Original Research

Validity of SOFA score as a prognostic tool for critically ill elderly patients with acute infective endocarditis

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The prognostic value of the sequential organ failure assessment (SOFA) score for critically ill elderly patients with acute infective endocarditis (IE) remains unknown. From January 2015 to December 2019, 111 elderly (≥65 years) patients with acute IE were consecutively included and divided into a low SOFA (<6) group (n = 71) and a high SOFA (≥6) group (n = 40). Endpoints included in-hospital and long-term (12–36 month) mortality. A high SOFA score was related to higher incidence of in-hospital mortality (30.0%) with an area under the curve (AUC) of 0.796. In multivariate analysis, age [odds ratio (OR) = 2.21, 95% confidence intervals (CI), 1.16–6.79, p = 0.040], SOFA ≥6 (OR = 6.38, 95% CI, 1.80–16.89, p = 0.004) and surgical treatment (OR = 0.21, 95% CI, 0.05–0.80, p = 0.021) were predictive of in-hospital mortality. A Cox proportional-hazards model identified age [Hazard ratios (HR)= 2.85, 95% CI, 1.11–7.37, p = 0.031], diabetes mellitus (HR = 3.99, 95% CI, 1.35–11.80, p = 0.013), SOFA ≥6 (OR = 3.38, 95% CI, 1.26–9.08, p = 0.001) and surgical treatment (HR = 0.24, 95% CI, 0.08–0.68, p = 0.021) as predictors of long-term mortality. A high SOFA score predicts a poor outcome including in-hospital and long-term mortality in critically ill elderly patients with acute IE.

Keywords

SOFA; Elderly patients; Acute infective endocarditis; In-hospital mortality; Long-term mortality

1. Introduction

The epidemiology of infective endocarditis (IE) is changing with a growing proportion of patients who are elderly [1]. The incidence of IE in elderly patients is 4.6 times higher than in the general population, with delayed diagnosis [2, 3]. Medical or surgical treatment for IE in elderly patients remains controversial because of associated high incidence of morbidity and mortality [4]. Accordingly, early identification of patients with an elevated risk of death from IE is essential to improve outcomes in elderly patients. The sequential organ failure assessment (SOFA) score has been confirmed as an effective prognostic tool in the management of sepsis, as well as in IE patients [5–7]. However, limited data is available on the prognostic value of SOFA in patients with IE who are elderly.

We conducted the first multicenter prospective observational study that evaluated the prognostic value of the SOFA score for in-hospital and long-term mortality of patients aged 65 years and older who were treated for acute IE.

2. Patients and methods

2.1 Patient enrollment

A multicenter prospective observational trial involving acute IE in elderly patients (≥65 years) was conducted at 3 university-affiliated medical centers (Shenzhen People's Hospital, Longgang District People's Hospital of Shenzhen and Guangdong General Hospital) in China. Using modified Duke criteria for IE diagnosis [8], a total of 348 patients diagnosed with IE were consecutively screened from January 2015 to December 2019. After exclusion of patients with age <65 years, patients not requiring ICU admission (n = 210), patients with prior IE diagnoses (n = 10) and repeat hospitalizations (n = 17), 111 elderly patients with acute IE requiring ICU were included in this study. IE was categorized as either acute (developing over hours or 14 days) or subacute (progressive over 2 weeks to months). Surgery was performed provided that surgical criteria were met. Conservative drug therapy was initiated in circumstances of extremely poor health conditions or inability to afford the expense of operation.

2.2 Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the Ethics Committee of Shenzhen People's Hospital (approval number: SZLY0122). All participants provided informed consent prior to participation in the study.

2.3 Data collection

Transthoracic echocardiography and SOFA score were assessed within 24 hours of admission. Transesophageal echocardiography was performed if necessary. Serum samples were collected and analyzed immediately upon admission [C-reactive protein (CRP), 0–5 mg/L; erythrocyte sedimentation rate (ESR), 20 mm/h]. Follow-up data were acquired by telephone at 1 month, 3 months, 6 months and 12 months after discharge from hospitalization.

2.4 Study endpoints

The primary study endpoint was in-hospital mortality. Secondary endpoint measures included other predictors of in-hospital mortality and all cause death during follow-up.

2.5 Statistical analysis

Statistical analysis was performed by SPSS 22.0 (Chicago, IL, USA). Data were reported as mean ± standard deviation (SD) or counts (percentage). Group comparison of continuous data was conducted by Student's *t*-test, analysis of variance (ANOVA) or Kruskal-Wallis test. Group comparison of categorical data was calculated by Chi-square or Fisher Exact test. Optimal cut-off points for SOFA scores were calculated by receiver operator characteristic curve (ROC) analysis. Univariable and multivariable logistic regression analyses were applied to evaluate adjusted odds ratio (OR) for in-hospital mortality, and reported with 95% confidence intervals (CI). Kaplan-Meier curves, evaluated with log-rank tests and Cox proportional-hazards models, were used to evaluate the long-term survival. Hazard ratios (HR) are also reported with 95% CI. Statistical significance was defined as $p < 0.05$.

3. Results

3.1 Characteristics of patients in high SOFA and low SOFA groups

One hundred and eleven elderly patients with acute IE were included in this study (29 females, mean age 71.86 ± 5.48 years), among which 17 patients (15.32%) died during hospitalization. Patients were divided into low SOFA (<6, n = 71) and high SOFA (≥6, n = 40) score. Patients with high SOFA scores had higher incidence of embolic complications (35% vs. 15.49%, p = 0.040), neurological failure determined by Glasgow Coma Score (GCS ≤12, 25% vs. 8.45%, p = 0.028), heart failure determined by New York Heart Association (NYHA) class III–IV (50% vs. 25.35%, p = 0.029) and vegetation size ≥10 mm (55% vs. 33.8%, p = 0.045), and a lower rate of receiving surgical treatment (67.5% vs. 90.14%, p = 0.029) (Table 1).

Table 1. Baseline clinical characteristics of patients according to SOFA score.

Characteristics	Low SOFA (n = 71)	High SOFA (n = 40)	p-value
Age (years)	68 (66, 75.75)	71.5 (67, 77)	0.029
Females, n (%)	18 (25.35)	11 (27.50)	0.781
AIE, n (%)	14 (19.72)	10 (25.00)	-
SIE, n (%)	57 (80.28)	30 (75.00)	0.481
Hypertension, n (%)	18 (25.35)	14 (35.00)	0.389
Diabetes mellitus, n (%)	6 (8.45)	8 (20.00)	0.144
Affected valve			
Aortic valve, n (%)	38 (53.52)	18 (45.00)	0.325
Mitral valve, n (%)	38 (53.52)	22 (55.00)	0.900
Tricuspid valve, n (%)	8 (11.27)	4 (10.00)	0.951
#Multiple-valves, n (%)	8 (11.27)	9 (22.50)	0.745
Congenital heart disease, n (%)	5 (7.04)	5 (12.50)	0.492
Neurological failure (GCS ≤12), n (%)	6 (8.45)	10 (25.00)	0.028
Paravalvular abscess, n (%)	4 (5.63)	6 (15.00)	0.168
Embolic complications, n (%)	11 (15.49)	14 (35.00)	0.040
Stroke, n (%)	10 (14.08)	10 (25.00)	0.207
Heart failure, n (%)	40 (56.34)	29 (72.50)	0.106
NYHA III–IV, n (%)	18 (25.35)	22 (55.00)	0.029
LVEF (%)	62.90 ± 7.75	62.29 ± 9.24	0.717
Temperature, °C	38.8 ± 1.17	38.95 ± 0.57	0.627
CRP, mg/L	24.67 ± 22.07	37.89 ± 21.16	0.006
SOFA score (interquartile range)	3.9 (3, 5)	7.5 (6, 9)	0.001
ESR, mm/h	39.06 ± 34.33	39.50 ± 34.08	0.917
Pathogen, n (%)			
Staphylococcus aureus	10 (14.08)	7 (17.5)	0.416
Streptococcus spp	20 (28.17)	12 (30.00)	0.738
Healthcare-associated infection	2 (2.82)	1 (2.50)	0.730
Vegetation size ≤10 mm, n (%)	24 (33.80)	22 (55.00)	0.045
Surgery treatment, n (%)	64 (90.14)	27 (67.50)	0.029
In-hospital death	5 (7.04)	12 (30.00)	0.002
Long-term mortality	7 (9.86)	11 (27.50)	0.003

AIE, acute infective endocarditis; SIE, subacute infective endocarditis; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SOFA, sequential organ failure assessment; GCS, Glasgow Coma Score. #Affected value more than or 2 valves.

3.2 SOFA score for predicting in-hospital mortality

In-hospital mortality, the primary endpoint, was 30% in the high SOFA score group and 7.04% in the low SOFA score group (p = 0.002). ROC analysis indicated that a SOFA score of ≥6 could predict in-hospital mortality with sensitivity 76.47%, specificity 71.28% (AUC = 0.796, 95% CI, 0.814–0.904, $p < 0.001$) (Fig. 1).

Univariate analysis identified age (odds ratio (OR) = 3.05, p = 0.039), diabetes mellitus (OR = 3.94, p = 0.032), multiple-valves (OR = 2.10, p = 0.040), neurological failure (GCS ≤12; OR, 4.58, p = 0.012), paravalvular abscess (OR = 4.51, p = 0.034), NYHA III–IV (OR = 3.93, p = 0.041), CRP ≥18.6 mg/L (OR = 4.11, p = 0.035), SOFA ≥6 (OR = 6.65, p = 0.003) and surgical treatment (OR = 0.23, p = 0.011) as predictors for in-hospital mortality. Upon multivariate analysis, age (OR = 2.31, 95% CI, 1.16–6.79, p = 0.040), SOFA ≥6 (OR = 6.38, 95% CI, 1.80–16.89, p = 0.004) and surgical treatment (OR = 0.21, 95% CI, 0.05–0.80, p = 0.021) were confirmed as adjusted independent predictors for in-hospital mortality (Fig. 2).

3.3 SOFA score for predicting long-term outcome

Among the 94 patients surviving hospitalization, 1 patient (1.1%) was lost to follow-up and 18 patients (19.35%) died

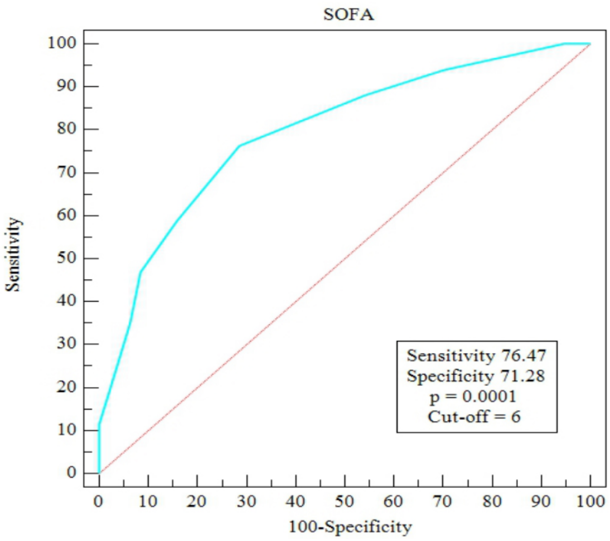

Fig. 1. The ROC curves for SOFA in predicting in-hospital mortality in elderly IE patients.

within the follow-up time of 12–36 months. Long-term mortality, a secondary endpoint, was 27.50% in the high SOFA score group and 9.86% in the low SOFA score group (p = 0.003). Kaplan-Meier analysis demonstrated a lower cumulative survival in patients with SOFA 6–9 and SOFA ≥10 (p = 0.001; Fig. 3A). The Cox proportional-hazards model of SOFA score for long-time survival over 3 years of follow-up showed that age (HR = 2.85, 95% CI, 1.11–7.37, p = 0.031), diabetes mellitus (HR = 3.99, 95% CI, 1.35–11.80, p = 0.013), SOFA ≥6 (HR = 3.38, 95% CI, 1.26–9.08, p = 0.001) and surgical treatment (HR = 0.24, 95% CI, 0.08–0.68, p = 0.021) were adjusted independent predictors (Fig. 3B and C).

4. Discussion

This study aims to evaluate the utility of SOFA for predicting mortality in critically ill elderly patients with acute IE. The major findings are: (i) a strong predictive value of high SOFA for in-hospital mortality; (ii) high SOFA was associated with long-term mortality; (iii) additionally, age, diabetes mellitus and surgical treatment were independent predictors of clinical outcomes.

With an increase in life expectancy, elderly people susceptible to infectious diseases are more common than ever for physicians. In particular, acute IE in elderly patients is a severe and challenging disease for cardiologists, with high in-hospital mortality rates ranging from 24.9% to 45.3% [9, 10]. Early identification of prognostic factors may offer the opportunity to improve the clinical outcomes of these patients. The SOFA score assesses respiration, coagulation, liver and renal function, cardiovascular health and the central nervous system, using fraction of inspiration O2, platelet count, serum bilirubin and creatinine, blood pressure/pressor use, and the Glasgow coma score, reflecting the severity of organ failure and predicting underlying comorbidities [11, 12]. A SOFA score of 2 or more has been recommended as a criterion for sepsis and has been confirmed as a significant predictor of ICU mortality [7]. Therefore, it is reasonable to expect that obtaining a SOFA score on admission could predict the severity and prognosis of acute IE.

In our study, SOFA ≥6 (OR, 6.38) could predict in-hospital mortality with sensitivity 76.47% and specificity 71.28% (AUC, 0.796, 95% CI, 0.814–0.904). The score of AUC in our study was much lower than that in the study of Nobuhiro (AUC, 0.915, sensitivity 76.9%, specificity 89.6%), which included coagulase negative bacteremia patients without IE as control group, but the cut-off point (6) was similar. Kim and colleagues found that a higher SOFA cut-off value (7 [4, 11] vs. 3 [1, 5], $p < 0.001$) predicted poor outcomes in IE with *Staphylococcus aureus* [13] bacteremia (SAB). The mortality rate for methicillin-resistant SAB (MRSAB) is 32% and for methicillin susceptible SAB (MSSAB) is 14%, both higher than in other infections. Wei found that increased CRP and red blood cell distribution width, especially in combination, were associated with in-hospital mortality in patients with blood culture-negative infective endocarditis [14]. Other biochemical markers such as troponin, B-Type Natriuretic Peptide and D-dimer are reliable prognostic biomarkers associated with adverse outcomes in patients with IE [15–17]. However, sensitivity and specificity were lower than in our study.

Advanced age (OR, 2.31) has been associated with poor prognosis in acute IE. Our results were in accordance with studies by Netzer [18] and Selton-Suty [19], who found that mortality was higher in elderly patients (>65 or >70 years, respectively) than in younger ones (25% vs. 11% or 28% vs. 13.5%, respectively). Another study showed mortality rates up to 32% in patients aged >60 years [20]. In-hospital mortality in our study was 15.32%, lower than in previous studies. This may be attributed to a high percentage (81.98%) of the elderly patients in our study receiving surgical treatment, which our data showed to be associated with better outcomes (OR, 0.21 for mortality). Our results were in accordance with those observed by Di Salvo [1], in which in-hospital mortality in patients who received surgery was lower than in those treated without surgery, and elderly patients who received surgical treatment had better outcomes (11% mortality).

Our data also showed that high SOFA (SOFA ≥6, HR, 3.38) was associated with long-term mortality. SOFA-based assessment could be performed at admission, allowing for an evidence-based decision-making process for prognostic management. SOFA was initially proposed for organ dysfunction quantification in general critically ill patients, and was further confirmed as a prognostic tool for mortality prediction [21]. Additionally, patient characteristics, including older age (HR, 2.85) and diabetes mellitus (HR, 3.99), were main factors leading to adverse prognosis. These results are in agreement with the study of Lin and Duval [22, 23], in which age and diabetes mellitus were significantly associated with the short-time outcome in patients with IE. Though early surgery reduced incidence of in-hospital and 1-year mortal-

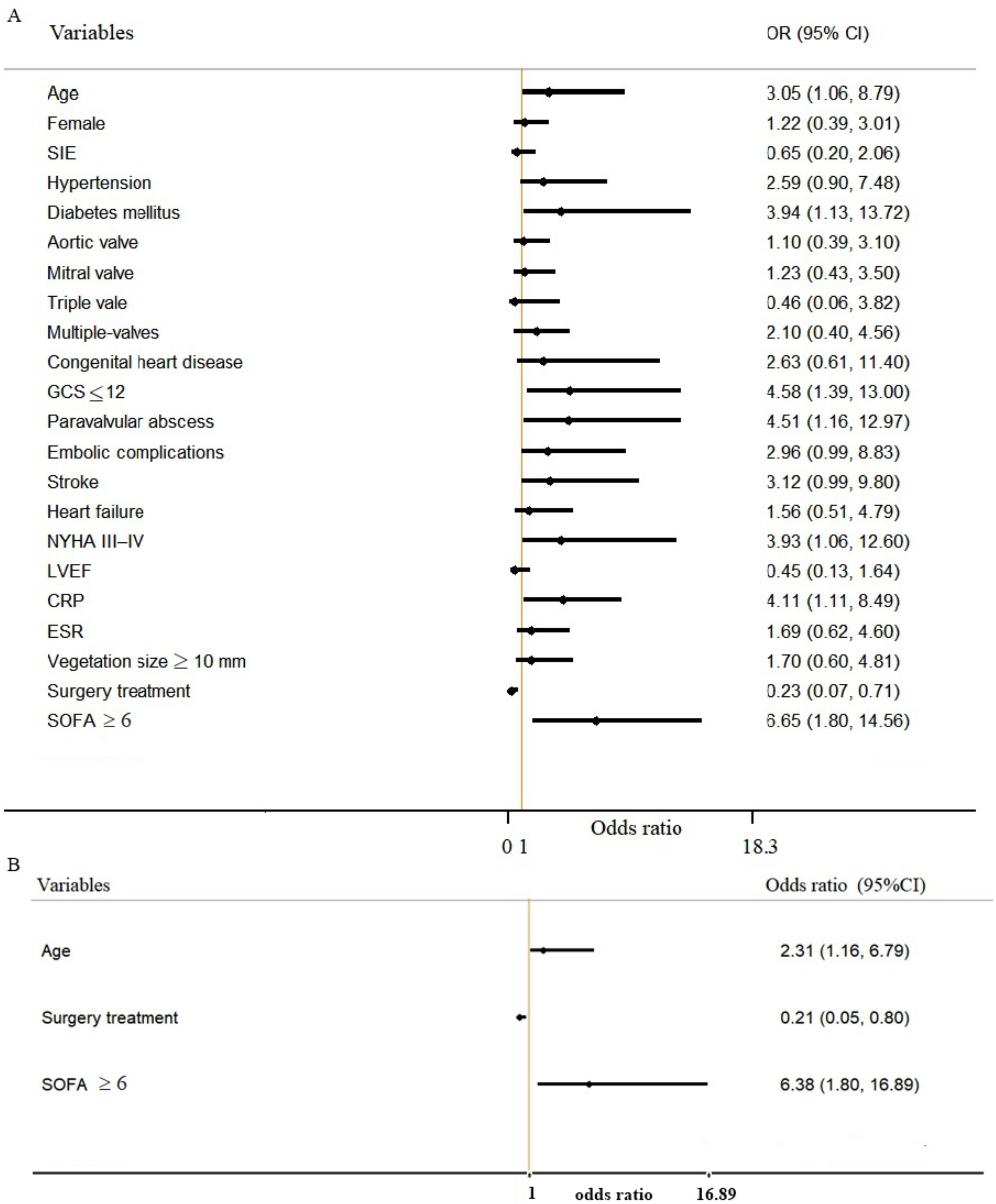

Fig. 2. Univariate (A) and multivariate analyses (B) of factors associated with in-hospital mortality.

ity in patients with native or prosthetic valve IE [24], fewer elderly patients with acute IE received surgical treatment. In fact, cardiovascular surgeons frequently refuse to operate on a patient over 80 years of age and hesitate for patients from 75 to 80 years old due to higher perioperative or post-operative complications and mortality. However, the ratio of morbidity and mortality in patients who have undergone surgery treatment was reduced in our study, which may be ascribed to improved surgical techniques. In our study, surgical treatment was performed in 81.98% of patients and was confirmed as a strong predictor (HR, 0.24) of good outcome with follow-up in elderly patients. With the development of surgeon experience and advancement in surgical techniques, success rates of surgery are higher and complication rates are lower than previously. Accordingly, surgical treatment was almost routinely recommended for IE in this study. Age alone should probably not be regarded as a contraindication to surgery. A more frequent use of surgery and greater co-

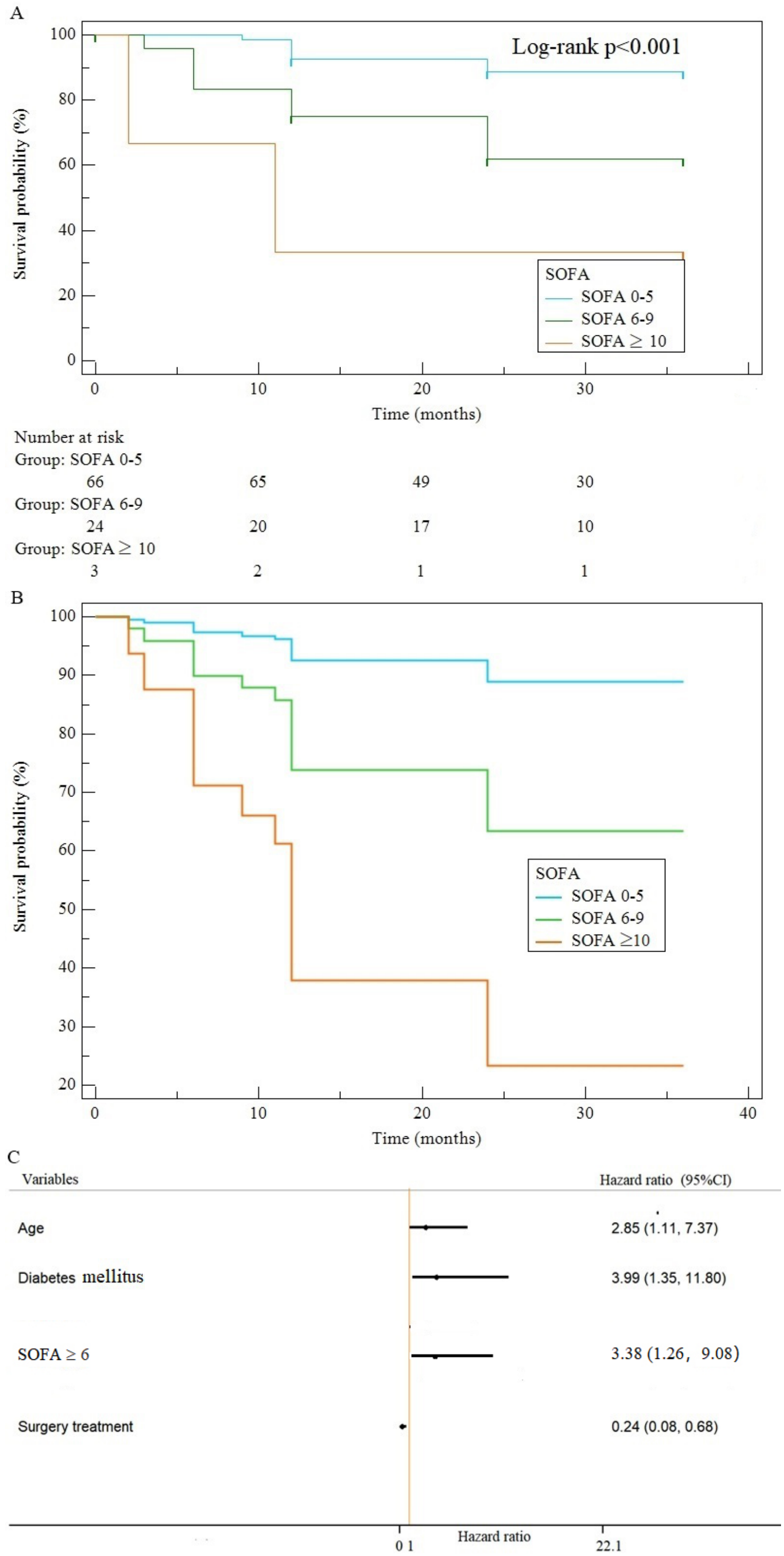

Fig. 3. Kaplan-Meier analysis (A), Cox regression analysis (B) and Cox proportional-hazards model (C) of SOFA score for survival over 3 years of follow-up.

operation between cardiologists and geriatricians could help improve the management of elderly patients with IE [25].

We should acknowledge the limitations of the present study. First, this is a prospective observational trial involving a small population. Thus, there might be a bias in data selection and analysis. Secondly, younger IE patients (age <65 years) were excluded; therefore, the comparison between SOFA scores of different ages (age <65 years and age

>65 years) with mortality in acute IE was lacking. Finally, the SOFA score may differ significantly during hospital stay. Evaluation of SOFA scores including different periods during hospitalization needs further study.

5. Conclusions

SOFA is a straightforward prognostic tool to use for critically ill elderly patients with acute IE. A SOFA score ≥6 is significantly associated with in-hospital and long-time mortality.

Author contributions

YWL, MSW, SHD, FL and HYQ designed, collected, analyzed and wrote this manuscript. BHL, SYG, FL, HDL, JY and DQY assisted in the conduct of study. BHL, SYG, HDL, JY, DQY and HYQ performed the research. YWL, MSW and SHD was the principal investigator.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the Ethics Committee of Shenzhen People's Hospital (approval number: SZLY0122). All participants provided informed consent prior to participation in the study.

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Conflict of interest

The authors declare no conflict of interest.

References

[1] Di Salvo G, Thuny F, Rosenberg V, Pergola V, Belliard O, Derumeaux G, *et al.* Endocarditis in the elderly: clinical, echocardiographic, and prognostic features. European Heart Journal. 2003; 24: 1576–1583.

[2] Hoen B, Alla F, Selton-Suty C, Béguinot I, Bouvet A, Briançon S, *et al.* Changing profile of infective endocarditis: results of a 1-year survey in France. Journal of the American Medical Association. 2002; 288: 75–81.

[3] Werner GS, Schulz R, Fuchs JB, Andreas S, Prange H, Ruschewski W, *et al.* Infective endocarditis in the elderly in the era of transesophageal echocardiography: clinical features and prognosis compared with younger patients. American Journal of Medicine. 1996; 100: 90–97.

[4] Remadi JP, Nadji G, Goissen T, Zomvuama NA, Sorel C, Tribouilloy C. Infective endocarditis in elderly patients: clinical characteristics and outcome. European Journal of Cardio-Thoracic Surgery. 2009; 35: 123–129.

[5] Heiro M, Helenius H, Sundell J, Koskinen P, Engblom E, Nikoskelainen J, *et al.* Utility of serum C-reactive protein in assessing the outcome of infective endocarditis. European Heart Journal. 2005; 26: 1873–1881.

[6] Asai N, Shiota A, Ohashi W, Watanabe H, Shibata Y, Kato H, *et al.* The SOFA score could predict the severity and prognosis of infective endocarditis. Journal of Infection and Chemotherapy. 2019; 25: 965–971.

[7] Raith EP, Udy AA, Bailey M, McGloughlin S, MacIsaac C, Bellomo R, *et al.* Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for in-Hospital Mortality among Adults with Suspected Infection Admitted to the Intensive Care Unit. Journal of the American Medical Association. 2017; 317: 290–300.

[8] Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Ryan T, *et al.* Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clinical Infectious Diseases. 2000; 30: 633–638.

[9] Lu KJ, Kearney LG, Ord M, Jones E, Burrell LM, Srivastava PM. Age adjusted Charlson Co-morbidity Index is an independent predictor of mortality over long-term follow-up in infective endocarditis. International Journal of Cardiology. 2013; 168: 5243–5248.

[10] Durante-Mangoni E, Bradley S, Selton-Suty C, Tripodi MF, Barsic B, Bouza E, *et al.* Current features of infective endocarditis in elderly patients: results of the International Collaboration on Endocarditis Prospective Cohort Study. Archives of Internal Medicine. 2008; 168: 2095–2103.

[11] Innocenti F, Palmieri V, Guzzo A, Stefanone VT, Donnini C, Pini R. SOFA score and left ventricular systolic function as predictors of short-term outcome in patients with sepsis. Internal and Emergency Medicine. 2018; 13: 51–58.

[12] Innocenti F, Tozzi C, Donnini C, De Villa E, Conti A, Zanobetti M, *et al.* SOFA score in septic patients: incremental prognostic value over age, comorbidities, and parameters of sepsis severity. Internal and Emergency Medicine. 2018; 13: 405–412.

[13] Kim C, Song K, Park K, Kim M, Choe PG, Oh M, *et al.* Impact of antimicrobial treatment duration on outcome of Staphylococcus aureus bacteraemia: a cohort study. Clinical Microbiology and Infection. 2019; 25: 723–732.

[14] Wei X, Liu Y, He P, Zhou Y, Tan N, Chen J, *et al.* Combined efficacy of C-reactive protein and red blood cell distribution width in prognosis of patients with culture-negative infective endocarditis. Oncotarget. 2017; 8: 71173–71180.

[15] Postigo A, Vernooij RWM, Fernández-Avilés F, Martínez- Sellés M. Cardiac troponin and infective endocarditis prognosis: a systematic review and meta-analysis. European Heart Journal. Acute Cardiovascular Care. 2021; 10: 356–366.

[16] Shiue AB, Stancoven AB, Purcell JB, Pinkston K, Wang A, Khera A, *et al.* Relation of level of B-type natriuretic peptide with outcomes in patients with infective endocarditis. American Journal of Cardiology. 2010; 106: 1011–1015.

[17] Lin Y, Jiang M, Wei X, Huang J, Su Z, Wang Y, *et al.* Prognostic value of D-dimer for adverse outcomes in patients with infective endocarditis: an observational study. BMC Cardiovascular Disorders. 2021; 21: 279.

[18] Netzer RO, Zollinger E, Seiler C, Cerny A. Native valve infective endocarditis in elderly and younger adult patients: comparison of clinical features and outcomes with use of the Duke criteria. Clinical Infectious Diseases. 1999; 28: 933–935.

[19] Selton-Suty C, Hoen B, Grentzinger A, Houplon P, Maignan M, Juillière Y, *et al.* Clinical and bacteriological characteristics of infective endocarditis in the elderly. Heart. 1997; 77: 260–263.

[20] Watanakunakorn C, Burkert T. Infective endocarditis at a large community teaching hospital, 1980–1990. A review of 210 episodes. Medicine. 1993; 72: 90–102.

[21] Minne L, Abu-Hanna A, de Jonge E. Evaluation of SOFA-based models for predicting mortality in the ICU: a systematic review. Critical Care. 2008; 12: R161.

[22] Duval X, Alla F, Doco-Lecompte T, Le Moing V, Delahaye F, Mainardi J, *et al.* Diabetes mellitus and infective endocarditis: the insulin factor in patient morbidity and mortality. European Heart Journal. 2007; 28: 59–64.

[23] Lin CJ, Chua S, Chung SY, *et al.* Diabetes Mellitus: An Independent Risk Factor of In-Hospital Mortality in Patients with Infective Endocarditis in a New Era of Clinical Practice. International Journal of Environmental Research and Public Health. 2019; 16: 2248.
[24] Kiefer T, Park L, Tribouilloy C, Cortes C, Casillo R, Chu V, *et al.* Association between Valvular Surgery and Mortality among Patients with Infective Endocarditis Complicated by Heart Failure. Journal of the American Medical Association. 2011; 306: 2239–2247.
[25] Oliver L, Lavoute C, Giorgi R, Salaun E, Hubert S, Casalta J, *et al.* Infective endocarditis in octogenarians. Heart. 2017; 103: 1602–1609.