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Clinical features and predictors for mortality in patients with infective endocarditis at a university hospital in Taiwan from 1995 to 2003

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SUMMARY

The clinical features and microbiological characteristics of 315 patients with definite or possible infective endocarditis (IE) from January 1995 to December 2003 were evaluated. There were 187 males and 128 females with a mean age of 51 years (range, 1 month to 92 years). Ninety-three patients (30%) had a diagnosis of valvular heart disease and 24 (8%) had received prosthetic valve replacement. Blood culture was negative in 62 patients (20%). Staphylococci (91 patients, 32%), including methicillin-susceptible *Staphylococcus aureus* (15%), methicillin-resistant *S. aureus* (11%), and coagulase-negative staphylococci (6%), were the most commonly encountered pathogens followed by viridans group streptococci (77 patients, 24%). Eight patients (25%) had various neurological, renal, embolic, and cardiac complications. Patients with neurological complications [odds ratio (OR) 8·175, $P<0·001$], nosocomial IE (OR 6·661, $P<0·001$), underlying malignancy (OR 4·993, $P<0·001$), elevated serum creatinine level (OR 3·132, $P=0·001$), or elevated WBC count ($>15\,000/mm^3$) (OR 2·537, $P=0·007$) were at significantly increased risk of mortality. This study found mortality from IE was associated with several factors, among which neurological complications were the most hazardous. Patients with more than one risk factor had poorer prognosis. These results suggest the need for more aggressive management in patients with IE when multiple risk factors for mortality are identified.

INTRODUCTION

Infective endocarditis (IE) was always fatal in the pre-antibiotic era [1]. Despite advances in antibiotic therapy and valve surgery in recent decades, and the widely adoption of transoesophageal echocardiography (TEE) as the primary diagnostic modality, the reported in-hospital mortality rate from IE remains high (14–31%) [2–7]. The majority (55–75%) of patients with native valve endocarditis have predisposing conditions including rheumatic heart disease, congenital heart disease, mitral valve prolapse, degenerative heart disease, asymmetrical septal hypertrophy, or intravenous drug abuse [8, 9]. In patients with IE, development of conditions including heart failure, neurological complications, renal failure, fungal infection, valve ring or myocardial abscesses or with prosthetic valve IE has frequently been associated with poor prognosis [10–12].

Numerous studies had been conducted to elucidate the factors contributing to the high mortality and morbidity rates of patients with IE [7, 13–17]. Wallace

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et al. [7] found that among clinical, microbiological, and echocardiographic features, only white blood cell (WBC) count and serum albumin were independent predictors of short-term death. Cabell et al. [13] reported an association between infection with *Staphylococcus aureus* and death. Hasbun et al. [14] found that comorbid illness, mental status, heart failure, causative organism, and surgical therapy were important factors determining 6-month survival. Mourvillier et al. [15] reported that septic shock, cerebral emboli, immunocompromised state, and cardiac surgery independently predict the outcome of native valve IE, while the outcome of prosthetic valve IE was associated with septic shock, neurological complications, and immunocompromised states. Prognosis is good in young intravenous drug abusers with *S. aureus* infection of the tricuspid valve [16, 17]. There has been a lack of large-scale study of IE in Taiwan and few retrospective studies of its prognostic determinants [18, 19].

The goal of this study was to delineate the clinical profile of IE in patients from Taiwan, and to identify the risk factors for mortality by multivariate analysis. The results of this study may have implications for treatment strategy which could improve prognosis.

PATIENTS AND METHODS

Study population

We reviewed the medical records of all the patients with a discharge diagnosis of IE at National Taiwan University Hospital (Taipei, Taiwan), a 2000-bed tertiary care hospital, from January 1995 to December 2003. Data collected for each patient included age, sex, chief complaint, presumptive diagnosis on admission, underlying cardiac or other medical illness (congenital heart disease, valvular heart disease, diabetes, hypertension, old stroke, chronic kidney disease, chronic liver disease, chronic lung disease, haematological malignancies, other malignant diseases, and autoimmune disease), history of IE, prosthetic valve, and intravenous drug abuse. WBC count, C-reactive protein (CRP), serum albumin, renal function test, and liver function test results obtained on admission or just before the manifestations of nosocomial IE noted during hospitalization were also recorded. In addition, echocardiographic findings (vegetation site and size), causative organisms identified by blood culture, and complications associated with IE, including neurological, renal, cardiac, and embolic complications were also evaluated.

Definitions

All included patients fulfilled the modified Duke criteria for definite or possible IE, as proposed by Li et al. [20]. Renal dysfunction was defined as a serum creatinine level $>1{\cdot}5$ mg/dl (133 μmol/l), and liver dysfunction as elevation of liver enzymes by more than twice the upper limit of normal [aspartate aminotransferase (AST) >74 U/l ($1{\cdot}23$ μkat/l), alanine aminotransferase (ALT) >82 U/l (1363 μkat/l)]. Neurological complications included cerebral emboli or ischaemic stroke, mycotic aneurysm with or without leading to cerebral haemorrhage, and cerebral abscess. Renal complications included acute renal failure, defined as an increase of serum creatinine by $>0{\cdot}5$ mg/dl (44 μmol/l) during admission, or glomerulonephritis. Embolic complications included splenic infarct or abscess, coronary embolism with myocardial infarction, pulmonary embolism, and peripheral limb embolization, but cerebral embolization was not included. Cardiac complications included new atroventricular conduction block, intracardiac abscess, and heart failure.

Statistical analysis

All analyses were performed using the Statistical Package for the Social Science (SPSS for Windows 11.0, SPSS Institute, Chicago, IL, USA). In univariate analyses, Pearson's χ^2 test and Fisher's exact test were used for comparison of categorical variables between fatal and non-fatal cases, while the Student's t test was used for analysis of continuous variables. Homogeneity of variance was assessed by Levene's test. All variables that were identified as significant indicators of mortality in the univariate analysis were included in the multivariate analysis with stepwise linear regression. All tests were two-tailed, and a P value of $<0{\cdot}05$ was considered to be statistically significant.

RESULTS

Characteristics of the study population

Within the 9-year period of study, there were 346 patients who had a discharge diagnosis of IE. Among these patients, 31 were excluded because their clinical conditions did not fulfil the study criteria of definite or possible IE. The remaining 315 patients were

Table 1. *Demographics, underlying diseases, and clinical features of 315 patients with infective endocarditis at National Taiwan University Hospital from 1995 to 2003*

Characteristics	Value
Case numbers (male/female)	315 (187/128)
Age (mean ± S.D.)	50·61 ± 22·22
Clinical presentations	
Fever	190 (60·3%)
Dyspnoea	36 (11·4%)
Neurological symptoms[a]	34 (10·8%)
Gastrointestinal symptoms[b]	13 (4·1%)
Constitutional symptoms[c]	8 (2·5%)
Chest pain	7 (2·2%)
Miscellaneous[d]	27 (8·6%)
Predisposing conditions	
Valvular heart disease	93 (29·5%)
Congenital heart disease	36 (11·4%)
Prosthetic valve	24 (7·6%)
Central venous devices	26 (8·3%)
Previous infective endocarditis	22 (7·0%)
Intravenous drug abuse	14 (4·4%)
Laboratory findings	
White blood cell (/mm³)	12 540 ± 7867
C-reactive protein (mg/l)	7·11 ± 5·79
Serum albumin level (g/dl)	3·06 ± 0·59
Renal dysfunction	83 (26·3%)
Liver dysfunction	43 (16·0%)

[a] Neurological symptoms included limb weakness, headache, seizure, or change in consciousness.
[b] Gastrointestinal symptoms included diarrhea, nausea, vomiting, or abdominal pain.
[c] Constitutional symptoms included fatigue, general malaise, or loss of body weight.
[d] Miscellaneous symptoms included other cardiovascular symptoms (arrhythmia or conduction disturbance, or palpitation, other than chest pain and dyspnoea), musculoskeletal symptoms (arthralgia, muscle ache, or non-specific limb pain), pedal oedema, haematological symptoms (petechiae, bleeding).

included in the analysis. Table 1 shows the demographic characteristics, underlying diseases, and clinical features of the patients. There were 187 males and 128 females; male-to-female ratio 1·46. The mean age was 50·6 years, ranging from 1 month to 92 years.

Diabetes mellitus was present in 47 patients (14·9%), and hypertension in 59 (18·7%). Valvular heart disease was found in 93 patients (29·5%) and was the most commonly encountered predisposing factor in adults. Twenty-four patients (7·6%) had received valve replacement with a prosthetic valve. Fourteen patients (4·4%) were intravenous drug abusers. Central venous devices, including port-A catheter, pacemaker or double-lumen catheter were placed before the development of IE in 26 patients (8·25%).

On admission, patients had an average WBC count of 12 540 ± 7867 (1/mm³), mean CRP of 7·11 ± 5·79 (mg/l), and mean serum albumin of 3·06 ± 0·59 g/dl (30·6 ± 5·9 g/l). Renal dysfunction was noted in 83 patients (26·34%). Forty-three patients (15·99%) had liver dysfunction. Fever was the most commonly encountered chief complaint. The frequency of other major manifestation at presentation was detailed in Table 1.

Thirty-six patients (11·4%) had congenital heart disease, which was the most frequent predisposing factor in children. The most frequent types of congenital heart diseases included: ventricular septal defects in 13 patients (36·1%), including two patients with concomitant ventricular septal defect and patent ductus arteriosus, complex congenital heart disease in seven patients (19·4%), tetralogy of Fallot in five patients (13. 9%), and bicuspid aortic valve in four patients (11·1%). Other identified congenital anomalies included patent ductus arteriosus (8·3%), atrial septal defect (5·6%), Marfan syndrome (2·8%), and arteriovenous fistula (2·8%).

Echocardiographic findings included vegetations noted on the mitral valve in 129 patients (41·0%), on the aortic valve in 116 patients (36·8%), on the tricuspid valve in 41 patients (13·0%), on the pulmonic valve in 10 patients (3·2%), and had vegetations noted on other sites in 12 patients (3·8%), including left or right ventricular outflow tract, interventricular septum, on the wall of pulmonary artery, or pacemaker lead. Less than one-tenth of patients had negative findings on echocardiography (28 patients, 8·9%). The mean vegetation size was 13·47 ± 6·63 mm. IE was classified as definite in 212 patients and as possible in 103 patients. The mortality rate was 21·6%. All the nine patients with *Streptococcus bovis* bacteraemia underwent colon fibreoscopy examinations. Among these patients, one had rectal cancer, six had colorectal adenoma, and one each had rectal xanthoma and internal haemorrhoid.

Table 2 shows the microbiological spectrum of patients with IE. Streptococci and staphylococci were found with equal frequency, with each noted in 97 patients (30·8%). Viridans streptococci were the most common causative *Streptococcus* spp. responsible for IE in 77 patients (24·4%). Methicillin-susceptible *S. aureus* (MSSA) was the most common causative

Table 2. *Causative microorganisms yielded on blood cultures from 315 patients with infective endocarditis at National Taiwan University Hospital from 1995 to 2003*

Microorganism	No. (%) of patients
Gram-positive facultative aerobes	
Streptococcus spp.	97 (30·8)
Group B	4 (1·3)
Group G	1 (0·3)
Viridans group	77 (24·4)
Streptococcus bovis	9 (2·9)
Streptococcus pneumoniae	2 (0·6)
Abiotrophia or *Granulicatella* spp.	4 (1·3)
Staphylococcus spp.	101 (32·1)
Methicillin-susceptible *Staphylococcus aureus*	48 (15·2)
Methicillin-resistant *Staphylococcus aureus*	35 (11·1)
Coagulase-negative staphylococci	18 (5·7)
Enterococcus spp.	17 (5·4)
Gemella spp.	1 (0·3)
Corynebacterium jeikeium	2 (0·6)
Gram-negative facultative aerobes	
HACEK group	5 (1·6)
Haemophilus aphrophilus	1 (0·3)
Haemophilus parainfluenzae	1 (0·3)
Cardiobacterium hominis	2 (0·6)
Eikenella corrodens	1 (0·3)
Non-HACEK group	17 (5·4)
Enterobacter cloacae	4 (1·3)
Acinetobacter baumannii	3 (0·9)
Chryseobacterium indologenes	2 (0·6)
Pseudomonas aeruginosa	2 (0·6)
Salmonella enterica serotype *Choleraesuis*	2 (0·6)
Burkholderia cepacia	1 (0·3)
Escherichia coli	1 (0·3)
Klebsilla pneumoniae	1 (0·3)
Serratia marcescens	1 (0·3)
Anaerobes	7 (2·3)
Peptostreptococcus anaerobius	3 (1·0)
Bacteroides spp.	3 (1·0)
Lactobacillus acidophilus	1 (0·3)
Fungi	6 (1·9)
Candida spp.	5 (1·6)
Cryptococcus neoformans	1 (0·3)
Negative blood cultures	62 (19·7)

HACEK, *Haemophilus parainfluenzae*, *Haemophilus aphrophilus*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* spp.

Staphylococcus spp. with methicillin-resistant *S. aureus* (MRSA) more prevalent than coagulase-negative staphylococci at rates of 35·1% and 5·7% of isolates respectively. Seventeen patients (5·4%) were infected with enterococci, and another 17 patients were infected with Gram-negative bacilli. There were five patients (1·59%) infected by HACEK group bacteria. Sixty-two patients (19·7%) had negative blood cultures.

Complications developed in 80 patients (25·4%). These included neurological complications in 31 patients, the most common of which was embolic stroke (21 patients). Subarachnoid haemorrhage due to rupture of mycotic aneurysm was also documented in 7 patients. Twenty-three (7·3%) patients had embolic events, which presented as splenic infarct in 8 patients, distal limb emboli in 8 patients, or pulmonary embolism in 7 patients. Cerebral embolism was classified as a neurological complication. Seventeen patients (5·4%) had renal complications, and acute renal failure and glomerulonephritis were the most common causes. Cardiac complications were noted in 17 patients (5·4%). Myocardial infarction developed in 2 patients due to coronary arterial embolization. IE involving the aortic valve was associated with a higher rate of cardiac complication (9·2% *vs.* 3·1%, $P=0·037$). This association was at least partially due to the anatomical contiguity of the aortic valve and conduction system. Tricuspid valve involvement was associated with a lower mortality rate (9·8%), possibly due to a reduced rate of neurological complications (0% *vs.* 16·9%, $P=0·021$). The deposition of vegetation emboli in the pulmonary circulation might explain the reduced rate of neurological complications unless paradoxical embolism due to intracardiac right-to-left shunt occurred.

Characteristics of culture-positive *vs.* culture-negative patients

Blood culture results were positive in 253 patients (80·3%) and negative in 62 patients (19·7%). Comparison of these two groups by univariate analysis revealed that culture-negative patients had a significantly higher rate of diagnosis of valvular heart disease (26·5% *vs.* 41·9%, $P=0·020$). This might have been because positive blood culture is one of the requirements, either as a major or a minor criterion, for defining IE with the modified Duke criteria. Culture-positive patients had a higher rate of placement of central venous devices (10·3% *vs.* 0%, $P=0·004$). Most culture-positive patients met the criteria for definite IE, while most culture-negative patients only met the criteria for possible IE. This is easily explained by the fact that positive blood culture was one of the criteria used to define IE. Other

Table 3. *Characteristics of 315 patients with infective endocarditis according to the results of blood culture*

Characteristics	Culture-positive ($n=253$)	Culture-negative ($n=62$)	P
Age	50·89 ± 22·12	49·45 ± 22·78	0·649
WBC (1/mm³)	12 633 ± 8143	12 161 ± 6670	0·680
CRP (mg/l)	6·91 ± 5·19	8·20 ± 8·38	0·338
Albumin (g/dl)	3·04 ± 0·59	3·12 ± 0·56	0·396
Vegetation size (mm)	13·47 ± 6·38	13·46 ± 8·27	0·995
Intravenous drug abuse	11 (4·35%)	3 (4·84%)	0·743
Congenital heart disease	31 (12·25%)	5 (8·06%)	0·504
Valvular heart disease	67 (26·48%)	26 (41·94%)	0·020[a]
Prosthetic valve	18 (7·11%)	6 (9·68%)	0·645
History of IE	16 (6·32%)	6 (9·68%)	0·402
Central venous devices	26 (10·28%)	0 (0%)	0·004[a]
Positive echocardiography	226 (89·33%)	61 (98·39%)	0·023[a]
Definite *vs.* possible IE	203 *vs.* 50	9 *vs.* 53	<0·001[a]
Complication	67 (26·48%)	13 (20·97%)	0·419
Renal complication	14 (5·53%)	3 (4·84%)	1·000
Neurological complication	25 (9·88%)	6 (9·68%)	1·000
Embolic complication	22 (8·70%)	1 (1·61%)	0·090
Cardiac complication	14 (5·53%)	3 (4·84%)	1·000
Nosocomial IE	38 (15·02%)	4 (6·45%)	0·095
Mortality	56 (22·13%)	12 (19·35%)	0·732

IE, Infective endocarditis.
[a] $P<0·05$.

parameters, such as clinical characteristics, underlying medical illness, site and size of vegetations, or laboratory findings such as WBC count, CRP, and serum albumin on admission were not associated with differences in the of yield rate of blood culture. There was also no significant difference in the complication rate or mortality rate between these two groups of patients (Table 3).

Predictors for mortality

Univariate analysis was used to compare the characteristics of the 68 patients (21·6%) who died and 247 patients who survived (Table 4). There were many factors that showed a significant correlation with mortality including: advanced age (56·7 *vs.* 48·9 years, $P=0·010$), diabetes mellitus (25·0% *vs.* 12·2%, $P=0·012$), hypertension (29·4% *vs.* 15·79%, $P=0·014$), chronic renal disease (26·5% *vs.* 11·3%, $P=0·003$), and malignancy (23·5% *vs.* 7·3%, $P=0·001$). Laboratory examination on admission showed that mortality rate was significantly associated with higher WBC count (15 758 *vs.* 12 540/mm³), lower serum albumin level (2·82 *vs.* 3·12 g/l, $P=0·002$), and renal or liver dysfunction (45·6% *vs.* 21·05% and 27·9% *vs.* 9·7% respectively, both $P<0·001$). Neurological complications and nosocomial IE were also associated with a higher mortality rate (both $P<0·001$). The only predictor of lower mortality rate was intravenous drug abuse, but this association was of marginal significance (0% *vs.* 5·7%, $P=0·046$).

The independent risk factors for mortality identified in the multivariate analysis were neurological complications (OR 8·175, $P<0·001$), nosocomial IE (OR 6·661, $P<0·001$), underlying malignancy (OR 4·993, $P<0·001$), renal dysfunction (OR 3·132, $P=0·001$), and elevated WBC count (OR 2·537, $P=0·007$) (Table 5). Low serum albumin level (<3 g/l) (OR 1·643, $P=0·138$) and advanced age (>65 years) (OR 1·472, $P=0·255$) were not significantly related to mortality. As shown in the Figure, the Kaplan–Meier survival curves for patients without risk factors were significantly different from those with one risk factor ($P<0·001$), and this difference was also significant between those with one and those with two or more risk factors. The differences in survival were mainly due to risk factors which developed in the early stage of disease.

DISCUSSION

IE remains the fourth most important life-threatening infectious syndrome [21]. The overall mortality rates

Table 4. *Univariate analysis of outcome for 315 patients with infective endocarditis*

Characteristics	Died ($n=68$)	Survived ($n=247$)	P value
Sex (male : female)	43 : 25	144 : 103	0·489
Age	56·71 ± 23·48	48·93 ± 21·61	0·010[a]
White blood cell count (/μl)	15 758 ± 10 287	11 650 ± 6816	< 0·001[a]
C-reactive protein (mg/l)	8·10 ± 6·21	6·90 ± 5·70	0·348
Albumin (g/dl)	2·82 ± 0·53	3·12 ± 0·58	0·002[a]
Vegetation size (mm)	14·00 ± 7·99	13·40 ± 6·48	0·780
Diabetes mellitus	17 (25·00 %)	30 (12·15 %)	0·012[a]
Hypertension	20 (29·41 %)	39 (15·79 %)	0·014[a]
Chronic renal disease	18 (26·47 %)	28 (11·34 %)	0·003[a]
Malignancy	16 (23·53 %)	18 (7·29 %)	0·001[a]
Intravenous drug abuse	0 (0·00 %)	14 (5·67 %)	0·046[a]
Congenital heart disease	5 (7·35 %)	31 (12·55 %)	0·286
Valvular heart disease	20 (29·41 %)	73 (29·55 %)	1·000
Prosthetic valve	3 (4·41 %)	21 (8·50 %)	0·506
History of IE	1 (1·47 %)	21 (8·50 %)	0·056
Central venous devices	9 (13·24 %)	17 (6·88 %)	0·131
Site involved			
Aortic valve	27 (39·71 %)	41 (16·60 %)	0·779
Mitral valve	30 (44·11 %)	109 (44·13 %)	1·000
Tricuspid valve	4 (5·88 %)	37 (14·98 %)	0·065
Pulmonary valve	3 (4·41 %)	7 (2·83 %)	0·455
Other sites	1 (1·47 %)	12 (4·86 %)	0·312
Renal dysfunction[b]	31 (45·59 %)	52 (21·05 %)	< 0·001[a]
Liver dysfunction[c]	19 (27·94 %)	24 (9·72 %)	< 0·001[a]
Definite *vs.* possible IE	48 : 20	164 : 83	0·562
Complication present	26 (38·24 %)	54 (21·86 %)	0·008[a]
Renal complications[d]	5 (7·35 %)	12 (4·86 %)	0·379
Neurological complications[e]	16 (23·53 %)	15 (6·07 %)	< 0·001[a]
Embolic complications[f]	3 (4·41 %)	20 (8·10 %)	0·584
Cardiac complications[g]	2 (2·94 %)	15 (6·07 %)	0·543
Nosocomial IE	21 (30·88 %)	21 (8·50 %)	< 0·001[a]

IE, Infective endocarditis.

[a] $P < 0·05$.

[b] Indicates serum creatinine level higher than 1·5 mg/dl on admission or at the occurrence of nosocomial IE.

[c] Indicates elevated liver enzyme of more than two times normal (AST > 74 U/l, ALT > 82 U/l).

[d] Indicate acute renal failure defined by increase of serum creatinine level by more than 0·5 mg/dl during admission, and glomerulonephritis.

[e] Indicate cerebral emboli or ischaemic stroke, mycotic aneurysm with or without leading to cerebral haemorrhage, or cerebral abscess.

[f] Indicate splenic infarct or abscess, coronary embolism with myocardial infarction, pulmonary embolism, and peripheral limb embolization. Cerebral embolization was not included.

[g] Indicate conduction disturbance, intracardiac abscess, and heart failure.

for both native-valve and prosthetic-valve endocarditis are as high as 20–25 %, with death resulting primarily from central nervous system embolic events and haemodynamic deterioration [22]. There have been few multivariate analyses of the prognostic determinants in IE [23–27], and only one report including Chinese patients (80 cases) has been published in medical literature [26].

Mortality correlates in the univariate analysis included age, WBC count, serum albumin level, diabetes, hypertension, chronic renal disease, malignancy, previous history of IE, renal or liver dysfunction, neurological complication and nosocomial IE. Intravenous drug addiction was associated with a significantly reduced mortality rate, compatible with a previous report [28], and might be related to

Table 5. *Multivariate logistic regression for risk factors of mortality in 315 patients with infective endocarditis at National Taiwan University Hospital from 1995 to 2003*

Parameter	OR (95% CI)	*P* value
Neurological complications[a]	8·175 (3·295–20·282)	<0·001
Nosocomial infection	6·661 (2·987–14·855)	<0·001
Malignancy	4·993 (2·112–11·806)	<0·001
Renal dysfunction[b]	3·132 (1·604–6·116)	0·001
Elevated WBC count[c]	2·537 (1·295–4·969)	0·007
Albumin <3 g/dl	1·643 (0·852–3·168)	0·138
Age >65 years	1·472 (0·757–2·861)	0·255

OR, Odds ratio; CI, confidence interval.
[a] Indicates limb weakness, headache, seizure, or change in consciousness.
[b] Indicates serum creatinine level higher than 1·5 mg/dl on admission or at the occurrence of nosocomial IE.
[c] Indicates WBC count >15 000/μl.

younger age, less concomitant comorbidity, and a higher rate of tricuspid involvement. Tricuspid IE was associated with a trend towards lower mortality rate, but this difference was not significant. Its impact on mortality was masked by its positive effect on neurological complications. These factors were included in multivariate logistic regression analysis, which identified variables independently associated with nosocomial IE, presence of neurological complications, malignancy, renal dysfunction, and high WBC count. Nosocomial IE was associated with worse clinical condition, more comorbidity, neurological complications, and subsequent sequelae. Thus, our study found that nosocomial IE and neurological complications were the greatest contributors to mortality in patients with IE. A previous study found that neurological complications were independent markers for mortality in patients with IE [29].

Studies, which evaluated the ability of echocardiography to predict complications of IE, revealed that vegetation size was a predictor of embolic events [27, 30]. Jaffe et al. [25] reported a trend towards a higher risk of embolization in patients with vegetations >10 mm. However this echocardiographic finding did not predict worse outcome or death in our study. Embolization to sites other than the brain might have a more minor negative effect on prognosis. Fewer patients with prosthetic IE included in our study and the Framingham criteria adopted by Chu et al. for detecting early heart failure or heart failure unrelated to IE might be the cause for a lower

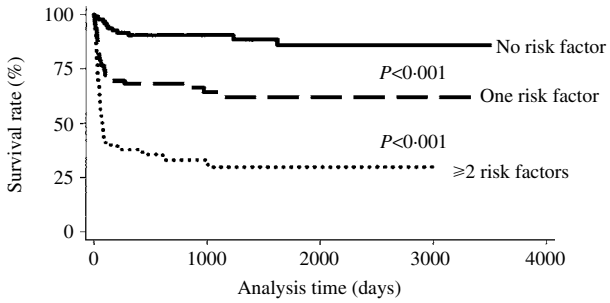

Fig. Kaplan–Meier survival curves for patients with infective endocarditis according to number of risk factors.

rate of cardiac complication than that previously reported [31].

Underlying malignancy also predicted worse outcome due to poorer baseline condition or haematological and immunological damage following chemotherapy. In this study age only showed a trend towards a higher mortality rate, while a previous study in southern Taiwan found age to be an independent predictor on multivariate analysis [19]. These conflicting data may reflect selection bias or differences in the definition of elderly patients [32–35].

Serum albumin is an acute phase reactant indicating inflammation, as well as WBC count. Factors responsible for changes of albumin level in inflammation include haemodilution, increased vascular permeability, increased local consumption, and decreased synthesis due to inhibition by cytokines. Changes in these parameters with more prominent inflammation may explain their association with worse outcome. However, only high WBC count was a significant risk factor for mortality in this study. Impaired renal function implicates underlying renal insufficiency, worse haemodynamics, or immunological or embolic complications caused by IE, and thus, may also result in worse outcome.

There were several limitations to our study. First, a lower proportion of streptococci causing IE and more culture-negative cases than most recent endocarditis cohorts are of interest. Information about antibiotic exposure prior to IE diagnosis is important and would be helpful to explain these phenomena. However, a large proportion of the patients in this study were transferred from other local hospitals or outpatient clinics. However, such information was not available for the majority of our patients. Many patients might have received antibiotic treatment (prescribed by the physicians in local hospitals or outpatient clinics) before they were admitted to our hospital. Second, our data was from patients treated

at a tertiary referral centre, which suggests a selection bias towards patients with greater illness severity, and higher rates of complications and mortality. Third, because this study was conducted at a single centre, regional and institutional variation in the microbiology, diagnosis and treatment of IE may have influenced results. Finally, this was an observational study, and data on all clinical parameters were obtained by retrospective review of medical records. In addition, some data were unavailable. These situations may have led to detection bias. Further studies about other factors influencing outcomes of patients with IE, such as different regimens of antibiotic therapy, types of causative organisms, and timing of administration of appropriate antibiotics and surgical intervention (valve replacement), are needed.

In conclusion, consideration of risk factors for mortality in patients with IE is important to determine the appropriate treatment. Obtaining at least three sets of blood culture for patients with suspected IE before any antibiotics are started is crucial. An aggressive treatment strategy and earlier intervention before the development of complications appears to be indicated in high-risk patients.

DECLARATION OF INTEREST

None.

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