



Profile of infective endocarditis at a tertiary-care hospital in Japan over a 14-year period: characteristics, outcome and predictors for in-hospital mortality



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SUMMARY

Objectives: The aims of this study were to describe the epidemiological features and clinical characteristics of infective endocarditis (IE) at a tertiary-care hospital in Japan and to identify the factors associated with in-hospital mortality.

Methods: A retrospective observational study was conducted at a 925-bed tertiary-care teaching hospital in Japan. All adult patients diagnosed with definite IE between August 2000 and July 2014 according to the modified Duke criteria were included.

Results: A total of 180 patients (60.6% men; mean age, 69.1 years) with definite IE were included. The most common pathogen was *Staphylococcus aureus* (27.2%). Nine patients (5.0%) had culture-negative IE. Transthoracic and transoesophageal echocardiography were performed in 180 (100%) and 132 patients (73.3%), respectively, and vegetations were detected in 128 patients (71.1%). Surgical therapy was performed in 31 patients (17.2%). Overall, the in-hospital mortality rate was 26.1%. The independent predictors of in-hospital mortality were methicillin-resistant *S. aureus* (MRSA), vascular phenomena, health care-associated IE and heart failure.

Conclusions: MRSA, vascular phenomena, health care-associated IE and heart failure were independent predictors of in-hospital mortality. The unique characteristics in our cohort were the very high mean age, low rate of culture-negative IE, high rate of definite IE without detected vegetations and predominance of *S. aureus*.

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1. Background

Infective endocarditis (IE) has a high mortality rate.^{1–3} Its characteristics and causative pathogens differ by country and have changed over time.^{4–6} The increasing opportunities of contact with pathogens in the health care setting and the use of invasive procedures are important reasons for the variations in causative pathogens.⁷

To improve the outcome of this highly lethal disease, the early identification of patients who are at a high risk of mortality is important. Although several studies^{6,8–15} have evaluated possible

predictors of mortality in patients with IE, reports from Japan are scarce.

We conducted this study to describe the epidemiological features and clinical characteristics of IE in a tertiary-care hospital in Japan and to identify the factors associated with in-hospital mortality.

2. Methods

2.1. Study design and setting

This retrospective cohort study was conducted at Kameda Medical Center, a large tertiary-care teaching hospital with 925 beds, in Japan. The study was approved by the Committee for Ethics of Kameda Medical Center under the condition that personal data be kept confidential. Because of the retrospective,

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observational nature of the study, the requirement for informed consent was waived.

2.2. Participant selection

Patients diagnosed with IE between August 2000 and July 2014 were potentially eligible for study inclusion. We extracted information for these patients from the electronic medical record and our department database. The clinical information regarding these patients was retrospectively obtained from the electronic medical records. The modified Duke criteria¹⁶ were used to screen definite IE cases, and possible IE cases were excluded.

2.3. Definition of variables

The demographic data obtained were age, gender and comorbidities, such as diabetes, cancer, the use of glucocorticoids, haemodialysis and prosthetic valve involvement. Diabetes was considered present when it was listed in the patient record as a comorbid condition or if the patient's HbA1c (Japan Diabetes Society) was >6.2%, which is equivalent to HbA1c (National Glycohemoglobin Standardization Program) >6.6%. Cancer was considered present when patients had any active disease or if they had received chemotherapy for cancer. Glucocorticoid users were defined as those receiving an equivalent of ≥ 10 mg of prednisolone for >1 month. Haemodialysis use was considered present if a patient had undergone maintenance haemodialysis.

Information regarding clinical characteristics, including the presence of shock, altered mental status, heart failure, persistent bacteraemia, vascular phenomena, immunological phenomena, vegetations and causative pathogens, was also obtained. Shock was defined as a systolic blood pressure <90 mmHg that did not recover after intravascular volume resuscitation. The Framingham criteria¹⁷ were used to diagnose chronic heart failure. Persistent bacteraemia was defined as at least two positive blood cultures obtained on different calendar days during the same infectious episodes.¹⁸ Vascular phenomena include major arterial emboli, septic pulmonary infarcts, mycotic aneurysms, intracranial haemorrhages, conjunctival haemorrhages and Janeway lesions. Immunological phenomena included glomerulonephritis, Osler's nodes, Roth spots and rheumatoid factor positivity. Vascular and immunological phenomena were considered negative when no findings of these phenomena were documented. Vegetations were considered to be present when detected by either transthoracic echocardiography (TTE) or transoesophageal echocardiography (TEE). The location of the vegetations was documented when it was specified in the records.

IE was classified according to the mode of acquisition on the basis of the definitions in a previous study.⁷ Community-acquired IE was that diagnosed at the time of admission or ≤ 48 h of admission in patients not fulfilling the criteria for health care-associated IE. Health care-associated IE was subclassified into nosocomial IE or non-nosocomial health care-associated IE. Nosocomial IE was that developing in patients hospitalized for >48 h before the onset of signs or symptoms of IE. Non-nosocomial health care-associated IE was that diagnosed ≤ 48 h of admission in outpatients with extensive health care contact, as evidenced by one the following criteria: (1) if they received intravenous therapy, wound care or specialized nursing care at home ≤ 30 days before IE onset; (2) if they attended a hospital or haemodialysis clinic and/or had received intravenous chemotherapy ≤ 30 days before IE onset; (3) if they were hospitalized in an acute care hospital for ≥ 2 days in the 90 days before IE onset; or (4) if they resided in a nursing home or long-term care facility.

Appropriate empirical antimicrobial therapy was defined as the empirical administration of antimicrobials to which the

subsequently isolated pathogens had *in vitro* susceptibility before the first report of microbiology cultures. If the causative pathogen was not detected, empirically administered antimicrobial agents that were recommended after consultation with the Infectious Diseases department were regarded as appropriate. These recommendations were usually based on either the American Heart Association guidelines¹⁹ or the European Society of Cardiology guidelines.²⁰ Patients were considered to have undergone surgical therapy if it was performed during the course of antimicrobial treatment. In-hospital mortality was chosen as an outcome variable.

2.4. Statistical analysis

The odds ratio for in-hospital mortality was calculated with 95% confidence intervals for each variable of interest in univariate logistic regression. All variables with theoretical clinical importance and those that achieved a P value of <0.10 in the univariate analysis were included in the multivariate analysis. A backward stepwise method was used to select most useful predictors of the outcome. All analyses were performed using the R version 3.0.2. (<http://www.r-project.org>) with the EZR frontend.²¹

3. Results

In total, 180 patients were diagnosed with definitive IE and were treated during the study period. A summary of the patients' demographics, clinical characteristics, therapy and outcome is presented in Table 1. The mean age of the patients was 69.1 years, and 109 patients (60.6%) were men. The most common comorbidity

Table 1
Summary of patients' demographics, clinical characteristics, therapy and outcomes (n = 180)

Variables	(n = 180)
Mean age, years (\pm SD)	69.1 (\pm 14.0)
Sex, men, n (%)	109 (60.6)
Comorbidities, n (%)	
Diabetes	25 (13.8)
Cancer	15 (8.3)
Glucocorticoid use	11 (6.11)
Haemodialysis	19 (10.6)
Conditions, n (%)	
Shock	21 (11.7)
Altered mental status	35 (19.4)
Heart failure	50 (27.8)
Vascular phenomena	107 (59.4)
Immunological phenomena	51 (28.3)
Persistent bacteraemia	107 (59.4)
Echocardiogram and vegetation findings, n (%)	
Performance of TTE	180 (100)
Performance of both TTE and TEE	132 (73.3)
Vegetation detected by TTE	97 (53.9)
Vegetation detected either by TTE or TEE	128 (71.1)
Aortic valve	58 (32.2)
Mitral valve	76 (42.2)
Pulmonic valve	1 (0.6)
Tricuspid valve	1 (0.6)
Multi	11 (6.1)
Others	5 (2.8)
Type of IE, n (%)	
Prosthetic valve involvement	35 (19.4)
Community acquired	106 (58.9)
Non-nosocomial health care associated	47 (26.1)
Nosocomial health care associated	27 (15.0)
Treatment and Outcome, n (%)	
Appropriate empirical antimicrobial therapy	70 (38.9)
Surgery	31 (17.2)
In-hospital mortality	47 (26.1)

SD: standard deviation; TTE: transthoracic echocardiogram, TEE: transoesophageal echocardiogram

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