Prognostic Importance of Predischarged Troponin T Levels in Acute Anterior Myocardial Infarction

Bulent MUTLU,1 MD, Ahmet YILMAZ,1 MD, Kenan SONMEZ,1 MD, Elif EROGLU,1 MD, Muhsin TURKMEN,1 MD, and Yelda BASARAN,1 MD

SUMMARY

The baseline cardiac troponin T (cTnT) level strongly predicts short-term mortality in acute coronary syndromes, but the added value of predischarged (7th day) measures to predict short-term outcome and left ventricular (LV) remodeling in patients with ST elevation myocardial infarction (MI) is controversial.

Baseline, peak and predischarged cTnT results were evaluated in 52 patients (15 females, 37 males, mean age, 54.4 ± 8.8 years) with first acute anterior MI. There were 4 deaths (all cardiac origin) during the 30 day follow up period. Kaplan-Meier analysis revealed patients with a predischarged serum cTnT level higher than the median level (1.2 ng/mL) had a higher mortality rate than those with submedian levels (P < 0.05). Additionally, the highest correlation rate was found between predischarged cTnT values and LV ejection fraction (LV-EF, r = -0.58, P < 0.002). There were no differences between the groups in the 7th day left ventricular diastolic parameters, but the 30th day isovolumetric relaxation time and mitral E wave deceleration time were shorter (146.9 ± 30.1 vs 129 ± 23.4 msec, P = 0.025 and, 185.8 ± 51.8 vs 144.6 ± 58.1 msec, P = 0.012) in patients with higher predischarged cTnT level.

High levels of predischarged cTnT levels in patients admitted with first acute anterior MI defines a subgroup. These patients have poor systolic and diastolic functions and are at increased risk of short term mortality. This group of patients may have benefit from early intensive treatment strategies before discharge. (Jpn Heart J 2004; 45: 43-52)

Key words: Troponin, Myocardial infarction, Remodeling

ACCUMULATING data show that serum cardiac Troponin T (cTnT) and I are the most sensitive markers for myocardial injury. The greatest potential may lie in risk stratification because these parameters are more closely linked to mortality than CKMB or myoglobin.1-5

Short and long-term left ventricular functions are important prognostic criteria in acute myocardial infarction. Presence of myocardial damage and its severity in these patients can be assessed from the myocardial proteins appearing from the Department of Cardiology, Kosuyolu Heart and Research Hospital, Istanbul, Turkey.

Address for correspondence: Bulent Mutlu, MD, Department of Cardiology, Kosuyolu Heart and Research Hospital, Kadikoy, 81190, Istanbul, Turkey.

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in the circulation. Availability of cardiac specific tests like cTnT and Troponin I give us a chance to improve the clinical assessment, compared with other routine cardiac markers such as CK, CKMB, and myoglobin.\textsuperscript{1-5} Furthermore, the presence of cTnT in the circulation within 24 hours after AMI strongly reflects the degradation of myofilaments in irreversibly damaged cells on the first day of MI and is not affected by coronary status.\textsuperscript{6}

The aim of this study was to compare the traditional cardiac markers with early and predischarged bedside cTnT levels in order to determine their prognostic and diagnostic importance and estimation of LV function in anterior myocardial infarction.

**METHODS**

**Patient population:** We conducted a prospective study on consecutive patients admitted to the Coronary Care Unit of the Kosuyolu Heart and Research Hospital, for suspected large anterior MI, established by the presence of a typical pericardial pain lasting 30 minutes and an increase of 0.1 mV in ST displacements in 3 leads from V1-V6. Diagnosis of Q-wave MI was confirmed by both new Q-wave appearance and increased creatine kinase (CK) to more than the normal value (190 U/L). Exclusion criteria were any of the following: a previous myocardial infarction, left bundle branch block, myocardiopathy or valvular disease, atrial fibrillation, renal impairment (serum creatinin levels more than 2.5 mg/dL), or any other serious concomitant disease.

Thrombolytic therapy or primary PTCA was based on clinical criteria. The study protocol was approved by the ethics committee of the hospital and written informed consent was obtained from every patient who participated.

**Analysis of troponin T:** Three serial blood samples were obtained at admission, at the 12\textsuperscript{th} hour and on the 7\textsuperscript{th} day. Cardiac troponin T was measured quantitatively by a whole blood rapid bedside test (TROPT, Roche Diagnostics; Mannheim Germany). The detection limit of this assay was 0.2-2 ng/mL quantitatively.

**Analysis of creatinine kinase-MB:** Serial samples of blood, approximately 5 mL each, were drawn on arrival to the coronary care unit at admission and 3 h, 6 h, 12 h, 18 h, 24 h and 48 h after admission. The samples were assayed for creatinine kinase-MB utilizing a commercially available assay (Konelab 60i, Thermo Clinical Labsystem, Finland). A value of total creatinine kinase-MB of more than 25 IU/L was considered to be positive for detection of myocardial infarction.

**Echocardiography:** Two-dimensional echocardiography was performed with a Vingmed CFM 800 (Sonotron; Horten, Norway) and a 3.25-MHz transducer. We used apical 4- and 2-chamber views to determine left ventricular ejection fraction.
and left ventricular volumes using the biplane summation-of-disks method recommended by the American Society of Echocardiography. Mitral inflow parameters, including the early diastolic peak velocity (E), peak velocity at atrial contraction (A), E/A ratio, and mitral deceleration time (EDT) were measured using pulsed Doppler from the apical 4-chamber position with the sample volume position at the tips of the mitral valve leaflets during diastole. The isovolumetric relaxation time (IVRT), defined as the time from aortic valve closure to mitral valve opening, was assessed by simultaneously measuring the flow into the LV outflow tract and mitral inflow by Doppler echocardiography. All echocardiographic measurements were assessed on the 7th and 30th days of myocardial infarction.

**Follow-up:** All patients were invited to the hospital for noninvasive evaluation at the 30th day of the myocardial infarction. In patients who did not come to the hospital, follow-up was performed by telephone contact. Survival status and cause of death were established for all patients. Cause of death was classified according to the American Heart Association criteria.

**Statistical analysis:** Data were analyzed using the SPSS software package (version 10.1, SPSS, Chicago, Illinois, USA). Continuous variables are reported as the mean (SD) and categorical variables as percentages. Differences in the baseline demographics and outcome measures between the two cTnT groups were tested by nonparametric x² statistics. Correlations were tested by the Spearman rank correlation test (rₛ). Echocardiographic parameters were compared by Students t-test. Cumulative survival was assessed by the Kaplan-Meier method and groups were compared using the log rank test. A probability value of \( P < 0.05 \) was considered significant.

**RESULTS**

**Baseline characteristics:** Sixty-five patients out of 122 were classified according to the criteria above as acute anterior myocardial infarction. Only the first admission was included in the analysis; thus 52 patients were finally studied. Overall there were 4 deaths, all of cardiac origin, in the study group. One patient died suddenly after being discharged while 3 patients died due to refractory heart failure.

**Serum cTnT levels, baseline characteristics, and perfusion time:** The patients were divided into two groups according to the median 7th day cTnT level: the high (> 1.2 ng/mL) and the low (< 1.2 ng/mL) cTnT groups. The high cTnT group had a higher Killip classification and higher mortality rate than the low cTnT group (Table I). The low cTnT group had a shorter symptom to reperfusion therapy time (Table II).
Serum cTnT levels and left ventricular ejection fraction: Significant negative correlations were seen between admission cTnT, the 7th day cTnT, and CKMB peak values with the 7th day left ventricular ejection fraction (Table III). The serum 7th day cTnT level had the highest significant negative correlation with left ventricular ejection fraction in the chronic phase with first anterior myocardial infarction (n = 48, r = -0.50, P < 0.001, Table III).

Table I. Correlation Coefficients Between Biochemical Cardiac Markers and Left Ventricular Ejection Fractions

<table>
<thead>
<tr>
<th></th>
<th>r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission cTnT-LVEF 7th day</td>
<td>-0.57</td>
<td>0.0001</td>
</tr>
<tr>
<td>12th hour cTnT-LVEF 7th day</td>
<td>-0.20</td>
<td>NS</td>
</tr>
<tr>
<td>7th day cTnT-LVEF 7th day</td>
<td>-0.58</td>
<td>0.0001</td>
</tr>
<tr>
<td>Admission CK-MB-LVEF 7th day</td>
<td>-0.49</td>
<td>0.0001</td>
</tr>
<tr>
<td>CK-MBmax-LVEF 7th day</td>
<td>-0.55</td>
<td>0.0001</td>
</tr>
<tr>
<td>7th day cTnT-LVEF first month</td>
<td>-0.39</td>
<td>0.04</td>
</tr>
<tr>
<td>12th hour cTnT-LVEF first month</td>
<td>-0.20</td>
<td>NS</td>
</tr>
<tr>
<td>7th day cTnT-LVEF first month</td>
<td>-0.50</td>
<td>0.0001</td>
</tr>
<tr>
<td>Admission CKMB-LVEF first month</td>
<td>-0.39</td>
<td>0.047</td>
</tr>
<tr>
<td>CK-MBmax-LVEF first month</td>
<td>-0.42</td>
<td>0.004</td>
</tr>
</tbody>
</table>

cTnT = troponin-t; LVEF = left ventricular ejection fraction; CK-MB = creatin kinase myocardial isoenzyme.

Table II. Baseline Characteristics and 30-Day Mortality Values of Patients According to 7th Day cTnT Subgroups

<table>
<thead>
<tr>
<th></th>
<th>cTnT 1.2 (26)</th>
<th>cTnT &gt; 1.2 (26)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (% female)</td>
<td>8 (31%)</td>
<td>6 (23%)</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.9 ± 8.3</td>
<td>56.7 ± 8.6</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6 (23%)</td>
<td>9 (34%)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>20 (76%)</td>
<td>17 (65%)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>12 (46%)</td>
<td>13 (50%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8 (31%)</td>
<td>9 (35%)</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>119 ± 21.7</td>
<td>123 ± 26.5</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>70 ± 11.5</td>
<td>73 ± 13.0</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate</td>
<td>80.7 ± 9.2</td>
<td>83.4 ± 9.1</td>
<td>NS</td>
</tr>
<tr>
<td>Killip Classification</td>
<td>I 23 (89%)</td>
<td>12 (46%)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>II 3 (11%)</td>
<td>11 (42%)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>III 0</td>
<td>2 (8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV 0</td>
<td>1 (4%)</td>
<td></td>
</tr>
<tr>
<td>30-day mortality</td>
<td>0</td>
<td>4 (15.4%)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

cTnT = Troponin-T.
Serum cTnT levels and left ventricular systolic and diastolic parameters: The high cTnT group had a lower ejection fraction in the 7th day and 30th day measurements. There were no differences between the two groups in the 7th day diastolic measurements, but the high cTnT group had a higher mitral E/A ratio and shorter EDT and IVRT in the 30th day echocardiographic measurements (Table IV).

**DISCUSSION**

This study shows that the presence of cTnT concentrations of 1.2 ng/mL on the 7th day in patients who have sustained an anterior myocardial infarction identifies a group at significant risk for left ventricular dysfunction, remodeling, and cardiac death on subsequent short term follow-up.
For over twenty years cardiac markers have played an important role in the diagnosis of acute coronary syndromes. These cardiac markers also play an important role in the diagnosis of patients with suspected AMI and ST segment elevation, but have been deemed to have little clinical and prognostic value. CKMB, which is being used as a gold standard in the diagnosis of MI, becomes positive only when myocardial necrosis develops. Additionally, CKMB values in long-term prognoses are quite low. In patients with non-Q wave MI, even though the CKMB values are quite low, the recurrence of ischemia is greater and the area under ischemia is larger than the others. Because of these limitations, new markers have been developed for the determination of myocardial injury. cTnT, which is one of these markers, is a regulatory protein in the thin filaments of myocardial cells and has been shown to have very high sensitivity and specificity in the diagnosis of myocardial injury and necrosis.\(^1\)\(^{-6}\),\(^\text{12}\) Besides its diagnostic value, cTnT is an important marker in acute coronary syndromes and/or in the prognostic evaluation of patients who have been admitted to a coronary care unit with angina pectoris. Additionally, the early presence of one of these new, highly specific cardiac structural proteins, cTnT, has been found to have important prognostic significance in patients with unstable angina pectoris.\(^\text{12}\)\(^{-14}\)

The level of myocardial injury and the degree of LV dysfunction are the most important factors in the definition of prognosis and clinical development. Furthermore, there are very few studies that have shown the prognostic value of cTnT in patients with Q wave MI and the relationship between LV functions.\(^\text{14}\)

Traditional biochemical markers such as CK and CKMB do not have high sensitivity and specificity rates in diagnosing small infarcts and the area under risk.\(^3\)\(^{,6}\),\(^\text{15-19}\) In addition, cTnT has high sensitivity and specificity rates in the determination of myocardial injury, and a close chimeric relationship has been shown between myocardial destruction and the cTnT released from cells.\(^5\) With these qualifications, in our study, the values of cTnT in the prediction of LV function have been investigated using a rapid bedside assay.\(^\text{13}\),\(^\text{19-24}\) Quantitative bedside cTnT measurements were preferred because they are rapid and independent from laboratory assessment.

The aim of our study was to compare the traditional cardiac markers with cTnT in terms of their prognostic and diagnostic values and their importance in the prediction of LV function. First, the correlation between cTnT and LV function was investigated and then the median value of the 7\(^{\text{th}}\) day cTnT values, which is 1.2 ng/mL, was taken as the cutoff value for the classification of subgroups. Clinical, echocardiographic, biochemical, and treatment differences were evaluated between these subgroups.

**cTnT and left ventricular function:** In our study, we obtained results similar to these of previous studies in terms of the comparison of first, maximal, 7\(^{\text{th}}\) day val-
ues and LV function between cTnT and classical cardiac markers.\(^5,25\) We also found a statistically significant high correlation between early phase LV function and first and 7th day cTnT and CKMB values. Therefore, the correlations between late phase LV function and all other data are found to be decreased, except for the high negative correlation of 7th day cTnT. When this correlation was evaluated, it was found that both the 24th hour and peak CKMB values were very important in the evaluation of early phase functions; at later phases these values lose their qualifications. Therefore, it is not absolutely certain that serum cTnT levels and the levels after 24 hours have an importance in long-term prognosis and in the prediction of LV function. In patients who were admitted to the CPU with AMI, cTnT levels on day 1 are strongly correlated with coronary reperfusion and the levels of free cTnT released from myofilaments. In contrast, the kinetics of cTnT released 1 day after AMI are unaffected by coronary reperfusion and reflect the degradation of myofilaments in irreversibly damaged cells.\(^5\) Previous studies have demonstrated a negative correlation between cTnT levels and LV function, and late term mortality, especially on the 3rd to 5th days after AMI.\(^26\)

cTnT and left ventricular diastolic parameters: In our study, we examined not only early and late term LV systolic function, but also diastolic function as well. It is known that LV systolic function is an important predictor in mortality and morbidity after MI.\(^26,27\) Doppler echocardiography is used in examining diastolic function in MI and a restrictive flow pattern in particular has been shown to be correlated with the development of congestive heart failure and an increase in mortality.\(^28-33\) Therefore, in our study, systolic function as well as diastolic function were evaluated by pulsed wave Doppler in patients with acute anterior MI. In the subgroup comparison conducted using the 7th day median cTnT values, no differences were found in early phase diastolic parameters, whereas a difference was observed in the late phase measurements (Table III). In particular, the LV diastolic pattern changes in patients with higher predischarged cTnT are seen to be independent from LV systolic function (Table III). In previous studies, diastolic function has been shown to have an importance in remodeling and a prognostic value in increasing mortality and morbidity in AMI patients. The incidences of CHF and sudden death were shown to be increased in patients with an EDT < 140 ms.\(^34\) In our study, considering that almost half of the patients in group 2 had EDT values under 140 ms, it could be said that high 7th day cTnT values are the marker of remodeling.

cTnT reperfusion specifications: After evaluating all of the echocardiographic parameters, we conclude that the cases with lower predischarged cTnT were successful and the reperfusion ratios of that group were high (Table IV). After eval-
uation of the onset time of MI and style of reperfusion in this group, it was seen that all cases which primary PTCA have been performed, were from this group and also the reperfusion process was started earlier, whereas there were no differences between these two groups in terms of thrombolytic therapy and administration incidence (Table IV).

These results show that not only reperfusion alone but also its onset, and dependently, the myocardial area that survived without damage, demonstrate the importance of remodeling and its prognostic value in the late phase.

**Clinical approach:** The importance of LVEF and LV function in remodeling and early and late term mortality have been demonstrated in large trials. Evaluation of LV function, especially diastolic parameter measurements, is time consuming and thus not applicable to all cases, whereas the quantitative bedside cTnT measurement is rapid, easy, and independent from the laboratory so it can easily be used for the estimation of early and late phase LV function and mortality. Early identification of this group of patients might increase both the benefits of the medical therapies and the early invasive treatment approaches.

**Study limitations:** Bedside cTnT measurement, which has had limitations in diagnostic evaluations, could not be done in most of the cases in terms of the definition of prognosis and LV functions because its maximum value is 2 ng/mL. Because of this limitation no correlation was observed between its peak values and LVEF.

The importance of late term cTnT values has been proven in early and late term prognosis and the estimation of LV function. Also, an EDT value less than 140 msec was shown to be important in remodeling, late phase CHF development and prognosis.34) This is why we assessed the mean values of mitral flow instead of diastolic function in subgroups as a basic value. Patients without previous MI and with anterior MI have been included in our study. Therefore, the results cannot be extrapolated to all myocardial infarction groups.

**Conclusion:** Rapid bedside 7th day cTnT measurement is not only a diagnostic and prognostic marker, but also an easy, practical, and potent noninvasive method in the definition of late and early phase LV systolic and/or diastolic function, as well as the estimation of remodeling development in late phase.

**REFERENCES**


