test was used for comparison of mean troponin T levels with number of coronary vessels involved. P < 0.05 was considered to indicate statistical significance. All calculations were performed with SPSS version 12.0 software. Informed consent was obtained from all the patients.
RESULTS
Baseline characteristics
Total 210 patients were enrolled in this study. The mean age was 53.3 ± 10.53 years. 165 (76%) were male. All patients had chest pain (100%), 35.7% patients were diabetic, 52.9% hypertensive, 48% hyperlipidemic, 35.2% has family history of CHD, 37.1% were smoker and 7.1% had no risk factor.

Troponin T status
Total patients (N=210) were grouped into five quartiles according to the level of Troponin T measured; 13.8% (n=29) had Troponin T level ≤ 0.01 ng/ml, 8.6% (n=18) had Troponin T level 0.02 to 0.04 ng/ml, 9% (n=19) had Troponin T level 0.05 to 0.12 ng/ml, 21.9% (n=46) had Troponin T level 0.13 to 0.32 ng/ml and 46.7% (n=98) had Troponin T > 0.32 ng/ml. (Table I). The cutoff value used for Cardiac Troponin T was 0.10 ng/ml. Approximately two-thirds patients had Troponin T levels > 0.10 ng/ml and they were considered as Troponin T positive.

Coronary angiographic findings:
All patients (N=210) underwent coronary angiography before discharge. All coronary angiograms were evaluated without knowledge of clinical or Troponin T status. Left main disease was present in 13.3% (n=28). More than 70% luminal narrowing at least in one vessel was present in 95.2% of the patients, 3.3% had calcification, 67.6% had occlusion and 6.2% had visible thrombus. Out of 210 patients, 26.7% had single vessel disease, 27.1% two vessel disease and 41.4% three vessel disease. Normal coronary angiogram was noted in 4.8%.

Table I: Sex wise distribution of patients according to Troponin-T status

<table>
<thead>
<tr>
<th>Troponin-T Status</th>
<th>Frequency</th>
<th>% Age</th>
<th>Frequency</th>
<th>% Age</th>
<th>Frequency</th>
<th>% Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.01 ng/ml</td>
<td>22</td>
<td>12.3</td>
<td>7</td>
<td>15.6</td>
<td>29</td>
<td>13.8</td>
</tr>
<tr>
<td>0.02 to 0.04 ng/ml</td>
<td>14</td>
<td>8.5</td>
<td>4</td>
<td>8.9</td>
<td>18</td>
<td>8.6</td>
</tr>
<tr>
<td>0.05 to 0.12 ng/ml</td>
<td>16</td>
<td>9.7</td>
<td>3</td>
<td>6.7</td>
<td>19</td>
<td>9.0</td>
</tr>
<tr>
<td>0.13 to 0.32 ng/ml</td>
<td>35</td>
<td>21.2</td>
<td>11</td>
<td>24.4</td>
<td>46</td>
<td>21.9</td>
</tr>
<tr>
<td>&gt; 0.32 ng/ml</td>
<td>78</td>
<td>47.3</td>
<td>20</td>
<td>44.4</td>
<td>98</td>
<td>46.7</td>
</tr>
<tr>
<td>Total</td>
<td>165</td>
<td>100</td>
<td>45</td>
<td>100</td>
<td>210</td>
<td>100</td>
</tr>
</tbody>
</table>

Mean (S.D) 0.754 (1.183) 0.779 (1.439) 0.759 (1.239)

Comparison of mean Troponin T level with number of coronary vessels involved shows no vessel involvement (n=10) when mean Troponin T level was 3.300ng/ml, single vessel disease was seen in 56 patients with mean Troponin T level 3.4107 ng/ml, double vessel disease in 57 patients with mean Troponin T level 3.7719 ng/ml and 87 patients had triple vessel disease with mean Troponin T level 4.1033 ng/ml. P-value remained significant (p=0.03). (Table II)

DISCUSSION
Unstable angina (UA) non-ST elevation myocardial infarction (NSTEMI) are very common manifestations of coronary heart disease. UA/NSTEMI constitutes a clinical syndrome that is caused by atherosclerotic coronary artery disease and associated with an increased risk of cardiac death and myocardial infarction.9 In clinical studies Troponin T has been suggested to be better (i.e, more sensitive and specific) marker of myocardial necrosis than CK-MB, and measurement serum Troponin in patients with unstable angina detect patients with “micronecrosis”.10,11,12 Patients with elevated Troponin have more extensive coronary artery disease, more complex and severe coronary lesions, multi-vessel disease, greater coronary narrowing and a greater burden of intracoronary thrombus on coronary angiography.8,13,14 In our study, total (N=210) patients were grouped into five quartiles according to the level of Troponin T measured (According to CAPTURE trial). First quartile had Troponin T level ≤ 0.01 ng/ml in 13.8% (n=29) patients, second quartile had troponin T level ranges from 0.02 to 0.04 ng/ml in 8.6% (n=18) patients, third quartile had Troponin T level ranges from 0.05 to 0.12 ng/ml in 9% (n=19) patients, fourth quartile had Troponin T level ranges from 0.13 to 0.32 ng/ml in 21.9% (n=46) patients and fifth quartile had Troponin T level > 0.32 ng/ml in 46.7% (n=98) patients. Third quartile ranges from 0.05 to 0.12 ng/ml which
overlaps both positive and negative, the cut off being 0.10 ng/ml. We did this study to determine the association between quantitative Troponin T levels and angiographic findings in unstable angina / non-ST elevation myocardial infarction. We included patients with unstable angina and their Troponin levels measured, whether positive or negative and preformed their coronary angiogram. The present analysis of this study shows that 13.3% patients has left main stem disease, 41.4% patients had three vessel disease, 27.1% patients has two vessel disease, 26.7% patients has single vessel disease, 95.2% patients has more than 70% stenosis in at least one vessel, 67.6% has occlusion, 3.3% has calcification and 6.2% patients has visible thrombus.

In our study, coronary arteries (n=10) were normal in patients with the elevated mean Troponin T levels, the possible explanation may be: Patients with minor myocardial injury (micronecrosis) also has raised Troponin T levels which lyses spontaneously or due to anti-thrombotic treatment, this micro-thrombus may be resolved and coronary arteries may be normal at the time of coronary angiography, there may be other causes than ischemic origin like myocarditis, left ventricular dysfunction, subendocardial injury due to increased wall stress, episodes of extreme hypertension, pericarditis and pulmonary embolism. In the present study, there was a low incidence of thrombus even in Troponin T positive patients. Coronary angiography was not performed acutely. No comparable study was found in Pakistan in literature review.

DeFilippi et al evaluated the relation between cardiac Troponin T level, the presence and severity of coronary artery disease and long term prognosis in patients with chest pain but no ischemic ECG changes who has short term observations. Patients with positive cTnT had 26 % single vessel disease, 40 % two vessel disease and 23 % has three vessel disease. In our study 41.4 % patients had three vessel disease. However, there were several limitations in this study. One is that a positive cTnT test was an indication of coronary angiography. Secondly, they detected no thrombi. Of note, in patients with unstable angina the reported incidence of thrombus is highly variable, ranging from 1% to 52%. Thirdly, this study used the first generation ELISA for cTnT, which has been replaced by second and third generation assay. These have a greater specificity for the cTnT cardiac isoforms.

Jurlander et al sought to identify differences in coronary anatomic pathology in patients with unstable angina and elevated versus non elevated serum troponin T values. All patients underwent coronary angiography, one -third (n=37) of the patients with unstable angina had increase in serum troponin T values. They has a higher incidence of three vessel disease (46%), left main disease (16%), and visible thrombus (22%). Comparing with our study the number of patients in this study is limited. Two thirds (n=150) of the patients with unstable angina has increase in serum Troponin T levels, the possible explanation may be: Patients with minor myocardial injury (micronecrosis) also has raised Troponin T levels which lyses spontaneously or due to anti-thrombotic treatment, this micro-thrombus may be resolved and coronary arteries may be normal at the time of coronary angiography. There may be other causes than ischemic origin like myocarditis, left ventricular dysfunction, subendocardial injury due to increased wall stress, episodes of extreme hypertension, pericarditis and pulmonary embolism. In the present study, there was a low incidence of thrombus even in Troponin T positive patients. Coronary angiography was not performed acutely. No comparable study was found in Pakistan in literature review.

Heeschen et al related the angiographic data to the TnT status of the CAPTURE trial patients. This study demonstrated a significant relationship between angiographic lesion complexity, presence of thrombus and a TnT level > 0.10 ng/ml. In this study there was a low incidence of thrombus, even in TnT positive patients (14.3%). Angiography is not a very sensitive method for the detection of thrombus. Neither intravascular ultrasound nor angioscopic evaluation was performed in the CAPTURE trial, these methods might have provided a higher sensitivity for the detection of thrombus formation. However, despite its low sensitivity for the detection of mural thrombus, angiography remains highly specific for larger luminal thrombi.

CONCLUSION
Our study demonstrated that there was a significant association between elevated quantitative Troponin T levels and number of diseased vessels. Therefore, Troponin T positive patients should be evaluated by coronary angiography to know the severity of the disease.
REFERENCES