Cardiac Emergency Triage and Therapeutic Decisions Using Whole Blood Rapid Troponin T Test for Patients With Suspicious Acute Coronary Syndrome

Kunio Tanaka, MD; Yoshihiko Seino, MD*; Kanji Ohbayashi, MD; Teruo Takano, MD*

Emergency triage and therapeutic decisions using the recently developed whole blood rapid troponin T test were evaluated and compared with conventional electrocardiographic (ECG) diagnosis in a total of 155 patients with chest pain who visited 16 emergency outpatient clinics in the Tokyo metropolitan area. Thirty-seven patients (23.9%) had a final diagnosis of acute myocardial infarction or high-risk unstable angina requiring emergency coronary intervention and these events were defined as acute coronary syndrome. Diagnostic values using the second-generation rapid troponin T test were evaluated according to 3 time-windows in 85 patients. The sensitivity of the test was 10% for patients assessed within 3h after the onset, 62.5% for 3–6h after, and 75% for more than 6h, whereas conventional ECG diagnosis had 100% sensitivity at any time-window. In contrast, the specificity of the rapid troponin T test was 100%, 100%, and 97.4%, whereas that of conventional ECG diagnosis was 25%, 57.1%, and 42.2%, respectively for the 3 time-windows. The positive predictive value of ECG diagnosis was inferior to the rapid troponin T test, which reflected the prudent attitude of physicians taking ECG decisions as positive when myocardial ischemia was suspected. The diagnostic efficacy of the rapid troponin T test was remarkable in patients with the non-ST elevation type of acute coronary syndrome. A questionnaire survey on therapeutic decisions revealed that only 10% of Tokyo outpatient institutes performed prehospital thrombolytic therapy, 30–33% administered aspirin or nitrate, and 16.7% gave heparin. The rapid troponin T test is extremely useful for cardiac emergency triage and therapeutic decision making. There is a requirement for practical guidelines for the primary therapeutic decisions for patients with suspicious acute coronary syndrome. (Jpn Circ J 2001; 65: 424–428)

Key Words: Acute coronary syndrome; Acute myocardial infarction; Prehospital care; Troponin T

Cardiac emergency triage and the therapeutic decision are the most important issues in the management of acute coronary syndrome (ACS), which consists of a wide spectrum of lethal coronary events such as rapidly developing unstable angina, acute myocardial infarction (AMI), non-Q wave infarction, and cardiac sudden death. The clinical diagnosis of ACS is based on the symptoms, clinical imaging, physical findings, electrocardiographic (ECG) findings, and laboratory tests. However, conventional laboratory tests have several limitations related to laboratory equipment, laboratory staff, and the time required for biochemical assay of cardiac markers. Therefore, a new diagnostic system using rapid and easier biochemical assay has been requested for cardiac emergency management.

Approximately 94% of cardiac troponin T exists as a component of the structural protein of myofibrils, and the remaining 6% is a soluble fraction in the cytoplasm. Therefore, the release kinetics of troponin T reflects 1 of 2 types of myocardial injury; that is, either the loss of the integrity of the cell membrane or progressive irreversible necrosis of myofibrils. We previously reported that measuring the level of troponin T is useful not only for early diagnosis of AMI, but also for detecting high-risk unstable angina and non-Q wave infarction. However, the quantitative measurement of cardiac troponin T by enzyme-linked immunosorbent assay requires specific laboratory equipment and time for the assay to be conducted.

A whole blood rapid troponin T test, which facilitates simple and rapid evaluation of increased troponin T using a whole blood sample at bedside, was released in 1995 and we reported on the clinical utility of that first-generation rapid troponin T panel test for diagnosing acute coronary syndrome in a cooperative study with office cardiologists in the Tokyo metropolitan area (Tokyo Troponin T Trial: 4T). In the present study, using the upgraded second-generation rapid troponin T test, we analyzed the test’s diagnostic efficacy in detail according to 3 time-windows from the onset to the evaluation and ECG changes on admission. Furthermore, we conducted a questionnaire survey on the current therapeutic decisions in medical clinics in the Tokyo metropolitan area for acute coronary syndrome.

Methods

The subjects consisted of 155 patients (age: 34–99 years, 78 males and 77 females) with suspected AMI or unstable angina who visited cardiac emergency outpatient clinics of 16 institutes (listed in Appendix) that are affiliated with the First Department of Medicine, Nippon Medical School or 4T, Tokyo. All the physicians involved in the cardiac emer-
Emergency Triage by Rapid Troponin T Test


The present study was conducted in the context of patient presentations to the cardiac emergency service. In this context, the emergency team consisted of cardiologists. An ECG was recorded in all patients before assessment using the whole blood rapid troponin T test. The first-generation rapid troponin T test (TROP T®, Boehringer-Mannheim, Germany) was assessed in 70 patients, and both the first- and the second-generation (TROP T® sensitive, Roche, Germany) rapid troponin T tests were assessed in 85 patients. The treating physician read the tests on site. Conventional diagnosis was based on the symptoms, physiological findings and ECG changes and classified as positive (‘markedly suspicious’ and ‘suspicious’) or negative (‘unlikely’).

**Definition of Acute Myocardial Infarction and High-Risk Unstable Angina**

The diagnosis of AMI was based on the presence of (1) prolonged chest pain, (2) development of a new Q wave following ST elevation or prolonged ST-T changes, and (3) characteristic elevation of serum creatine kinase (CK) (> twice the upper limit) and CK-MB (>10% of total CK). High-risk unstable angina was defined as unstable angina required emergency coronary intervention such as emergency percutaneous transluminal coronary angioplasty (PTCA) or emergency coronary artery bypass grafting (CABG). Both AMI and high-risk unstable angina were defined as acute coronary syndrome in the present study. The indication for emergency coronary intervention was based on the ACC/AHA guidelines for the management of AMI.11–13

The diagnostic efficacy of the rapid troponin T test for acute coronary syndrome was evaluated precisely in the 85 patients who were assessed by the second-generation assay (age: 34–99 years, 46 males and 39 females), and compared with the conventional diagnosis. The diagnostic efficacy of the test was analyzed according to 3 time-windows from onset to presentation.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Time-Windows and the Electrocardiographic Findings at the Cardiac Emergency Visit</th>
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<tbody>
<tr>
<td></td>
<td>Total (%)</td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>ST elevation</td>
<td>35 (22.6)</td>
</tr>
<tr>
<td>ST depression/inverted T</td>
<td>39 (25.2)</td>
</tr>
<tr>
<td>Abnormal Q</td>
<td>18 (11.5)</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>16 (10.3)</td>
</tr>
<tr>
<td>Arrhythmia (AF, pacemaker etc)</td>
<td>16 (10.3)</td>
</tr>
<tr>
<td>No specific abnormalities</td>
<td>35 (22.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Performance of the Rapid Panel Test for Detecting Acute Coronary Syndrome (ACS) at 3 Time Windows Following the Onset of Chest Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance</td>
<td>0–3 (n=18)</td>
</tr>
<tr>
<td>ACS+</td>
<td>ACS−</td>
</tr>
<tr>
<td>Positive diagnosis</td>
<td>1</td>
</tr>
<tr>
<td>Negative diagnosis</td>
<td>9</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>10</td>
</tr>
<tr>
<td>Specificity</td>
<td>100</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>100</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>47.1</td>
</tr>
</tbody>
</table>

Fig 1. Diagnostic efficacy of rapid troponin T test: Analysis according to time-windows from onset to presentation. Tree bars represent the diagnostic value for 0–3h, 3–6h, and more than 6h after the onset of symptoms to the clinical evaluation.
the onset of symptoms to the clinical evaluation (within 3h
of onset: n=18; between 3 and 6h of onset: n=15; and
>6h: n=50), and also according to the ECG changes on ad-
mission; namely, ST elevation (n=20), non-ST elevation (ST
depression or T wave inversion, n=22), and others. Two
patients in whom the time of onset of the symptoms could
not be clarified were excluded from the time-windows
analyses.
A questionnaire survey was also conducted to inves-
tigate the therapeutic decisions being made by cardiologists in 29
cardiology outpatient clinics, including the 16 involved in
the present troponin T study. The issues canvassed were (1)
whether the physician was performing prehospital throm-
bolysis, or administering aspirin, heparin or nitrate
as anti-ischemic therapy before transfer to hospital, (2)
routes of emergency transfer, and (3) future perspectives on
cardiac primary care.

Results
Symptoms and Electrocardiographic Findings
The chief complaints on presentation at the outpatient
clinic were chest pain or chest oppression (124 patients,
80%), dyspnea (21 patients, 13.5%), palpitation (18 patients,
11.6%), back pain (10 patients, 6.5%), and syncope or
consciousness disturbance (9 patients, 5.8%). The number
of patients assessed in each of the 3 time-windows was in
25 patients (16.1%) in 3h, 22 patients (14.2%) between
3 and 6h, and 107 patients (69.0%) at more than
6h (Table 1). ST elevation was recorded in 35 patients
(22.6%), and ST depression or T wave inversion in 39
patients (25.2%) (Table 1).
Of the 155 patients, 37 (23.9%) had a final diagnosis of
acute coronary syndrome (ie, AMI or high-risk unstable
angina requiring emergency coronary intervention).

Diagnostic Efficacy of Rapid Troponin T Test:
Analysis by Time-Windows
The second-generation test gave a positive test result
much earlier (3–3.5h after the onset) in contrast with the
first-generation test, which gave a positive result at 4.5–5h
after the onset. Comparing the diagnostic value of the 2
tests, the second-generation panel test had superior diag-
nostic value compared with the first-generation panel test: 50%
vs 26.7% for sensitivity, 98.2% vs 98.2% for specificity,
93.7% vs 88.9% for positive predictive value and
79.7% vs 71.1% for negative predictive value, respectively.
Precise analysis of the test’s diagnostic efficacy for acute
coronary syndrome was done in the 85 patients who under-
went evaluation using the second-generation test (Table 2).
The sensitivity of the rapid troponin T test was
10% for patients being assessed within 3h after the onset,
62.5% for those between 3 and 6h, and 75% for those more
than 6h after onset, whereas the conventional ECG diagnos-
sis had 100% sensitivity at any time-window. The speci-
ficity of the rapid troponin T test was 100% for those
within 3h and between 3 and 6h, and 97.4% for more
than 6h, but for the conventional ECG diagnosis specificity
was 25% for those within 3h, 57.1% for those between 3
and 6h, and 42.2% for those more than 6h after onset. The
positive predictive value of the rapid troponin T test was
100% for within 3h and between 3 and 6h, and 90% for
more than 6h after onset, in contrast to conventional diag-
nosis for which it was 62.5% for within 3h, 72.7% for
3–6h, and 33.3% for more than 6h after onset (Table 3).

Diagnostic Efficacy: Analysis by Electrocardiographic Changes
In patients showing ST elevation, the positive predictive
value of the conventional ECG diagnosis was 95% (19/20),
whereas that of the rapid troponin T test was 100%. The
diagnostic efficacy for diagnosing acute coronary syndrome
was satisfactory with either method. In contrast, in patients
showing non-ST elevation, the positive predictive value of
conventional diagnosis was 36.4% (8/22), whereas that of
rapid troponin T test was 75% (16/22). Therefore the diag-
nostic efficacy of the rapid troponin T test was superior to
that of conventional diagnosis in patients showing non-ST-
elevation type changes. Furthermore, this method was
useful for diagnosing patients complicated by bundle
branch block, those with previous myocardial infarction,
and those who had undergone pacemaker implantation.

Questionnaire Survey on Prehospital Care
The replies to the questionnaire survey from 29 institutes
are shown in Table 4. When the diagnosis of AMI was
established, only 3 institutes (10.3%) were administering
intravenous thrombolytic therapy before or during transfer
to the hospital, and 24 institutes (82.7%) were not using
prehospital thrombolysis, even within 6h of onset because
of (1) the difficulty in countering adverse events, such as
the development of reperfusion arrhythmias or bleeding
tendency (15 institutes, 51.7%); (2) the coronary care unit
(CCU) is located within a short distance and patient can be
rapidly transferred within 20 to 40min (12 institutes,
41.1%); and (3) difficulty in obtaining informed consent (6

Table 3 Diagnostic Efficacy of Rapid Troponin T Test: Analysis According to Time-Windows

<table>
<thead>
<tr>
<th>Time Window</th>
<th>Conventional diagnosis</th>
<th>Rapid troponin test</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3h</td>
<td>100 100 100</td>
<td>62.5 75</td>
</tr>
<tr>
<td>3–6h</td>
<td>57.1 42.2 33.3</td>
<td>100 100</td>
</tr>
<tr>
<td>&gt;6h</td>
<td>100 100 100</td>
<td>97.4 90</td>
</tr>
</tbody>
</table>

Table 4 Questionnaire Survey on Current Status of Prehospital Care

**Q1: Performing prehospital thrombolysis?**
Yes 3/29 (10.3%), No 24/29 (82.7%), Others 2

**Reason for not performing**
- Difficulty for countering adverse events: 15 institutes, 51.7%
- CCU is located within a short distance: 12 institutes, 41.1%
- Trouble in obtaining informed consent: 6 institutes, 20.7%

**Q2: Prehospital medication**
- Aspirin (81–162 mg): 8 institutes, 33.3%
- Nitrates (sublingual or patch): 7 institutes, 29.2%
- Intravenous heparin (3,000–5,000 units): 4 institutes, 16.7%
- Nothing: 12 institutes, 50%

Table 2 Electrocardiographic Changes

<table>
<thead>
<tr>
<th>Time Window</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3h</td>
<td>100</td>
<td>25</td>
<td>62.5</td>
<td>100</td>
</tr>
<tr>
<td>3–6h</td>
<td>72.7</td>
<td>57.1</td>
<td>73.3</td>
<td>100</td>
</tr>
<tr>
<td>&gt;6h</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
institutes, 20.7%). As prehospital medication, aspirin (81–162 mg, 8 institutes, 33.3%), nitrates (sublingual or percutaneous patch, 7 institutes, 29.2%), or intravenous heparin (3,000–5,000 units, 4 institutes, 16.7%) were used, although 12 institutes (50%) replied that patients were directly transferred to the cardiovascular specialist hospital without specific medication.

Concerning the choice of hospital, 12 institutes (50%) replied that the choice was made by the emergency team of the Tokyo CCU network belonging to the Tokyo Fire Department, and the other 12 institutes (50%) replied that the choice was made by the treating physician. Finally, 18 institutes (75%) noted the requirement for clinical guidelines for the primary and prehospital care of acute coronary syndrome patients in Japan.

**Discussion**

In 1996 and 1999, the ACC/AHA Task Force proposed guidelines for the management of patients with AMI, in which the importance of early risk stratification and primary care at the cardiac emergency room was emphasized. Furthermore, measurement of cardiac troponin T and I was recommended rather than conventional cardiac markers, such as CK or CK-MB, because these new markers give an early diagnosis of not only AMI but also high-risk unstable angina. The use of the new, simple and rapid whole blood assay for cardiac troponin T is recommended in the guidelines. In addition, the guidelines emphasize the importance of the therapeutic decisions for the primary care at the cardiac emergency room, which will differ according to the ECG changes (ie, ST elevation type, non-ST elevation (ST depression or T wave inversion) and others). Furthermore, the joint committee of the European Society of Cardiology and American College of Cardiology has recently redefined myocardial infarction, in which the biochemical diagnosis has been changed to evaluation of cardiac troponins rather than CK or CK-MB. The redefined diagnostic criteria include high-risk unstable angina with minor myocardial damage detected by elevation of troponin T.

*Diagnostic Efficacy of the Rapid Troponin T Test and Its Clinical Utility*

The introduction of a rapid biochemical diagnosis using the first-generation troponin T test for office cardiology was revolutionary because it facilitated rapid bedside evaluation and risk stratification in patients with suspected acute coronary syndrome. However, the positive test result was not obtained until 4.5–5.5 h after the onset of symptoms because of the time lag in the release kinetics of troponin T from injured cardiomyocytes. Therefore, the diagnostic sensitivity of the first-generation assay had a temporal limitation for patients presenting in the superacute phase. The present study has shown that the diagnostic efficacy has improved and positive test results are available much earlier (ie, 3 h after the onset) when using the second-generation assay. However, there is still a temporal limitation for patients presenting in the superacute phase (within 3 h of onset), for which the sensitivity of the upgraded test was 10%, still a low value. The specificity of rapid troponin T test was excellent. The development of new biochemical markers that facilitate earlier risk stratification in the superacute phase is anticipated.

A multicenter study of cardiac emergencies in the United States, the Chest Pain Evaluation in the Emergency Room (CHEER), reported that approximately 50% of patients hospitalized with suspected unstable angina were noncardiac, and that 2–5% of patients with AMI were not diagnosed in the emergency room. They conducted a chest pain observation study that could establish the differential diagnosis of chest pain based on a 6-h protocol of serial monitoring of the ECG and CK isozyme measurements, and recommended this as a safe, effective, and cost-saving means of cardiac primary care for patients with suspected acute coronary syndrome. Although they did not use a rapid biochemical assay in their study, their results and our data highlight the clinical utility of the rapid biochemical test in cardiac emergencies.

In the GUSTO-IIa trial, Ohman et al demonstrated that the plasma level of troponin T on admission was an important prognostic factor that independently predicted the mortality within 30 days after onset in patients with acute coronary syndrome. The mortality rate was significantly higher in patients exhibiting troponin T levels greater than 0.1 ng/ml than those with troponin T levels below 0.1 ng/ml. A substudy of FRISK also demonstrated that the maximal troponin T level obtained within the initial 24 h after onset is a most satisfactory predictive factor of the prognosis regardless of whether unstable angina or non-Q wave infarction has been diagnosed. Moreover, it has been verified that the absence of troponin T elevation is the most reliable factor for identifying the lowest-risk patients with acute coronary syndrome.

The high-risk group identified in those reports would be almost identical to the present patients showing a positive test result with the rapid troponin T test (troponin T >0.15 ng/ml). Early risk stratification would become much easier and faster in cardiac emergency situations in Japan if the rapid troponin T test was used. Although we have not yet performed a follow-up study, the large-scale studies described earlier have already suggested the significant contribution of early risk stratification in cardiac emergencies. We need a further follow-up study in Japan to confirm the therapeutic implication of the whole blood rapid panel test.

In contrast, the ECG diagnosis had lower specificity and positive predictive values in the present study, which reflects the prudent attitude of physicians taking ECG changes as a positive result when myocardial ischemia was suspected. Concerning the pattern of the ECG changes, the diagnosis was almost accurately established by the conventional method in patients showing ST elevation, and the rapid panel test was not necessarily an improvement in the diagnosis for this group. However, its positive predictive value was superior to that of the conventional method (75% vs 36.4%) in patients with an ECG of the non-ST elevation type.

*Issues in the Therapeutic Decisionmaking*

The questionnaire survey in this study revealed that primary medications, such as prehospital thrombolysis, aspirin, or heparin, were not being administered in approximately 50% of Tokyo outpatient institutes before transferring the patient to the hospital even when the diagnosis of AMI or unstable angina was established. The reasons for not performing prehospital thrombolysis were fear of adverse events, difficulty in obtaining informed consent or the relatively short distance to the CCU. According to the ACC/AHA guidelines, there are practical therapeutic strate-
gies for patients with acute coronary syndrome. Thrombolytic therapy or primary PTCA is recommended in patients with AMI of the ST-elevation type, whereas aspirin, low molecular heparin, and glycoprotein IIb/IIIa inhibitors are recommended for patients with AMI of the non-ST elevation type. In the CAPTURE trial, Hamm et al reported that anti-platelet therapy with the IIb/IIIa antagonist, Abciximab, was especially useful in patients with intractable unstable angina exhibiting troponin T levels greater than 0.1 ng/ml. Moreover, in the PRISM study, Heeschen et al reported similar results using Tirofiban, another glycoprotein IIb/IIIa antagonist. It is already established that aspirin or intravenous heparin is absolutely beneficial for the prevention of cardiac events in such patients regardless of the pattern of ECG changes. However, in our Tokyo survey only 33% institutes gave aspirin and 17% gave heparin in such situations. Therefore, the present questionnaire survey strongly suggests the necessity of practical guidelines for the primary care of acute coronary syndrome and that the cardiac emergency network requires much more effective communication between the general practitioners, emergency rooms specialist hospitals and the Fire Department.

Acknowledgment
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References

Appendix

The following centers participated in this study:
Nippon Medical School, The First Department of Medicine; Ohbayashi Cardiology Clinic; Hakuijai Memorial Hospital; Ishikawa Cardiology Clinic; Okusawa Cardiology Clinic; Otoh Cardiology Clinic; Kamei Cardiovascular Clinic; Kenseidou Hospital; Kohda Cardiology Clinic; Hosoda Cardiology Clinic; Chiku Cardiology Clinic; Suzuki Cardiology Clinic; Hashimoto Cardiology Clinic; Morisugi Cardiology Clinic; Yamada Cardiology Clinic.