Serum Cardiac Troponin T in Patients with Acute Myocardial Infarction

Detection of Coronary Reperfusion and Prediction of Cardiac Function

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Summary

Serum troponin T, a myocardial contractile protein, has been reported to be a sensitive marker for the diagnosis of acute myocardial infarction. However, there have been few reports on its ability to detect coronary reperfusion and to predict left ventricular function in the chronic stage.

Twenty-two patients (20 males and 2 females, 61 ± 10 y.o.) with acute myocardial infarction were enrolled in this study. They were divided into 2 groups, one with successful reperfusion (group A: n = 13) and one without reperfusion (Group B: n = 9) and the serial changes of their serum troponin T levels were evaluated. Serum myosin light chain was measured in another group of patients with acute myocardial infarction without history of old myocardial infarction (group C: n = 8). The slope of the logarithm of serum troponin T on a time-value curve was calculated from the time of admission to the first peak within 24 hours of the onset of acute myocardial infarction. The correlation coefficient between the late peak of serum troponin T and the left ventricular ejection fraction in 11 patients with first Q wave acute myocardial infarction was compared with that between the serum myosin light chain peak and the left ventricular ejection fraction in group C.

1) The slope of the logarithm of serum troponin T on the time-value curve in group A was greater than that in group B (0.57 ± 0.45 vs. 0.22 ± 0.16) (p < 0.05). 2) There was a good correlation between the late peak of serum troponin T (78 ± 10 hours after the onset) and the left ventricular ejection fraction in 11 patients with first Q wave acute myocardial infarction (r = −0.84, p < 0.01), which was similar to that of the serum myosin light chain peak and the left ventricular ejection fraction (r = −0.72, p < 0.05). On the other hand, there was no correlation between the peak level of serum creatine phosphokinase and the left ventricular ejection fraction (r = −0.55, NS). The serum
troponin T levels 24, 36, 48 and 60 hours after the onset also correlated well with the left ventricular ejection fraction ($r = -0.65, -0.7, -0.65$ and $-0.89$, respectively). We conclude that the serial measurement of serum troponin T in patients with acute myocardial infarction is useful in the evaluation of left ventricular function in the chronic stage and that it is a potential non-invasive predictor of coronary reperfusion. ([Jpn Heart J] 36: 293–303, 1995)

**Key words:** Serum troponin T  
Acute myocardial infarction  
Reperfusion therapy  
Left ventricular function

SERUM levels of creatine phosphokinase and its isoenzymes have been used widely to evaluate the extent of myocardial necrosis and to detect coronary reperfusion in patients with acute myocardial infarction. However, their application is limited because they are also present in skeletal muscle and coronary reperfusion causes a rapid washout. Therefore, new non-invasive markers which can detect the reperfusion status and predict accurately left ventricular function in the chronic stage are necessary in this modern era of reperfusion therapy. It has been reported that the measurement of serum troponin T is useful in the diagnosis of acute myocardial infarction because of its cardiac specificity and unique release time course. However, there are few reports on the effect of reperfusion. The goal of this study is to determine whether the serial measurement of serum troponin T is useful in the detection of coronary reperfusion and whether it can predict cardiac function in the chronic stage in patients with acute myocardial infarction.

**METHODS**

**Study protocol:** Twenty two patients with acute myocardial infarction (20 males and 2 females, 61 ± 10 years of age) who were admitted to the Coronary Care Unit within 24 hours after the onset of acute myocardial infarction were enrolled in this study. Acute myocardial infarction was diagnosed by the following criteria: 1) typical chest pain lasting more than 30 minutes, 2) ST elevation (>0.1 mV) in at least 2 leads of the standard 12 lead electrocardiogram, 3) typical time course of changes in serum cardiac enzymes. Emergency coronary angiography was performed in all patients and intracoronary thrombolysis and/or percutaneous transluminal coronary angioplasty was done in eligible patients. After reperfusion, intravenous heparin was continued for 72 hours and aspirin (81 mg/day) was administered. For confirmation of the patency of the infarct-related coronary artery and evaluation of cardiac function, coronary angiography and biplane left ventriculography (30° right and 60° left anterior oblique views) were performed 4 weeks after the onset of acute myocardial infarction (= chronic stage). The left ventricular ejection fraction was calculated by the area-length...
formula with the use of an HP 5659 ventricular angiography workstation (Hewlett Packard, Mountain View, CA). Depending on the result of reperfusion therapy, the 22 patients were divided into two groups: successful reperfusion (group A: n = 13) and no reperfusion (group B: n = 9). Successful reperfusion was defined as an improvement of coronary flow to TIMI grade 2 or 3.\textsuperscript{12} In group A, all infarct-related coronary arteries were confirmed to be open in the chronic phase. In group B, 6 patients had unsuccessful recanalization and 3 patients did not receive recanalization therapy. Coronary angiography in the chronic stage showed all infarct-related arteries were occluded in group B. Serum myosin light chain was measured in eight other patients with acute myocardial infarction who had no prior myocardial infarction (group C).

**Blood sampling:** Blood samples were obtained on admission and every 3 hours during the first 24 hours, every 6 hours during the next 48 hours, then every 12 hours until 7 days after admission. Serum troponin T and conventional cardiac enzymes (creatine phosphokinase, glutamic oxaloacetic transaminase and lactate dehydrogenase) were also measured in the same blood samples.

**Serum cardiac troponin T, myosin light chain and creatine phosphokinase assay:** Serum troponin T was measured by enzyme-linked immunosorbent assay as previously reported.\textsuperscript{9} This assay is manufactured as a test kit consisting of 7 components: antibody-coated test tubes, monoclonal antibody-enzyme complex, incubation buffer, troponin T standard, control serum, substrate buffer, and the diammonium salt of 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid). For serum troponin T measurements, the antibody-enzyme complex, troponin T standards, and the diammonium salt of 2,2'-azino-bis substrate are dissolved in the buffer solution provided in the test kit and mixed thoroughly with a vortex mixer. Troponin T standards or unknown patient serum (200 ml) is added manually to the test tubes, and 1 ml of antibody-enzyme complex (45 IU) and all the remaining solutions are added by a batch enzyme-linked immunosorbent assay analyzer (Enzyme Test ES 22; Boehringer Mannheim, Germany). Solid-phase antibody, troponin T-coating solutions, and antibody-enzyme complex are incubated at room temperature for 60 minutes. The tubes are then emptied by suction and washed twice with tap water. To each test tube 1 ml substrate solution is added, and the substrate conversion is measured as color formation after 30 minutes of incubation at room temperature. The normal range in this assay is reported to be less than 0.5 µg/l.

Myosin light chain is measured with the radio immunoassay developed by Isobe et al.,\textsuperscript{13} and creatine phosphokinase is measured spectrophotometrically at 340 nm as described by Rosalki.\textsuperscript{14}

**Detection of reperfusion from serial changes of troponin T:** Because coronary reperfusion would influence the rate of appearance in the serum, the rate of
increase of serum troponin T soon after admission was calculated. The logarithm of the troponin T level from admission to the first peak within 24 hours was plotted against time, and the slopes of the time-logarithm of the troponin T level curves of group A and group B were compared. Sensitivity and specificity for the detection of coronary reperfusion were calculated as follows:

\[
\text{Sensitivity} = \frac{\text{number of true detections of reperfusion in group A}}{\text{number of all detections of reperfusion in both groups}}; \quad \text{specificity} = \frac{\text{number of true detections of no reperfusion in group B}}{\text{number of all detections of no reperfusion in both groups}}.
\]

**Evaluation of left ventricular function:** The late peak of serum troponin T and the peak of creatine phosphokinase were correlated with the left ventricular ejection fraction in the chronic stage in 11 patients with first Q wave acute myocardial infarction (7 patients in group A and 4 patients in group B) to determine whether the peak level of serum troponin T reflects infarct size. The correlation coefficient between serum troponin T 24, 36, 48 and 60 hours after the onset of acute myocardial infarction and the left ventricular ejection fraction in the chronic stage was also determined (TnT-24, TnT-36, TnT-48 and TnT-60, respectively). The correlation between the peak of serum myosin light chain and the left ventricular ejection fraction in the chronic stage in group C was also calculated.

**Statistical analysis:** All data are expressed as the mean ± SD. Correlation was determined by linear regression analysis. Comparison among groups was carried out by unpaired Student's test and the chi-square test. The level of statistical significance was defined as \( p < 0.05 \).

**Results**

The background data of the patients are listed in Table I. Changes in the serum troponin T level are shown in Table II. Age, gender and site of acute myocardial infarction did not differ between the two groups. As shown in Figure 1, the time course of serum troponin T was biphasic in 10 patients of group A and 6 patients of group B. Both time to early peak and time to late peak were similar in group A and group B. However, the first peak of serum troponin T level was significantly higher in group A than in group B (\( p < 0.05 \)). In contrast, the interval from the onset of acute myocardial infarction to the time of maximal serum creatine phosphokinase level in group A was shorter than in group B (\( p < 0.01 \)). The peak creatine phosphokinase values in the two groups were not significantly different.

**Detection of reperfusion:** The slope of the logarithm of the serum troponin T-time curve was significantly steeper in group A (0.57 ± 0.45/hour) than in group
Table I. Patients Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Age (y.o.)</td>
<td>61 ± 9</td>
<td>63 ± 13</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Site of AMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANT</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>INF</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Number of diseased vessel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVD</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>MVD</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Time to reperfusion (min.)</td>
<td>274 ± 76</td>
<td>(−)</td>
</tr>
<tr>
<td>Peak CPK (IU/l)</td>
<td>4019 ± 2036</td>
<td>2819 ± 1690</td>
</tr>
<tr>
<td>Time to peak CPK (min.)</td>
<td>813 ± 241</td>
<td>1469 ± 527</td>
</tr>
</tbody>
</table>

_n = number; y.o. = years old; AMI = acute myocardial infarction; ANT = anterior; INF = inferior; SVD = single vessel disease; MVD = multivessel disease (significant stenosis was defined as > 75% diameter stenosis); *p < 0.05 vs group A.

Table II. Indexes Derived from Serum Troponin T Level

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to early peak (hours)</td>
<td>15.3 ± 6.0</td>
<td>19.0 ± 4.5</td>
</tr>
<tr>
<td>Troponin T at early peak (μg/l)</td>
<td>17.8 ± 15.0</td>
<td>5.9 ± 3.4*</td>
</tr>
<tr>
<td>Time to late peak (hours)</td>
<td>78.4 ± 14.0</td>
<td>72.0 ± 16.0</td>
</tr>
<tr>
<td>Troponin T late peak (μg/l)</td>
<td>8.0 ± 5.1</td>
<td>6.7 ± 2.8</td>
</tr>
</tbody>
</table>

*p < 0.05 vs group A

Figure 1. A representative case in group A. The left panel shows the time course of the serum troponin T level and the right panel shows the slope of the logarithm of the serum troponin T-time curve. TnT = troponin T.
B \(0.22 \pm 0.16/\text{hour}\). When the cut off level was set at 0.27/\text{hour}, the sensitivity was 90\% and the specificity was 73\% for the detection of coronary recanalization (Figure 2).

**Correlation between variables and left ventricular ejection fraction:** Correlation coefficients between variables and left ventricular ejection fraction in 11 patients with first Q wave acute myocardial infarction are shown in Table III. The late peak of their serum troponin T was observed \(77.9 \pm 12.8\) hours after the onset of acute myocardial infarction. There was a good correlation between the peak value of serum troponin T and the left ventricular ejection fraction in the chronic stage \((r = -0.84, p < 0.01)\), which was similar to that between myosin light chain and the left ventricular ejection fraction \((r = -0.72, p < 0.05)\) (Figure 3). Especially in group A, there was a good correlation between the late peak of serum troponin T and the left ventricular ejection fraction \((r = -0.94)\). However, there was no correlation between peak level of creatine phosphokinase and the left ventricular ejection fraction in any group \((r = -0.59\) and \(-0.66,\) respectively).

![Figure 2. Slope of the logarithm of the serum troponin T-time curve in each group. Note that the slope in group A (open circle) is greater than that in group B (open square). TnT = troponin T.](image)

**Table III.** Correlation Coefficients between Peak Serum Troponin T and Creatine Phosphokinase and Left Ventricular Ejection Fraction

<table>
<thead>
<tr>
<th></th>
<th>(r) peak TnT vs. LVEF</th>
<th>(p)</th>
<th>(r) peak CPK vs. LVEF</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recanalization (+)</td>
<td>-0.94</td>
<td>(p &lt; 0.01)</td>
<td>-0.59</td>
<td>n.s.</td>
</tr>
<tr>
<td>Recanalization (-)</td>
<td>-0.35</td>
<td>n.s.</td>
<td>-0.66</td>
<td>n.s.</td>
</tr>
<tr>
<td>All</td>
<td>-0.84</td>
<td>(p &lt; 0.01)</td>
<td>-0.55</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

\(n = \text{number}; \ n.s. = \text{not significant}; \ p = \text{probability}; \ TnT = \text{troponin T}; \ LVEF = \text{left ventricular ejection fraction}\)
Figure 3. Correlation between late peak of serum troponin T (left panel), peak creatine phosphokinase (center panel) and peak of serum myosin light chain (right panel) and left ventricular ejection fraction. The correlation coefficient between the serum level of the troponin T and the left ventricular ejection fraction was similar to or better than that between the serum myosin light chain level and the left ventricular ejection fraction ($p<0.05$), but there was no significant correlation between the creatine phosphokinase level and the left ventricular ejection fraction. TnT = troponin T; LVEF = left ventricular ejection fraction; MLC = myosin light chain.

Figure 4. Correlation between troponin T levels at various times after the onset and left ventricular ejection fraction. Correlations between TnT-24, 36, 48, 60 and the left ventricular ejection fraction are significant. LVEF = left ventricular ejection fraction. TnT-24, 36, 48 and 60 = serum levels of troponin T 24, 36, 48 and 60 hours after onset of acute myocardial infarction.
A significant correlation was also observed between TnT-24, 36, 48, 60 and the left ventricular ejection fraction in the chronic stage (Figure 4). Although there was no statistically significant difference in correlation coefficients among these values, TnT-60 appeared to have the highest correlation coefficient.

DISCUSSION

We have shown that the peak value of serum troponin T has a good correlation with left ventricular ejection fraction in the chronic stage of acute myocardial infarction and that the rate of increase in serum troponin T may predict coronary reperfusion.

Detection of coronary reperfusion: In the modern era of reperfusion therapy for acute myocardial infarction, the estimation of infarct size from conventional cardiac enzyme levels seems inappropriate. The conventional markers such as early increase of creatine phosphokinase, early disappearance of chest pain and early decrease of ST elevation in the 12-lead electrocardiograph have been found to have only low reliability. Serum myoglobin has been reported to be able to detect coronary reperfusion quickly because of its rapid kinetics. However, it has a low specificity for cardiac injury because it is also present in skeletal muscle, and its rapid disappearance from serum may lead to misjudgment of recanalization. Cardiac troponin T is a component of contractile proteins and 6% of all troponin T exists in the cytosol in a soluble unbound form. Serum troponin T has been reported to start rising 3.5 hours after the onset of acute myocardial infarction (slightly earlier than serum creatine phosphokinase), persists for more than 10 days and has a high diagnostic potential because of its cardiospecificity. As shown in this study, the release of troponin T in acute myocardial infarction is typically biphasic, and it has been reported that the first peak of serum troponin T is composed mainly of soluble unbound troponin T and the late peak reflects continuing myocardial damage. Recently, Abe et al reported that an increase in serum troponin T 60 minutes after reperfusion therapy can be applied to detect successful reperfusion in patients with acute myocardial infarction. In this study, the slope of the logarithm of the serum troponin T-time curve in the early phase of reperfusion after acute myocardial infarction was higher than that when there was no reperfusion. Although the index used in this study is different from theirs, our results support their conclusion. When successful reperfusion was achieved, the first peak of serum troponin T may be composed mainly of washout of unbound troponin T from the cytosol due to reperfusion of the occluded coronary artery. Thus, release of unbound troponin T in the cytosol must be sensitive to reperfusion, and measurement of the rate of this release might detect coronary reperfusion. However, the specific-
itivity of the detection of reperfusion by the slope of the logarithm of the serum troponin T-time curve was 73%, which seems relatively low. This may be due to the small number of samplings. If sampling is done more often during the early phase of acute myocardial infarction and the time needed to measure serum troponin T can be shortened, a better non-invasive judgment of coronary reperfusion may be possible.

**Evaluation of left ventricular function:** Although peak creatine phosphokinase has been in general use for the evaluation of infarct size, it does not necessarily correlate with the left ventricular function at the chronic stage when successful reperfusion is achieved, probably because of the false increase in peak creatine phosphokinase due to the washout phenomenon. In this study, the peak creatine phosphokinase level was examined in 11 patients with first Q-wave acute myocardial infarction, and there was no significant correlation between the left ventricular ejection fraction and peak creatine phosphokinase, because this group contained both reperfused and non-reperfused acute myocardial infarction patients. Thus, without information about the reperfusion situation, one cannot predict left ventricular function in the chronic stage from the peak creatine phosphokinase value. In contrast, correlation coefficients between the troponin T level and the left ventricular ejection fraction were excellent in the same patient group. Isobe et al reported that the serum level of myosin light chain reflected changes in left ventricular function after acute myocardial infarction regardless of the presence or absence of coronary reperfusion. In this study, we have shown that the predictive ability of troponin T is similar to or better than that of serum myosin light chain. Serum contractile proteins such as troponin T and myosin light chain appear to reflect myocardial necrosis better than do conventional cardiac enzymes. However, myosin light chain is more influenced by renal dysfunction and has lower cardiospecificity (12% cross-reactivity with skeletal muscle) than troponin T (1–2%). Therefore, troponin T may have an advantage over myosin light chain in the prediction of left ventricular function in the chronic stage. Moreover, the troponin T level 60 hours after the onset of acute myocardial infarction showed a correlation coefficient similar to the late peak of troponin T, indicating that it may be possible to predict infarct size by measuring serum troponin T at a single sampling point about 60 hours after the onset of acute myocardial infarction. This would be economically useful.

**Limitations of this study:** The major limitation of judging the presence of coronary reperfusion from serum troponin T is that the assay takes about 90 min, which makes it too late to decide the next strategy after intravenous thrombolysis has failed. Moreover, troponin T in the first sample of serum was elevated in only 11 of the 22 patients with acute myocardial infarction in this series. Therefore, we hope to improve the method of serum troponin T assay and shorten the time
required to obtain results.

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REFERENCES