Implication of Different Cardiac Troponin I Levels for Clinical Outcomes and Prognosis of Acute Chest Pain Patients

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OBJECTIVES We compared outcomes in patients with non–ST-segment elevation acute coronary syndromes (ACS) according to the degree of cardiac troponin I (cTnI) elevation.

BACKGROUND Controlled trials of high-risk patients have found that troponin elevations identify an even higher risk subset. It is unclear whether outcomes are similar among a lower risk, heterogeneous patient group. Also, few studies have reported outcomes other than myocardial infarction (MI) or death, based on the peak troponin value.

METHODS Consecutively, admitted patients without ST-segment elevation on the initial electrocardiogram underwent serial marker sampling using creatine kinase (CK), CK-MB fraction, and cTnI. Patients were grouped according to peak cTnI: negative = no detectable cTnI; low = peak greater than the lower limit of detectability but less than the optimal diagnostic value; intermediate = peak greater than or equal to the optimal diagnostic value but less than the manufacturer’s suggested upper reference limit (URL); and high = peak greater than or equal to the URL. Thirty-day outcomes included cardiac death, MI based on CK-MB, revascularization, significant disease, and a reversible defect on stress testing. Six-month mortality was also determined. Negative evaluations for ischemia included nonsignificant disease, no reversible stress defect, and negative rest perfusion imaging.

RESULTS Of the 4,123 patients admitted, 893 (22%) had detectable cTnI values. Cardiovascular events and positive test results at 30 days and 6-month mortality increased significantly with increasing cTnI values. Negative evaluations for ischemia were significantly and inversely related to peak cTnI values. Although adverse events were significantly more common in patients with a low cTnI value than in those with negative cTnI, negative evaluations for ischemia were frequent.

CONCLUSIONS Increased cTnI values are associated with worse outcomes. Although low cTnI values are associated with adverse events, they do not have the same implication as higher cTnI values, and nonischemic evaluations are frequent.

Both cardiac troponin T (cTnT) and I (cTnI) have a higher sensitivity for detecting myocardial necrosis than do traditional cardiac markers (1,2). They also add significant incremental diagnostic and prognostic value to routine clinical and electrocardiographic (ECG) variables for identifying patients at risk of cardiac events (3,4). These advantages led a joint committee of the European Society of Cardiology and American College of Cardiology (ESC/ACC) to recommend that patients who have detectable cardiac troponin, as a result of myocardial ischemia, be diagnosed as having acute myocardial infarction (MI) (5).

Patients with troponin elevations appear to benefit preferentially from antiplatelet (6–8) and antithrombotic treatment (9), as well as early coronary angiography (2). As a result, these treatment strategies have been incorporated into recommendations for the treatment of patients with non–ST-segment elevation acute coronary syndromes (ACS) (3,4). However, these recommendations were based primarily on studies that evaluated outcomes in higher risk patients enrolled in ACS trials. In addition, the definition of positive troponin varies substantially among the studies (2,6,7,10–12). Therefore, the conclusions drawn are difficult to apply and may not be valid in lower risk patients, such as those undergoing an evaluation in the emergency department (ED), particularly those with lower troponin concentrations. In this study, we assessed outcomes based on different peak cTnI values in a large, consecutive group of patients admitted from the ED for exclusion of myocardial ischemia.

METHODS This study was performed at a 600-bed, inner-city hospital with approximately 85,000 ED visits and 1,500 coronary...
Abbreviations and Acronyms

ACS = acute coronary syndromes
CCU = coronary care unit
CI = confidence interval
CK = creatine kinase
cTnI = cardiac troponin I
cTnT = cardiac troponin T
CV = coefficient of variation
ED = emergency department
ESC/ACC = European Society of Cardiology/ American College of Cardiology
LLD = lower limit of detectability
MI = myocardial infarction
MPI = myocardial perfusion imaging
URL = upper reference limit

A total of 4,567 consecutive patients were admitted to the CCU from June 1996 through March 2000. For patients with multiple admissions during each study period, only the first admission was included in the analysis. Patients with ST-segment elevation who met criteria for ACS (e.g., absence of ischemic ECG changes) underwent further risk stratification using rest myocardial perfusion imaging (MPI) (13). Moderate-risk patients are admitted as observation patients and undergo serial marker sampling to exclude MI. Low-risk patients undergo rest MPI in the ED and are discharged and scheduled for outpatient stress testing if the images are either negative or unchanged from previous studies. Markers are not routinely measured in these patients. Patients with positive MPI are considered high risk and admitted for MI exclusion.

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Markers. All patients underwent serial testing for creatine kinase (CK) and CK-MB by mass assay at 0, 3, 6, and 8 h and cTnI at 0 and 8 h after presentation. Patients who had positive markers or recurrent or continuing symptoms had sampling continued at 6- to 8-h intervals until a peak value was reached or a diagnosis was made. The peak cTnI value during the first 24 h was used for analysis.

Centrifuged plasma was filtered before CK-MB and cTnI analyses. Two different diagnostic assays for CK-MB and cTnI were used. From June 1996 to May 1998, the Opus Magnum Analyzer (Behring Diagnostics, Boston, Massachusetts) was used. The lower limit of detectability (LLD) for this assay was 0.5 ng/ml, and the suggested diagnostic value for MI (upper reference limit [URL]) was 2.5 ng/ml (14). The 99th percentile for patients without coronary disease was <0.5 ng/ml. The coefficients of variation (CV) reported by the manufacturer were 12% and 5% for cTnI values of 3.0 and 19 ng/ml, respectively. The CV values for lower cTnI values were not available. Outcomes for these patients have been reported in detail previously (15). The current study represents expansion of outcomes assessed, as well as analysis using different cTnI diagnostic values from a previous study (15). From May 1998 to April 2000, cTnI was analyzed using the Bayer assay (Bayer Corp., Tarrytown, New York). The LLD for this assay was 0.1 ng/ml, and the suggested diagnostic value for MI was 0.9 mg/ml (10). The 99th percentile determined in 200 patients without evidence of coronary disease was <0.1 ng/ml. The CV for this assay at our institution was <15% at a cTnI concentration of 0.3 ng/ml. For CK-MB, an URL of 8.0 ng/ml was used for both assays.

For each of the two assays, we chose an optimal diagnostic value for cTnI (Opus, 1.0 ng/ml; Bayer, 0.3 ng/ml), which improved specificity without affecting sensitivity, compared with the reference standard CK-MB MI definition. Sensitivity (96% vs. 97%) and specificity (93% vs. 92%) at the optimal diagnostic value were similar and not statistically different for the two assays. In addition, they were equivalent to the recent ESC/ACC definition of MI. Patients were then separated into four groups according to peak cTnI values: 1) negative = no detectable cTnI; 2) low = peak cTnI values greater than or equal to the LLD and less than the optimal diagnostic value; 3) intermediate = peak cTnI values greater than or equal to the optimal diagnostic value but less than the URL; and 4) high = peak cTnI values greater than or equal to the URL.

The results from the two assays were subsequently combined because the areas under the receiver-operating characteristics curve for the two assays (Opus assay, 0.977 ± 0.04; Bayer assay, 0.971 ± 0.04) were comparable and not significantly different, indicating similar diagnostic test performance. In addition, there was no significant difference between the two groups in the baseline characteristics associated with adverse cardiac outcomes and test results in ACS patients (Table 1).

Outcomes. Patient outcomes occurring within 30 days of admission were assessed. When a patient experienced more than one cardiac event, only one was considered, based on the following order: cardiac death, criteria for MI at the time of admission, late CK-MB MI (>24 h but within 30 days), revascularization, significant coronary disease, and a reversible defect on stress imaging. Negative evaluations for ischemia were assessed in a similar fashion and included nonsignificant disease on angiography, a normal or fixed defect on stress MPI, and negative rest MPI during the ED evaluation. Cardiac death was defined as death due to MI, coronary artery disease, or arrhythmia. In addition, six-month cardiac mortality was also assessed. Mortality was determined using chart review, scripted phone interviews,
and death registry data from the Virginia Division of Health Statistics and the Social Security Death Index. The definition of CK-MB MI was an elevation of CK-MB ≥8.0 ng/ml, with a relative index ≥4.0 (CK-MB × 100/total CK), in association with a characteristic marker rise and fall. Significant coronary disease was defined as ≥60% left main stenosis and ≥70% stenosis in a major coronary artery, its branches, or a bypass graft supplying myocardium at ischemic risk. Stress testing was performed using symptom-limited exercise or pharmacologic stress with single-photon emission computed tomographic MPI and was considered abnormal if there was a reversible defect. Rest MPI was considered positive if there was a perfusion defect in conjunction with abnormal wall motion or thickening (13). An ischemic ECG was defined as transient ST-segment elevation, ST-segment depression ≥1 mm, or ischemic T-wave inversion (symmetrical T-wave inverted ≥2 mm).

Statistical analysis. Results were compared using the Student t test for continuous variables and chi-square analysis for dichotomous variables. A value of p ≤ 0.05 was considered significant in most cases. When differences in cardiac outcomes were compared among the different cTnI groups, a value p < 0.017 was required to correct for multiple comparisons. Cardiovascular mortality was shown using the Kaplan-Meier method, with comparisons made using the log-rank test. Significance of the trend toward an increasing incidence of adverse outcomes and a decreasing incidence of negative ischemic evaluations was assessed using linear regression analysis. A Cox regression model was used to model the hazard of six-month cardiac mortality as a function of cTnI positivity. The Wald test was used to test for all pairwise difference in hazard rates. The Bonferroni correction was used for multiple testing. Statistical analyses were performed using SAS version 8.2 (Cary, North Carolina).

RESULTS

The characteristics and demographic variables of the 4,123 patients are shown in Table 1. A total of 346 patients (8.4%) had CK-MB MI. Of the 893 patients (22%) who had detectable cTnI values, 425 (10%) had cTnI values greater than the URL (high cTnI), 198 (4.8%) had cTnI values less than the URL but greater than or equal to the optimal diagnostic value (intermediate cTnI), and 270 (6.5%) had cTnI values less than the optimal diagnostic value but greater than the LLD (low cTnI). Serial testing made a difference in classifying these patients, as the initial cTnI often did not reflect the final classification. Among the low cTnI group, 45% had negative cTnI initially. Similarly, 49% of patients in the intermediate cTnI group had initial cTnI values that were negative (29%) or low (20%), and 52% of those who had high cTnI values had initial values that were negative (29%), low (13%), or intermediate (9%). Therefore, if only the initial cTnI were used, 50% of the patients with detectable cTnI values would have been misclassified.

Thirty-day and six-month follow-up was complete in 92% and 96%, respectively. Patients who did not have follow-up were significantly less likely to have cTnI elevations and revascularization, were younger, had fewer risk factors for coronary disease, and were more likely to have an evaluation negative for ischemia. Additional diagnostic testing was performed within 30 days of admission in 73% of patients (n = 3,020). A total of 1,508 patients (37%) underwent coronary angiography, with 579 (14%) undergoing revascularization. Stress MPI was performed in 1,116 patients (27%) who did not undergo coronary angiography, and 396 patients (9.6%) had negative rest MPI during the initial ED evaluation but did not undergo further diagnostic testing, other than serial marker sampling. At least one end point (cardiac death or CK-MB MI, or additional diagnostic testing) was present in 76%, 69%, 67%, and 92% of patients who had negative, low, intermediate, or high peak cTnI values, respectively. The distribution of test results based on peak cTnI values are shown in Table 2.

Six-month cardiac mortality is shown in Figure 1. There was a highly significant (p < 0.0001) stepwise increase in cardiac mortality as peak cTnI increased. After correcting
for multiple comparisons, mortality was significantly higher in all cTnI groups, including the low cTnI group, compared with the negative cTnI group (p < 0.01). In addition, mortality was significantly different between the low and intermediate cTnI groups and the intermediate and high cTnI groups were not statistically significant. Compared with the negative cTnI group, the hazard ratio for the low cTnI group was 2.5 (95% confidence interval [CI] 1.4 to 4.4), 3.9 for the intermediate cTnI group (95% CI 2.3 to 6.8), and 6.1 for the high cTnI group (95% CI 4.2 to 8.7).

Thirty-day outcomes based on peak cTnI values are shown in Figure 2. In each of the outcome categories, the trend toward an increasing incidence of ischemic outcomes with increasing peak cTnI was highly significant. Figure 2 also shows the differences between each cTnI group. Only a small minority of patients who had low or negative cTnI values met CK-MB criteria for MI. In contrast, the majority of patients with high cTnI values had CK-MB MI. The results were essentially unchanged after excluding patients who had CK-MB MI at the time of admission (Fig. 3).

The incidence of evaluations that were negative for ischemia showed an inverse relation to peak cTnI values, decreasing as peak cTnI values increased. An evaluation that was negative for ischemia (CK-MB MI excluded and either nonsignificant coronary disease, no reversible stress defect, or negative rest MPI) was found in 54% of those without cTnI elevations, 42% of those with low cTnI values (p < 0.001 vs. negative cTnI group), 22% of those with intermediate values (p < 0.001 vs. low cTnI group), and only 8.7% of those with high cTnI values.

Because the distinction between negative cTnI and low cTnI values was of particular interest, the two groups were further analyzed. When the two groups were compared, the differences in six-month cardiac mortality was significant (p < 0.02) (Fig. 1). Events at 30 days (including the combinations of death and MI; death, MI, and revascularization; and death, MI, and significant disease) also differed significantly (Figs. 2 and 3). When patients in the low cTnI group who had an ischemic evaluation were compared with those who did not, the only variables different were the presence of an ischemic ECG (22% vs. 10%, p < 0.05) and ECG evidence of previous MI (20% vs. 9%, p < 0.05).

When outcome and test results were analyzed individually, a similar gradient appeared, with the incidence of death, MI, revascularization, and significant disease increasing as cTnI values increased. Also, the incidence of negative cardiac evaluations decreased as peak cTnI values increased.

| Table 2. Cardiac Outcomes and Test Results Based on Peak Cardiac Troponin I Value |
|---------------------------------|-------|-------|----------|----------|---------|----------|----------|
|                                 | Death | MI    | Revasc.  | Sig Dz   | (+) Stress | Non-Sig Dz | (-) Stress | (-) MPI  |
| None (n = 3,229)                | 22 (0.7%) | 8 (0.2%) | 306 (9.5%) | 541 (17%) | 298 (9.2%) | 488 (15%) | 967 (30%) | 353 (11%) |
| Low cTnI (n = 270)              | 6 (2.2%)   | 3 (1.1%)  | 42 (16%)  | 59 (22%)  | 19 (7.0%)  | 37 (14%)  | 56 (21%)  | 29 (11%)  |
| Intermediate cTnI (n = 198)    | 6 (3.0%)   | 29 (15%)  | 49 (25%)  | 67 (34%)  | 6 (3.0%)   | 20 (10%)  | 22 (11%)  | 9 (4.5%)  |
| High cTnI (n = 426)            | 30 (7.0%)  | 306 (72%) | 186 (44%) | 264 (62%) | 14 (3.3%)  | 31 (7.3%) | 15 (3.5%) | 5 (1.2%)  |

A patient could have more than one event or test result. Data are expressed as the number (%) of subjects.

cTnI = cardiac troponin I; MI = myocardial infarction; MPI = myocardial perfusion imaging; Revasc. = revascularization; Sig Dz = significant disease; (+) = positive; (−) = negative.

Figure 1. Kaplan-Meier curves of six-month cardiac mortality for the different cardiac troponin I (cTnI) values. The trend toward increased mortality and increased cTnI was highly significant (p < 0.001). In addition, mortality was significantly different (p < 0.01) between the negative (neg) cTnI and low, intermediate (inter), and high cTnI groups.
The only exception was a positive stress test result, which was likely due to coronary angiography being performed as the preferred initial evaluation.

**DISCUSSION**

In this large study of ED chest pain patients without ST-segment elevation on the initial ECG, we found a significant incremental increase in cardiac events and positive test results as the peak cTnI value increased. Low peak cTnI values predicted cardiac events, but negative evaluations for ischemia were also common. Importantly, these relationships persisted after excluding CK-MB MI at the time of admission as an end point.

We separated patients into four groups based on their peak cTnI value, using the URL, LLD, and optimal diagnostic value as decision limits. The first two were chosen because they are the most commonly used values in research studies and clinical practice (2,10,16,17). The third—the optimal diagnostic value—was chosen using receiver operating characteristic curve analysis, which allows...
more appropriate selection of a diagnostic value through optimization of sensitivity and specificity (18). This value was similar to the one proposed by the ESC/ACC (10% CV) (5).

**Non-MI end points.** The majority of reports analyzing outcomes based on troponin positivity used only the "hard" end points of MI and death. However, these outcomes occur in only a minority of patients; therefore, this approach provides only a limited assessment of the diagnostic ability of troponin. It also fails to identify patients in whom outcomes may be impacted by subsequent treatment, such as revascularization. Studies that have reported other outcomes, such as stress testing (19,20) or coronary angiography (21), typically included too few patients to analyze outcomes based on different troponin levels. Only two studies did include sufficient numbers, allowing stratification by troponin concentration (22,23). Although performed in a population of predominately high-risk ACS patients, both studies reported results similar to ours: increasing troponin values were associated with a higher prevalence of positive stress tests, significant coronary disease, and revascularization procedures (22,23). Our results extend this finding to lower risk patients. In addition, we found that negative ischemic evaluations increased with decreasing cTnI values.

**Low cTnI and outcomes.** Because cardiac troponin is not normally found in the blood, small amounts of damage, which may not meet traditional criteria for MI, can be detected. Studies performed in high-risk ACS patients did not find any concentration of detectable troponin that was not associated with increased risk (1,2,5,24). This observation led to the current recommendation that, in the proper setting, any detectable troponin should be considered pathologic and indicative of MI (5). In addition to identifying troponin as the preferred diagnostic marker, the recommendations also specified that the diagnostic cut-off value should be >99th percentile. The LLD for the two assays used in the present study met this criteria, as they were undetectable in large control groups.

Several studies that used the LLD for cTnI (2,25) and cTnT (2) observed that the presence of these minor elevations was associated with a significantly higher cardiac event rate, compared with the absence of detectable troponin. In contrast, other studies performed in lower risk patient populations found no such difference (16,26–28). This discrepancy can be attributed to two factors: patient risk and cohort size. Unlike patients in most ACS trials which have a high prevalence of MI, most ED patients have a low overall risk. Greater numbers of patients are therefore required to demonstrate a significant difference in outcomes. The large number of patients in the current study allowed us to demonstrate a stepwise increase in events with increasing cTnI values, confirming that even small cTnI elevations have prognostic significance.

However, evaluations that were negative for ischemia were common in patients with low cTnI values. One explanation is that previous treatment and preprocedural delays resulted in thrombus resolution by the time angiography was performed (29). Positive cTnI values in patients with negative imaging could be related to the relative insensitivity of MPI, as approximately 3% to 5% of myocardium must be ischemic for detection (30). Another possible mechanism is the release of small amounts of troponin resulting from global ischemia and patchy necrosis, such as during a hypertensive crisis or severe heart failure, rather than through prolonged ischemia and infarction from epicardial coronary artery disease. However, the high number of patients with low cTnI elevations who did not have events suggests that most discrepancies represent analytical false-positive results due to the assays themselves, rather than necrosis.

Troponin I values just above the LLD have been a source of considerable diagnostic confusion. In contrast to ACS trials, only a minority of ED patients with chest pain have diagnostic ECG changes. Because atypical presentations are frequent, the presence of troponin elevations is often the primary, if not only, criterion used to diagnose these patients as having MI. Spurious elevations have been frequent enough in some studies (31–33) so that the term "troponinosis" (33) has been coined to describe them.

A high prevalence of analytical false-positive results has important implications for the treatment of chest pain patients. Troponin-positive patients appear to benefit preferentially from more intensive antiplatelet and antithrombotic therapy (6,7,12,16,34), as well as early coronary angiography with revascularization, when appropriate (2,12). Recommendations for the treatment of patients with non–ST-segment elevation ACS now use the detection of troponin to guide diagnostic and therapeutic measures (3,4). Given the high frequency of negative subsequent evaluations in chest pain patients with low troponin elevations, such intensive treatment may not be warranted in all patients (16,35). Rather, treatment decisions should be based on clinical variables indicative of high risk, such as an ischemic ECG or previous MI.

The high frequency of analytical false-positive troponin values near the LLD led to the ESC/ACC recommendation of ≤10% CV at the diagnostic value (5). Almost none of the currently available cTnI assays (36–38) or the current cTnT assay (39) are able to achieve this. Thus, fulfilling this requirement will require a higher diagnostic value, often two to three times the LLD. Values that fall between the LLD and the diagnostic value are therefore indeterminate and are not to be considered diagnostic of MI.

It is unclear what these indeterminate troponin values should be called. Based on the ESC/ACC definition, they would be considered negative. However, our data, as well as those of others (2), indicate that these lower cTnI values have prognostic value, so disregarding them is not appropriate. Our data suggest that until assays meeting the criteria specified by the ESC/ACC are available, the use of two decision limits, as suggested by the National Academy
of Clinical Biochemists (40), may be necessary. The MI would be diagnosed if the troponin value exceeded the diagnostic limit, whereas lower values would be considered equivocal, with further clinical correlation and evaluation required.

**Study limitations.** Although the current study is observational, it has several advantages over many previous studies in which troponin analyses were reported as substudies of controlled clinical trials. In most multicenter trials, sampling was performed at only one time point, reducing accuracy. In contrast, we performed serial sampling in all patients. The prespecified inclusion and exclusion criteria used in multicenter trials frequently lead to high-risk, relatively homogeneous populations (1,6–12) in which women and the elderly are under-represented (17). Assessing a test’s performance in only a high-risk population results in substantial bias, thus limiting the ability to generalize the results. Therefore, studies such as ours are important to complement the information obtained from randomized, clinical trials. Although this was a single-center study, the patient characteristics and outcomes, including the proportion of patients who had CK-MB MI (25,28,41,42) and troponin elevations without CK-MB MI (25,27,28,42), were similar to those reported in both single- and multicenter studies, indicating that these results should be generalizable to other sites, as long as the definition of troponin positivity is consistent with the recent consensus recommendations (5).

Not all patients underwent diagnostic testing beyond serial marker analysis. This reflects actual clinical practice in which individual patient variables and clinical judgment ultimately determine what, if any, additional testing is necessary. However, the trend toward increased events as cTnI values increased was consistent across the spectrum of outcome events. Also, physicians were not blinded to the cTnI values; therefore, further care was based in part on these results. Although clinical trials blind physicians to troponin values, myocardial markers, including cTnI, are routinely assessed in all patients admitted to most U.S. hospitals (43). The range of diagnostic testing performed in patients with and without cTnI elevations suggests that the decisions were based on the entire clinical presentation rather than the cTnI results alone. We used cardiac rather than all-cause mortality as an end point. In contrast to clinical trials, in which the majority of patients have a high prevalence of coronary disease, many of the patients included in the current study had a nonischemic cause for their chest pain, which would have increased the overall mortality in the lower risk patients. Although follow-up was not complete, it was comparable to previous studies, and patients without follow-up were at lower risk. Our use of the Virginia Death Registry, as well as the Social Security Death Index, which has been demonstrated to have a high specificity (44), further supports the veracity of our conclusions.

**Conclusions.** Cardiac troponin I elevations are associated with an increased adverse event rate, although low cTnI values are frequently associated with a high rate of negative evaluations for ischemia. Therefore, the degree of troponin elevation, as well as clinical variables such as previous MI and an ischemic ECG, should be considered when deciding treatment.

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**REFERENCES**


16. Heeschen C, Hamm CW, Goldmann B, Deu A, Langenbrink L, White HD. Troponin concentrations for stratification of patients with acute coronary syndromes in relation to therapeutic efficacy of tirofi-


29. Heeschen C, van den Brand MJ, Hamm CW, Simoons ML. Angio-

30. Verani MS, Jeroudi MO, Mahmorian JJ, et al. Quantification of myocardial infarction during coronary occlusion and myocardial sal-


33. Ng SM, Krishnaswamy P, Morrisey R, Clopton P, Fitzgerald R, Maisel AM. Mitigation of the clinical significance of spurious eleva-
tions of cardiac troponin I in settings of coronary ischemia using serial testing of multiple cardiac markers. Am J Cardiol 2001;87:994–7.


42. Zimmerman J, Fromm R, Meyer D, et al. Diagnostic marker coop-
