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Original Article

# The SOFA score could predict the severity and prognosis of infective endocarditis☆

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ABSTRACT

*Introduction:* Although infectious endocarditis (IE) is a potentially severe infectious disease, there are no prognostic tools for in-hospital mortality for IE patients. This is the first report documenting that the Sequential Organ Failure Assessment (SOFA) score could evaluate the severity and outcome among IE patients.

*Patients and methods:* From 2007 to 2018, we reviewed all patients who were diagnosed as having IE at our institue. Patients diagnosed as definite IE according to the modified Duke criteria or by surgical procedure were included in this study.

*Results:* A total of 66 IE patients were enrolled in this study. They were 45 males (68%) and the median age was 70 years. As for prognostic factors for in-hospital death among IE patients, SOFA score ≥6, CCI ≥3, surgical procedure, heart failure, immunological phenomena and detection of *S. aureus* as a causative pathogen were identified as prognostic factors by univariate analysis. Of these 6 factors, SOFA score ≥6 (OR 7.6, 95%CI 1.3–46.6, $p = 0.029$), heart failure (OR 9.7, 95%CI 1.1–86.1, $p = 0.042$), surgery (OR 0.1, 95% CI 0–0.8, $p = 0.037$) and immunological phenomena (OR 0.1, 95%CI 0–0.9, $p = 0.042$) were independent prognostic factors for in-hospital mortality among IE by logistic regression analysis.

*Conclusion:* The SOFA score could be a good prognostic tool to use for IE patients. Also, SOFA score ≥6, surgery, immunological phenomena and heart failure were independent prognostic factors for in-hospital mortality among IE patients.



## 1. Introduction

Infective endocarditis (IE) is one of the most serious septic infectious diseases showing a high in-hospital mortality of 16–26% [1–3]. Although a variety of diagnostic tools and antibiotic therapy have been developed, its prognosis has not differed over the decades. Nowadays, IE has become a common disease for physicians due to emergence of biologics, chemotherapy and immunotherapy for cancer and collagen vascular diseases. However, there is no predictive tool in the management of IE. Recently, it has been reported that quick Sequential Organ Failure Assessment (qSOFA) and Sequential Organ Failure Assessment (SOFA) scores were effective as prognostic tools in the management of sepsis and other infections [4–6]. We conducted this retrospective study for the purpose of clarifying whether qSOFA and SOFA score could correctly evaluate the severity and the prognosis of IE. This is the first report documenting that the SOFA score could correctly predict outcomes among IE patients.

☆ All authors meet the ICMJE authorship criteria.

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## 2. Patients and methods

### 2.1. Study design and setting

This retrospective cohort study was conducted at Aichi Medical University hospital in Japan, a large tertiary-care teaching hospital with 900 beds. This study was approved by the Institutional Review Board of Aichi Medical University Hospital.

### 2.2. Participant selection

From 2007 to 2018, we reviewed all patients who were diagnosed as having IE at Aichi Medical University Hospital. Patients diagnosed as definite IE according to the modified Duke criteria or by surgical procedure were included in this study. Patients diagnosed as having possible IE according to the modified duke criteria were excluded in this study.

### 2.3. Control group

We selected coagulase negative bacteremia patients without IE who were admitted to our institute during the study period as the control group as shown in Table 1.

### 2.4. Definition of variables

Patients' characteristics, outcomes, pathogens isolated and sites of infection were evaluated. Comorbidity was evaluated by CCI [7]. The severity of IE was evaluated by qSOFA and SOFA score. Vascular phenomena include major arterial emboli, septic pulmonary infarcts, mycotic aneurysms, intracranial hemorrhages, conjunctival hemorrhages and Janeway lesions. Immunological phenomena included glomerulonephritis, Osler's nodes, Roth spots, decrease of complements in serum level and rheumatoid factor positivity. Vascular and immunological phenomena were considered negative when none of these phenomena were documented. Disseminated intravascular coagulation (DIC) was diagnosed according to the disseminated intravascular coagulation diagnostic criteria established by the Japanese Association for Acute Medicine (JAAM DIC diagnostic criteria) [8].

Antibiotic treatment was classified as appropriate or as inappropriate when the identified pathogens were sensitive and resistant respectively to the initially prescribed antibiotics. The antibiotic susceptibility was assessed with minimum inhibitory concentration testing according to the guidelines of the Clinical and Laboratory Standards Institute [9]. Cases of IE were categorized as community-acquired or health care-associated, and as nosocomial or non-nosocomial health care-associated infection. Cases were considered community-acquired if they were diagnosed within 48 h of admission, and if signs or symptoms consistent with infective endocarditis developed in a patient without extensive out-of-hospital contact with health care interventions or systems. Cases were considered nosocomial health care-associated if they occurred in a patient hospitalized for more than 48 h prior to the onset of signs or symptoms consistent with infective endocarditis. Cases were considered non-nosocomial health care associated if they were diagnosed within 48 h of admission, and if signs or symptoms consistent with infective endocarditis developed prior to hospitalization in patients with extensive out-of-hospital contact with health care interventions or systems, defined as: 1) receipt of intravenous therapy, wound care, or specialized nursing care at home within the 30 days prior to the onset of native valve endocarditis; 2) receipt of hemodialysis or intravenous chemotherapy in the 30 days before the onset of native valve endocarditis; 3) hospitalization for 2 or more days in the 90 days before the onset of native valve endocarditis; or 4) residing in a nursing home or long-term care facility.

### 2.5. Evaluation of comorbidities

Comorbidities were evaluated by the Charlson Comorbidity index (CCI). This index predicts ten-year mortality for 22 different comorbid conditions, including heart disease, AIDS, and cancer. Each condition is assigned a score of 1, 2, 3, or 6 depending on the risk of dying. For each patient, the sum of these scores is used as the total score to predict mortality. Because patients are often unaware of the severity of their conditions, each patient's chart was reviewed to determine the appropriate comorbid conditions and the resulting CCI score [7].

### 2.6. Factors of analysis

Clinical data were collected by a review of electronic medical records. All of the patients' data at the time of diagnosis as IE were reviewed in our institute. Forty candidate predictors were chosen from published clinical studies as potential prognostic factors [10–13].

Continuous variables of the factors were divided into two categories as follows: age (≧70, <70 years); body temperature (BT) (≧37.1, <37.1 °C); systemic blood pressure (SBP) (<100, ≧100 mmHg); Glasgow coma scale (GCS) (<15, 15); PaO2/FiO2 ratio (P/F) (<285, ≧285); white blood cell (WBC) (<4000 or ≧9000, 4000–9000 cells/μL); hemoglobin (Hb) (<11, ≧11 g/dL); platelet (Plt) (<150,000, ≧150,000/μL); total bilirubin (TB) (≧1.2, <1.2 mg/dL); C-reactive protein (CRP) (≧11, <11 mg/dL); creatinine (Cr) (≧1.2, <1.2); albumin (Alb) (<4.0, ≧4.0 g/dL); CCI (≧3, <3); SOFA score (≧6, <6). The cut-off points for age and CRP was set on the median values, while BT, SBP, GCS, R/F ratio, WBC, Hb, Plt, TB, Cr and Alb were set at the value that demarcated the normal and abnormal ranges. The cut-off points for CCI and SOFA score was set based on Youden index. qSOFA was not evaluated as prognostic factors because 6 of 61 patients had no records of respiratory rate.

### 2.7. Statistical analysis

To identify factors associated with in-hospital death, the Fisher's exact or $\chi^2$ statistic test were performed using the 40 parameters among IE patients. Factors showing $p$-value < 0.1, were considered candidate predictors significantly related to in-hospital mortality and were extracted and multivariate analysis was performed for these factors using logistic regression analysis. Differences were assumed to be significant if $p < 0.05$. Continuous variables with a normal distribution were compared using Student's $t$-test and the Wilcoxon rank-sum test for non-normally distributed variables. The $\chi^2$ statistic or Fisher's exact test were used to compare categorical variables. All the analyses were performed using SPSS version 23.

## 3. Results

Patients' characteristics, outcomes and pathogens isolated are showed in Table 1. A total of 66 IE patients were enrolled in this study. They were 46 males (70%) and 20 females (30%). The median age was 70 years (range 19–88). As for the type of IE, community-acquired, healthcare-associated and hospital-associated IE were seen in 32 (49%), 28 (41%) and 6 (9%), respectively. As for healthcare-associated factors, prior hospital stay within 90 days is the most commonly seen in 14 of the 28 patients (50%), followed by prior antibiotics use within 90 days in 11 of the 28 patients (39%). IE patients had native and prosthetic valves in

**Table 1**
Patients' characteristics and pathogens isolated in IE patients.

| | IE patients (n = 66) | Control (n = 45) | *p*-value |
|---|---|---|---|
| Median age (range, years) | 70 (19–88) | 77 (20–93) | 0.002 |
| Age ≧70 years | 35 (53) | 35 (78) | 0.01 |
| < 70 years | 31 (47) | 10 (22) | |
| Male sex (n, %) | 46 (70) | 29 (64) | 0.68 |
| Outcome (n, %) | | | |
| 30-day mortality (%) | 8 (12) | 6 (13) | 1.000 |
| In-hospital mortality (%) | 16 (24) | 8 (18) | 0.486 |
| Comorbidity (n, %) | | | |
| Cardiac disease | 26 (39) | 13 (29) | 0.416 |
| Diabetes mellitus | 21 (32) | 10 (22) | 0.291 |
| Chronic pulmonary disease | 8 (12) | 6 (13) | 1.000 |
| Gastroesophageal reflux disease | 3 (5) | 2 (4) | 1.000 |
| Malignancy | 16 (24) | 21 (47) | 0.023 |
| Collagen vascular disease | 7 (11) | 4 (9) | 1.000 |
| Cerebrovascular disease | 12 (18) | 14 (31) | 0.17 |
| Kidney disease | 19 (29) | 10 (22) | 0.513 |
| Liver dysfunction | 5 (8) | 5 (11) | 0.523 |
| Prior dental procedure (n, %) | 7 (11) | NE | |
| Past history of IE | 5 (8) | NE | |
| Healthcare associated factors (n, %) | 28 (42) | NE | |
| Residence of nursing home | 3 (11) | | |
| Requiring any help (PS ≧ 3) | 2 (7) | | |
| Heamodailysis | 9 (10) | | |
| Chemotherapy | 1 (4) | | |
| Immunosuppressive agents use | 4 (10) | | |
| Tube feeding | 0 | | |
| Prior antibiotics use within 90 days | 11 (39) | | |
| Prior hospital stay within 90 days | 14 (50) | | |
| Procedures of echo (n, %) | | NE | |
| TTE | 66 (100) | | |
| TEE | 30 (45) | | |
| Existence of vegetation | | | |
| Yes | 46 (70) | | |
| No | 20 (30) | | |
| Type of IE (n, %) | | NE | |
| Community-acquired infection | 32 (49) | | |
| Healthcare-associated infection | 28 (42) | | |
| Hospital-associated infection | 6 (9) | | |
| Native valve involvement | 53 (80) | | |
| Prosthetic valve involvement | 13 (20) | | |
| Infection site | | | |
| Aortic valve | 20 (30) | | |
| Mitral valve | 35 (53) | | |
| Pulmonic valve | 0 | | |
| Tricuspid valve | 7 (11) | | |
| Multiple valves | 6 (9) | | |
| Unknown | 10 (15) | | |
| Symptoms (n, %) | | NE | |
| Immunological phenomena | 23 (32) | | |
| Vascular phenomena | 44 (71) | | |
| Heart failure | 9 (14) | | |
| CNS disorder | 17 (26) | | |
| Charlson comorbidity index (mean ± SD) | 2.1 ± 2.2 | 3.5 ± 2.0 | <0.001 |
| ≧3 (n, %) | 19 (29) | 31 (69) | <0.001 |
| Condition (n, %) | | | |
| DIC | 13 (20) | 8 (18) | 1.000 |
| Quick SOFA ≥ 2 (n, %) | 15/60 (25) | 5/41 (12) | 0.133 |
| SOFA scores (mean ± SD) | 3.8 ± 2.7 | 2.7 ± 2.5 | 0.036 |
| Initial treatment regimen (n, %) | | NE | |
| Monotherapy | 25 (38) | | |
| Combination therapy | 41 (62) | | |
| β-lactams + other agents | 37 (56) | | |
| Anti-MRSA agents | 29 (44) | | |
| Combination therapy with aminoglycosides | 19 (29) | | |
| Inappropriate antibiotic treatment | 9 (61) | | |
| Surgical intervention (n, %) | | NE | |
| Yes | 19 (29) | | |
| No | 47 (71) | | |
| Pathogens isolated (n, %) | | 45 (100) | |
| *Staphylococcus aureus* | 23 | | |
| MSSA | 17 | | |
| MRSA | 6 | | |
| Coagulase-negative staphylococci | 12 | | |

(*continued on next page*)

**Table 1** (*continued*)

| | IE patients (n = 66) | Control (n = 45) | *p*-value |
|---|---|---|---|
| *Streptococcus* group | 11 | | |
| β-hemolytic streptococci | 2 | | |
| Viridans group streptococci | 9 | | |
| *Enterococcus* species | 9 | | |
| Gram-negative rods | 2 | | |
| Fungi | 4 | | |
| HACEK | 3 | | |
| Others | 6 | | |
| Multiple-pathogens isolated | 10 (15) | | |
| Unknown | 4 (6) | | |

CNS, central nervous system; DIC, disseminated intravascular coagulation; IE, infective endocarditis; MSSA, methicillin-susceptible *Staphylococcus* aureus; MRSA, methicillin-resistant *Staphylococcus* aureus; NE, not evaluated; qSOFA, quick Sequential Organ Failure Assessment; SOFA, Sequential Organ Failure Assessment; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

53 (80%) and 13 (20%), respectively. Transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE) were accomplished in 66/66 (100%) and 30/66 (45%), respectively. Vegetations by TTE and TEE were seen in 46/66 (70%). Prior dental works were seen in 7/66 (11%). The most common comorbidity was cardiac disease in 26/66 (39%), followed by kidney disease in 19/66 (29%). The most common valve involved was mitral valve in 35/66 (53%), followed by aortic valve in 20/66 (30%). The median CCI was 2 (range 0–6). As for the initial antibiotic treatment, combination antibiotic therapy of β-lactams and other agents was prescribed most frequently in 37/66 (56%). Combination therapy with aminoglycoside was seen in 19/66 (29%). Nineteen of 66 patients (29%) required surgical interventions, such as AVR or MVR. Inappropriate treatment was seen in 9/61 (15%). Vascular and immunological phenomena were seen in 44 (71%) and 23 (32%), respectively. Heart failure and CNS disorders were seen in 9 (14%) and 17 (26%), respectively.

In terms of causative pathogens isolated, *Staphylococcus aureus* including MRSA, was seen most commonly in 23/66 (30%), followed by Streptococci in 11/66 (17%). Ten of 66 (15%) had multiple pathogens. HACEK group pathogens were seen in 3/66 (5%), and no pathogens were identified in 4/66 (6%). The 30-day, or in-hospital mortality rates were 12 and 24%, respectively.

### 3.1. Comparison with survival and death groups

In terms of the comparison of the survival and death groups, there were no differences among age and sex. Both CCI (3.4 vs. 1.6, $p = 0.003$) and SOFA scores (6.9 vs. 2.8, $p < 0.001$) were much higher in death groups than in survival groups. *S. aureus* including MRSA, was seen more frequently in death group than in survival group without a statistical significance (9/16, v.s. 14/50, $p = 0.068$).

As for the relationship between qSOFA and outcomes, in-hospital mortality among IE patients with qSOFA ≧ 2 was much higher than those with qSOFA 0–1 (77 vs. 10%, $p < 0.001$).

Receiver-operating characteristic (ROC) curves for SOFA score and CCI among IE patients.

With respect to the diagnostic value of predictive values for in-hospital mortality among IE patients, the area under the curve of ROCs (AUROC)s of SOFA score and CCI were 0.915 ($p < 0.001$) and 0.788 ($p = 0.001$), respectively (Fig. 1). The SOFA score cutoff value was 6 and had a sensitivity of 76.9%, a specificity of 89.6%, a positive predictive value of 66.7%, and a negative predictive value of 93.5%. The cutoff was set according to the Youden Index.

As for 15 patients with qSOFA ≧ 2, AUROCs of SOFA score and CCI were 0.977 ($p = 0.006$) and 0.83 ($p = 0.055$), respectively (Fig. 2). Since there were no records of respiratory rate in 6 of 66 patients, qSOFAs were not evaluated in these 6 patients.

### 3.2. ROC curves for SOFA score among the control group

With respect to the diagnostic value of predictive values for in-hospital mortality among the control group, AUROC of SOFA score was 0.649 ($p = 0.191$).

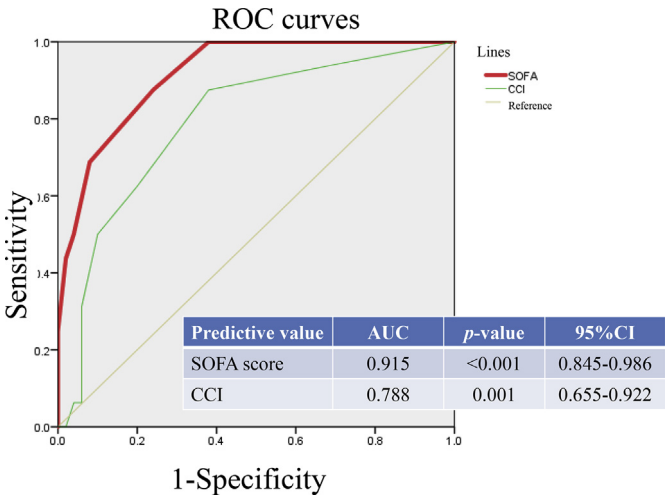


**Fig. 1.** Shows ROC curves of SOFA score and CCI among IE patients for in-hospital death.

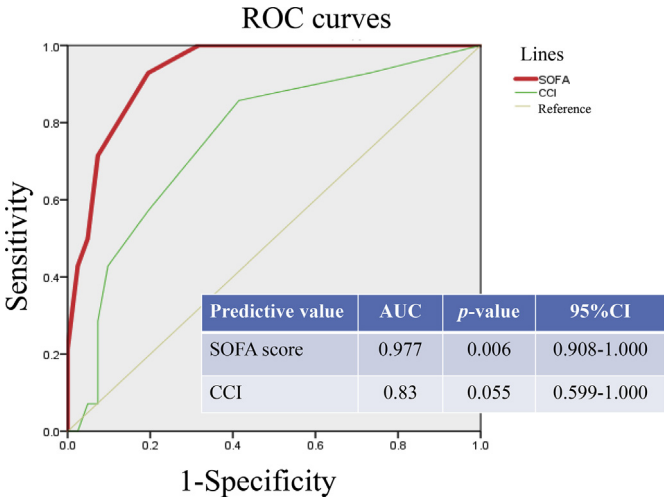


**Fig. 2.** Shows ROC curves of SOFA score and CCI among IE patients with qSOFA≧2 for in-hospital death.

### 3.3. Prognostic factors for in-hospital mortality among IE patients

We analyzed prognostic factors for in-hospital mortality of IE (Tables 2 and 3). SOFA score ≥6, CCI ≥3, surgical procedure, heart failure, immunological phenomena and detection of *S. aureus* as a causative pathogen were found as prognostic factors by a univariate analysis. Of these 6 factors, Logistic regression analysis showed SOFA score ≥6 (OR 7.6, 95%CI 1.3–46.6, $p = 0.029$), heart failure (OR 9.7, 95%CI 1.1–86.1, $p = 0.042$), surgery (OR 0.1, 95%CI 0–0.8, $p = 0.037$) and immunological phenomena (OR 0.1, 95%CI 0–0.9, $p = 0.042$) were independent prognostic factors for in-hospital mortality among IE.

To remove duplicate data, malignancy, kidney disease and hemodialysis were excluded in this analysis because these are included in CCI index. In addition, P/F ratio, GCS < 15, SBP < 100 mmHg, Plt < 150,000/μL and Cr > 1.2 mg/dL were excluded in this analysis because these are included in the SOFA score.

**Table 2**
Prognostic factors for in-hospital death among IE patients by univariate analysis.

| Variables | Odds ratio | 95%CI | *p*-value |
|---|---|---|---|
| Age≧70 years | 1.7 | 0.5–5.3 | 0.407 |
| Male sex | 0.7 | 0.2–2.3 | 0.759 |
| Nursing home and healthcare associated factors | 2.1 | 0.7–6.6 | 0.25 |
| Past history of IE | 0.8 | 0.1–7.4 | 1.000 |
| Prior dental work | 0.2 | 0–3.3 | 0.182 |
| Prosthetic valve | 1.5 | 0.4–5.8 | 0.719 |
| Disseminated intravascular coagulation | 0.9 | 0.2–3.9 | 1.000 |
| Body temperature≧37.1 °C | 0.9 | 0.3–3.0 | 1.000 |
| Systemic blood pressure<100 mmHg | 3.6 | 1.1–11.6 | 0.054 |
| Glasgow coma scale<15 | 12.0 | 3.2–45.2 | <0.001 |
| P/F < 285 ($PO_2$ < 60) | 3.8 | 0.8–17.6 | 0.09 |
| White cell count≧9,000, <4,000 | 1.5 | 0.4–4.9 | 0.571 |
| Hemoglobin<11.0 g/dL | 1.6 | 0.5–5.1 | 0.566 |
| Platelet count<150,000/μL | 1.6 | 0.5–5.1 | 0.566 |
| Total bilirubin≧1.2 mg/dL | 1.8 | 0.6–5.5 | 0.384 |
| C-reactive protein≧11 mg/dL | 1.4 | 0.4–4.3 | 0.768 |
| Creatinine≧1.2 mg/dL | 5.3 | 1.5–18.0 | 0.009 |
| Albumin<4.0 g/dL | 1.0 | 0.1–9.9 | 1.000 |
| Vascular phenomena | 0.9 | 0.3–2.9 | 1.000 |
| Immunological Phenomena | 0.2 | 0–1.0 | 0.035 |
| Surgery | 0.2 | 0–1.0 | 0.027 |
| Inappropriate antibiotic therapy on initial treatment | 2.7 | 0.6–11.5 | 0.224 |
| Persistent bacteremia | 1.8 | 0.5–6.8 | 0.465 |
| Presence of vegetation | 0.9 | 0.3–3.2 | 1.000 |
| Cardiac disease | 1.3 | 0.4–4.0 | 0.772 |
| Diabetes mellitus | 2.0 | 0.6–6.4 | 0.355 |
| Malignancy | 3.5 | 1.0–12.0 | 0.049 |
| Kidney disease | 3.6 | 1.1–11.6 | 0.054 |
| Chronic pulmonary disease | 0.4 | 0–2.5 | 0.668 |
| Hepatic disease | 2.2 | 0.3–14.8 | 0.588 |
| Gastroesophageal reflux disease | 0.4 | 0–8.4 | 1.000 |
| Cerebrovascular disease | 1.8 | 0.5–6.8 | 0.465 |
| Collagen disease | 1.3 | 0.2–7.4 | 1.000 |
| Immunosuppressive state | 1.4 | 0.3–6.3 | 0.695 |
| Dementia | 3.4 | 0.4–26.6 | 0.245 |
| Heart failure | 5.2 | 1.2–22.7 | 0.032 |
| Hemodialysis | 7.1 | 1.5–34.4 | 0.017 |
| Detection of *S.aureus* | 3.3 | 1.0–10.6 | 0.068 |
| Detection of *Enterococcus* species | 0.9 | 0.2–4.7 | 1.000 |
| ICU stay at an initial treatment | 0.8 | 0.2–3.4 | 1.000 |
| SOFA≧6 | 19.8 | 4.9–80.6 | <0.001 |
| CCI≧3 | 5.1 | 1.5–17.2 | 0.001 |

CCI, Charlson Comorbidity Index; CI, confidential interval; ICU, intensive care unit; IE, infective endocarditis; P/F, $PO_2/FiO_2$ ratio; *S. aureus*, *Staphylococcus* aureus; SOFA, Sequential Organ Failure Assessment.

**Table 3**
Prognostic factors for in-hospital mortality among IE by univariate and multivariate analyses.

| Variables | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95%CI | *p*-value | Odds ratio | 95%CI | *p*-value |
| SOFA score ≥6 | 19.8 | 4.9–80.6 | <0.001 | 7.6 | 1.3–46.6 | 0.029 |
| CCI ≥3 | 5.1 | 1.5–17.2 | 0.001 | | | |
| Immunological phenomena | 0.2 | 0–1.0 | 0.035 | 0.13 | 0.2–0.9 | 0.042 |
| Surgery | 0.2 | 0–1.0 | 0.027 | 0.1 | 0–0.8 | 0.037 |
| Heart failure | 5.2 | 1.2–22.7 | 0.032 | 24.1 | 1.1–86.1 | 0.042 |
| *Detection of S.aureus* | 3.3 | 1–10.6 | 0.068 | | | |

CCI, Charlson Comorbidity Index; CI, confidential interval; IE, infective endocarditis; SOFA, Sequential Organ Failure Assessment.

## 4. Discussion

While it is well known that IE has a poor prognosis, showing a high in-hospital mortality of 16–26% [1–4], there is no predictive value among IE patients for in-hospital death. Our study concluded that the SOFA score could probably evaluate the prognosis of IE. Recent studies showed that SOFA score could predict the severity and the prognosis of community-acquired, healthcare-associated pneumonia and acute pyelonephritis [5,6,14]. SOFA score is a tool reflecting the severity of organ failure such as kidney or liver [4]. IE is a systemic infection caused by endocarditis with bacteremia, which could lead to immunological reaction. Therefore, it is reasonable that the SOFA score could reflect the severity and prognosis of IE. CCI is a useful tool for evaluating patients' conditions with underlying diseases [7]. Non-survivor among IE patients had much higher CCI scores than those who survived in our study. Some documented that CCI would be one of the most useful tools for predicting some infections and ALI [15,16]. Although CCI was not an independent prognostic factor for in-hospital mortality among IE patients, we speculate that CCI might be a prognostic tool. Further study should be needed to conclude whether CCI is a prognostic tool.

Our results showed that SOFA $\geqq$ 6 and heart failure were independently poor prognostic factors for in-hospital death among IE patients, while surgery was an independent favorable prognostic factor. Some have already demonstrated that MRSA, vascular phenomena, APACHE II score, increasing age, prosthetic valve, heart failure and healthcare-associated IE were independent prognostic factors [10–13]. However, our study could not reproduce them, and found other prognostic factors among IE patients except for heart failure and surgery. These discrepancies may be because of the lack of uniformity of variables and differences in our study design.

In the present study, detection of vegetations by echocardiogram and a history of requiring surgical procedures were seen in 69% and 25% which were much lower than those of previous large cohorts [17,18]. These rates were similar to the study by Hase et al. [11]. This discrepancy may be attributable to the fact that while our study population was quite different from previous large cohorts [17,18], it was just the same as the one of Hase [11]. In our study, 32% of patients (52%) were older than 70 years. The elderly tended to refuse TEE due to their poor conditions, resulting in the low rate of TEE procedures. As for surgery, poor ADL and more comorbidities among patients might be associated with the low rate of surgical procedures. While our rate of surgical procedures was lower than previous studies, in-hospital mortality rate was as same as in previous large cohorts [17,18]. This favorable result may be attributable to the fact that despite as many as 11% patients were without any abnormal findings by echocardiogram, they could be diagnosed as definite IE by modified Duke criteria, namely positive blood culture and three minor criteria resulting in the early treatment. Furthermore, advanced diagnostic testing such as Matrix-assisted laser desorption/ionization-time of flight mass spectrometry might have contributed to the early diagnosis and the favorable outcomes. While antibiotic therapy and diagnostic testing are advancing, IE still remains a life-threatening infection. Our results demonstrated that the SOFA score could be one of the useful prognostic tools in evaluating the severity of IE. In addition, our study showed that surgical treatment was a favorable prognostic factor among IE patients. While admission to ICU for initial treatment was not associated with in-hospital mortality (data not shown), surgery was a favorable prognostic factor in this study. This might mean an early surgical intervention could contribute to improving the high mortality rate among IE patients. We could suggest that IE patients with high SOFA scores should be treated by surgery for a better prognosis.

There are limitations in our study. First, this is a retrospective study in a small population. Thus, there might be a bias in data selection and analysis. Second, we evaluated only patients diagnosed as definite IE by modified Duke criteria. In general practice, more patients with possible IE by modified Duke criteria exist. Then, all patients including definite and possible IE by the criteria should be studied in the future. Third, there was a difference of patients' characteristics between IE patients and the control group. More patients should be estimated and analyzed by propensity score matching analysis for identifying a prognostic factor among IE patients.

## 5. Conclusion

SOFA score could correctly reflect the severity and prognosis of IE. SOFA score $\geq$6, surgery, immunological phenomena and heart failure were independent prognostic factors for in-hospital mortality among IE.

## Conflicts of interest

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