CLINICAL RESEARCH STUDY

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Incidence and Significance of a Positive Troponin Test in Bacteremic Patients Without Acute Coronary Syndrome

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ABSTRACT

BACKGROUND: Since the introduction of troponin for the diagnosis of myocardial infarction, several studies have shown additional conditions in which troponin is elevated, including sepsis. The objective of this study was to determine the incidence of an elevated troponin in patients with bacteremia and its significance.

METHODS: This was a prospective, noninterventional study. Patients with a positive blood culture were included. Cardiac troponin I (cTnI) was determined within 4 days of blood culture. A repeat electrocardiogram was obtained in a sample of patients with elevated cTnI and in patients with a negative troponin test. Demographic, clinical, and microbiological data were obtained for all patients.

RESULTS: A total of 159 bacteremic patients were included. Positive cTnI was detected in 69 patients (43%). Elevated cTnI was associated with a number of underlying diseases, hospitalization ward, severity of the systemic inflammatory condition, and kidney function ($P < .05$-$.001$). A repeat electrocardiogram was performed in 39 patients with a positive cTnI and in 28 patients with a negative cTnI. Two of 39 patients (5%) in the positive cTnI group had ischemic changes and 2 patients (5%) had nonspecific changes, whereas only 1 patient (4%) with a negative cTnI had nonspecific changes. Bivariate analysis revealed a statistically significant association for positive cTnI and mortality; however, on multivariate analysis this was no longer significant.

CONCLUSION: Forty-three percent of bacteremic patients had an elevated cTnI. Risk factors for elevated cTnI were severity of the underlying infection, renal function, and underlying cardiac disease. Increased cTnI was found to be a dependent risk factor and a surrogate marker for death.

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KEYWORDS: Bacteremia; Cardiac troponin I; Mortality; Sepsis; Septic shock

In the past decade, the diagnosis of myocardial infarction has become far more sensitive with the introduction of methods for determining the serum level of cardiac troponin. Cardiac troponin T and I (cTnT, cTnI) are proteins with myocardium unique amino acid sequences. Currently, serum troponin is considered the most sensitive and specific laboratory marker for myocardial injury.[1,2] However, since the introduction of the troponin test for clinical use, several studies have demonstrated noncoronary conditions in which serum troponin levels may be increased.[3-5] Among these conditions are pericarditis, myocarditis, pulmonary embolism, congestive heart failure, stroke, and sepsis. In most of these cases, the mechanism of myocardial injury is still unclear. Troponin levels have also been shown to be increased after cardiac procedures, such as angioplasty, cardiac conversion, and ablation, and when taking cardiotoxic drugs.[6,7]

As mentioned, one of the reported causes of an elevated troponin level in patients without acute coronary syndrome is sepsis. Previous reports describe patients who had severe sepsis and septic shock, and were usually treated in intensive care units. These reports involved only small numbers of patients.[8-10] A few studies dealt with the possible association between a positive troponin test and specific bacteria. In one study, an association with *Streptococcus pneu-*

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moniae[8] was found, whereas no association with any organism was found in another study.[10] Several studies have concluded that an elevated troponin level in septic patients is an adverse prognostic factor for in-hospital mortality, duration of hospitalization, and left ventricular function.[9,10] One study even suggested that an elevated troponin level is an independent prognostic factor in addition to the APACHE score.[11]

The main objective of the current study was to determine the incidence of an elevated troponin in patients with bacteremia without an acute coronary syndrome. Secondary objectives were to determine the prognostic significance of this finding and possible association with specific bacterial species.

CLINICAL SIGNIFICANCE

- Forty percent of bacteremic patients without acute coronary syndrome may have an elevated cTnI.
- Risk factors for elevated cTnI include greater severity of underlying infection, renal dysfunction, and underlying cardiac disease.
- An increased cTnI was found to be a dependent risk factor serving as a surrogate marker for adverse outcome in these patients.

MATERIALS AND METHODS

This was a prospective, comparative, and noninterventional study. Data were collected between May 1, 2005, and May 16, 2006. The study population included patients who were hospitalized at Shaare Zedek Medical Center, Jerusalem, a 550-bed general hospital, and from whom clinically significant bacteria were isolated from at least 1 blood culture. The following bacteria were defined as clinically insignificant bacteria (ie, likely contaminants) unless they were isolated from more than 1 culture: coagulase-negative *Staphylococcus*, alpha-hemolytic *Streptococcus*, *Micrococcus, Bacillus,* and diphtheroids. Among patients with a positive blood culture, a subgroup of patients were identified with urinary tract infection who had a positive urine culture with growth of the same organism. Patients with a cardiac event (ie, myocardial infarction, cardiac or thoracic surgery, cardiopulmonary resuscitation, cardioversion, endocarditis, myocarditis, and rapid atrial fibrillation) during the month before the positive cultures were excluded.

cTnI testing was performed on 1 blood sample, which was sent for an unrelated clinical indication, from all the study patients. Because troponin levels remain elevated for approximately 1 week after myocardial infarction,[12] only samples sent within 4 days of the blood culture drawing were tested for troponin. cTnI levels were determined with the Beckman Coulter AccuTnI kit on the Access2 (Beckman Coulter, Fullerton, Calif). According to the manufacturer, the cutoff level for determination of cTnI is 0.06 μg/L. However, in our laboratory, the cutoff used is 0.08 because this is the concentration at which the interassay coefficient of variation is less than or equal to 20% (functional sensitivity or limit of quantification). The 10% coefficient of variation is between 0.08 and 0.1, and for this study we used 0.11 μg/L as the cutoff value for elevated cTnI to ensure that only patients with a clinically relevant elevated troponin were included. To facilitate a more advanced statistical analysis, the cTnI level was divided into 8 subgroups. Serum creatinine was determined from the same sample from which the troponin level was tested or from another blood sample obtained on the same day.

A repeat electrocardiogram (ECG) could be obtained in 39 of the patients with a positive cTnI and in a control group consisting of 28 patients with a positive blood culture but negative cTnI. A cardiologist compared the ECG with the admission ECG. If no admission ECG was found, the ECG was compared with that from a previous hospitalization. Patient charts were reviewed for documentation of symptoms suggesting any acute cardiac symptoms in the period between the 2 ECG recordings. Any change between the ECGs was recorded.

In each patient, we determined whether infection was community or hospital acquired. Patients whose blood culture was drawn and found positive more than 48 hours after hospitalization were defined as having a hospital-acquired infection.[13,14] Bacteria were identified by accepted methods. Appropriateness of empiric antibiotic treatment was determined on the basis of the antimicrobial susceptibilities.

For each adult patient, a mortality probability model (MPM) score[15] was calculated. Its aim was to determine the risk for fatal outcome and severity of disease at the time of admission. The data used for the MPM score included indication for admission, Glasgow Coma Scale, need for resuscitation, need for surgery at admission, presence of malignancy as part of the presenting disease, presence of infection as part of the index disease, presence of chronic renal failure, hospitalization in an intensive care unit during the previous 6 months, age, heart rate, and diastolic blood pressure in the emergency department. The result is a continuous qualitative value between 0 and 1.

Determination of the systemic inflammatory response syndrome[15,16] was done for each patient with data from the day on which the positive blood culture was taken. These data included fever ($>$38.0°C or $<$35.0°C), heart rate ($>$90 beats/min), respiratory rate ($>$20 breaths/min), and white blood cell count ($>$12,000 μ/mm^3, $<$4,000 μ/mm^3, or $>$100 μ/mm^3 of bands). In addition, in patients with the systemic inflammatory response syndrome, we determined whether bacteremia was associated with sepsis, severe sepsis, or septic shock according to standard criteria.[16,17] We measured the duration of hospitalization and the interval between the time of the blood culture and the day of discharge or death.