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ORIGINAL RESEARCH

Impact of Valve Culture Positivity on Prognosis in Patients with Infective Endocarditis Who Underwent Valve Surgery

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ABSTRACT

Introduction: Infective endocarditis (IE) is a severe and fatal infection with high in-hospital and overall mortality rates of approximately up to 30%. Valve culture positivity was associated with in-hospital mortality and postoperative complications; however, few studies have analyzed the relationship between valve cultures and overall mortality over a long observation period. This study aimed to compare the association of valve culture positivity with overall mortality in patients with IE who underwent valve surgery.

Methods: A total of 416 IE patients admitted to a tertiary hospital in South Korea from November 2005 to August 2017 were retrospectively reviewed. A total of 202 IE patients who underwent valve surgery and valve culture were enrolled. The primary endpoint was long-term overall mortality. Kaplan–Meier curve and Cox proportional hazards model were used for survival analysis.

Results: The median follow-up duration was 63 (interquartile range, 38–104) months. Valve cultures were positive in 22 (10.9%) patients. The overall mortality rate was 15.8% (32/202) and was significantly higher in valve culture-positive patients (36.4%, $p = 0.011$). Positive valve culture [hazard ratio (HR) 3.921, $p = 0.002$], Charlson Comorbidity Index (HR 1.181, $p = 0.004$), Coagulase-negative staphylococci (HR 4.233, $p = 0.001$), new-onset central nervous system complications (HR 3.689, $p < 0.001$), and new-onset heart failure (HR 4.331, $p = 0.001$) were significant risk factors for overall mortality.

Conclusions: Valve culture positivity is a significant risk factor for long-term overall mortality in IE patients who underwent valve surgery. The importance of valve culture

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positivity needs to be re-evaluated, as the valve culture positivity rate increases with increasing early surgical intervention.

Keywords: Endocarditis; Heart valves; Mortality; Tissue culture

Key Summary Points

- Infective endocarditis (IE) is still associated with high mortality rates
- The association of valve culture positivity with long-term mortality is unclear
- Positive valve culture is related to local infection and systemic infection burden
- Positive valve culture increases long-term mortality in IE patients with surgery

INTRODUCTION

Infective endocarditis (IE) is a severe and potentially fatal infection with high in-hospital and overall mortality rates of approximately 10–20% and up to 30%, respectively, despite appropriate antibiotic treatment and improved surgical interventions [1–3]. Advanced age, structural heart disease, prosthetic valve, intravascular catheter, and prior IE are well-known risk factors for IE [4]. Patients with prosthetic valves and previous episodes of IE are at the highest risk and require antibiotic prophylaxis [5].

Several prognostic factors for increased mortality have been identified, including host factors, pathogen-specific factors, and treatment-related factors. Age, comorbidities, and a history of IE have also been associated with IE mortality [6–8]. Surgical intervention is important to reduce complications and mortality, and is recommended in about half of all IE patients [9, 10]. However, even with surgical intervention, the overall mortality is still approximately 10–17% [11].

In addition, positive tissue valve culture has been associated with in-hospital mortality and postoperative complications [12–14]. Valve culture is an independent predictor of in-hospital mortality in active left-sided IE [12]. Therefore, the European Society of Cardiology (ESC) guideline recommends that positive valve culture should guide antibiotic choice and treatment duration [13]. Positive valve culture also increases the risk of postoperative complications, such as acute respiratory distress syndrome (ARDS) and paravalvular leakage [13, 14]. However, few studies have analyzed the relationship between valve cultures and overall mortality over a long observation period.

This study aimed to compare the difference in long-term overall mortality according to valve culture results in IE patients who underwent surgical intervention.

METHODS

Patient Selection

We retrospectively reviewed 416 IE patients admitted to Severance Hospital, a 2400-bed tertiary hospital in South Korea, from November 2005 to August 2017. We defined IE according to the modified Duke criteria, and included cases of "definite IE" and "possible IE" [15]. Eligibility criteria were as follows: age > 18 years, valve surgery, and appropriate valve culture. Patients who received a prolonged course of antibiotics after surgery, such as those with tuberculosis or fungal infection, were excluded from this study ($n = 2$). We also excluded cases in which valve culture was not performed or only a swab culture at the surgical site was performed ($n = 43$) [16]. In cases of multiple episodes in the same patient, only data from the first episode were analyzed, and subsequent events were described as recurrence. This study was approved by the institutional review boards (IRBs) of Yonsei University College of Medicine (IRB no. 4-2018-0248). Informed consent was waived due to the retrospective nature of the study, which complied with the Good Clinical Practice guidelines and the Declaration of Helsinki.

Definition of Variables

Antibiotics were selected according to the ESC guidelines [5]. The duration of antibiotic treatment was considered when one of the compounds was effective against the causative microorganism, and when the antibiotic was administered intravenously; specifically, if one of the empirically started antibiotics was susceptible to the identified strain, this was counted from the first entry date, whereas if no empirically started antibiotic was susceptible to the identified strain, this was counted from the date of change according to susceptibility [17]. Surgical intervention was recommended, based on a multidisciplinary team decision according to the American Heart Association and ESC guidelines [5, 18]. Appropriate valve culture was performed using aseptically removed valve specimens during surgery [19]. Causative microorganisms were defined as pathogens cultured from blood or tissue samples [20]. Reoperation was defined as a case requiring additional surgery on the same heart valve for the treatment of IE recurrence or postoperative valve complications [21]. The Charlson Comorbidity Index was used to estimate the risk of death from comorbidities present on admission [22]. The European System for Cardiac Operative Risk Evaluation II (EuroSCORE) is used for surgical risk stratification in IE patients [23]. The mortality data were obtained from the Ministry of the Interior and Safety of South Korea, which collects mortality data of all Korean citizens. The primary endpoint of this study was overall mortality during the observational period. Overall mortality was defined as death from any cause. The secondary endpoints were in-hospital mortality, 1-year mortality, 1-year reoperation, overall reoperation, and postoperative complications, such as new-onset heart failure (HF), conduction abnormality, and paravalvular and embolic complications.

Statistical Analysis

Between-group comparison was performed using the chi-squared and Fisher's exact tests for categorical variables and the Mann–Whitney *U* test for continuous variables. A *p*-value of < 0.05 was considered statistically significant. A Kaplan–Meier curve was drawn using patient survival from the time of admission to either death or date of the last follow-up. The log-rank test was used to determine whether there was a difference in survival distributions between the two groups. Hazard ratios (HRs) and 95% confidence intervals (CIs) of variables for overall mortality were analyzed using a Cox proportional hazards model. Variables for multivariable analysis were selected based on the clinically significant risk factors in univariable analysis. Statistical analysis was performed using IBM SPSS Statistics for Windows v.25 (IBM, Armonk, NY, USA).

RESULTS

Patient Characteristics

Of 416 IE patients in total, 247 patients who underwent valve surgery were enrolled (Fig. 1). Of 247 patients, only 81.8% underwent appropriate valve culture. The valve culture results were positive in 10.9% and negative in 89.1% of patients. The median age of the study population was 53 [interquartile range (IQR), 39–65] years, and 65.3% of patients were male (Table 1). The most affected valves were the mitral valve (64.9%) and aortic valve (48.5%). Multiple valve involvement occurred in 19% of patients. Approximately 40.1% of patients had a previous history of valve dysfunction, including prosthetic valve (10.9%), previous valve surgery (14.9%), cardiac devices (2.5%), and other structural problems, such as rheumatic heart disease, mitral valve prolapse, and bicuspid aortic valve. The most frequently isolated microorganisms were streptococci (40.1%), followed by coagulase-negative staphylococci (CoNS) (8.4%), and *Staphylococcus aureus* (7.9%). Sixty-one patients (30.2%) had negative blood culture results. There were no differences in sex, IE history, history of valve dysfunction, affected valves, comorbidities, microorganisms, duration of total antibiotic treatment, and vegetation size between patients with positive and negative valve culture results. However, patients

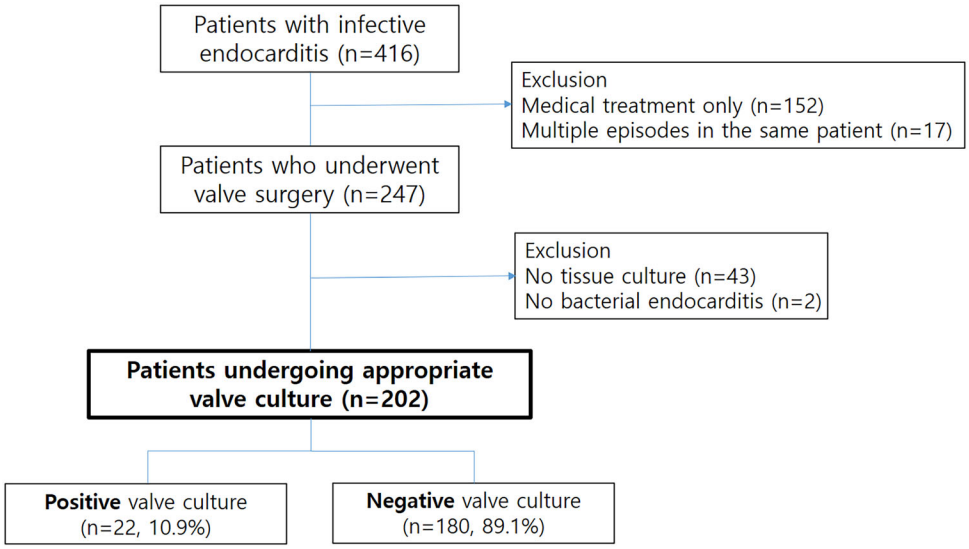

Fig. 1 Flow chart of study patients with infective endocarditis. A total of 416 infective endocarditis (IE) patients admitted to a 2400-bed tertiary hospital in South Korea from November 2005 to August 2017 were retrospectively reviewed. IE patients who underwent valve surgery and appropriate valve culture were enrolled in this study ($n = 202$). Patients who were indicated to receive prolonged antibiotics (for instance, for tuberculosis or fungal infection) after surgical intervention were excluded from this study ($n = 2$). Cases in which valve culture was not performed or only a swab culture was performed at the surgical site were excluded ($n = 43$). Multiple episodes in the same patient were counted only at the first time, and subsequent events were described as recurrence ($n = 17$). Multiple episodes in the same patient they were counted only at the first time, and subsequent events were described as recurrence; No tissue culture cases in which valve culture was not performed or only a swab culture was performed at the surgical site were excluded; No bacterial endocarditis Patients who were indicated to receive prolonged antibiotics (for instance, for tuberculosis or fungal infection) after surgical intervention were excluded from this study

with positive valve culture results had a higher rate of left ventricular dysfunction (63.6% vs. 36.1%, $p = 0.013$), were older [62 (IQR, 45–72) vs. 52 (IQR, 38–63), $p = 0.033$], had a higher Charlson Comorbidity Index [3 (IQR, 0–5) vs. 1 (IQR, 0–3), $p = 0.035$], and a higher EuroSCORE value [2.70 (IQR, 2.07–4.20) vs. 2.06 (IQR, 1.53–2.82), $p = 0.003$] than patients with negative valve culture results.

Outcomes According to Valve Culture Results

The median follow-up duration was 63 (IQR, 38–104) months. The 1-year mortality rate (31.8% vs. 8.9%, $p = 0.005$) and overall mortality rate (36.4% vs. 12.9%, $p = 0.011$) were significantly higher in IE patients with positive valve cultures (Table 2). This significant difference in overall mortality between patients with positive and negative valve cultures was confirmed by the Kaplan–Meier curve and log-rank test ($p = 0.002$) (Fig. 2). In-hospital mortality tended to be higher in valve culture-positive patients than in valve culture-negative patients; nevertheless, this difference was not statistically significant (18.2% vs. 6.1%, $p = 0.064$) (Table 2).

No statistically significant difference in complications was identified between the valve culture-positive and -negative groups, as follows: new-onset HF (13.6% vs. 13.3%, $p = 0.999$), new conduction abnormality (9.1% vs. 8.9%, $p = 0.999$), paravalvular complications (22.7% vs. 13.9%, $p = 0.336$), CNS embolic events (36.4% vs. 30.6%, $p = 0.579$), renal failure (18.2% vs. 10.0%, $p = 0.271$), peripheral arterial occlusive disease (4.5% vs. 1.1%,

Table 1 Baseline characteristics of infective endocarditis patients who underwent valve surgery

	Total (n = 202)	Valve culture		p value
		Negative (n = 180, 89.1%)	Positive (n = 22, 10.9%)	
Age (years)	53 (39–65)	52 (38–63)	62 (45–72)	0.033
Male sex	132 (65.3%)	118 (65.6%)	14 (63.6%)	0.858
Nosocomial infection	22 (10.9%)	19 (10.6%)	3 (13.6%)	0.715
Previous IE	6 (3.0%)	6 (3.3%)	0 (0.0%)	0.999
Underlying cardiac valve conditions	81 (40.1%)	72 (40.0%)	9 (40.9%)	0.935
Prosthetic valve	22 (10.9%)	19 (10.6%)	3 (13.6%)	0.715
Previous valve surgery	30 (14.9%)	25 (13.9%)	5 (22.7%)	0.336
Cardiac devices	5 (2.5%)	3 (1.7%)	2 (9.1%)	0.093
Affected valve				
Aortic valve	98 (48.5%)	87 (48.3%)	11 (50.0%)	0.883
Mitral valve	131 (64.9%)	118 (65.6%)	13 (59.1%)	0.549
Tricuspid valve	10 (5.0%)	7 (3.9%)	3 (13.6%)	0.081
Pulmonary valve	6 (3.0%)	5 (2.8%)	1 (4.5%)	0.504
Multiple valves	39 (19.3%)	34 (18.9%)	5 (22.7%)	0.774
Other comorbidities				
Diabetes mellitus	30 (14.9%)	24 (13.3%)	6 (27.3%)	0.107
Chronic heart failure	12 (5.9%)	10 (5.6%)	2 (9.1%)	0.624
Renal disease	13 (6.4%)	10 (5.6%)	3 (13.6%)	0.156
Liver disease	9 (4.5%)	8 (4.4%)	1 (4.5%)	0.999
Solid cancer	13 (6.4%)	11 (6.1%)	2 (9.1%)	0.638
Hematologic malignancy	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.999
Connective tissue disease	7 (3.5%)	6 (3.3%)	1 (4.5%)	0.560
Immunosuppressive therapy	5 (2.5%)	5 (2.8%)	0 (0.0%)	0.999

Table 1 continued

	Total (n = 202)	Valve culture		p value
		Negative (n = 180, 89.1%)	Positive (n = 22, 10.9%)	
Antibiotic treatment within 30 days	25 (12.4%)	21 (11.7%)	4 (18.2%)	0.488
Central venous access	6 (3.0%)	4 (2.2%)	2 (9.1%)	0.13
Charlson Comorbidity Index	1 (0–3)	1 (0–3)	3 (0–5)	0.035
EuroSCORE value (median, IQR)	2.08 (1.53–2.86)	2.06 (1.53–2.82)	2.70 (2.07–4.20)	0.003
Clinical signs and symptoms (initial)				
Fever (≥ 38 °C)	144 (71.3%)	128 (71.1%)	16 (72.7%)	0.874
LV dysfunction (EF < 50%)	79 (39.1%)	65 (36.1%)	14 (63.6%)	0.013
Sepsis (including septic shock)	131 (64.9%)	114 (63.3%)	17 (77.3%)	0.196
CNS embolic complications	65 (32.2%)	56 (31.1%)	9 (40.9%)	0.353
Peripheral embolic complications	18 (8.9%)	16 (8.9%)	2 (9.1%)	0.999
Skin lesions	4 (2.0%)	4 (2.2%)	0 (0.0%)	0.999
Microbiology				
Coagulase-negative staphylococci	17 (8.4%)	14 (7.8%)	3 (13.6%)	0.406
Staphylococcus aureus	16 (7.9%)	13 (7.2%)	3 (13.6%)	0.392
MSSA	12 (5.9%)	11 (6.1%)	1 (4.5%)	0.999
MRSA	4 (2.0%)	2 (1.1%)	2 (9.1%)	0.059
Enterococcus species	16 (7.9%)	13 (7.2%)	3 (13.6%)	0.392
Streptococcus species	81 (40.1%)	73 (40.6%)	8 (36.4%)	0.705
HACEK	2 (1.0%)	1 (0.6%)	1 (4.5%)	0.206
Gram-negative bacilli (except for HACEK)	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.999
Others	8 (4.0%)	7 (3.9%)	1 (4.5%)	0.999
Duration of total antibiotic treatment	33 (27–42)	32 (27–41)	38 (28–47)	0.248
Duration of preoperative antibiotic treatment	10 (5–19)	9 (5–17)	5 (2–16)	0.479

Table 1 continued

	Total (n = 202)	Valve culture		p value
		Negative (n = 180, 89.1%)	Positive (n = 22, 10.9%)	
Duration of postoperative antibiotic treatment	23 (15–29)	22 (15–29)	27 (14–38)	0.306
Patients with vegetations (initial)	186 (92.1%)	167 (92.8%)	19 (86.4%)	0.392
Median maximal vegetation size (cm)	1.10 (0.70–1.73)	1.10 (0.70–1.70)	1.30 (0.95–2.25)	0.128

Continuous variables are described as median and interquartile range (IQR), and discrete variables were described as numbers (percentages)

IE infective endocarditis; *EuroSCORE* European System for Cardiac Operative Risk Evaluation; *LV* left ventricular; *EF* ejection fraction; *CNS* central nervous system; *CoNS* Coagulase-negative staphylococci; *MSSA* methicillin-susceptible *Staphylococcus aureus*; *MRSA* methicillin-resistant *Staphylococcus aureus*; *HACEK Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella*

$p = 0.294$), other embolic complications (9.1% vs. 8.9%, $p = 0.999$), and reoperation rate (4.5% vs. 3.9%, $p = 0.999$) (Table 2).

Univariable and Multivariable Analyses of Overall Mortality

Univariable analysis showed that Charlson Comorbidity Index ($p = 0.01$), positive valve culture ($p = 0.001$), new-onset central nervous system (CNS) complications ($p < 0.001$), and new-onset HF ($p = 0.002$) were associated with an increase in overall mortality (Table 3).

In the multivariable model, Charlson Comorbidity Index ($p = 0.004$), CoNS ($p = 0.001$), positive valve culture ($p = 0.002$), new-onset CNS complications ($p < 0.001$), and new-onset HF ($p = 0.001$) had a significant impact on increasing overall mortality (Table 3).

DISCUSSION

Our study showed that positive valve culture increased the risk of overall mortality in IE patients who underwent valve surgery over a long-term follow-up period, and revealed that new-onset CNS complications, new-onset HF, and Charlson Comorbidity Index were significant predictive factors influencing long-term overall mortality.

Numerous studies have evaluated predictors of poor outcomes and mortality in IE patients. HF and neurological complications are independent predictive factors for mortality in IE patients who underwent surgery [6–8, 24]. Several models included predictive factors that can affect mortality, such as prior cardiac surgery, number of treated valves/prostheses, left ventricular ejection fraction, comorbidities, and microorganisms [25, 26]. Our study showed that positive valve culture was a significant risk factor for overall mortality over a long-term follow-up period.

Positive valve culture is required for the diagnosis of "definite" IE according to the modified Duke criteria [15]. Positive valve culture is also a crucial factor influencing antibiotic choice and duration of treatment after surgical intervention (Class IIa; Level of Evidence B)

Table 2 Postoperative outcomes of patients with infective endocarditis after valve surgery

Postoperative outcomes	Total ($n = 202$)	Valve culture		p value
		Negative ($n = 180$, 89.1%)	Positive ($n = 22$, 10.9%)	
In-hospital mortality	15 (7.4%)	11 (6.1%)	4 (18.2%)	0.064
1-year mortality	23 (11.4%)	16 (8.9%)	7 (31.8%)	0.005
Overall mortality	32 (15.8%)	24 (12.9%)	8 (36.4%)	0.011
New-onset heart failure	27 (13.4%)	24 (13.3%)	3 (13.6%)	0.999
New conduction abnormality	18 (8.9%)	16 (8.9%)	2 (9.1%)	0.999
Paravalvular complications	30 (14.9%)	25 (13.9%)	5 (22.7%)	0.336
Embolic complications				
CNS involvement	63 (31.2%)	55 (30.6%)	8 (36.4%)	0.579
Renal failure	22 (10.9%)	18 (10%)	4 (18.2%)	0.271
PAOD	3 (1.5%)	2 (1.1%)	1 (4.5%)	0.294
Other systemic emboli	18 (8.9%)	16 (8.9%)	2 (9.1%)	0.999
1-year reoperation[a]	5 (2.5%)	4 (2.2%)	1 (4.5%)	0.442
Overall reoperation[a]	7 (3.5%)	7 (3.9%)	1 (4.5%)	0.999

CNS central nervous system; *PAOD* peripheral arterial occlusive disease

[a]Reoperation: a case requiring additional surgery on the same heart valve, not only for the recurrence of infective endocarditis but also for postoperative valve complications

[5, 18]. A previous study suggested that the duration of antibiotic treatment and vegetation size were independent predictive factors for positive valve culture [13]. Data from a randomized controlled trial and large meta-analysis support early surgical intervention in IE [10, 27]. Early surgical intervention reduced the risk of HF and emboli, but increased the proportion of positive valve cultures [13]. A positive valve culture result could be due to a higher grade of bacteremia, insufficient therapeutic time, or antibiotic treatment failure [12]. Further, positive valve culture was indicative of active local infection in IE patients undergoing cardiac surgery [12].

In addition, positive valve culture was associated with poor clinical outcomes in IE patients who underwent surgery; for example, positive valve culture increased the risk of postoperative ARDS and paravalvular leakage [13, 14], and was associated with higher in-hospital mortality rates [12]. Our study showed no difference in paravalvular leakage or other complications according to the valve culture results, but 1-year (31.8% vs. 8.9%, $p = 0.005$) and overall mortality (36.4% vs. 12.9%, $p = 0.011$) were significantly higher in patients with positive valve cultures compared to those with negative valve cultures. Thus, positive valve culture is an important determinant of IE diagnosis and treatment, and is also associated with the duration of appropriate antibiotic treatment, vegetation size, postoperative complications, and mortality.

CoNS is an important causative pathogen in prosthetic valve endocarditis (PVE) and native valve endocarditis (NVE). CoNS invades and destroys native tissue and forms biofilms by binding with polymer surfaces of foreign bodies [28, 29]. Some studies have found that CoNS increases the risk of in-hospital mortality and relapse in patients with PVE [30, 31]. NVE

Table 3 Univariable and multivariable analyses of overall mortality in patients with infective endocarditis using a Cox proportional hazards model

Characteristics	*n*	Univariable analysis			Multivariable analysis		
		HR	95% CI	*p*-value	HR	95% CI	*p* value
Sex							
Male	132	1					
Female	70	0.605	0.255–1.439	0.256			
Multiple valve involvement	39	0.731	0.270–1.979	0.538			
Previous infective endocarditis	6	1.029	0.118–8.985	0.979			
Previous valve problem history[a]	81	2.029	0.880–4.679	0.097			
Charlson Comorbidity Index		1.177	1.040–1.331	0.01	1.181	1.054–1.324	0.004
Microbiology							
CoNS	17	5.208	0.836–32.444	0.077	4.233	1.788–10.023	0.001
S. aureus	16	1.308	0.176–9.705	0.793			
Enterococcus	16	0.898	0.095–8.487	0.925			
Streptococcus	81	0.728	0.127–4.167	0.722			
Blood culture-negative	61	1.817	0.268–12.325	0.541			
Valve culture							
Negative	180	1					
Positive	22	5.608	2.071–15.188	0.001	3.921	1.681–9.145	0.002
New-onset CNS complications	63	4.166	1.883–9.217	< 0.001	3.689	1.783–7.633	< 0.001
New-onset HF	27	4.214	1.671–10.628	0.002	4.331	1.839–10.196	0.001

HR hazard ratio; *CI* confidence interval; *CoNS* coagulase-negative staphylococci; *S. aureus*, *Staphylococcus aureus*; *CNS* central nervous system; *HF* heart failure

[a]Previous valve problem history: prosthetic valve, previous valve surgery, cardiac devices, rheumatic heart disease, mitral valve prolapse, bicuspid aortic valves, and other valve structural causes

caused by CoNS was also associated with poor outcomes and high overall mortality, despite the high rate of surgical procedures [32]. In our study, CoNS infection was also a significant risk factor associated with overall mortality.

IE leads to HF by destroying structures important to hemodynamics through multiple mechanisms including vegetations, destructive valve lesions, and abscess formation [33]. HF is the most frequent complication, affecting up to 60% of IE patients, and is also the main cause of death in IE patients [6]. HF is also the most common indication for surgical intervention in IE, and early surgery is associated with reduced mortality [9]. Of note, HF remained an independent predictor of in-hospital and 1-year mortality in IE patients, despite appropriate surgical intervention [6, 7]. Several studies have shown that HF is also the main cause of long-term mortality in IE patients [34, 35]. These findings are consistent with our own observations showing that HF was a significant risk factor for long-term overall mortality.

CNS complications occur in up to 30% of IE patients, and are the result of emboli, which are related to vegetation length and mobility

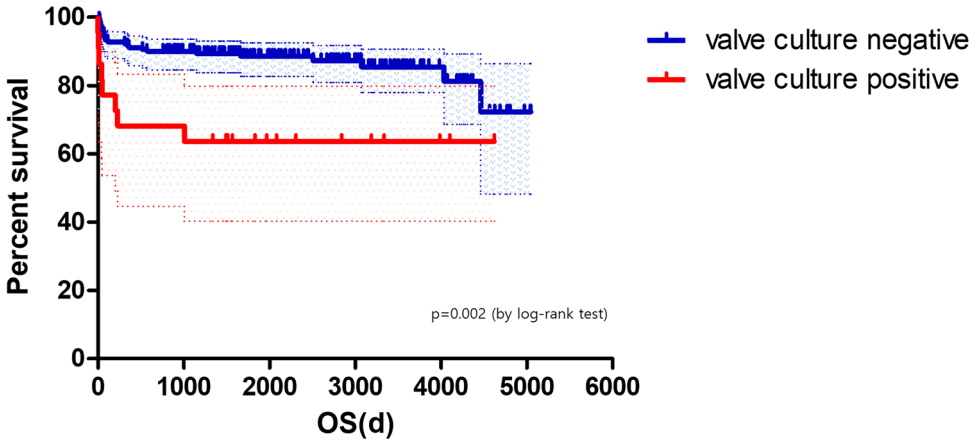

Fig. 2 Kaplan–Meier curve for overall mortality in patients with infective endocarditis who underwent valve surgery according to valve culture result. Significant differences in the overall mortality of infective endocarditis patients were observed between positive and negative valve cultures using the Kaplan–Meier curve and log-rank test ($p = 0.002$). *OS, overall survival

[8, 11]. Initiating appropriate antibiotic therapy is important to prevent these neurological complications and to lower the risk of emboli [36]. Surgical intervention in IE can be safely performed after asymptomatic CNS complications, and may improve survival in selected IE patients without intracranial hemorrhage [37]. However, CNS complications, such as ischemic stroke and brain hemorrhage, were significantly associated with overall mortality [8, 38]. In our study, CNS complications were significant prognostic factors for overall mortality in IE patients.

Various comorbidities have been reported to be associated with mortality in IE patients who undergo surgery. The EuroSCORE II is the best-known predictive model for in-hospital mortality in these patients, and renal impairment, poor mobility, and chronic lung disease are suggested as comorbidities associated with mortality [23]. Other comorbidities, such as the Acute Physiology, Age, Chronic Health Evaluation II score, diabetes mellitus, and Charlson Comorbidity Index, are also reported as major risk factors for in-hospital and 1-year mortality [6, 39]. This trend is also seen in long-term mortality, and several studies have shown that various comorbidities, such as the Charlson Comorbidity Index, renal impairment, and hepatic dysfunction, are associated with mortality in IE patients [40, 41]. We also showed that the Charlson Comorbidity Index was crucial risk factor for overall mortality in IE patients.

Our study has some limitations. First, this was a retrospective study with a relatively small sample size of positive valve cultures. Second, although many variables that can affect treatment were well balanced between valve culture-positive and -negative groups, such as composition of microorganisms, previous IE history, previous valve history, affected valves, comorbidities, vegetations, and duration of antibiotic treatment [36, 39, 42–44], age and Charlson Comorbidity Index were not completely balanced. Nevertheless, we attempted to overcome this limitation by considering potential confounders through the Cox regression multivariable analysis. Therefore, further larger prospective studies are warranted. Although the study population differed from that in our study, Munoz discussed the false positivity of valve culture [45]. Whole-genome sequencing or 16S rDNA sequencing may reduce the false positivity and increase diagnostic accuracy [46]. Another strength of our study was the long observation period (median 63 months, IQR 38–104), which improves the reliability of our results regarding the long-term prognosis of IE patients.

CONCLUSION

Positive valve culture was an important factor influencing long-term overall mortality in IE patients who underwent valve surgery. Therefore, it is critical to perform appropriate valve culture during surgery in IE patients. Based on our study, the importance of valve culture positivity needs to be re-evaluated, as the valve culture positivity rate increases with increasing early surgical intervention.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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