PROGNOSTIC FACTORS AND IN-HOSPITAL OUTCOME OF NATIVE VALVE ENDOCARDITIS IN TURKEY. A MULTICENTER STUDY

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ABSTRACT

Aim: To investigate the predisposing factors, demographic and clinical characteristics, echocardiographic and prognostic features, and outcomes of patients with native valve infective endocarditis (IE) in Turkey in a multicenter based study.

Materials and methods: The study population consisted of 158 consecutive patients with native valve IE (NVE). Data on demographics, medical history, medications, clinical procedures, predisposing factors, clinical examination, microbiology, antibiotic therapy, echocardiography, surgery, complications, and outcome were collected and compared.

Results: The mean age of the patients was 47±19 (range 13-87). Seventy seven patients (49%) were female. Of the 158 NVE patients, 49 died during hospitalization. Mortality rate was 31%. Twenty eight patients experienced a stroke. The patients who died during hospitalization were significantly older than the survivors and had higher mean heart rate, white blood cell, C reactive protein, creatinine, poor NYHA functional class, multiple vegetations and large vegetations. Culture-negative endocarditis was seen in 54 cases (34%). Staphylococci were the most common causative organisms (28%). Eighty patients had undergone surgical treatment (51%). Hemoglobin, presence of multiple vegetation, vegetation size (>10 mm), septic shock and poor NYHA class on admission were independent risks for in hospital mortality and stroke. Beside these variables C reactive protein was also an independent risk for in hospital mortality.

Conclusion: Native valve IE in Turkey was associated with high in-hospital mortality. Rheumatic heart disease continues to be the most common underlying heart condition and echocardiographic findings on admission were the most important independent predictors of mortality or stroke.

Key words: native valve endocarditis, prognostic factors, mortality.

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Introduction

In spite of medical improvements, infective endocarditis (IE) remains a very serious health problem with a high mortality rate1,2. Over the past decades there has been a change in the age-related incidence of infective endocarditis from younger to more elderly patients in the developed countries. However in the rest of the world, IE more frequently affects younger patients with a larger spectrum of causative microorganisms. Increase in intravenous drug users, degenerative valvular lesions, longevity and more frequent rheumatic valvular disease prevalence; determine the risk groups in the developing countries. Despite these changes, the prevalence and general aspects of IE has not changed much3,4.

We sought to determine the predisposing factors, demographic and clinical characteristics, echocardiographic and prognostic features, and outcomes of patients with native valve infective endocarditis in Turkey in a multicenter based study.

Methods

The study population consisted of 158 consecutive Turkish patients with IE treated at 13 major hospitals in Turkey from 2005 to 2012. All hospitals are tertiary referral centers, which receive patients from surrounding hospitals. These hospitals were located in different cities throughout Turkey. The diagnosis of definite IE was confirmed using the modified Dukes criteria5. A standard report
form was used at all sites to collect data. Data on demographics, medical history, medications, clinical procedures, predisposing factors, clinical examination, microbiology, antibiotic therapy, echocardiography, surgery, complications, and outcome were collected. The presence of the following characteristics was investigated on echocardiography: presence of vegetation, new moderate or severe valvular regurgitation, cordal rupture, new dehiscence and abscess. Measurements of the vegetation length were performed in various planes, and the maximal length was measured. Transthoracic (TTE) and/or transesophageal echocardiography (TEE), were performed as clinically indicated.

Complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rates (ESR), serum chemistry, and urine analysis, the antibiotic regimen, aspects related to the surgical approach and in-hospital outcome were also recorded. The study was approved by the local Medical Ethics Committee.

**Statistical analysis**

Statistical Package for Social Sciences software (SPSS 12, Chicago, IL, USA) was used for analysis. Descriptive parameters were shown as mean ± standard deviation or in percentages. Student’s t-test was used to compare continuous variables. Categorical data were compared with chi-square test. Variables, which were not normally distributed, were compared using Mann-Whitney U test. Multivariate logistic regression analysis was used to assess the independent risks for in-hospital mortality and major adverse outcome (mortality or disabling stroke). The covariates included in the analysis were age, white blood cell, creatinine, heart rate, vegetation size and poor NYHA functional class on admission (class III or IV). A p value of < 0.05 was considered statistically significant.

**Results**

The mean age of the patients was 47±19 (range 13-87). Seventy seven patients (49%) were female. Of the 158 NVE patients, 49 died during hospitalization. Mortality rate was 31%. Twenty eight patients experienced a stroke and 24 of them died which showed a very high rate of in-hospital mortality (85%). Clinical, echocardiographic and microbiological variables of survivors and patients who died were compared in Tables I and II.

<table>
<thead>
<tr>
<th></th>
<th>Survivors (n=109)</th>
<th>dead (n=49)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>44±19</td>
<td>52±18</td>
<td>0.013</td>
</tr>
<tr>
<td>Gender Female n,</td>
<td>52 (48%)</td>
<td>24 (49%)</td>
<td>0.882</td>
</tr>
<tr>
<td>Patient history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic renal failure, n</td>
<td>19 (17%)</td>
<td>23 (47%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes Mellitus, n</td>
<td>16 (15%)</td>
<td>6 (12%)</td>
<td>0.683</td>
</tr>
<tr>
<td>Weight loss, n</td>
<td>16 (15%)</td>
<td>12 (24%)</td>
<td>0.135</td>
</tr>
<tr>
<td>Fever (&gt;38.3°C), n</td>
<td>91 (83%)</td>
<td>30 (61%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>118±15</td>
<td>107±18</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>72±10</td>
<td>66±10</td>
<td>0.001</td>
</tr>
<tr>
<td>Pulse, bpm</td>
<td>85±11</td>
<td>101±12</td>
<td>0.001</td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>11.3±2.3</td>
<td>9.8±2</td>
<td>0.001</td>
</tr>
<tr>
<td>White blood cell, n/ml</td>
<td>13889±5244</td>
<td>16979±9872</td>
<td>0.011</td>
</tr>
<tr>
<td>Sedimentation rate, mm/hour</td>
<td>64±25</td>
<td>71±28</td>
<td>0.119</td>
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<tr>
<td>C reactive protein, mg/dl</td>
<td>62±46</td>
<td>86±75</td>
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</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>1.4±1.5</td>
<td>2.5±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA FC &gt;2, n</td>
<td>34 (31%)</td>
<td>44 (90%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septic shock, n</td>
<td>2 (2%)</td>
<td>24 (49%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke, n</td>
<td>4 (4%)</td>
<td>24 (49%)</td>
<td>&lt;0.001</td>
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<tr>
<td>Embolism, n</td>
<td>15 (14%)</td>
<td>18 (37%)</td>
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<tr>
<td>Atrial fibrillation, n</td>
<td>7 (6%)</td>
<td>6 (12%)</td>
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</tr>
<tr>
<td>Abscess, n</td>
<td>2 (2%)</td>
<td>5 (10%)</td>
<td>0.016</td>
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</table>

**Table 1:** Comparison of baseline demographic and clinical characteristics on admission.

Continuous variables were represented as mean ± SD. NYHA; New York Health Association functional class.characteristics on admission

The patients who died during hospitalization were significantly older than the survivors and had higher mean heart rate, white blood cell, C reactive protein, creatinine, poor NYHA functional class, multiple vegetations and large vegetations. A pathogenic microorganism was isolated from blood cultures in 104 cases (66%). Staphylococci were the most common causative organisms (28%), followed by streptococci, which were identified in 11% of cases.

Community-acquired methicillin-resistant S. aureus was found in 9 patients (6%) and coagulase-negative staphylococci in 7%. The next most common etiologic agents were enterococci (11%). Culture-negative endocarditis occurred in 54 patients (34%).
Mean duration of hospital stay was 27±18 days. Eighty patients had undergone surgical treatment (51%) patients during index hospitalization. The main indication for surgery was refractory heart failure, persistent large vegetation, pulmonary embolism and persistent infection. Among the 49 (31%) patients who received medical therapy alone, hospital mortality was 37%. Twenty one of the patients who had treated with surgery died during hospital stay (mortality rate among patients treated with surgery was 26%).

In order to understand independent risks for major adverse events logistic regression analysis was performed. Hemoglobin, presence of multiple vegetation, vegetation size (>10 mm), septic shock and poor NYHA class on admission were independent risks for in hospital mortality and stroke. Beside these variables C reactive protein was also an independent risk for in hospital mortality (Table III).

<table>
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<td>Age</td>
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<td>0.990-1.069</td>
<td>0.144</td>
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<tr>
<td>Hemoglobin, g/dl</td>
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<td>0.471-0.859</td>
<td>0.003</td>
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<tr>
<td>White blood cell, n/ml</td>
<td>1</td>
<td>1.000-1.000</td>
<td>0.228</td>
</tr>
<tr>
<td>C- Reactive protein, mg/dl</td>
<td>1.028</td>
<td>1.008-1.049</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Table 2: Comparison of echocardiographic and microbiological variables in patients with NVE survivors and patients died during hospitalization.

Continuous variables were represented as mean ± SD, NVE; Native Valve Endocarditis

In order to understand independent risks for major adverse events logistic regression analysis was performed. Hemoglobin, presence of multiple vegetation, vegetation size (>10 mm), septic shock and poor NYHA class on admission were independent risks for in hospital mortality and stroke. Beside these variables C reactive protein was also an independent risk for in hospital mortality (Table III).

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Table 3: Multivariate logistic regression analysis assessing the independent risks for in-hospital major adverse events.

NYHA; New York Health Association functional class.

Discussion

This multicenter study provided significant data on the epidemiology, microbiology, clinical characteristics, prognostic features, treatment and outcome of IE in tertiary referral centers in Turkey.

In the present study, in-hospital mortality was 31%, which is mildly higher than that observed in other countries (9-12) including some other developing countries (13,14). This higher mortality may have been due to the relatively more complex cases being admitted to our centers, such as cases with late diagnosis, which have been already complicated on admission and the high proportion of IE
involving staphylococci. It is well known that the clinical features of IE substantially differ between patients from referral centers and those seen in primary-care centers(19).

In West, the epidemiologic characteristics of IE have changed over the past few decades. These changes is attributed to a number of factors including increasing patient longevity and a concomitant increase in cases of degenerative valvarul disease, reduction in the incidence of acute rheumatic disease, early correction of congenital cardiac defects and more frequent use of invasive central vascular catheters associated(6,16,14). In our study, the mean age of the patients was 47 years (range 13 to 87 years) and rheumatic heart disease was the most common underlying heart disease for IE (38%). Compared to other reports from Turkey, our patient population was relatively older (5,7). But the rate of rheumatic fever when compared with these studies is higher in our study (60/158, 38% and 11/68, 16.2%, respectively). In a recently published domestic paper, rheumatic heart disease (36.1% including patients with prosthetic valves) was the most common pre-existing valvular abnormality in IE patients, constituting four times higher incidence than degenerative valvarul disease as the predisposing risk factor for IE(19). Although the incidence of acute rheumatic fever has decreased in the last decade, it still continues to be an important public health problem in Turkey(20). Therefore, we assume that the high frequency of rheumatic valvarul disease will be one of the most important predisposing risk factors in the prevalence of IE in the near future.

Culture-negative endocarditis was seen in 54 cases (34%) of our study population and is among the lowest rate reported from the developing countries(6,16,21,22). The high culture positivity rates are extremely important as the optimal and effective therapy of IE depends on culture and antibiotic sensitivity results. Low blood culture positivity is related with three major reasons: previous administration of antimicrobial agents, inadequate microbiological techniques, and infection with highly fastidious bacteria or non-bacterial pathogens(23).

Our findings showed that echocardiographic findings performed on admission had a significant prognostic value showing one of the highest odds ratios for major adverse events (combined end point of mortality or stroke). Our results are concordant with the literature data with the recent prospective multicenter studies(22,24).

The study done by Thuny et al showed that large vegetations (>10 mm) and/or high vegetation mobility were associated with an increased embolic risk(25). In the current study, presence of a large vegetation (>10 mm) was associated with an 8.5 times risk of death or stroke. Similarly, multiple vegetations on admission carried a risk of 250 times of in-hospital mortality. Concordant with these results, Hill et al. observed that vegetation length >10 mm was independently associated with six-month mortality(25). On the other hand, in a series from Brazil, vegetation length >13 mm was the only independent predictor of in-hospital mortality(22).

**Conclusions**

Native valve IE in Turkey was associated with high in-hospital mortality. Rheumatic heart disease continues to be the most common underlying heart condition and echocardiographic findings on admission were the most important independent predictors of mortality or stroke.

**References**


Acknowledgements
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