Cost of care for a critically ill patient is approximately 3 times more than the cost for a patient on a general medicine unit. Therefore, to allocate resources appropriately and assign patients to a suitable acute care unit, intensive care practitioners must assess patients’ severity of illness and prognosis. Cost of care is especially important for hospitals that predominantly serve a culturally diverse community where poverty is high, and most of the patients have multiple, complicated comorbid conditions and are more likely to be admitted to a critical care unit than to a general unit. Care of long-term care residents dependent on mechanical ventilation is particularly complicated because the patients often have infections caused by multidrug-resistant organisms.
including organisms that produce *Klebsiella pneumoniae* carbapenemase, that are associated with high mortality. As a result, these patients have a high readmission rate to mixed medical-surgical intensive care units (ICUs) and cardiac care units (CCUs), commonly because of sepsis. The high readmission rates are often associated with prolonged wait time for ICU or CCU bed availability because patients from the emergency department or acute care units have more severe illnesses. Further confounding ICU and CCU bed availability is the often prolonged length of stay for patients already in the units. Among the conditions responsible for this situation, sepsis, acute renal failure, and acute respiratory failure are independent predictors of in-hospital mortality among hospitalized patients from nursing homes across the United States.

Although several validated scoring systems are available for assessing severity of illness in critically ill patients, such as the Acute Physiology and Chronic Health Evaluation (APACHE) II, these systems are prone to interrater variability depending on the time of the data collection and the interobserver subjectiveness in the clinical assessment of illness severity. In critically ill patients without acute coronary syndrome (ACS), a potentially reliable objective parameter for predicting illness severity is the serum level of cardiac troponin I (CTnI). CTnI is a component of protein complexes essential for the contraction and relaxation of cardiac striated muscle. More specifically, CTnI binds to actin to support the troponin-tropomyosin complex needed for contraction and relaxation of the sarcomere. CTnI is present exclusively in the myocardium, and any mechanical or inflammatory stress on the myocardium will result in serum elevations in CTnI and decrease the functionality of the myocardium. Causes for CTnI elevation include sepsis, heart failure, respiratory failure, pulmonary embolism, chronic obstructive pulmonary disease (COPD), and renal failure due to ischemia associated with myocardial demand and inadequate oxygenation. For patients with ACS, higher serum levels of CTnI are associated with a poorer prognosis than are lower levels. In patients without ACS, CTnI elevation is more sensitive for detection of ischemia than are levels of creatine kinase MB and total creatine kinase. Evaluations of the correlation between CTnI levels and severity-of-illness findings determined by using currently existing scoring systems are limited.

Published findings on the prognostic value of serum CTnI levels are conflicting. Previous investigations, mostly retrospective observational studies, have indicated that serum levels of CTnI and/or troponin T subunits are reliable prognostic markers for multiple outcomes, including severity of traumatic brain injury as indicated by scores on the Glasgow Coma Scale, hospital mortality and length of stay, and ICU length of stay, among critically ill patients across different medical specialties, including cardiothoracic surgery, neurology, and general surgery (Table 1). However, Minkin et al and Stein et al found that CTnI levels within 24 hours of ICU admission or peak levels during the ICU stay correlated poorly with hospital length of stay, readmission rates, and mortality at 6 months after discharge. The results of these 2 retrospective studies suggest that CTnI level is a poor predictor for such outcomes in non-ACS patients and conflict with the findings of Garrett et al. Only 3 studies were conducted prospectively and outside the United States, and none of the studies included an evaluation of the prognostic value of CTnI levels in long-term care patients. As mentioned earlier, cardiovascular disease is the most common cause of death among long-term care residents.

The objectives of our study were to determine if CTnI levels in non-ACS patients admitted to the ICU or the CCU have any prognostic value and to improve the quality of care and allocation of resources at our institution.
**Methods**

In a prospective observational study, all patients admitted to either the ICU or the CCU during 115 consecutive days were screened for eligibility. Inclusion criteria included at least 1 elevated serum level of CTnI within 24 hours of admission to the ICU or CCU, with the highest CTnI level within the stated time window recorded for the study’s results. Patients were excluded if they had ACS as indicated by medical history, physical examination, clinical features, cardiac biomarkers, and electrocardiographic findings as defined by the American College of Cardiology and the American Heart Association anytime during their current admission; were less than 18 years old; or declined to participate in the study. Patients with a known history of ACS were eligible for enrollment only if the ACS had occurred more than 10 days before the patient was examined in the emergency department, because serum levels of CTnI can remain elevated for up to 10 days after a myocardial ischemic event. Patients were divided into 2 groups on the basis of their highest CTnI level: if the peak serum level was more than 0.049 ng/mL, they were enrolled in the elevated CTnI group.
CTnI group (CTnI-positive); if the level was 0.049 ng/mL or less, they were placed into the normal CTnI group (CTnI-negative).

The Access AccuTnI Reagent (Beckman Coulter Inc) was used to detect CTnI. The functional sensitivity, defined as the lowest CTnI concentration measurable with an assay coefficient of variation or total imprecision of 20% or less for the presence of a myocardial infarction, is 0.046 ng/mL,\(^2^6\) which is close to the assay’s cutoff value for the detection of a CTnI level considered elevated (CTnI-positive). The sensitivity of different methods of measurement vary.\(^1^1,1^2\) In several studies,\(^2^5\) the functional sensitivity of other assays with a similar coefficient of variation (≤20%) was 0.03 ng/mL. However, the cross-reactivity of the Access AccuTnI Reagent with cardiac troponins C and T subunits, creatine kinase MB, actin, myosin, tropomyosin, and myoglobin is 0.001% or less,\(^2^6\) and as a result the assay is highly specific for CTnI. The detectable range of the assay is 0.01 to 100 ng/mL.\(^2^6\) The lowest median detection limit of the immunoassay reported is 0.004 ng/mL.\(^2^6\) The third universal definition of myocardial infarction defines an increased concentration of cardiac troponins as a value exceeding the 99th percentile of the concentration of a normal reference population consisting of apparently healthy volunteers free from heart disease.\(^2^7\) Apple\(^2^8\) recommends that the concentration of cardiac troponin to be considered indicative of myocardial infarction be based on a level that must be measured with an imprecision less than or equal to a 10% coefficient of variation.

Regardless of baseline characteristics, hospital mortality was significantly higher in the CTnI-positive group than in the CTnI-negative group.

The following data were collected for each patient within 24 hours of admission to the ICU or CCU: demographic information (eg, age); where they were admitted from; admitting diagnosis; medical history for specific diseases (eg coronary artery disease); current smoking status; presence of an implantable cardioverter defibrillator; peak CTnI and creatine kinase MB levels; serum levels of sodium, potassium, urea nitrogen, glucose, and creatinine; platelet and white blood cell counts; the need for invasive mechanical ventilation or hemodialysis; presence of sepsis or shock; use of intravenous vasopressors; and prophylaxis status for venous thromboembolism. All laboratory data were obtained at the same time as the CTnI and creatine kinase MB levels. If completed, the initial electrocardiographic findings were also assessed to determine if the patient met the exclusion criteria for ACS. The following data were collected daily until discharge: mortality, ICU length of stay, hospital length of stay, use of intravenous vasopressors, and respiratory status. The primary outcome was hospital mortality due to any cause. Secondary outcomes included ICU and hospital lengths of stay; admitting diagnosis of sepsis, shock, acute renal failure, or acute respiratory failure; use of intravenous vasopressors; incidence of intubation; successful extubation if the patient was intubated; and disposition at discharge.

Continuous variables are reported as median and interquartile range; categorical variables are reported as proportions with matching percentages. For univariate comparison of categorical variables between the CTnI-positive group and the CTnI-negative group, the Fisher exact test was used. The Mann-Whitney test was used for categorical independent variables with continuous dependent variables between both groups, with disposition at discharge analyzed with the multiple regression test in relationship to all baseline continuous variables, including CTnI levels. Spearman rank correlation was used to assess for correlation between continuous variables. The unpaired Kruskal-Wallis test was used for analysis of disposition of patients after discharge from the hospital. All tests were 2-tailed except for the Kruskal-Wallis test. A significance level of .05 was used for all analyses. For relative risk, 95% CIs were calculated. Analyses were performed by using SPSS, version 16.0, software (IBM SPSS).

Results

During the study period, 90 patients qualified for inclusion in the study. Of these, 40 (44%) were in the CTnI-positive group and 50 (56%) in the CTnI-negative group. The median CTnI levels were 0.08 and 0.01 ng/mL, respectively (\(P<.001\); Table 2). Baseline characteristics were similar in both groups except that compared with the CTnI-negative patients, CTnI-positive patients had a higher median white blood cell count (\(P=.02\)), were less likely to be admitted from home (\(P=.009\)), and were more likely to have underlying COPD (\(P=.04\)).

Regardless of baseline characteristics, hospital mortality was significantly higher in the CTnI-positive group than in the CTnI-negative group: 35% vs 12%, respectively; relative risk (RR), 1.35; 95% CI, 1.05-1.73;
P = .01 (Table 3). CTnI-positive patients were also more likely than CTnI-negative patients to be intubated anytime during the current admission period: 41% vs 17%, respectively; RR, 1.34; 95% CI, 1.02-1.76; P = .02. The 2 groups did not differ significantly in median length of stay in the ICU or CCU (4 vs 3 days; P = .52), median hospital length of stay (9 vs 8 days; P = .44), admission because of sepsis (38% vs 22%; RR, 1.23; 95% CI, 0.94-1.66; P = .16), shock (40% vs 20%; RR, 1.04; 95% CI, 0.99-1.78; P = .06), or acute renal failure (10% vs 6%; RR, 1.04; 95% CI, 0.92-1.18; P = .48), and the use of intravenous vaspressors (38% vs 18%; RR, 1.31; 95% CI, 0.99-1.72; P = .06). Among the patients who survived until hospital discharge, CTnI-negative patients (46%) were more likely than CTnI-positive patients (25%) to be discharged to home directly from the hospital (RR, 0.72; 95% CI, 0.52-0.98; P = .04), although multiple regression analysis indicated no significant difference between CTnI levels and other baseline continuous variables for hospital disposition (R² = 0.111; P > .05 for all variables assessed).

ICU or CCU length of stay correlated positively with sepsis (P < .001), shock (P = .005), and use of intravenous...
reported by Lim et al. The exact pathophysiological mechanism of CTnI elevation among non-ACS critically ill patients remains unclear. Potential mechanisms include underlying coronary artery disease; small-vessel thrombosis due to low levels of activated protein C, leading to myocardial necrosis and depressed left ventricular ejection fraction; tachycardia and hypotension associated with septic shock; and use of intravenous vasopressors. The prevalence of underlying coronary artery disease and other chronic preexisting conditions did not differ between the 2 groups, although significantly more patients in the CTnI-positive group had a history of COPD. COPD often results in poor systemic and myocardial perfusion, which may result in cardiac-demand ischemia and ultimately decrease functionality of CTnI. Using a combination of coronary angiography, dobutamine stress echocardiography, and autopsy studies, Ammann et al detected no flow-limiting coronary

### Discussion

In our study, elevated serum levels of CTnI were associated with higher hospital mortality among non-ACS critically ill patients. This finding agrees with the results of other studies. The exact pathophysiological mechanism of CTnI elevation among non-ACS critically ill patients remains unclear. Potential mechanisms include underlying coronary artery disease; small-vessel thrombosis due to low levels of activated protein C, leading to myocardial necrosis and depressed left ventricular ejection fraction; tachycardia and hypotension associated with septic shock; and use of intravenous vasopressors. The prevalence of underlying coronary artery disease and other chronic preexisting conditions did not differ between the 2 groups, although significantly more patients in the CTnI-positive group had a history of COPD. COPD often results in poor systemic and myocardial perfusion, which may result in cardiac-demand ischemia and ultimately decrease functionality of CTnI. Using a combination of coronary angiography, dobutamine stress echocardiography, and autopsy studies, Ammann et al detected no flow-limiting coronary
artery disease or small-vessel thrombosis in 72% of critically ill non-ACS patients with sepsis and CTnI elevation. Therefore, the theoretical mechanisms for CTnI elevation are not supported by our findings or by the results of Ammann et al.

Use of intravenous vasopressors has been associated with elevated CTnI levels and may reflect low levels of irreversible or reversible myocardial ischemia associated with dopamine and intravenous norepinephrine. However, in our study, the 2 groups of patients did not differ in the use of vasopressors despite a positive correlation between vasopressor use and ICU length of stay \((\rho=0.331; P=.001)\). In critically ill patients without ACS, possible alternative causes for elevation in CTnI include sepsis, acute renal failure, and acute respiratory failure, and, as mentioned earlier, these conditions are significant independent predictors of in-hospital mortality among hospitalized nursing home residents. However, we found no significant difference for these variables between the 2 groups of patients in our study.

Other causes for CTnI elevation in non-ACS patients relevant to an ICU include COPD and asthma exacerbations, renal failure, heart failure, and presence of an implantable cardioverter defibrillator. We found no significant difference between our 2 groups for any of these causes except underlying COPD, which was more prevalent in the CTnI-positive group \((P=.04)\), although the need for intubation among COPD patients and successful extubation were similar between both groups (Table 2). Pulmonary embolism is also known to cause CTnI elevation, although this embolism is difficult to diagnose because of its nonspecific signs and symptoms and the lack of sensitivity, specificity, or both among the diagnostic tests currently available. We used computed tomography pulmonary angiography to screen 7 patients in the CTnI-positive group and 13 in the CTnI-negative group for pulmonary embolism; we found only 1 confirmed case, in the CTnI-positive group. Although our 2 groups

### Table 4: Correlation between clinical variables and length of stay in the medical/surgical intensive care unit and cardiac care unit

<table>
<thead>
<tr>
<th>Clinical variable</th>
<th>Spearman rank correlation with length of stay in medical or cardiac intensive care</th>
<th>(P^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.142</td>
<td>.18</td>
</tr>
<tr>
<td>Cardiac troponin I</td>
<td>0.156</td>
<td>.14</td>
</tr>
<tr>
<td>Weight</td>
<td>0.036</td>
<td>.74</td>
</tr>
<tr>
<td>Height</td>
<td>-0.071</td>
<td>.51</td>
</tr>
<tr>
<td>Creatine kinase MB</td>
<td>0.121</td>
<td>.26</td>
</tr>
<tr>
<td>Serum urea nitrogen</td>
<td>-0.025</td>
<td>.82</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>-0.114</td>
<td>.28</td>
</tr>
<tr>
<td>Serum sodium</td>
<td>-0.085</td>
<td>.43</td>
</tr>
<tr>
<td>Serum potassium</td>
<td>-0.133</td>
<td>.21</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>-0.027</td>
<td>.80</td>
</tr>
<tr>
<td>Platelet count</td>
<td>-0.149</td>
<td>.16</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0.286</td>
<td>.006</td>
</tr>
<tr>
<td>Shock</td>
<td>0.291</td>
<td>.005</td>
</tr>
<tr>
<td>Use of intravenous vasopressors</td>
<td>0.331</td>
<td>.001</td>
</tr>
</tbody>
</table>

\(^a\) \(P\) values less than .05 were considered significant.

### Table 5: Correlation between clinical variables and overall length of stay in the hospital

<table>
<thead>
<tr>
<th>Clinical variable</th>
<th>Spearman rank correlation with length of stay in hospital</th>
<th>(P^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.121</td>
<td>.26</td>
</tr>
<tr>
<td>Cardiac troponin I</td>
<td>0.024</td>
<td>.82</td>
</tr>
<tr>
<td>Weight</td>
<td>-0.004</td>
<td>.97</td>
</tr>
<tr>
<td>Height</td>
<td>-0.01</td>
<td>.92</td>
</tr>
<tr>
<td>Creatine kinase MB</td>
<td>0.127</td>
<td>.23</td>
</tr>
<tr>
<td>Serum urea nitrogen</td>
<td>-0.087</td>
<td>.41</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>-0.068</td>
<td>.53</td>
</tr>
<tr>
<td>Serum sodium</td>
<td>-0.079</td>
<td>.46</td>
</tr>
<tr>
<td>Serum potassium</td>
<td>-0.164</td>
<td>.12</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>0.111</td>
<td>.30</td>
</tr>
<tr>
<td>Platelet count</td>
<td>-0.105</td>
<td>.31</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0.115</td>
<td>.28</td>
</tr>
<tr>
<td>Shock</td>
<td>0.176</td>
<td>.10</td>
</tr>
<tr>
<td>Use of intravenous vasopressor(s)</td>
<td>0.135</td>
<td>.20</td>
</tr>
</tbody>
</table>

\(^a\) \(P\) values less than .05 were considered significant.
of patients did not differ in the use of pharmacological prophylactic agents, mechanical prophylactic devices (eg, sequential compression device), and no prophylaxis for venous thromboembolism, pulmonary embolism may occur with any of the 3 methods, even when both pharmacological and mechanical prophylaxis are used simultaneously.11

As mentioned, CTnI is elevated if any mechanical or inflammatory stress is exerted on the myocardium.8,9 In pulmonary embolism, oxygen delivery to the myocardium is decreased, and left ventricular volume decreases as a result of right ventricular distention; the decrease in left ventricular volume leads to a decrease in stroke volume.42

The reduction of both oxygenation and ventricular volume result in an increase in heart rate, a type of mechanical stress, as a physiological reflex in an attempt to increase stroke volume.44 Without adequate oxygenation, the increase in heart rate ultimately leads to dyspnea and demand ischemia of the myocardium, resulting in partial loss of CTnI functionality, which ultimately leads to detectable serum levels of CTnI.8,3 Both dyspnea and tachycardia are common indications of pulmonary embolism and the need for supplemental oxygen.42 Therefore, silent pulmonary embolism remains a possible cause for the increased need for intubation and mortality in the patients in our study.

Scoring systems for severity of illness, such as the APACHE II, the Simplified Acute Physiology Score (SAPS II), and the Mortality Probability Model (MPM II) may be used to predict the probability of mortality and to assess objectively the quality of care provided by an ICU.65 However, use of these systems has several limitations. Unlike the APACHE II and the MPM II, the SAPS II was derived from studies of European, not North American, patients; consequently, it may not be appropriate to apply this predictor model in the United States.67 When severity-of-illness scores were calculated by using each of these systems, the input data were the most abnormal serum CTnI levels obtained within the initial 24 hours after an admission to the ICU,4 with the exception of the MPM II, in which a value obtained after 24 hours may be incorporated. The physiological status of ICU patients can change dramatically within 24 hours, and consequently, the most abnormal value may be difficult to determine. The Glasgow Coma Scale is a component of the APACHE II, SAPS II, and MPM II scoring systems. The scale is subjective, and consistency between evaluators may be moderate at best.44 Therefore, an objective marker such as the CTnI level may help reduce interrater variability. Theoretically, as long as the CTnI assays are identical, levels of the biomarker could be used for assessment of prognosis in critically ill patients in different institutions. However, validation of this possibility would require a multicenter study with a large number of patients.

CTnI levels are often obtained to help rule out ACS, and a CTnI-negative result might lead to a confirmation bias that the patient is not at high risk for morbidity and mortality.

Limitations

Our study had several limitations. Although each severity-of-illness scoring system has its own limitations, we did not use any of these systems during the study. Hence, all patients were included rather than only the most ill. A power analysis was not performed before the start of the study. As a result, we used nonparametric tests for all analyses. This step may account for the lack of significant differences in ICU or CCU length of stay and hospital length of stay; admitting diagnosis of sepsis, shock, acute renal failure, and acute respiratory failure; and the correlation of CTnI levels with ICU or CCU length of stay. Nevertheless, significant differences in mortality...
and need for intubation were found in favor of the CTnl-negative group. Another potential limitation was the CTnl stratification into only 2 categories of normal and abnormal. In other studies, CTnl levels were stratified into multiple tiers, and the investigators evaluated whether higher levels were associated with poorer clinical prognosis. Limitations of other studies include a lack of specification about the assays used, as mentioned; lack of standardization among the commercially available CTnl assays; conflicting results; and arbitrary stratification between studies. Because of these limitations, we opted not to categorize our patients into more than 2 groups. Not all patients were screened for pulmonary embolism via computed tomography pulmonary angiography, although this situation may have occurred because pulmonary embolism was not considered a possibility. In addition, screening was avoided to prevent potential harm to patients whose unstable hemodynamic status precludes transfer out of the ICU or CCU to undergo such a test. Autopsy reports for confirmation of the presence of pulmonary embolism were not collected for any patient.

Conclusion
Elevation of CTnl within 24 hours of an ICU admission has prognostic value for hospital mortality and incidence of intubation in non-ACS critically ill patients. Further studies are needed to determine whether this finding will be applicable in other clinical settings.

Acknowledgments
This research was done at Kingsbrook Jewish Medical Center. The study was approved by the appropriate institutional review board in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

Financial Disclosures
None reported.

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