INTRODUCTION

The measurement of cardiac biomarkers is an integral step in the management of patients with ischemic heart disease. Cardiac biomarkers have long been used to estimate infarct sizes that closely correlate with five-year mortality. Infarct size can be estimated from creatine kinase MB and myoglobin but repeated estimations are required during a small time window. Moreover although they are related, it is the infarct size rather than residual left ventricular function that is measured.

Left ventricular function is the single best individual predictor of mortality after acute myocardial infarction. Late mortality and morbidity after myocardial infarction is improved by treatment with Angiotensin Converting Enzyme (ACE) inhibitors, particularly in patients with heart failure or those having Left Ventricular Ejection Fraction (LVEF) ≤ 40%. It has been shown that biomarkers predict left ventricular ejection fraction and help in the early identification of patients with poor LV function. Serum troponin-T concentration has been found to be inversely correlated with LVEF as a consequence of inverse relation between infarct size and LVEF.

As primary Percutaneous Coronary Intervention (PCI) is now the preferred modality of reperfusion for acute STEMI, the role of cardiac enzymes in predicting infarct size and hence LVEF in patients undergoing primary PCI is uncertain. A recent study showed that post STEMI troponin-I peak occurs at 12-24 hours and is better correlated with LVEF. Levels of troponin-I and T can be used as a non-imaging modality to identify patients with LVEF ≤ 40% who need early aggressive therapy.

ABSTRACT

Objective: To determine the serum levels of troponin-I in identifying left ventricular ejection fraction (LVEF) of ≤ 40% in patients with first anterior ST Elevation Myocardial Infarction (STEMI).

Study Design: Case series.

Place and Duration of Study: At the Tabba Heart Institute, Karachi, from May to November 2008.

Methodology: Consecutive patients presenting with first anterior STEMI were studied. Troponin-I concentration was measured by MEIA (microparticle enzyme immunoassay) method and LVEF was visually assessed. Analysis of relation between troponin-I levels and LVEF by the Receiver-Operator Characteristic (ROC) curve was performed to determine the cut off values of troponin-I in identifying LVEF ≤ 40% in patients, who had received streptokinase or undergone primary Percutaneous Coronary Intervention (PCI).

Results: Out of the 90 patients studied, 50 patients received streptokinase and the remaining 40 patients underwent primary PCI. Mean age was 54.6 ± 9 years and 82% were male. Troponin-I levels of > 63.5 ng/ml predicted LVEF ≤ 40% with a sensitivity of 94% and specificity of 97% in patients receiving streptokinase, whereas in patients undergoing primary PCI, troponin-I levels of > 87.5 ng/ml predicted LVEF < 40% with a sensitivity of 86% and specificity of 100%.

Conclusion: Troponin-I concentration of > 63.5 ng/ml and > 87.5 ng/ml can predict LVEF ≤ 40% in patients treated with either streptokinase or primary PCI respectively for first anterior STEMI. Troponin-I can be used as a non-imaging tool to identify patients with LVEF ≤ 40% who need early aggressive therapy.

Key words: Myocardial infarction. Troponin-I. Streptokinase.
METHODOLOGY

A case series study was conducted on 90 consecutive patients, presenting to the Emergency Department of Tabba Heart Institute, Karachi, from May to November 2008. All patients regardless of age and gender presenting with acute anterior wall STEMI within 12 hours of symptoms onset, with ST segment elevation of > 1 mm in precordial leads, or presumably new onset Left Bundle Branch Block (LBBB) (depending on availability of prior electrocardiogram). Anginal symptoms included chest heaviness and squeezing or discomfort with or without radiation to arms, neck, lower jaw or back.

Out of 90 patients, 50 patients received streptokinase and the remaining 40 patients underwent primary PCI. In the emergency department, all patients received aspirin 300 mg, clopidogrel 600 mg, parenteral beta blockers as per indications and an initial weight-based bolus of unfractionated heparin. Glycoprotein (GP) IIb/IIIa antagonist (epifibatide) was administered to patients undergoing primary PCI. All patients were admitted in the coronary care unit.

Troponin-I levels were measured by the MEIA (microparticle enzyme immunoassay) method at the laboratory after 12 and 24 hours of presentation and peak troponin levels were recorded. On the 4th day of hospitalization, an echocardiogram was performed and LVEF was visually estimated and recorded by the staff physician. The main outcome variable of the study was to determine the cut off values of serum troponin-I levels, which identifies LVEF of < 40% in patients undergoing either thrombolytic therapy or primary PCI. Both MEIA and echocardiography was performed and recorded by a laboratory technician. The staff physician not involved in the study so as to minimize bias.

All the variables of age, gender, history of diabetes (defined as a fasting glucose ≥ 126 mg/dl or on treatment), hyperlipidemia (fasting cholesterol ≥ 200 mg/dl or on treatment), hypertension (systolic blood pressure ≥ 140/90 mmHg or on treatment), smoking, positive family history of Coronary Artery Disease (CAD) in first degree relatives (age < 55 years in male and < 65 years in female relatives), peak troponin-I levels and LVEF were recorded in the proforma.

The data was entered into the Statistical Package for Social Sciences Software, version 14. Descriptive statistics were used to summarize the continuous variables like age, duration of pain, door to needle/door to balloon time (minutes). Troponin-I and ejection fraction values were reported as mean ± S.D. Frequency and percentages were reported for categorical variables such as gender, diabetes, dyslipidemia, hypertension, smoking, family history and LVEF ≤ 40%. Sensitivity and specificity of troponin-I levels to identify LVEF ≤ 40% were determined by Receiver-Operator Characteristic (ROC) curve. The Pearson correlation co-efficient was used to determine the relationship between troponin-I and LVEF of ≤ 40%. P-value ≤ 0.05 was considered significant.

RESULTS

Ninety patients were included in this study. The mean age was 54± 9 years. There were 74 (82%) males and 16 (18%) females. There were 39 (43%) diabetics, 44 (48%) hypertensive patients, Sixty one (68%) were dyslipidemic and 50 (55%) smokers. Twenty seven (30%) had a positive family history of coronary artery disease. Table I shows the demographic characteristics of patients undergoing either streptokinase therapy or primary PCI separately.

The mean duration of pain (onset of symptoms till ER arrival) was 124±41 minutes in patients who received streptokinase and 140±30 minutes in patients who underwent primary PCI. The mean door to needle time was 24.4±8 minutes and the mean door to balloon time was 100±15 minutes (Table I).

<table>
<thead>
<tr>
<th>Patients characteristics</th>
<th>Streptokinase group</th>
<th>Primary PCI group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) [mean (SD)]</td>
<td>54.92±8.75</td>
<td>54.30±9.26</td>
</tr>
<tr>
<td>Male</td>
<td>43 (86)</td>
<td>31 (77.5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>24 (48)</td>
<td>15 (37.5)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21 (42)</td>
<td>23 (57.5)</td>
</tr>
<tr>
<td>Dyslipidima</td>
<td>36 (72)</td>
<td>25 (62.5)</td>
</tr>
<tr>
<td>Smoking</td>
<td>36 (72)</td>
<td>14 (35.0)</td>
</tr>
<tr>
<td>Family history</td>
<td>11 (22)</td>
<td>16 (40.0)</td>
</tr>
<tr>
<td>Duration of pain (minutes)</td>
<td>124.12±41.30</td>
<td>140±30</td>
</tr>
<tr>
<td>Door to needle/balloon time (minutes)</td>
<td>24.4±8</td>
<td>100±15</td>
</tr>
</tbody>
</table>

Mean serum troponin-I levels measured by the MEIA method were 74.7±65 ng/ml in patients who received streptokinase and 81.5±50 ng/ml in patients who underwent primary PCI. Mean LVEF on the fourth day of admission was 42.7±10% and 41±9% in patients who received streptokinase or had primary PCI respectively (Table II).

A strong negative (Pearson’s correlation coefficient = -0.79), statistically significant (p < 0.001) correlation was found between troponin-I and a LVEF of ≤ 40%. Analysis of the relationship between troponin-I levels and LVEF by receiver-operator characteristic curve was performed.
to determine the cut off values of troponin-I in identifying LVEF of ≤ 40% (Figures 1 and 2).

A troponin-I concentration of > 63.5 ng/ml predicted a LVEF of ≤ 40% with a sensitivity of 94% and specificity of 97% in patients who received streptokinase. A troponin-I concentration of > 87.5 ng/ml predicted a LVEF < 40% with a sensitivity of 86% and a specificity of 100% in patients who had undergone primary PCI (Table II).

**DISCUSSION**

An assessment of myocardial damage after STEMI is crucial in evaluating the efficacy of reperfusion therapy and predicting prognosis. Serum troponin-T and I are accepted as highly reliable biochemical markers for diagnosing myocardial infarction and the extent of myocardial damage.

The kinetics of troponin-I release are reperfusion dependent – reaching an earlier maximal level and having a correspondingly faster decline compared with that seen in non-revascularized STEMI, patients. Troponin-I peak concentrations are attained nearly at 12 hours and remained elevated 72 hours after reperfusion. Single troponin measurement between 12-24 hours of myocardial infarction is well correlated with infarct size. It is determined by SPECT imaging (p < 0.001), irrespective of reperfusion.

Similar data is available for troponin-T. A troponin-T concentration of > 2.8 µg/l predicted a LVEF ≤ 40% in patients with STEMI who had received thrombolytic therapy with a sensitivity of 95.5% and specificity of 88.1%. Another study showed that troponin-I measurement at 12 and 48 hours were inversely related (p < 0.001) to LVEF assessed both early and at 3 months after STEMI. Troponin-I levels >14.8 µg/l at 48 hours predicted LVEF of < 40% at 3 months, with a sensitivity of 100%, specificity of 65%.

No study was found which addressed the utility of troponin-I levels in patients with anterior STEMI, who had undergone either streptokinase therapy or primary PCI, to identify the relationship of troponin-I with LVEF and to determine cut off values of troponin-I for non-imaging identification of patients with LVEF of ≤ 40%.

In this study, the cut off values of troponin-I were determined to identify LVEF of ≤ 40% in patients undergoing either pharmacological or catheter-based reperfusion for first anterior STEMI. Patients with anterior STEMI were particularly selected because of the larger area of myocardium at risk and the higher probability of postinfarction poor LVEF.

A strong, negative, statistically significant correlation was found between serum troponin-I concentration measured 12-24 hours after postmyocardial infarction and LVEF. This finding was also noted in a previous study by Rao.

**Table II: Serum troponin-I levels and LVEF in patients receiving streptokinase or underwent primary PCI.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patient who received streptokinase (n=50) (%)</th>
<th>Patients having undergone primary PCI (n=40) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin I (mean ± (SD))</td>
<td>74.76 ± 65.77</td>
<td>81.52 ± 50.51</td>
</tr>
<tr>
<td>EF values (mean ± (SD))</td>
<td>42.70 ± 10</td>
<td>41.00 ± 9</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 40</td>
<td>33 (66)</td>
<td>24 (65)</td>
</tr>
<tr>
<td>&gt; 40</td>
<td>17 (34)</td>
<td>14 (35)</td>
</tr>
<tr>
<td>Troponin-I levels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Predict LVEF ≤ 40%)</td>
<td>&gt; 63.5 ng/ml (Sensitivity: 94%)</td>
<td>&gt; 87.5 ng/ml (Sensitivity: 86%)</td>
</tr>
<tr>
<td></td>
<td>(Specificity: 97%)</td>
<td>(Specificity: 100%)</td>
</tr>
</tbody>
</table>

**Figure 1:** ROC curve of patients who received streptokinase or underwent primary PCI.

**Figure 2:** Scattergram of patients who received streptokinase or underwent primary PCI.
Analysis of the relation between troponin-I values and visually estimated LVEF by receiver-operator characteristic curve showed that troponin-I concentration of > 63.5 ng/ml predicted LVEF of ≤ 40%, with a sensitivity of 94% and specificity of 97%, in patients who received streptokinase. A troponin-I concentration of > 87.5 ng/ml, predicted LVEF ≤ 40% with a sensitivity of 86% and specificity of 100%, in patients who underwent primary PCI. Stanely et al. demonstrated that using a threshold value of 55 ng/ml, troponin-I had 90% sensitivity and 52% specificity in predicting LVEF < 40%, in patients undergoing primary PCI.

This study showed higher cut off values of troponin-I levels in predicting LVEF of ≤ 40%, in patients who had undergone primary PCI. The mean duration of symptoms in patients who received streptokinase or underwent primary PCI, were almost similar and the door to needle time of 24.4 ± 8 minute and door to balloon time of 100 ± 15 minutes were near standards. The likely possible reason for higher troponin-I levels would be distal embolization of small fragments of the atherosclerotic plaque, side branch occlusion or temporary vessel occlusion in patients who had undergone primary PCI.

CONCLUSION

A troponin-I concentration of > 63.5 ng/ml and > 87.5 ng/ml can predict LVEF ≤ 40% in patients treated with either streptokinase or primary PCI respectively for first anterior STEMI. Considering the socioeconomic background of our population and the facilities available in health sector, troponin-I can easily be used as a non-imaging tool to early identify patients with LVEF of ≤ 40%, who need early aggressive therapy.

REFERENCES


11. Rao AC, Collinson PO, Canepa-Anson R, Joseph SP. Troponin-T measurement after myocardial infarction can identify left ventricular ejection of less than 40%. Heart 1998; 80:223-5.


