Original article

# Clinical features of infective endocarditis: Comparison between the 1990s and 2000s

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## ARTICLE INFO

## ABSTRACT

*Background:* The circumstances surrounding infective endocarditis (IE) are under constant change due to an increase in drug-resistant organisms, a decrease in rheumatic valve disease, progress in surgical treatment, and aging society. The purpose of this study was to compare clinical features of IE between the 1990s and 2000s and to elucidate the determinants of death or clinical event.
*Methods:* All hospital admission records between January 1990 and December 2009 were retrospectively analyzed. The definition of IE was based on modified Duke criteria. Clinical presentation, blood culture, laboratory results, and echocardiography findings were compared between the 1990s and 2000s.
*Results:* There were 112 patients with definite or probable IE according to modified Duke criteria. The most frequent organism causing IE was *Streptococcus viridians* both in the 1990s and 2000s. The determinants of in-hospital death were hemodialysis and congestive heart failure. The in-hospital mortality of IE was 5.4% in the 1990s and 13.3% in the 2000s. Composite events of in-hospital death and central nervous system disorders were significantly higher in the 2000s compared with the 1990s.
*Conclusion:* The most frequent causative organism of IE was *S. viridians*, both in the 1990s and 2000s. Independent predictors of in-hospital mortality in IE were hemodialysis and congestive heart failure.

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## Introduction

The circumstances surrounding infective endocarditis (IE) are under constant change. In terms of the frequency of underlying valve heart disease on the host side, a decrease in rheumatic valve disease and increase in degenerative aortic stenosis in aging society are reported to be changing the etiology of IE [1,2]. Regarding the causative organisms, an increase in intravenous drug abuse (IVDA) brought differences among ages and countries [3]. In European countries and the USA, streptococci were the dominant pathogens in the past [4–6], while recently staphylococci have been increasing compared with streptococci [7–11]. However, in Japan and Korea, streptococci remain dominant [12–16]. The prevalence of new antibiotics and immunosuppressive drugs promoted multi-drug resistant organisms including methicillin resistant *Staphylococcus aureus* (MRSA) [8,17,18].

In terms of the treatment, the timing of surgical intervention for IE with embolic complications of the central nervous system (CNS) is still controversial [19,20]. Recent prospective studies reported that surgical treatment in the early stage of active IE was superior to conservative therapy with reduction of composite event of all-cause death and embolic events [15,21,22]. The aim of this study was to elucidate the most current clinical spectrum of the microbiology, and the relationship between surgical treatment and in-hospital outcome of a consecutive series of patients with IE in the 1990s and 2000s.

## Methods

### Study design

All hospital admission records at Saitama Medical Center, Jichi Medical University between January 1990 and December 2009 were retrospectively reviewed for clinical presentation, blood cultures, laboratory results, and echocardiographic findings. A flowchart of patient inclusion is shown in Fig. 1. The definition of IE was based on modified Duke criteria [23]. The following data were extracted: age, sex, predisposing factors, affected valves, causative
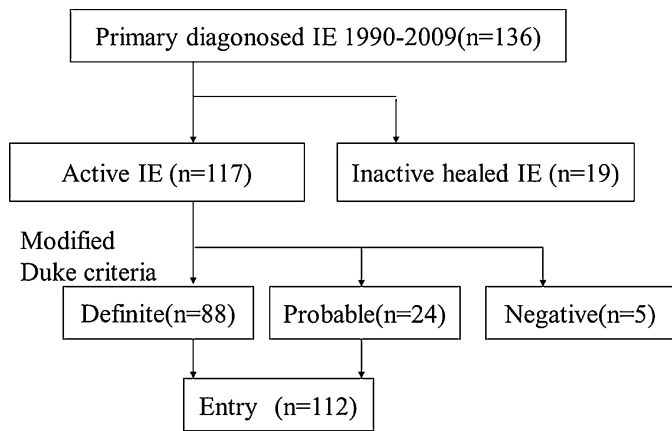
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**Fig. 1.** Flow chart of patient inclusion.

microorganisms, treatment, and outcome. These variables were compared between 1990–1999 (1990s) and 2000–2009 (2000s).

### Definition of clinical presentation

Active IE was defined as on-going active infection associated with elevation of white blood cell count and C-reactive protein level and/or continuous fever. CNS disorders were defined as positive findings of infarction or bleeding in computed tomography or magnetic resonance imaging after treatment.

### Statistical analysis

Statistical analysis for the comparison of data between the 2 study periods was performed by chi-square test or Fisher's exact test for categorical variables and the unpaired Student $t$ test for continuous variables. Univariate and multivariate analysis was performed with logistic regression test using a statistics software (SPSS, Chicago, IL, USA). Significance was defined as a probability value of $p < 0.05$. Data are shown as mean $\pm$ SD.

### Results

The demographic and clinical characteristics of patients are shown in Table 1. There were 69 men and 43 women ranging from 16 to 82 years of age. There was no significant difference in characteristics of patients between the two groups. There was no IVDA either in the 1990s or 2000s. As for underlying cardiac risk factors, the percentage of prosthetic valves was not different between

**Table 1**
Patient characteristics.

|  | 1990s ($n = 37$) | 2000s ($n = 75$) | $p$-Value |
|---|---|---|---|
| Age, years | 52.2 ± 14.9 | 54.4 ± 17.6 | NS |
| Male | 25 (67.6%) | 44 (58.7%) | NS |
| ≥65 years | 8 (21.6%) | 27 (36.0%) | NS |
| Diabetes mellitus | 4 (10.8%) | 4 (5.3%) | NS |
| Hemodialysis | 1 (2.7%) | 4 (5.3%) | NS |
| IVDA | 0 (0%) | 0 (0%) | NS |
| In-hospital infection | 1 (2.7%) | 3 (4.0%) | NS |
| Pre-existing VHD | 7 (18.9%) | 24 (32%) | NS |
| MVP | 5 (13.5%) | 5 (6.7%) | NS |
| Congenital heart disease | 3 (8.1%) | 6 (8%) | NS |
| VSD | 2 (5.4%) | 5 (6.7%) | NS |
| Hypertrophic cardiomyopathy | 1 (2.7%) | 3 (5.3%) | NS |
| Pacemaker | 0 (0%) | 1 (1.3%) | NS |
| Prosthetic valve | 5 (13.2%) | 10 (13.3%) | NS |

IVDA, intravenous drug abuse; VHD, valvular heart disease; MVP, mitral valve prolapse; VSD, ventricular septal defect.

the two groups. Affected valves were similar in the two groups (Table 2). Mitral valve was the most commonly infected throughout the two decades. The most frequent organism causing IE was *S. viridians* both in the 1990s and 2000s. The spectrum of organisms causing IE had not changed significantly in the 2000s as compared with the 1990s (Table 3).

The clinical presentation, treatment, and outcomes are shown in Tables 4 and 5. The surgical treatment with active IE was more frequently applied in the 1900s, and the rate of embolism in CNS was significantly higher in the 2000s. While in-hospital death was not significantly different between the two groups, composite events of in-hospital death and CNS embolism were significantly higher in the 2000s than the 1990s.

The results of univariate and multivariate analysis of in-hospital mortality are shown in Tables 6 and 7, respectively. Age, hemodialysis, congestive heart failure, and methicillin-resistant staphylococcal IE were significant factors of in-hospital mortality. Hemodialysis and congestive heart failure were independent predictors of in-hospital mortality in multivariate analysis.

**Table 2**
Affected valves.

|  | 1990s ($n = 37$) | 2000s ($n = 75$) | $p$-Value |
|---|---|---|---|
| Mitral valve | 28 (73.3%) | 47 (62.7%) | NS |
| Aortic valve | 12 (31.6%) | 33 (44%) | NS |
| Tricuspid valve | 2 (5.3%) | 7 (9.3%) | NS |
| Pulmonary valve | 0 (0%) | 3 (4%) | NS |
| Multiple valves | 5 (13.2%) | 13 (17.3%) | NS |
| PVE | 5 (13.2%) | 10 (13.3%) | NS |

PVE, prosthetic valve endocarditis.

**Table 3**
Causative microorganisms.

|  | 1990s ($n = 37$) | 2000s ($n = 75$) | $p$-Value |
|---|---|---|---|
| *Streptococcus viridans* | 16 (43.2%) | 29 (38.7%) | NS |
| *Streptococcus bovis* | 1 (2.7%) | 3 (4%) | NS |
| Other streptococci | 1 (2.7%) | 5 (6.7%) | NS |
| HACEK group | 0 (0%) | 0 (0%) | NS |
| *S. aureus* | 6 (16.2%) | 8 (10.7%) | NS |
| MRSA | 2 (5.4%) | 3 (4%) | NS |
| *Staphylococcus epidermidis* | 0 (0%) | 3 (4%) | NS |
| MRSE | 0 (0%) | 2 (2.7%) | NS |
| Enterococcus species | 4 (10.8%) | 10 (13.3%) | NS |
| Fungi | 1 (2.7%) | 0 (0%) | NS |
| Others | 1 (2.7%) | 4 (5.3%) | NS |
| Unknown | 7 (18.9%) | 13 (17.3%) | NS |

HACEK, haemophilus species (Haemophilus parainfluenzae, Haemophilus aphrophilus, Haemophilus paraphrophilus), Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella species. MRSA, methicillin-resistant *S. aureus*; MRSE, methicillin-resistant *S. epidermidis*.

**Table 4**
Clinical findings.

|  | 1990s ($n = 37$) | 2000s ($n = 75$) | $p$-Value |
|---|---|---|---|
| *Clinical presentation* |  |  |  |
| Congestive heart failure | 13 (34.2%) | 34 (44.2%) | NS |
| CNS disorder | 3 (7.9%) | 23 (29.9%) | 0.006 |
| Peripheral embolization | 7 (18.4%) | 17 (22.1%) | NS |
| *Echocardiographic findings* |  |  |  |
| Vegetation | 32 (84.2%) | 65 (84.4%) | NS |
| Abscess | 3 (3.9%) | 9 (11.7%) | NS |
| Perforation | 7 (18.4%) | 18 (23.4%) | NS |

CNS, central nervous system.