INTRODUCTION

Infective endocarditis (IE) is a serious endovascular infection and has a reported incidence of 1 per 1000 hospital admissions in the United States [1]. Despite major advances in diagnostic technology and antimicrobial treatment, the morbidity and mortality remain high; it has been reported that in-hospital mortality rate is nearly 20% [2-5]. Embolic events occur in 30% to 40% of patients with left-sided IE [6,7]. The utility of the Duke criteria [8,9] for the diagnosis of IE is well recognized [10,11]. Rapid diagnosis, effective treatment, prompt recognition of complication and risk factors for mortality are essential to good outcome. This study is designed to determine whether the echocardiographic findings and clinical features can serve as the risk factors of embolic events.

MATERIALS AND METHODS

Patient population

From January 1998 to December 2002, we identified 93 patients with definite IE according to modified Duke criteria [6] at the China Medical University Hospital.

For patients with repeat episodes of IE at our institution, only the first episode was included. Patients in which IE involved a prosthetic valve or patients with IE involving more than one valve were excluded.
The relationships between age, sex, microorganism, major embolic events, involved valve, vegetation size, peak C-reactive protein (CRP) and prognosis (in-hospital death) were analyzed.

**Classification of embolic events**

An embolic event was defined as the acute onset of organ system dysfunction consistent with ischemia [5]. Determination of major embolic events was made by review of the complete medical record, including brain embolism, pulmonary embolism, spleen embolism and kidney embolism. Patients with immune complex phenomena and microvascular emboli, such as cutaneous microinfarction, were not included in this study.

**Statistical methods**

Continuous variables are presented as mean ± SD for data distribution. Statistical testing was performed with the Student's *t* test for continuous variables. The influences of risk factors on the mortality and major embolic events were assessed by Fisher's exact test. Logistic regression modeling and ROC curve were used to determine the relationship between vegetation size and stroke. A *p* value < 0.05 was considered statistically significant.

**RESULTS**

The clinical characteristics of the 93 patients are listed in Table 1. Patients ranged in age from 3 to 83 years (mean, 44 yr). There was a male predominance (men/women: 75%:25%). Of the 93 patients with IE, 28 had major embolic events. In the non-fatal group (n = 71), a total of 18 patients had major embolic events, including 8 patients with brain embolism, 7 patients with pulmonary embolism and 3 patients with spleen embolism. In the fatal group (in-hospital death, n = 22), a total of 10 patients had major embolic events, including 8 patients with brain embolism and 2 patients with pulmonary embolism. The incidence of brain emboli was significantly higher in the fatal group (*p* = 0.019). We found that a brain embolic event was an independent predictor of death but other embolic events (pulmonary emboli, spleen emboli and kidney emboli) were not. The peak CRP was 60.2 ± 61.4 (mg/L) in the non-fatal group and 149.5 ± 75.3 (mg/L) in the fatal group (*p* = 0.004), indicating that elevation of CRP level was associated with increased risk of mortality in this study.

Stroke was associated with an increased risk of in-hospital death (*p* = 0.019) (Table 2). There was a higher incidence of stroke in IE patients with mitral valve involvement (*p* = 0.003) (Table 3). There were no incidences of stroke in patients with tricuspid infective endocarditis. Microorganisms were not associated with an increased risk of stroke (Table 4). Our data revealed that age, sex, microorganism, aortic valvular disease, and microvascular phenomena were not independent predictors of in-hospital death.

**Clinical characteristics**

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Gender (male/female)</th>
<th>CHF, Fc III and CHF, Fc IV</th>
<th>Intravenous drug abuser</th>
<th>Medical death</th>
<th>Brain emboli</th>
<th>Spleen emboli</th>
<th>Pulmonary emboli</th>
<th>Kidney emboli</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 ± 20</td>
<td>70/23</td>
<td>20</td>
<td>20</td>
<td>22</td>
<td>16</td>
<td>3</td>
<td>9</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are presented as the mean value ± SD or number. CHF = congestive heart failure; Fc III = function class III; Fc IV = function class IV.

**Comparison of clinical features in patients with and without stroke**

<table>
<thead>
<tr>
<th></th>
<th>Non-stroke (n = 77)</th>
<th>Stroke (n = 16)</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>44 ± 20</td>
<td>47 ± 18</td>
<td>0.6</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>58/19</td>
<td>12/4</td>
<td>1.0</td>
</tr>
<tr>
<td>Medical death</td>
<td>14</td>
<td>8</td>
<td>0.019</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>88.3 ± 66.8</td>
<td>96.8 ± 90.2</td>
<td>0.516</td>
</tr>
</tbody>
</table>

Data are presented as the mean value ± SD or number. CRP = C-reactive protein.

**Comparison of involved valves in patients with and without stroke**

<table>
<thead>
<tr>
<th></th>
<th>Non-stroke (n = 77)</th>
<th>Stroke (n = 16)</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral valve</td>
<td>25</td>
<td>12</td>
<td>0.003</td>
</tr>
<tr>
<td>Aortic valve</td>
<td>25</td>
<td>4</td>
<td>0.768</td>
</tr>
<tr>
<td>Tricuspid valve</td>
<td>20</td>
<td>0</td>
<td>0.019</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>0</td>
<td>0.599</td>
</tr>
</tbody>
</table>

The peak CRP was 60.2 ± 61.4 (mg/L) in the non-fatal group and 149.5 ± 75.3 (mg/L) in the fatal group (*p* = 0.004), indicating that elevation of CRP level was associated with increased risk of mortality in this study.

Stroke was associated with an increased risk of in-hospital death (*p* = 0.019) (Table 2). There was a higher incidence of stroke in IE patients with mitral valve involvement (*p* = 0.003) (Table 3). There were no incidences of stroke in patients with tricuspid infective endocarditis. Microorganisms were not associated with an increased risk of stroke (Table 4). Our data revealed that age, sex, microorganism, aortic valvular disease, and microvascular phenomena were not independent predictors of in-hospital death.
Brain Embolic in Infective Endocarditis

Table 4. Comparison of causative organisms in patients with or without stroke

<table>
<thead>
<tr>
<th></th>
<th>Non-stroke (n = 77)</th>
<th>Stroke (n = 16)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORSA</td>
<td>7</td>
<td>3</td>
<td>0.37</td>
</tr>
<tr>
<td>OSSA</td>
<td>18</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td><em>Streptococcus viridans</em></td>
<td>16</td>
<td>5</td>
<td>0.35</td>
</tr>
<tr>
<td>Other <em>Streptococcus</em></td>
<td>12</td>
<td>3</td>
<td>0.72</td>
</tr>
</tbody>
</table>
| ORSA = oxacillin resistant *Staphylococcus aureus*; OSSA = oxacillin sensitive *Staphylococcus aureus.*

Table 5. Comparison of the size of vegetation on mitral valve and aortic valve

<table>
<thead>
<tr>
<th></th>
<th>Aortic valve</th>
<th>Mitral valve</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length (mm)</td>
<td>8.5 ± 5.7</td>
<td>11.5 ± 7.1</td>
<td>0.139</td>
</tr>
<tr>
<td>Width (mm)</td>
<td>5.9 ± 4.1</td>
<td>7.9 ± 5.7</td>
<td>0.201</td>
</tr>
</tbody>
</table>

Figure. ROC curve of vegetation size to predict the risk of stroke. There was a higher risk of stroke in IE with the vegetation size greater than 1 cm and its sensitivity was 90% and specificity was 56% (p = 0.012) (arrow).

In this retrospective study, there were 31 patients whose conditions were diagnosed by transesophageal echocardiography (TEE). The results demonstrated that brain embolism was an independent predictor of in-hospital mortality. Heiro et al found that death during the acute phase of IE occurred in 24% of patients with neurologic complications and in 10% of patients without neurologic complications (p < 0.03) [12]. Chao et al demonstrated that neurologic complications were important prognostic predictors of in-hospital mortality in patients with IE [13]. Di Salvo et al reported that the risk factors for in-hospital mortality were age, prosthetic valve and cerebral embolism [14]. However, Vivian et al found that embolic events were independent predictors of death, although they demonstrated that any stroke (at time of admission or during hospitalization) was associated with an increased risk of death, and the occurrence of other embolic events (excluding stroke) was significantly more common in patients who died during hospitalization [15].

Anderson et al found that patients with mitral valve endocarditis have a greater risk of stroke than patients with aortic valve endocarditis. They demonstrated that the increased risk of stroke in MVE may be in part due to larger vegetations in these patients [16]; however, our data did not support that finding. Despite this difference in stroke risk between patients with MVE and AVE, no differences were detected in stroke severity, stroke subtype, vascular distribution, length of hospitalization, or survival [16]. Previous studies have evaluated predictors of major embolic events in IE. Durante et al demonstrated that young IE patients and/or IE patients with large vegetation and/or high serum CRP levels were at increased risk of major embolic complications during the in-hospital course of the disease [17].

Jaffe et al found that there was a higher risk of embolization in patients with vegetation...
> 10 mm in size [18]. Tischler et al also demonstrated that left-sided vegetation > 10 mm on echocardiograms poses a significantly increased risk of systemic embolization [19]. James et al demonstrated that the presence of vegetation on echocardiograms was not associated with a significantly higher risk for embolism in patients with left-sided native valve IE. The relative risk for embolic events associated with echocardiographically visualized vegetations may be microorganism dependent, with a significantly increased risk seen only in patients with *Streptococcus viridans* infection [6]. However, in our study, that microorganism was not associated with a higher risk for stroke.

In our study, elevation of CRP level was associated with increased risk of mortality \( (p = 0.004) \) but not associated with an increased risk of stroke \( (p = 0.516) \). This discrepancy may be due to the possibility that the CRP level used for analysis was not the real peak CRP level in the stroke group.

A number of limitations should be noted in interpreting the results of this study. Brain embolism was noted by retrospective chart review. Some patients with strokes that presented with mild or atypical signs and symptoms may not have been included. Many factors related to stroke, including old age, cholesterol, hypertension, diabetes mellitus and atrial fibrillation were not evaluated in this study. Vegetation size was measured by two dimensional echocardiography and may not have represented the actual size of vegetation.

In conclusion, brain embolism was a prognostic predictor of in-hospital mortality in patients with IE. We found a higher incidence of brain emboli in IE patients with mitral valve involvement and in IE patients with vegetation greater than 1 cm. There was no significant difference in the vegetation size between mitral or aortic valves. Age, sex, CRP level, and causative organisms were not predictors of brain emboli. Physicians should aggressively treat IE patients with mitral valve involvement and large vegetation.

**ACKNOWLEDGMENT**

We would like to thank Dr. Je-Jeul Hu (China Medical University Hospital) for assistance with statistical analysis.

**REFERENCES**


感染性心内膜炎患者併發腦栓塞之危險因子分析

鄭文君  白培英  周湘台

中國醫藥大學附設醫院  心臟內科

目的  栓塞的發生是感染性心內膜炎的併發症之一，且造成不良的生活品質，但在台灣卻很少有關於超音波的診斷、臨床表現及栓塞預後的相關性研究，本研究主要是探討感染性心內膜炎患者併發腦栓塞的危險因子。

方法  收集了從1998年1月至2002年12月發生感染性心內膜炎的病例，分析其年齡、性別、菌種、栓塞的發生、感染的瓣膜、赘生物大小、發炎指數和死亡率及相關性。

結果  此回溯性的研究，共收集93個病例，其中28人發生了栓塞。而發生栓塞的病例中有10人死亡，其中腦栓塞的發生率明顯較高，另外感染二尖瓣的心內膜炎及赘生物大於1公分者，其發生腦栓塞比例也明顯升高。

結論  腦栓塞是發生感染性心內膜炎死亡的重要因子，而感染二尖瓣的心內膜炎及赘生物大於1公分者，則為發生腦栓塞的危險因子。（中華醫學期刊2005;10:138-43）

關鍵詞
腦栓塞，感染性心內膜炎，赘生物大小

聯絡作者：白培英
地    址：404台中市北區育德路2號
        中國醫藥大學附設醫院  心臟內科
收文日期：2005年5月13日    修訂日期：2005年7月21日
接受日期：2005年7月28日