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Original Article

Comparison of the clinical manifestations of infective endocarditis between elderly and young patients — a 3-year study

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Background and purpose: Infective endocarditis (IE) is associated with high morbidity and mortality. This study investigated the clinical manifestations and outcomes of IE and compared them between old and young patients.

Methods: In this retrospective study, data for patients with IE who were treated from November 1, 2003 to October 30, 2006 were collected. Patients were identified as having IE if they met the modified Duke criteria for definitive IE.

Results: Seventy two patients were included. The most common symptoms were fever (81%) and dyspnea (50%). Fifty four patients (75%) had culture-positive IE. *Staphylococcus aureus* (35%) was the most common organism isolated, followed by *Streptococcus* spp. (26%). Vegetations were detected in 60 patients (83%): mitral valve (MV; 40%), aortic valve (AV; 24%), tricuspid valve (TV; 14%), MV and AV (4%), and pulmonary valve (1%). Thirty nine patients (54%) had embolic complications — 26 older patients (79%) and 13 younger patients (33%). Twenty two patients (31%) died in hospital. There were significant differences in clinical features between older and younger patients. Diabetes mellitus ($p \leq 0.01$), MV vegetation ($p \leq 0.01$), emboli ($p \leq 0.01$), and mortality ($p = 0.01$) were more common among older patients, while male sex ($p \leq 0.01$), intravenous drug use ($p \leq 0.01$), *S. aureus* endocarditis ($p \leq 0.01$), and TV vegetation ($p = 0.01$) were more common in younger patients.

Conclusion: While this study showed significant differences between older and younger patients, further investigation will be necessary to more precisely characterize the clinical spectrum of IE.

Key words: Aged; Endocarditis; Middle aged; Mortality; Young adult

Introduction

Despite advances in clinical medicine, infective endocarditis (IE) associated with morbidity and mortality remains a challenge in clinical medicine. The clinical features of IE have changed in recent years [1,2], and different age groups have different clinical characteristics and outcomes [3]. To ascertain the differences between old and young patients with IE in Taiwan, 125 episodes of IE were retrospectively analyzed for clinical presentation and outcomes.

Methods

The medical records of patients with IE treated at the Mackay Memorial Hospital, Taipei, Taiwan, from November 1, 2003 to October 30, 2006 were reviewed. Patients were identified as having IE if they met the modified Duke University criteria for definitive or possible IE [4].

Patients' medical records were examined for demographic information, comorbid conditions, previous

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heart disease, clinical characteristics, laboratory data, microbiological data, transthoracic echocardiogram (TTE), transesophageal echocardiogram (TEE), results of surgery, and in-hospital mortality.

Statistical analysis

The demographic data were examined for significant association with old and young age. For categorical variables, chi-squared or Fisher's exact tests, odds ratio of Mantel-Haenszel test, and univariate and multivariate logistic regression analyses were applied using the Statistical Package for the Social Sciences (SPSS) for Windows (Version 12.0; SPSS Inc, Chicago, IL, USA). A p value <0.05 was considered statistically significant.

Results

113 patients were treated for 125 episodes of clinically diagnosed IE during the study period. Forty one patients were excluded due to failure to meet the modified Duke criteria (definitive IE) or incomplete medical records. The patients' characteristics are shown in Table 1.

Patient and disease characteristics

The 72 patients who fulfilled the modified Duke's criteria for definitive IE were categorized as elderly (older than 65 years; n = 33) or young (65 years or younger; n = 39). The mean age of the patients was 57.8 years (range, 21-95 years). There were 36 men and 36 women. Men predominated in the young age group and women predominated in the older group. Twenty two patients (31%) had diabetes mellitus (DM), which occurred more frequently in the older group (n = 17; 52%) than in the younger group (n = 5; 13%) [$p \leq 0.01$]. Thirty seven patients (51%) had structural heart diseases (n = 20 in the older group vs n = 17 in the younger group; 2 patients in the older group had a prosthetic valve vs 1 in the younger group). Fourteen patients (19%) who were intravenous drug users (IVDUs) were in the younger group ($p \leq 0.01$).

The most common symptom was fever (n = 58; 81%), followed by dyspnea (n = 36; 50%). Leukocytosis (n = 59; 82%) and hypoalbuminemia (n = 65; 90%) were the most common laboratory findings.

Fifty five patients (76%) had culture-positive endocarditis. Overall, *Staphylococcus aureus* (n = 25; 35%) was the most common organism isolated (methicillin-sensitive *S. aureus* [MSSA] was isolated in 14 patients [64%] and methicillin-resistant *S. aureus* was isolated in 8 patients [36%]). Younger patients (n = 17) were affected significantly more often than elderly patients (n = 5) [$p \leq 0.01$]. Three patients (4%) had coagulase-negative staphylococci (CoNS) infection. *Streptococcus* spp. (n = 19; 26%) was the second most common organism isolated, including α-hemolytic streptococci in 11 patients, β-hemolytic streptococci in 4, γ-hemolytic streptococci in 1, *Streptococcus bovis* in 2, and *Streptococcus pneumoniae* in 1. The other organisms isolated were *Enterococcus* spp. in 2 patients, *Escherichia coli* in 2, *Klebsiella pneumoniae* in 1, *Enterobacter cloacae* in 1, *Enterobacter aerogenes* in 1, and *Corynebacterium* spp. in 3.

Vegetation was detected by TTE or TEE in 60 patients (83%). The most common valve involved was the mitral valve (MV; n = 29; 40%). Other vegetation locations were the aortic valve (AV; n = 17; 24%), tricuspid valve (TV; n = 10; 14%), pulmonary valve (PV; n = 1; 1%), and MV plus AV (n = 3; 4%). MV vegetation occurred more often in the older group than in the younger group ($p \leq 0.01$), while TV vegetation was noted more often in the younger group ($p = 0.01$).

Complications and outcomes

Thirty nine patients (54%) had complications of emboli, 26 (79%) from the older group and 13 (33%) from the younger group ($p \leq 0.01$). Nineteen of the 39 patients (49%) had a cerebrovascular event and 10 (26%) had pulmonary emboli. Other complications were renal emboli (n = 1), cutaneous emboli (n = 6), and splenic infarction (n = 3). All 72 patients received antimicrobial therapy. Surgical intervention was performed for 31 patients (43%). Twenty one patients with heart failure (29%) underwent valve surgery, 9 from the older group and 12 from the younger group. Uncontrolled infection was the indication for surgery for 6 patients, 2 from the older group and 4 from the younger group. Twenty two patients (31%) died in the hospital. The mortality rate in the older group was higher than in the younger group (15 [45%] vs 7 [18%]; $p = 0.01$).

Table 2 shows the characteristics of sex, DM, *S. aureus*, MV, TV, embolic complications, and mortality between the older and younger groups according to the Mantel-Haenszel test. Five variables of female sex, DM, MV, embolic complications, and mortality were significantly associated with older patients. MSSA and TV were significantly associated with younger patients.

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Table 1. Characteristics of the younger and older groups of patients with infective endocarditis.

Variable	Older group (n = 33) No. (%)	Younger group (n = 39) No. (%)	*p*
Sex			
Male	11 (33)	25 (64)	
Female	22 (66)	14 (36)	<0.01
Criteria			
2 major	19 (58)	25 (64)	0.57
1 major and 3 minor	14 (42)	14 (36)	0.57
Comorbid condition			
Diabetes mellitus	17 (52)	5 (13)	<0.01
Structural heart disease	20 (61)	17 (44)	0.15
Illicit intravenous drug use	0	14 (36)	<0.01
Human immunodeficiency virus	0	1 (3)	0.35
Symptom			
Fever	27 (82)	31 (79)	0.80
Dyspnea	15 (45)	21 (54)	0.48
Laboratory result			
Leukocytosis (>10,000 cells/μL)	26 (79)	33 (85)	0.52
Thrombocytopenia (<140,000 cells/μL)	9 (27)	10 (26)	0.88
Hypoalbuminemia (<3.5 g/dL)	32 (97)	33 (85)	0.08
Microbiology result			
Positive blood culture	24 (73)	30 (77)	0.68
Staphylococcus aureus	8 (24)	17 (44)	<0.01
Methicillin sensitive	1 (3)	13 (33)	
Methicillin resistant	4 (12)	4 (10)	
Other	3 (6)	0	
Streptococcus spp.	9 (27)	10 (26)	0.88
α-Hemolytic	3 (9)	8 (21)	
β-Hemolytic	4 (12)	0	
γ-Hemolytic	0	1 (3)	
Other	2 (6)	1 (3)	
Vegetation culture	2 (6)	0	
Echocardiography			
Vegetation	29 (88)	31 (79)	0.34
Atrial valve	8 (24)	9 (23)	0.91
Mitral valve	19 (58)	10 (26)	<0.01
Tricuspid valve	1 (3)	9 (23)	0.01
Pulmonary valve	1 (3)	0	
Atrial and mitral valves	0	3 (8)	
Embolic complication	26 (79)	13 (33)	<0.01
Pulmonary emboli	7 (21)	3 (8)	0.09
Cerebrovascular event	12 (36)	7 (18)	0.08
Renal emboli	1 (3)	0	0.27
Cutaneous emboli	3 (9)	3 (8)	0.83
Splenic infarction	3 (9)	0	0.05
Treatment			
Surgery	12 (36)	19 (49)	0.29
Congestive heart failure	9 (27)	12 (31)	
Uncontrolled infection	2 (6)	4 (10)	
Mortality	15 (45)	7 (18)	0.01

Table 3 shows the univariate and multivariate logistical regression analyses for factors of MV, embolic complications, and mortality. MV was significantly associated with female sex and older age. Embolic complications and mortality were significantly associated with older age. Women were significantly more likely to have MV.

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Table 2. Risk factors among the younger and older groups of patients with infective endocarditis according to individual factors.

Variable	Older group (n = 33) No. (%)	Younger group (n = 39) No. (%)	Odds ratio (χ^2)	*p*
Sex				
Male	11 (33)	25 (64)	0.3 (0.1-0.7)	0.011
Female	22 (67)	14 (36)	1.0	
Diabetes mellitus				
Positive	17 (52)	5 (13)	7.2 (2.3-23.1)	0.001
Negative	16 (48)	34 (87)	1.0	
Staphylococcus aureus	8 (21)	17 (44)		
Methicillin sensitive	1 (3)	13 (33)	0.1 (0.1-0.2)	0.020
Methicillin resistant	4 (12)	4 (10)	0.3 (0.1-1.8)	0.177
Other	3 (9)	0	1.0	
Mitral valve				
Positive	19 (58)	10 (26)	3.1 (1.2-8.1)	0.024
Negative	14 (42)	29 (74)	1.0	
Tricuspid valve				
Positive	1 (3)	9 (23)	0.1 (0.1-0.9)	0.037
Negative	32 (97)	30 (77)	1.0	
Embolic complications				
Positive	26 (79)	13 (33)	2.7 (1.1-7.1)	0.041
Negative	7 (21)	26 (67)	1.0	
Mortality				
Positive	15 (45)	7 (18)	3.8 (1.3-11.1)	0.014
Negative	18 (55)	32 (82)	1.0	

Abbreviation: χ^2 = chi-squared test.

Discussion

The clinical presentations of IE are changing due to increasing longevity in the population, new predisposing factors, and increasing nosocomial infection [1,2]. It has been well established that IE occurs most frequently in association with old age, male sex, uremia, DM, skin infections, and infectious episodes [5,6]. In this study, 46% of patients with IE were elderly people, but the male-to-female ratio was equal. More women with IE were elderly and more men were in the younger age group. This result is different from previous studies [1], which may be due to the small sample size in this study.

S. aureus was the most common cause of IE, accounting for 35% of all patients (n = 25). Seventeen patients with *S. aureus* (77%) were in the younger group ($p \leq 0.01$) and most were IVDUs. The influence of *S. aureus* is consistent with other studies showing increases in the overall rates of *S. aureus* bacteremia and related infections, such as vertebral osteomyelitis and IE [2,7,8]. Patients with IE caused by *S. aureus* had a significantly higher mortality rate than those with IE caused by other pathogens [7-9]. Eight patients with *S. aureus* IE (36%) died and 5 patients with *Streptococcus* spp. IE (23%) died. *Streptococcus* spp. was the second most common organism isolated (n = 19; 26%) but there were no significant differences between the older and younger groups.

Although right-sided IE accounts for only 5% to 10% of patients, it has been suggested that a significant increase in the proportion of right-sided IE is related to IVDU [10]. Among patients with IE due to IVDU, *S. aureus* is the most common causative pathogen [1,2,11]. The mortality rate for right-sided IE is generally lower and most patients respond to antimicrobial therapy [12]. In this study, all 14 IVDUs with IE were in the younger group ($p \leq 0.01$). The patients underwent tests for human immunodeficiency virus antibody but only 1 patient had a positive finding (with a CD4 count of 148/mL and a viral load of 247,000 copies/mL). Only 2 of the patients who were IVDUs died. Comparison of patients in the older group with patients in the younger group who were not IVDUs showed that *S. aureus* IE and TV vegetation was not significantly different between the groups. The influence of IVDU is therefore important.

The sensitivity and specificity of TEE is greater than that of TTE. In this study, TEE provided an accurate diagnosis of IE for 9 of 60 patients (15%) for

Table 3. Odds ratios (95% confidence intervals [CI]) for mitral valve involvement, embolic complications, and mortality in patients with infectious endocarditis according to individual factors and after adjustment for other factors.

Variable	Mitral valve involvement		Embolic complications	Mortality
	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Unadjusted odds ratio (95% CI)	Unadjusted odds ratio (95% CI)
Sex				
Male	0.3 (0.1-0.7)[a]	0.3 (0.1-0.9)[a]	1.3 (0.5-3.2)	0.8 (0.3-2.1)
Female	1.0	1.0	1.0	1.0
Age group				
Older	3.1 (1.2-8.0)[a]	2.3 (0.8-6.5)	2.7 (1.1-7.1)[a]	3.8 (1.3-11.1)[a]
Younger	1.0	1.0	1.0	1.0
Diabetes mellitus				
Positive	2.0 (0.7-5.4)	-	0.6 (0.2-1.7)	2.6 (0.9-7.6)
Negative	1.0	-	1.0	1.0
Staphylococcus aureus				
Methicillin sensitive	-	-	-	1.5 (0.3-8.2)
Methicillin resistant	-	-	-	3.7 (0.6-24.1)
Other	-	-	-	1.0
Streptococcus spp.				
α-Hemolytic	-	-	-	0.2 (0.1-2.7)
β-Hemolytic	-	-	-	0.3 (0.1-6.7)
Other	-	-	-	1.0
Atrial valve				
Positive	-	-	1.4 (0.5-3.8)	-
Negative	-	-	1.0	-
Mitral valve				
Positive	-	-	0.7 (0.3-1.7)	-
Negative	-	-	1.0	-
Tricuspid valve				
Positive	-	-	1.3 (0.3-4.9)	-
Negative	-	-	1.0	-
Embolic complication				
Positive	0.7 (0.3-1.7)	-	-	-
Negative	1.0	-	-	-
Surgery				
Positive	0.6 (0.2-1.5)	-	1.3 (0.5-3.4)	0.7 (0.2-1.9)
Negative	1.0	-	1.0	1.0
Mortality				
Positive	1.5 (0.5-4.1)	-	0.6 (0.2-1.7)	-
Negative	1.0	-	1.0	-

[a] $p < 0.05$.

whom TTE was negative. TEE is an essential tool when IE is suspected clinically in patients who are elderly or who may have prosthetic valve or nosocomial IE, and for the early detection of complications of IE [13,14].

Congestive heart failure and neurological events have the most common influence on the prognosis of IE. Several previous studies have reported that the rate of embolic events in patients with IE can be up to 60%. Neurological complications develop in 20% to 40% of all patients with IE [15,16]. Embolic complications were more common in the older group ($p \leq 0.01$). Specific embolic events of neurologic, pulmonary, renal, skin, and spleen were also more common in the older group, although the difference was not significant.

Mortality from IE was associated with several factors of vegetation location, the causative microorganism, comorbid conditions (DM, congestive heart failure, uremia), embolic complications, and medical treatment with or without surgery. The mortality rate for endocarditis is approximately 20% to 25% [1], with a range of 9% to 39%. In this study, the total crude

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mortality rate was 31%, and was higher among the older age group (p = 0.01). This result was different from that of Bouza et al's study, which found that mortality did not increase with age [2]. On univariate logistical regression analysis, MV, mortality, and embolic complications were significantly different in the older group (Table 3). In the mitral valve group, the adjusted female-to-male odds ratio was 1.0:0.3 (95% confidence interval, 0.1-0.9), which meant that men had a reduced risk for IE. There were no differences for the other groups. Although some studies have shown that older age is associated with a poor prognosis [3,17], old age did not appear to be a prognostic factor in the study of Netzer et al [18]. These conflicting results may be explained by factors such as small sample size and definition of old age.

This study has several limitations. Although uniform data collection methods were used, bias may have been present. The sample size was relatively small and the medical records were incomplete. The patients in this study were treated in a large medical center, in which the frequency, type, and severity of IE were likely to differ from a community hospital setting. Future investigations will be necessary to more precisely characterize the clinical spectrum of endocarditis.

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