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The usefulness of serum troponin levels to predict 1-year survival rates in infective endocarditis

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SUMMARY

Background and aim: Infective endocarditis (IE) is associated with increased mortality and morbidity. In this study, we aimed to evaluate the role of troponin levels in predicting long-term survival in patients with IE.

Methods: A retrospective analysis of the medical database of Yuksek Ihtisas Education and Research Hospital was performed to reach the patients that received the diagnosis of definite IE according to Duke criteria. Out of 84 definite IE cases, 48 patients (mean age 45.6±17.3, 39.6% female) that had troponin T levels measured upon hospital admission were included. The survival status of the study subjects was assessed during a follow-up period of 1 year.

Results: A total of 20 (41.7%) patients died during the follow-up. Baseline median troponin T levels were significantly higher in fatal cases (0.08 [0.02-0.24] ng/ml vs. 0.02 [0.01-0.04] ng/ml p=0.003). The optimal troponin T level to detect mortality was 0.05 ng/ml according to receiver operating characteristic curve (area under the curve 0.75, 95% Confidence Interval (CI) [0.61-0.9], p=0.003) with 70% sensitivity and 79% specificity. Patient with elevated troponin levels were older, were more likely to be male and tended to have enterococcal infection. These patients had also higher creatinine levels and increased systolic pulmonary pressures. In the multivariate Cox regression analysis, renal failure (hazards ratio (HR) 8.23, CI 95% 2.53-26.9, p<0.0001), heart failure (HR 4.48, CI 95% 1.73-11.61, p=0.002) and troponin T ≥ 0.05 ng/ml (HR 3.11, CI 95% 1.13-8.56, p=0.03) were associated with increased mortality rates.

Conclusions: IE has poor outcome and baseline troponin T levels may predict long-term survival rates in these patients.

1. Introduction

Infective endocarditis (IE) is associated with considerable mortality and morbidity rates despite recent improvements in the management of the cardiovascular diseases. In-hospital mortality rates range from 10% to 20%, while long-term mortality rates can be much higher [1–3].

IE has a broad range of course and identifying individuals who are at increased risk of adverse outcomes is challenging due to interaction of various factors. The immune status of the host, foreign body involvements, underlying heart disease, causative microorganism, and the region of the infection may all alter the course of this complex disease. Various clinical predictors have been proposed to estimate the outcome, but these parameters generally emerge overtime [1,4]. Indications and timing of the surgery, or duration of the antimicrobial therapy are still a matter of debate; therefore a powerful biomarker may facilitate risk stratification to make decision on these critical points, especially at the early stages of the disease.

Troponins are cardiac specific proteins that are released in case of myocardial injury. Besides well-known relationship with troponins and adverse outcome in acute coronary syndrome, similar associations have also been demonstrated in other cardiac and non-cardiac settings [5]. Recent studies have demonstrated that high troponin levels can be detected in IE and elevated troponin levels are associated with adverse outcome in patients with IE [6,7]. However, to date no study has evaluated the role of

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cardiac troponins in predicting long-term outcome. In the present study, we aimed to investigate the relationship between troponin levels and 1-year survival status in patients with IE.

2. Methods

2.1. Study Patients

The medical database of Yuksek Ihtisas Education and Research Hospital, Ankara, Turkey was reviewed retrospectively. Between January 2008 and January 2011, 84 consecutive patients diagnosed with definite IE according to the modified Duke criteria were enrolled [8]. Of all cases, 48 patients that had troponin T levels measured upon hospital admission (within 48 hours of initial admission) were included. Clinical, echocardiographic, and laboratory findings were recorded for each subject. Predisposing heart diseases including prosthetic valve, pre-existing valvular disease (rheumatic heart disease and degenerative valves), congenital heart disease, implantable cardiac device, nosocomial infection and previous history of IE were assessed. Hypertension was defined as blood pressure >140/90 mm Hg on >2 occasions during office measurements or use of antihypertensive treatment. Coronary artery disease was considered to be present when there was documented coronary stenosis of >50%.

Complications during hospitalization such as heart failure, renal failure, abscess formation, cerebrovascular events and surgical treatment for IE were recorded. Cerebrovascular events referred to the one of the following presentations: intracranial hemorrhage, ischemic stroke, and transient ischemic attacks. Renal failure was defined by serum creatinine concentration exceeding 2 mg/dl during hospital stay. The primary end point of the study was the incidence of all cause death within one year after the index hospitalization. Clinical event data were collected during the follow-up period for all patients by reviewing medical files and by telephone contacts. One-year follow-up was completed in all of the patients. The study was performed in accordance with the Declaration of Helsinki for human research and was approved by the local ethics committee.

2.2. Laboratory

Blood samples for troponin T were obtained upon admission and measured with an auto analyzer (Elecsys 2010) running commercial assays (Roche Diagnostics, Penzberg, Germany). This assay was reported in ng/ml and the upper reference limit (99th percentile) was < 0.01ng/ml in studies performed with healthy volunteers. Hemoglobin and white blood cell counts were measured using an automated hematology analyzer. C reactive protein (CRP), glucose and creatinine levels were measured accordingly. At least 3 sets of blood samples for cultures were obtained from each patient immediately after hospital admission. Any other available fluid, tissue (valves, vegetations or intracardiac abscesses removed at surgery) or foreign body samples (pacemaker leads, catheters) were used to isolate microorganisms.

2.3. Echocardiography

All patients underwent two-dimensional transthoracic echocardiography within 24 hours of admission. Echocardiographic examinations were performed with the Vivid 7 system (GE Healthcare, Wauwatosa, Wisconsin). Transesophageal echocardiography was performed when image quality with transthoracic echocardiography was not sufficient for an accurate diagnosis; or in cases of high clinical suspicion of IE, prosthetic valve involvement, and suspicion of complications. Vegetation, abscess formation, and valvular destruction (such as perforation of leaflet and chordal rupture) were noted. Vegetation size was measured by using different echocardiographic windows, and the maximal length was obtained. Existence of rocking motion of the prosthetic valve with an excursion of $> 15^{\circ}$ in at least one direction led to the diagnosis of dehiscence. Left ventricular ejection fraction was calculated by the modified Simpson method. Severe valvular regurgitation was identified according to guideline recommendations [9]. Continuous-wave Doppler of the tricuspid regurgitation jet signal using the Bernoulli equation estimated pulmonary artery systolic pressure [10].

2.4. Statistics

Continuous variables were expressed as mean ± SD or as median with interquartile range; and categorical variables were expressed as number and percentages. Categorical variables were compared with $\chi 2$ test or Fisher test; continuous variables were compared with Student's *t*-test or Mann-Whitney U test, as appropriate. Spearman correlation analysis was performed to evaluate the relation of troponin T with other variables. Receiver operating characteristic (ROC) curve was used to detect the optimal cut-off point of troponin T levels to estimate 1-year survival. Patients with IE were categorized into two groups on the basis of this cut-off value. Kaplan-Meier survival curves and log-rank values were used to assess survival in subgroups. Univariate Cox regression analysis was performed to assess the association of the variables with 1-year mortality. Variables that had $p<0.1$ in the univariate analysis were further analyzed with multivariate Cox regression model with conditional stepwise method. Results of the Cox regression analysis were reported with hazards ratios (HR) and 95% confidence intervals (CI). Statistical analysis was performed using SPSS software version 20.0 (SPSS Inc., Chicago, IL). A p value of 0.05 was considered statistically significant.

3. Results

Out of 84 definite IE cases, 48 patients had troponin T levels available. Supplement 1 shows baseline characteristics of the study subjects, and comparison of patients regarding the presence of troponin measurement. There were differences in various parameters of patients with and without troponin T levels, including presence of coronary artery disease, severe valvular regurgitation or enteroccocal infection, but these differences were not statistically significant.

Staphylococci species were the most common microorganisms. Presence of a prosthetic valve was the most common predisposing factor in the study cohort. Median duration of hospital stay was 31 days. A total of 20 (41.7%) patients died during the follow-up. Supplement 2 shows the differences between survivors and non-survivors. Renal failure, heart failure, and severe valvular regurgitation were significantly higher among non-survivors, whereas having a surgery due to IE was associated with lower mortality.

Baseline median troponin T levels were significantly high in fatal cases (0.08 [0.02-0.24] ng/ml vs. 0.02 [0.01-0.04] ng/ml, p=0.003). There was a modest correlation between troponin levels and age (r=0.38, p=0.008), CRP (r=0.32, p=0.03), creatinine (r=0.33, p=0.02), and systolic pulmonary artery pressure (r=0.49, $p<0.001$). The optimal troponin T level to detect mortality was 0.05 ng/ml according to ROC curve (area under the curve 0.75, 95% CI [0.61-0.9], p=0.003) with 70% sensitivity and 79% specifity (Figure 1). Of all patients, 19 (40%) had troponin T ≥ 0.05 mg/dl. To evaluate the association between troponin T and clinical outcome, patients were divided into 2 groups based on this cut-off value. Table 1