ELEVATED CARDIAC TROPONIN LEVELS IN CRITICALLY ILL PATIENTS: PREVALENCE, INCIDENCE, AND OUTCOMES

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BACKGROUND Levels of cardiac troponin, a sensitive and specific marker of myocardial injury, are often elevated in critically ill patients.

OBJECTIVES To document elevated levels of cardiac troponin I in patients in a medical-surgical intensive care unit and the relationship between elevated levels and electrocardiographic findings and mortality.

METHODS A total of 198 patients expected to remain in the intensive care unit for at least 72 hours were classified as having myocardial infarction (cardiac troponin I level ≥1.2 µg/L and ischemic electrocardiographic changes), elevated troponin level only (≥1.2 µg/L and no ischemic electrocardiographic changes), or normal troponin levels. Events were classified as prevalent if they occurred within 48 hours after admission and as incident if they occurred 48 hours or later after admission. Factors associated with mortality were examined by using regression analysis.

RESULTS A total of 171 patients had at least one troponin level measured in the first 48 hours. The prevalence of elevated troponin level was 42.1% (72 patients); 38 patients (22.2%) had myocardial infarction, and 34 (19.9%) had elevated troponin level only. After the first 48 hours, 136 patients had at least 1 troponin measurement. The incidence of elevated troponin level was 11.8% (16 patients); 7 patients (5.1%) met criteria for myocardial infarction, and 2 (1.5%) had elevated troponin level only. Elevated levels of troponin I at any time during admission were associated with mortality in the univariate but not the multivariate analysis.

CONCLUSIONS Elevated levels of cardiac troponin I in critically ill patients do not always indicate myocardial infarction or an adverse prognosis. (American Journal of Critical Care. 2006;15:280-289)
Elevated levels of cardiac troponin not due to acute coronary syndromes have been reported in various populations of patients in the intensive care unit (ICU): heterogeneous medical and surgical patients and critically ill patients with systemic hypotension and with conditions such as trauma, sepsis, pulmonary embolism, stroke, renal failure, and chronic obstructive pulmonary disease. The prevalence of increased levels ranges from 15% to 70% in the general ICU population, and estimates for the prevalence in critically ill patients with sepsis or septic shock are 31% to 80%. Abnormal serum levels of cardiac troponin have been detected in critically ill patients with non-cardiac diagnoses; in the study by Ammann et al, more than 70% of ICU patients with elevated cardiac troponin levels did not have flow-limiting coronary artery disease as indicated by stress echocardiography or by findings at autopsy.

Elevated troponin levels are clinically important because they may act as an adverse prognostic marker. The prognostic value of elevated serum levels of cardiac troponin is well recognized outside the ICU setting. However, in critically ill patients, the prognostic value and the relationship between elevated cardiac troponin levels and a diagnosis of myocardial infarction remain uncertain. In the consensus document of the Joint European Society of Cardiology/American College of Cardiology (ESC/ACC) Committee, myocardial infarction is defined on the basis of pathological findings or on the basis of a typical rise and fall in biochemical markers of myocardial necrosis and the presence of at least one of the following: ischemic signs and symptoms, electrocardiographic (ECG) signs of ischemia or necrosis, or a coronary artery intervention. In the ICU, endotracheal intubation, coma due to underlying illness, and use of sedatives and narcotics all limit the ability of patients to report symptoms associated with ischemia. Therefore, in practice, a combination of elevated levels of cardiac troponin and ECG changes indicating ischemia are frequently used to establish a diagnosis of myocardial infarction in the ICU. Use of coronary angiography, routine echocardiography, and continuous ECG recordings is either not feasible on a routine basis or has not been well studied in critically ill patients. Nevertheless, recognition of myocardial infarction in critically ill patients most likely is important because the development of myocardial infarction may contribute to increased morbidity and mortality.

Outside the ICU setting, patients with a diagnosis of myocardial infarction benefit from thrombolytic therapy, coronary revascularization, and use of anticoagulants, antiplatelet agents, β-blockers, statins, and angiotensin-converting enzyme inhibitors. However, myocardial infarction due to nonthrombotic mechanisms may not respond favorably to antithrombotic agents, and the impact of these therapies on outcomes in ICU patients with myocardial infarction is unknown. Furthermore, the risk-benefit ratio of these agents in the ICU may differ considerably from when they are used in patients with myocardial infarction outside the ICU. A fundamental understanding of the prognostic significance of elevated levels of cardiac troponin and their relationship to myocardial infarction in critically ill patients is therefore an important first step toward devising and testing appropriate management strategies.

We designed this study to document the prevalence and incidence of elevated serum levels of cardiac troponin I and myocardial infarction among critically ill patients; compare the morbidity and mortality of patients with myocardial infarction, patients with elevated levels of cardiac troponin I alone, and patients with normal cardiac troponin I levels; and assess whether elevated levels of cardiac troponin I are a predictor of ICU and hospital length of stay and mortality. We did not systematically screen patients by measuring levels of cardiac troponin and obtaining ECGs. Rather, we documented all the available results of tests ordered by the ICU team; hence, we determined the clinically recognized incidence and prevalence rates of elevated levels of cardiac troponin I and myocardial infarction.

Methods

Sample
All critically ill adults admitted to the 15-bed medical-surgical ICU at St Joseph’s Hospital, Hamilton, Ontario, between November 17, 2000, and January 17, 2002, who were expected to remain in the ICU for at least 72 hours were included in the study. Exclusion criteria included trauma, neurosurgery and cardiac surgery.
(due to regionalization in critical care), recent orthopedic surgery, pregnancy, and palliative care.

Data Collection

Patients in this study had been enrolled in a prospective cohort study to evaluate the incidence and prevalence of deep vein thrombosis. Prospectively, we collected demographic data, including patients’ age, sex, admitting diagnosis, and Acute Physiology and Chronic Health Evaluation II score.20 Daily, we collected the multiple organ dysfunction score21 and the need for advanced life support (mechanical ventilation, use of inotropic agents or vasopressors, and dialysis). We recorded duration of mechanical ventilation, length of ICU and hospital stays, and death. Retrospectively, we collected data on risk factors for cardiac disease, results of all assays of cardiac troponin I and ECGs performed during the ICU stay, and use of antithrombotic and cardiac medications. Although the medical center has a cardiac care unit, patients requiring mechanical ventilation are admitted to the ICU. The ICU team dictated the frequency and timing of assays of cardiac troponin I and ECGs, which were ordered as clinically indicated.

Analysis of Cardiac Troponin I Levels

Elevation of cardiac troponin I level was defined as a serum level greater than or equal to 1.2 µg/L. Troponin I was measured by using the Abbott AxSYM system (Abbott Laboratories, Mississauga, Ontario). The measurements have a coefficient of variation of 10%.22 The lower detection limit for the assay is 0.3 µg/L.

ECG Interpretation

12-Lead ECGs were recorded by using Pagewriter ECG machines (Hewlett-Packard, Palo Alto, Calif), which provide a computerized ECG interpretation at the top of each ECG. The ICU team dictated the frequency and timing of ECGs. All ECGs were reviewed by a cardiologist within 24 hours of recording, and modifications to the computerized interpretation were made. These reviewed ECGs with the cardiologists’ interpretations were used to classify the ECG findings into 3 categories: ischemic ECG abnormalities, nonischemic ECG abnormalities, and no ECG changes. New ECG findings indicative of ischemic changes were defined according to the joint ESC/ACC committee ECG criteria and included 1 or more of the following: ST-segment elevation 0.1 mV or greater in 2 or more contiguous leads, ST-segment depression, T-wave abnormality, and development of pathological Q waves. Occurrence of new left bundle branch block was also included in the ischemic ECG criteria, because its presence can obscure ST-segment elevation. Nonischemic ECG changes were any ECG abnormalities that did not meet ESC/ACC criteria.

Outcome Definitions

Patients were classified into the following groups on the basis of cardiac troponin I levels and ECG classifications: myocardial infarction, defined as 1 or more assays indicating an elevation in cardiac troponin I and ischemic ECG changes; elevated cardiac troponin I only, defined as 1 or more assays indicating an elevation in cardiac troponin I and nonischemic ECG changes (including patients with no ECG changes); and normal levels of cardiac troponin I. Myocardial infarction was defined according to the ESC/ACC guidelines,1 although symptoms of ischemia were not included in our definition because ICU patients are rarely able to report these symptoms. Patients with myocardial infarction were further classified into those with and without ST-segment elevation. All patients were classified in the category of their highest illness severity. Prevalent events were defined as those that occurred less than 48 hours after ICU admission; incident events, as those that occurred 48 hours or later after ICU admission.

Statistical Analysis

Continuous data were reported by using mean and SDs or by using median and interquartile ranges when data were skewed. Binary data were reported by using proportions and 95% CIs. Univariate and multivariate analyses were used to determine the association between ICU mortality and the following independent variables: Acute Physiology and Chronic Health Evaluation II score, use of mechanical ventilation, use of inotropic agents or vasopressors, dependence on acute or chronic dialysis, and elevated serum level of cardiac troponin I (maximum value). Variables associated with ICU mortality in the univariate analysis (P<.10) were retained in the multivariate analysis. A second logistic regression was completed to determine factors associated with hospital mortality. Regression results were expressed by using odds ratios and 95% CIs. The relationship between the degree of elevation of cardiac troponin I and these outcomes was assessed by using the following categories: less than 0.5 µg/L, 0.5 to 2.0 µg/L, 2.1 to 10.0 µg/L and greater than 10.0 µg/L.23 Statistical analyses were performed by using SAS, version 9.1, software (SAS Institute Inc, Cary, NC).

Results

Characteristics of the Sample

In the 14-month study period, 817 patients were admitted to the ICU; of these, 285 (34.9%) were 18
years or older and were expected to be in ICU for 72 hours or more. Of these 285, 22 (7.8%) were excluded for the following reasons: second admission to ICU (16), trauma (1), and withdrawal of life support (5). Of 263 eligible patients, 1 patient had no next of kin, and 1 patient’s family declined to consent to the study. A total of 261 patients were enrolled in the prospective study, and 198 (75.9%) had charts available for review. Among the 261 patients, 10 (5.1%) were in the cardiac care unit immediately before admission to the ICU; data on these patients were included in the primary analysis but were also analyzed separately as a sensitivity analysis. Characteristics of the patients enrolled in the study are listed in Table 1.

**Prevalence and Incidence of Elevated Cardiac Troponin I Levels**

The classification of patients by outcome is shown in the Figure. Table 2 gives the prevalence (<48 hours of ICU admission) and incidence (developing during ICU stay; ≥48 hours) of myocardial infarction and elevated level of cardiac troponin I only. Overall, 185 (93.4%) of the 198 eligible patients had at least 1 measurement of cardiac troponin I completed either at the time of admission or during their ICU stay. A total

### Table 1 Baseline characteristics of the sample (n = 198)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>66.3 (15.5)</td>
</tr>
<tr>
<td>Female</td>
<td>80 (40.4)</td>
</tr>
<tr>
<td>APACHE II score, mean (SD)</td>
<td>25.3 (8.2)</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>97 (49.0)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>176 (88.9)</td>
</tr>
<tr>
<td>Mechanical ventilation, median (IQR), days</td>
<td>6 (3, 12)</td>
</tr>
<tr>
<td>Intensive care unit mortality</td>
<td>51 (25.8)</td>
</tr>
<tr>
<td>Length of stay in intensive care unit, median (IQR), days</td>
<td>9 (6, 17)</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>75 (37.9)</td>
</tr>
<tr>
<td>Length of stay in hospital, median (IQR), days</td>
<td>25 (12, 55)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>88 (44.4)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>44 (22.2)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>38 (19.2)</td>
</tr>
<tr>
<td>Smoking</td>
<td>43 (21.7)</td>
</tr>
<tr>
<td>Medical admission</td>
<td>150 (75.8)</td>
</tr>
<tr>
<td>Admission diagnosis</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>72 (36.4)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>50 (25.3)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>29 (14.6)</td>
</tr>
<tr>
<td>Renal</td>
<td>16 (8.1)</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>14 (7.1)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>10 (5.1)</td>
</tr>
<tr>
<td>Other††</td>
<td>7 (3.5)</td>
</tr>
</tbody>
</table>

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; IQR, interquartile range.

*Values are number of patients (%) except where noted.
†Necrotizing fasciitis (3), diabetic ketoacidosis (1), facial surgery (1), mushroom poisoning (1), postpartum hemorrhage (1).

### Table 2 Prevalence and incidence of myocardial infarction and elevated troponin level only

<table>
<thead>
<tr>
<th>Event</th>
<th>Prevalence (n = 171)</th>
<th>Incidence (n = 136)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>38 (22.2)</td>
<td>12 (8.8)*</td>
</tr>
<tr>
<td>ST-segment elevation</td>
<td>5 (2.9)</td>
<td>0</td>
</tr>
<tr>
<td>No ST-segment elevation</td>
<td>33 (19.3)</td>
<td>7 (5.1)</td>
</tr>
<tr>
<td>Elevated troponin level only</td>
<td>34 (19.9)</td>
<td>4 (2.9)*</td>
</tr>
<tr>
<td>Without ischemic electrocardiographic (ECG) changes</td>
<td>29 (17.0)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>No ECG changes (normal ECG)</td>
<td>3 (1.8)</td>
<td>0</td>
</tr>
<tr>
<td>No ECG performed</td>
<td>2 (1.2)</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Total</td>
<td>72 (42.1)</td>
<td>16 (11.8)</td>
</tr>
</tbody>
</table>

*Five patients had both prevalent and incident myocardial infarction.
†Two patients had elevated troponin level only at admission, and elevations recurred during the stay in the intensive care unit.
The incidence of elevated cardiac troponin I level during the ICU admission was 11.8% (16 patients: 95% CI 6.8%-18.4%). Criteria for myocardial infarction were met by 12 patients (incidence 8.8%, 95% CI 4.6%-14.9%), although 5 of these patients met the criteria for myocardial infarction at the time of ICU admission (indicating that their incident myocardial infarction was a recurrent myocardial infarction); hence 7 patients had new myocardial infarction (incidence 5.1%, 95% CI 2.1%-10.3%), which were all of the non–ST-elevation type. A total of 4 patients had elevated cardiac troponin I only during their ICU stay (incidence 2.9%, 95% CI 0.8%-7.4%); elevations were present in 2 patients at admission and developed in 2 patients during the ICU stay (incidence 1.5%, 95% CI 0.2%-5.2%).

The prevalence of elevated cardiac troponin I level at the time of admission to the ICU was 42.1% (72 patients; 95% CI 34.6%-49.9%). Criteria for myocardial infarction were met by 38 of these patients (prevalence 22.2%, 95% CI 16.2%-29.2%); 5 had ST-segment elevation and 33 did not. A total of 34 patients (prevalence 19.9%, 95% CI 14.2%-26.7%) had elevated levels of cardiac troponin I only.

### Table 3 Characteristics and outcomes of patients by categories

<table>
<thead>
<tr>
<th>Baseline characteristics*</th>
<th>Myocardial infarction (n = 45)</th>
<th>Elevated troponin level only (n = 36)</th>
<th>Normal troponin level (n = 104)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>72.2 (11.0)</td>
<td>64.3 (18.5)</td>
<td>65.6 (14.7)</td>
<td>.02</td>
</tr>
<tr>
<td>Female</td>
<td>20 (44.4)</td>
<td>18 (50.0)</td>
<td>37 (35.6)</td>
<td>.26</td>
</tr>
<tr>
<td>APACHE II score, mean (SD)</td>
<td>27.2 (7.7)</td>
<td>26.3 (8.1)</td>
<td>24.6 (8.6)</td>
<td>.18</td>
</tr>
<tr>
<td>Admitting category</td>
<td></td>
<td></td>
<td></td>
<td>.006</td>
</tr>
<tr>
<td>Respiratory</td>
<td>13 (28.9)</td>
<td>8 (22.2)</td>
<td>46 (44.2)</td>
<td>.03</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>19 (42.2)</td>
<td>10 (27.8)</td>
<td>19 (18.3)</td>
<td>.08</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>6 (13.3)</td>
<td>5 (13.9)</td>
<td>17 (16.3)</td>
<td>.51</td>
</tr>
<tr>
<td>Renal</td>
<td>3 (6.7)</td>
<td>5 (13.9)</td>
<td>5 (4.8)</td>
<td>.46</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>1 (2.2)</td>
<td>1 (2.8)</td>
<td>11 (10.6)</td>
<td>.10</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3 (6.7)</td>
<td>3 (8.3)</td>
<td>4 (3.8)</td>
<td>.002</td>
</tr>
<tr>
<td>Other*</td>
<td>0</td>
<td>4 (11.1)</td>
<td>2 (1.9)</td>
<td>.03</td>
</tr>
<tr>
<td>Use of inotropic agents</td>
<td>27 (60.0)</td>
<td>23 (63.9)</td>
<td>44 (42.3)</td>
<td>.08</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>44 (97.8)</td>
<td>30 (83.3)</td>
<td>92 (88.5)</td>
<td>.51</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>9 (20.0)</td>
<td>6 (16.7)</td>
<td>14 (13.5)</td>
<td>.46</td>
</tr>
<tr>
<td>Hypertension</td>
<td>24 (53.3)</td>
<td>16 (44.4)</td>
<td>44 (42.3)</td>
<td>.10</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15 (33.3)</td>
<td>8 (22.2)</td>
<td>18 (17.3)</td>
<td>.002</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>17 (37.8)</td>
<td>4 (11.1)</td>
<td>15 (14.4)</td>
<td>.10</td>
</tr>
<tr>
<td>Smoking</td>
<td>8 (17.8)</td>
<td>4 (11.1)</td>
<td>27 (26.0)</td>
<td>.33</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>20 (44.4)</td>
<td>12 (33.3)</td>
<td>13 (12.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Maximum troponin level, median (IQR), µg/L</td>
<td>9.2 (5.1, 41.4)</td>
<td>3.1 (2.1, 12.8)</td>
<td>0.3 (0.3, 0.5)</td>
<td>.005†</td>
</tr>
</tbody>
</table>

### Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Myocardial infarction (n = 45)</th>
<th>Elevated troponin level only (n = 36)</th>
<th>Normal troponin level (n = 104)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay in intensive care unit, median (IQR), days</td>
<td>10 (8, 18)</td>
<td>8 (4, 13.5)</td>
<td>10 (6, 18)</td>
<td>.07</td>
</tr>
<tr>
<td>Length of stay in hospital, median (IQR), days</td>
<td>20 (11, 54)</td>
<td>13.5 (10.5, 45.5)</td>
<td>30 (15, 61)</td>
<td>.053</td>
</tr>
<tr>
<td>Intensive care unit mortality</td>
<td>15 (33.3)</td>
<td>13 (36.1)</td>
<td>21 (20.2)</td>
<td>.09</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>20 (44.4)</td>
<td>16 (44.4)</td>
<td>35 (33.7)</td>
<td>.33</td>
</tr>
</tbody>
</table>

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; IQR, interquartile range.
*Values are number of patients (%) except where noted.
†P value compares only myocardial infarction and elevated troponin level only groups.

of 171 (86.4%) patients had cardiac troponin I measured within 48 hours of ICU admission, and the number of patients in this subset was used as the denominator in the prevalence analysis. A total of 136 (68.7%) patients had cardiac troponin I measured after 48 hours of ICU admission; the number of patients in this subset was used as the denominator in the incidence analysis.

The prevalence of elevated cardiac troponin I level at the time of admission to the ICU was 42.1% (72 patients; 95% CI 34.6%-49.9%). Criteria for myocardial infarction were met by 38 of these patients (prevalence 22.2%, 95% CI 16.2%-29.2%); 5 had ST-segment elevation and 33 did not. A total of 34 patients (prevalence 19.9%, 95% CI 14.2%-26.7%) had elevated levels of cardiac troponin I only.

### Troponin I levels were elevated at ICU admission in 42% of subjects, but only 53% of these met the criteria for myocardial infarction.

### During the ICU stay, 11.8% of subjects had elevated troponin I levels, and 75% of these met the myocardial infarction criteria.
Association Between Patients’ Characteristics and Outcomes

The baseline characteristics and associated morbidity and mortality outcomes are shown in Table 3, divided as patients with myocardial infarction (n = 45), patients with elevated cardiac troponin level only (n = 36), and patients with normal cardiac troponin levels (n = 104). Patients with myocardial infarction more often were older, were admitted with cardiovascular-related diagnoses, had underlying hypercholesterolemia and previous myocardial infarction, and required inotropic agents at some point during their ICU stay. The mean of the maximum cardiac troponin I level was higher in patients with myocardial infarction than in patients with elevated cardiac troponin I level only. The proportion of patients requiring hemodialysis did not differ significantly among the 3 groups. In addition, length of ICU or hospital stay and ICU or hospital mortality did not differ significantly among the 3 groups.

Among patients classified as having myocardial infarction, those who received specific anti-ischemic and antithrombotic treatments (including heparin, β-blockers, angiotensin-converting enzyme inhibitors, and nitrates) and those who did not had similar ICU and hospital stays and ICU and hospital mortality (data not shown). These outcomes were also similar whether patients did or did not have ST-segment elevation.

Factors Associated With Mortality

The predictors of ICU and hospital mortality are shown in Table 4. In the univariate analysis, the presence of an elevated level of cardiac troponin I, the score on the Acute Physiology and Chronic Health Evaluation II, the need for inotropic agents or vasopressors, and the need for acute dialysis were all significantly associated with ICU mortality; the score on the Acute Physiology and Chronic Health Evaluation II, use of inotropic agents or vasopressors, mechanical ventilation, and acute dialysis were associated with hospital mortality. In the multivariate analysis, the need for inotropic agents or vasopressors was the only independent predictor of both ICU and hospital mortality. When levels of cardiac troponin I were divided into categories (<0.5 µg/L, 0.5-2.0 µg/L, 2.1-10.0 µg/L, and >10.0 µg/L), the odds ratios for ICU and hospital mortality increased with increasing levels of cardiac troponin I.

Proportion of Patients With Myocardial Infarction Receiving Antithrombotic and Cardiac Medications

Table 5 shows treatments administered for patients with myocardial infarction, divided into patients with and without ST-segment elevation. A total of 82.2% of patients received aspirin, and 48.9% received therapeutic doses of heparin. Unfractionated heparin was used in 73%, and low-molecular-weight heparin in 23%. Aspirin and therapeutic heparin were administered to all 5 patients with ST-segment elevation. Other recommended therapies in patients with coronary disease, including angiotensin-converting enzyme inhibitors, β-blockers, and statins, were used in 80% or less of the eligible patients with ST-segment elevation, and in 63% or less of the patients without ST-segment elevation.

Discussion

In this study of patients admitted to a medical-surgical ICU with an expected length of stay of at least 72 hours, the prevalence of an elevated level of cardiac troponin I was 42.1%. According to the defini-
tion of myocardial infarction in the consensus document by the joint ESC/ACC committee, 1 22.1% of these patients had myocardial infarction within 48 hours of ICU admission. Patients with myocardial infarction were more often admitted with cardiovascular diagnoses and had higher levels of cardiac troponin I and more cardiac risk factors than did patients without elevated levels of troponin I. However, inferences about comparisons of patients’ characteristics are limited. Patients who are known to have coronary artery disease, or who are admitted with cardiovascular diagnoses, may be more likely to have their cardiac risk factors documented in their medical records. Similarly, these patients may have more frequent measurements of cardiac troponin I, thus increasing the likelihood that an elevated level will be detected.

Table 5 Proportion of patients receiving antithrombotic and cardiac medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Myocardial infarction</th>
<th>ST-segment elevation</th>
<th>No ST-segment elevation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n = 45)</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Aspirin</td>
<td>37</td>
<td>82.2</td>
<td>5</td>
</tr>
<tr>
<td>Heparin</td>
<td>35</td>
<td>77.8</td>
<td>3</td>
</tr>
<tr>
<td>Prophylactic</td>
<td>22</td>
<td>48.9</td>
<td>5</td>
</tr>
<tr>
<td>Therapeutic</td>
<td>42</td>
<td>93.3</td>
<td>5</td>
</tr>
<tr>
<td>Any heparin</td>
<td>29</td>
<td>64.4</td>
<td>4</td>
</tr>
<tr>
<td>Angiotensin-</td>
<td>23</td>
<td>51.1</td>
<td>2</td>
</tr>
<tr>
<td>converting enzyme</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>inhibitor</td>
<td>12</td>
<td>26.7</td>
<td>0</td>
</tr>
<tr>
<td>Nitrites</td>
<td>26</td>
<td>57.8</td>
<td>3</td>
</tr>
</tbody>
</table>

Our results and the results of these other studies may differ for several possible reasons. First, differences among ICUs, including the case mix of critically ill patients with respect to cardiac risk factors and whether or not patients were systematically screened or had cardiac troponin levels measured as clinically indicated, would lead to different incidence and prevalence rates. Second, the type of assay used to measure cardiac troponin and the different thresholds used to classify levels of cardiac troponin as elevated would also influence the observed rates. Finally, and perhaps most important, the use of univariate analysis (which tends to suggest associations between cardiac troponin I levels and adverse outcomes that are unadjusted for other important covariates) in many studies could also account for the observed differences in results.

In other prospective studies, 10-12 15% to 70% of patients in a general ICU had at least a single measurement indicating an elevation in the serum level of cardiac troponin. The prevalence of elevation in cardiac troponin in specific ICU populations has been studied in patients who had sepsis, 2-5,10,11 cardiac surgery, 24,25 or noncardiac diagnoses. Prevalence estimates for patients with noncardiac diagnoses ranged from 16% to 55%. 14,15 In a study of 34 consecutive patients who were treated with mechanical ventilation or who underwent thoracic or vascular surgery, 11 (32%) had elevated levels of cardiac troponin T, and 4 (36%) of the 11 had ECG changes compatible with myocardial infarction. 26 These findings suggest that elevated levels of cardiac troponin are common among critically ill patients and that the prevalence of myocardial infarction among critically ill patients may be higher than is generally appreciated. However, the relevance of increased levels of cardiac troponin in relation to coronary ischemia and ECG changes still remains uncertain among ICU patients. The available studies suggest that cardiac troponin may be an adverse prognostic marker in the ICU; elevations in cardiac troponin I levels are associated with increased mortality in medical-surgical ICU patients, 10-12 including patients admitted for reasons other than acute coronary syndromes 13,27 and patients admitted with acute exacerbations of chronic obstructive pulmonary disease. 28 Elevations in cardiac troponin I levels have also been associated with increased ICU and hospital stays in surgical ICU patients. 19 Although supported by fewer studies, elevated levels of cardiac troponin T are similarly a predictor of mortality in ICU patients with early sepsis 2 and after cardiac surgery 24,25,29 and are associated with prolonged ICU stay after cardiac surgery.25

Our results and the results of these other studies may differ for several possible reasons. First, differences among ICUs, including the case mix of critically ill patients with respect to cardiac risk factors and whether or not patients were systematically screened or had cardiac troponin levels measured as clinically indicated, would lead to different incidence and prevalence rates. Second, the type of assay used to measure cardiac troponin and the different thresholds used to classify levels of cardiac troponin as elevated would also influence the observed rates. Finally, and perhaps most important, the use of univariate analysis (which tends to suggest associations between cardiac troponin I levels and adverse outcomes that are unadjusted for other important covariates) in many studies could also account for the observed differences in results.
Results of randomized trials indicate that antithrombotic therapy improves outcomes in patients with myocardial infarction. However, it is unclear if similar treatment of critically ill patients with elevated levels of cardiac troponin (which may be related to nonthrombotic causes) will similarly improve outcomes. Few of the patients with myocardial infarction in our study received all of the recommended antithrombotic and anti-ischemic therapies. Although use of aspirin and heparin was common in patients with myocardial infarction who had ST-segment elevation, cardiac medications were used in 80% or fewer of eligible patients with ST-segment elevation and in less than 63% of patients who met criteria for non–ST-segment elevation myocardial infarction. Inferences about use of medications in the group with ST-segment elevation are limited because of the small number of patients.

Our study has several limitations. First, although many of our data were prospectively collected for the original study, we collected data specific to myocardial infarction retrospectively. Because we did not screen all patients by obtaining daily measurements of cardiac troponin level and daily ECGs but recorded all available results of tests ordered by the ICU team, we determined the clinically recognized incidence and prevalence rates of elevated levels of cardiac troponin and myocardial infarction. Systematic screening with measurements of cardiac troponin levels and ECGs might lead to higher prevalence and incidence rates; however, this type of systematic screening is not routinely done in clinical critical care practice. Nonetheless, 86% of the patients had at least a single measurement of cardiac troponin I at the time of admission to the ICU, reflecting local practice patterns that may exist in other ICUs.

Second, the estimate of incidence was based on data for only 136 patients who had cardiac troponin I measured 48 hours or later after ICU admission, which resulted in a less precise estimate than estimates based on data for a larger number of patients would have been. Third, although our study included 198 patients, the number of patients in each group limited the power of our between-group comparisons to detect small differences. Fourth, only 1 reviewer abstracted data, a situation that may have resulted in abstraction errors; however, we minimized this risk by using pretested standardized data abstraction forms and classifying ECG changes according to the interpretation by cardiologists who were blinded to our study objectives. Last, we did not include all consecutive patients admitted to the ICU because our focus was not on patients admitted for overnight mechanical ventilation or postoperative monitoring; inclusion of these patients might have resulted in lower incidence and prevalence rates.

Strengths of our study include enrollment of patients during a period of more than 1 year and complete follow-up on all patients. We identified ECG changes indicative of ischemia by using the ECG criteria of the joint ESC/ACC committee, and we classified patients into categories reflecting myocardial ischemia as used in clinical practice, a method that indicated a high degree of illness in this cohort of critically ill patients. We used regression analysis to examine the independent contribution of elevated levels of cardiac troponin to mortality. In terms of generalizability, our ICU admits patients with cardiac conditions who need mechanical ventilation; in some centers, such patients may receive care in the cardiac care unit. Of the 10 patients transferred from the cardiac care unit, 4 met criteria for myocardial infarction (3 admitted with cardiac arrest, 1 with heart failure), 2 had elevated levels of cardiac troponin I only, and 4 had normal levels of cardiac troponin I. However, the overall prevalence of elevated levels of cardiac troponin I in our study cohort was still considerable (38.6%, n = 66) when data on patients transferred from the cardiac care unit (n = 10, of whom 4 had myocardial infarction) and on patients admitted with myocardial infarction with ST-segment elevation (n = 5) were not included in the analysis.

In summary, elevated levels of cardiac troponin reflecting myocardial infarction are common in critically ill medical-surgical patients. The role of elevations in cardiac troponin I as a prognostic marker in the ICU is still uncertain. Establishing the diagnosis of myocardial infarction in critically ill patients is challenging because of limitations in determining whether the patients have typical symptoms of ischemia and because of uncertainty about the interpretation of abnormal levels of cardiac troponin. Additional research is urgently needed on the appropriate diagnostic criteria for myocardial infarction in the ICU setting and the optimal management of critically ill patients who have elevated levels of cardiac troponin.

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REFERENCES
CE Test  
Test ID A061503: Elevated Cardiac Troponin Levels in Critically Ill Patients: Prevalence, Incidence, and Outcomes.  
Learning objectives:  
(1). Recognize the prevalence and incidence of elevated troponin levels in critically ill patients.  
(2). Describe the population of patients used in this study.  
(3). Identify relationships found in this study between elevated troponin levels, myocardial infarction, and mortality.  

1. Which of the following best describes the prevalence of elevated levels of cardiac troponin in critically ill patients with sepsis or septic shock?  
a. 15% to 70%  
b. 25% to 50%  
c. 31% to 80%  
d. >75%  

2. According to the European Society of Cardiology and the American College of Cardiology, myocardial infarction is defined on the basis of pathological findings or an increase or decrease in biochemical markers of myocardial necrosis and at least one other indicator.  
Which of the following is not considered one of those indicators?  
a. Ischemic signs and symptoms  
b. Decreased level of consciousness  
c. Electrocardiographic (ECG) signs of ischemia  
d. ECG signs of infarction  

3. According to the study by Ammann et al, what percentage of intensive care patients with elevated cardiac troponin levels had low-flow limiting coronary artery disease as indicated by stress echocardiography or by findings at autopsy?  
a. 30%  
b. 50%  
c. 70%  
d. 20%  

4. Which of the following factors limit the ability of critically ill patients to report signs of ischemia?  
1. Use of sedatives and narcotics  
2. Endotracheal intubation  
3. Altered level of consciousness due to underlying illness  
4. Preexisting cardiovascular disease  
a. All of the above  
b. None of the above  
c. b. and c. only  
d. a. and b. only  

5. Which of the following is true regarding treatment of myocardial infarction due to nonthrombotic mechanisms?  
a. Coronary revascularization has been found successful in treating these patients.  
b. Use of anticoagulants and antiplatelet agents has been found successful in treating these patients.  
c. These patients may not respond favorably to antithrombotic agents.  
d. Use of β-blockers, angiotensin-converting enzyme inhibitors, and statins reverses effects of nonthrombotic myocardial infarction.  

6. Which of the following best describes participants in this study?  
a. Critically ill children and adults admitted to the McMaster University Health Services Center medical-surgical intensive care unit (ICU) between November 2000 and January 2002  
b. Critically ill trauma patients admitted to the McMaster University Health Services Center ICU between November 2000 and January 2002  
c. Patients who did not receive anti-ischemic or antithrombotic treatments had decreased ICU and hospital mortality.  
d. Critically ill neurosurgical and cardiac surgery patients admitted to the McMaster University Health Services Center ICU between November 2001 and January 2003  

7. Which of the following was not included in the demographic data collected prospectively on the study participants?  
a. Patient's age and sex  
b. Patient's weight and height  
c. Acute Physiology and Chronic Health Evaluation II (APACHE II) score  
d. Patient's admitting diagnosis  

Test Answers: Mark only one box for your answer to each question. You may photocopy this form.  

1. a  
2. a  
3. a  
4. a  
5. a  
6. a  
7. a  
8. a  
9. a  
10. a  
11. a  
12. a  
13. a  

Test ID: A061503  
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