

Prognostic accuracy of initial and 24-h maximum SOFA scores of septic shock patients in the emergency department

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ABSTRACT

Background: We compared the prognostic accuracy of in-hospital mortality of the initial Sequential Organ Failure Assessment (SOFA_{ini}) score at the time of sepsis recognition and resuscitation and the maximum SOFA score (SOFA_{max}) using the worst variables in the 24 h after the initial score measurement in emergency department (ED) patients with septic shock.

Methods: This was a retrospective observational study using a multicenter prospective registry of septic shock patients in the ED between October 2015 and December 2019. The primary outcome was in-hospital mortality. The prognostic accuracies of SOFA_{ini} and SOFA_{max} were evaluated using the area under the receiver operating characteristic (AUC) curve.

Results: A total of 4860 patients was included, and the in-hospital mortality was 22.1%. In 59.7% of patients, SOFA_{max} increased compared with SOFA_{ini}, and the mean change of total SOFA score was 2.0 (standard deviation, 2.3). There was a significant difference in in-hospital mortality according to total SOFA score and the SOFA component scores, except cardiovascular SOFA score. The AUC of SOFA_{max} (0.71; 95% confidence interval [CI], 0.69–0.72) was significantly higher than that of SOFA_{ini} (AUC, 0.67; 95% CI, 0.66–0.69) in predicting in-hospital mortality. The AUCs of all scores of the six components were higher for the maximum values.

Conclusion: The prognostic accuracy of the initial SOFA score at the time of sepsis recognition was lower than the 24-h maximal SOFA score in ED patients with septic shock. Follow-up assessments of organ failure may improve discrimination of the SOFA score for predicting mortality.

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1. Introduction

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. The occurrence of sepsis is a major medical emergency requiring early recognition and management [1]. Sepsis-related morbidity and mortality remain high despite advances in intensive care [2–4]. For sepsis diagnosis, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) proposed clinical criteria using the Sequential Organ Failure Assessment (SOFA) score as a main measurement of organ dysfunction [1]. A change in SOFA score of 2 or more after infection is a defining characteristic of sepsis.

The original SOFA score was introduced by the Working Group of the European Society of Intensive Care Medicine. It was intended to quantify the failure severity of the six essential organ systems—respiration, coagulation, liver function, cardiovascular function, renal function, and central nervous system function—in sepsis patients in the intensive care unit (ICU) [5]. Each score of an organ system ranges from 0 to 4 using the worst value on each day. The original SOFA score was not designed to predict mortality. Rather, it has been widely used in clinical practice and research to define clinical sepsis and predict outcomes [6–9].

In the emergency department (ED) setting, the SOFA score is typically determined at the time of initial sepsis diagnosis. The maximum values on the first day may not be calculated. In previous clinical studies in EDs, data for the SOFA score were extracted at various intervals [10–13]. The aim of the present study was to compare the prognostic accuracy of in-hospital mortality using the initial SOFA score (SOFA_{ini}) at the time of sepsis recognition as well as the maximal SOFA (SOFA_{max}) score using variables measured during the 24 h after initial calculation for ED patients with early septic shock. We also evaluated the change in initial SOFA score to the 24-h maximum SOFA score.

2. Methods

2.1. Study design and population

This research was a retrospective observational study using the Korean Shock Society (KoSS) multicenter prospective registry between October 2015 and December 2019 [12,14]. KoSS was established in 2013 to improve the quality of diagnosing and managing septic shock. Beginning in October 2015, KoSS prospectively collected data from 12 university-associated hospital EDs in Republic of Korea during the study period. The registry included patients aged ≥ 19 years who were suspected of infection with refractory hypotension despite 20–30 mL/kg of fluid resuscitation or hypoperfusion. Hypotension was defined as systolic blood pressure (SBP) < 90 mmHg, mean arterial pressure < 70 mmHg, or SBP decrease > 40 mmHg from baseline; hypoperfusion was defined as blood lactate level > 4 mmol/L. In the registry, the following patients were excluded; 1) patients aged < 19 years, 2) patients who had limitations of resuscitation such as a do-not-resuscitate order, 3) patients who met the inclusion criteria only after 6 h from ED arrival, and 4) patients transferred to other hospitals from the ED [11,14]. Since the announcement of the Sepsis-3 definition, we have been collecting related data about the Sepsis-3 septic shock criteria, comprising hypotension requiring vasopressors to maintain a mean arterial pressure (MAP) ≥ 65 mmHg and serum lactate level > 2 mmol/L despite adequate fluid challenge [1].

The present study was approved by the Institutional Review Board of Samsung Medical Center (No. 2023-01-044). The need for informed consent was waived because this study was retrospective and observational, and the patient data were anonymized.

2.2. Data collection and outcome

We collected the following data from the web-based KoSS registry: demographic characteristics, including age and sex; comorbidities; source of infection; blood culture results; initial laboratory data; intervention, including vasopressor, mechanical ventilation, and renal replacement therapy; Acute Physiology And Chronic Health Evaluation II (APACHE II) score; and SOFA score [5,15]. The registry data included both SOFA_{ini} and SOFA_{max}. SOFA_{ini} was calculated when the refractory hypotension or hypoperfusion criteria were met; i.e., persistent hypotension (mean arterial pressure < 70 mmHg or systolic blood pressure < 90 mmHg) after adequate fluid treatment (20–30 mL/kg crystalloid solution), or a blood lactate concentration ≥ 4 mmol/L. SOFA_{max} was calculated using the worst value obtained during the 24 h after initial recognition of refractory hypotension or hypoperfusion. The primary outcome was in-hospital mortality, and the secondary outcome was 28-day or 90-day mortality.

2.3. Statistical analysis

The data are presented as median with interquartile range (IQR) or mean (standard deviation, SD) for continuous variables and as number of patients with percentages for categorical data. For comparison, continuous variables were analyzed using Wilcoxon rank-sum tests, while categorical variables were analyzed using Chi-square tests. The prognostic accuracy of SOFA score as a predictor for the outcomes was assessed using the area under the receiver operating characteristic (AUC) curve. For comparison of the AUC of SOFA_{ini} and SOFA_{max}, a nonparametric approach for dependent receiver operating characteristic curves was used [16]. The optimal cut-off of SOFA score was calculated by the Youden index. A two-tailed p-value < 0.05 was considered statistically significant. All analyses were performed using Stata 17.0 (Stata Corp., College Station, TX).

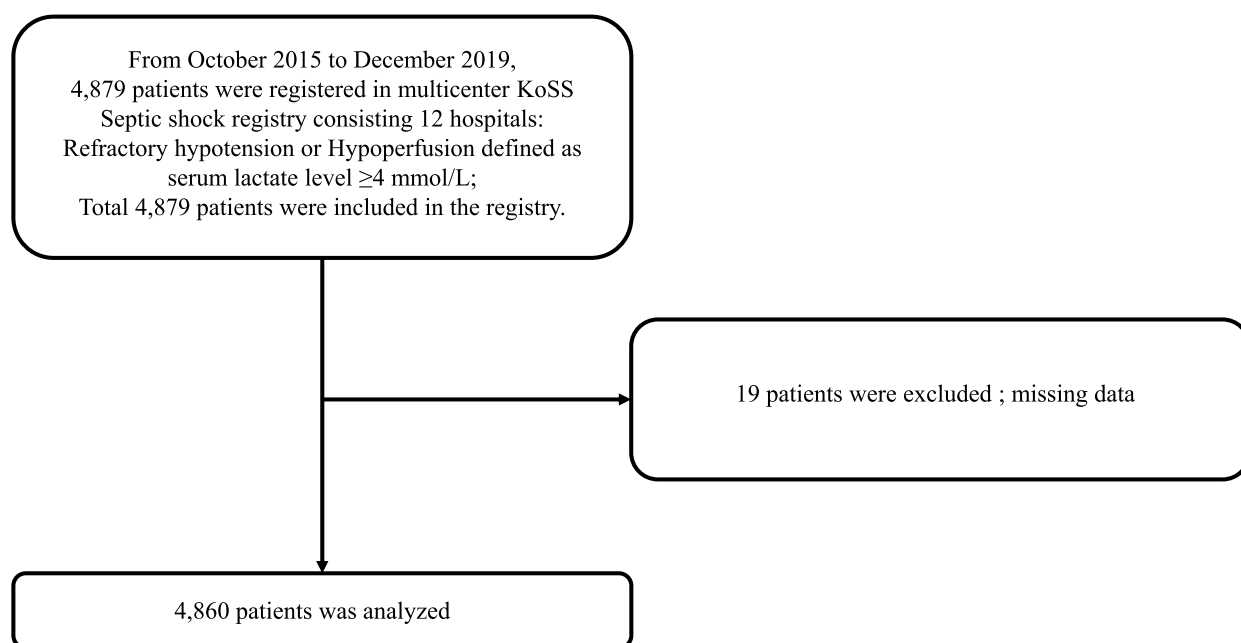


Fig. 1. Flowchart.

Table 1
Baseline characteristics.

Characteristics	Overall (n = 4860)	Survivor (n = 3784)	Non-survivor (n = 1076)	p
Age	70.5 (61.1–78.5)	70.2 (60.8–78.1)	71.7 (62.5–79.8)	<0.001
Male sex – n (%)	2776 (57.1%)	2122 (56.1%)	654 (60.8%)	0.006
Preexisting conditions – n (%)				
Hypertension	2034 (41.9%)	1604 (42.4%)	430 (40.0%)	0.155
Diabetes	1481 (30.5%)	1144 (30.2%)	337 (31.3%)	0.494
Chronic heart disease	644 (13.3%)	502 (13.3%)	142 (13.2%)	0.953
Chronic lung disease	379 (7.8%)	271 (7.2%)	108 (10.0%)	0.002
CVA	654 (13.5%)	501 (13.2%)	153 (14.2%)	0.406
Chronic renal disease	392 (8.1%)	289 (7.6%)	103 (9.6%)	0.040
Chronic liver disease	471 (9.7%)	340 (9.0%)	131 (12.2%)	0.002
Metastatic cancer	1246 (25.6%)	903 (23.9%)	343 (31.9%)	<0.001
Infection source – n (%)				
Lung	1576 (32.4%)	1079 (28.5%)	497 (46.2%)	<0.001
Urinary tract	1307 (26.9%)	1121 (29.6%)	186 (17.3%)	<0.001
Gastrointestinal	802 (16.5%)	575 (15.2%)	227 (21.1%)	<0.001
Hepatobiliary	970 (20.0%)	814 (21.5%)	156 (14.5%)	<0.001
Others	686 (14.1%)	534 (14.1%)	152 (14.1%)	0.990
Septic shock (Sepsis-3) – n (%)	2497 (51.3%)	1749 (46.2%)	748 (69.5%)	<0.001
Blood culture positive – n (%)	2013 (41.4%)	1560 (41.2%)	453 (42.1%)	0.607
Initial lactate level (mmol/L)	3.4 (1.9–5.5)	3.0 (1.8–4.9)	4.8 (2.9–7.7)	<0.001
Vasoactive drug – n (%)	4278 (88.0%)	3310 (87.5%)	968 (90.0%)	0.026
RRT – n (%)	674 (13.9%)	287 (7.6%)	387 (36.0%)	<0.001
Mechanical ventilation – n (%)	1370 (28.2%)	702 (18.6%)	668 (62.1%)	<0.001
APACHE II score	19 (13–25)	18 (13–24)	24 (18–32)	<0.001
SOFA score (initial)	6 (4–8)	6 (4–8)	8 (5–10)	<0.001
SOFA score (maximum)	8 (5–11)	7 (5–10)	10 (7–13)	<0.001

Data are shown as the median with interquartile range or n (%).

CVA, Cerebrovascular Accident; RRT, Renal Replacement Therapy; APACHE, Acute Physiology And Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment.

3. Results

3.1. Baseline characteristics

From October 2015 to December 2019, the number of patients added to the multi center KoSS Septic shock registry was 4879; and

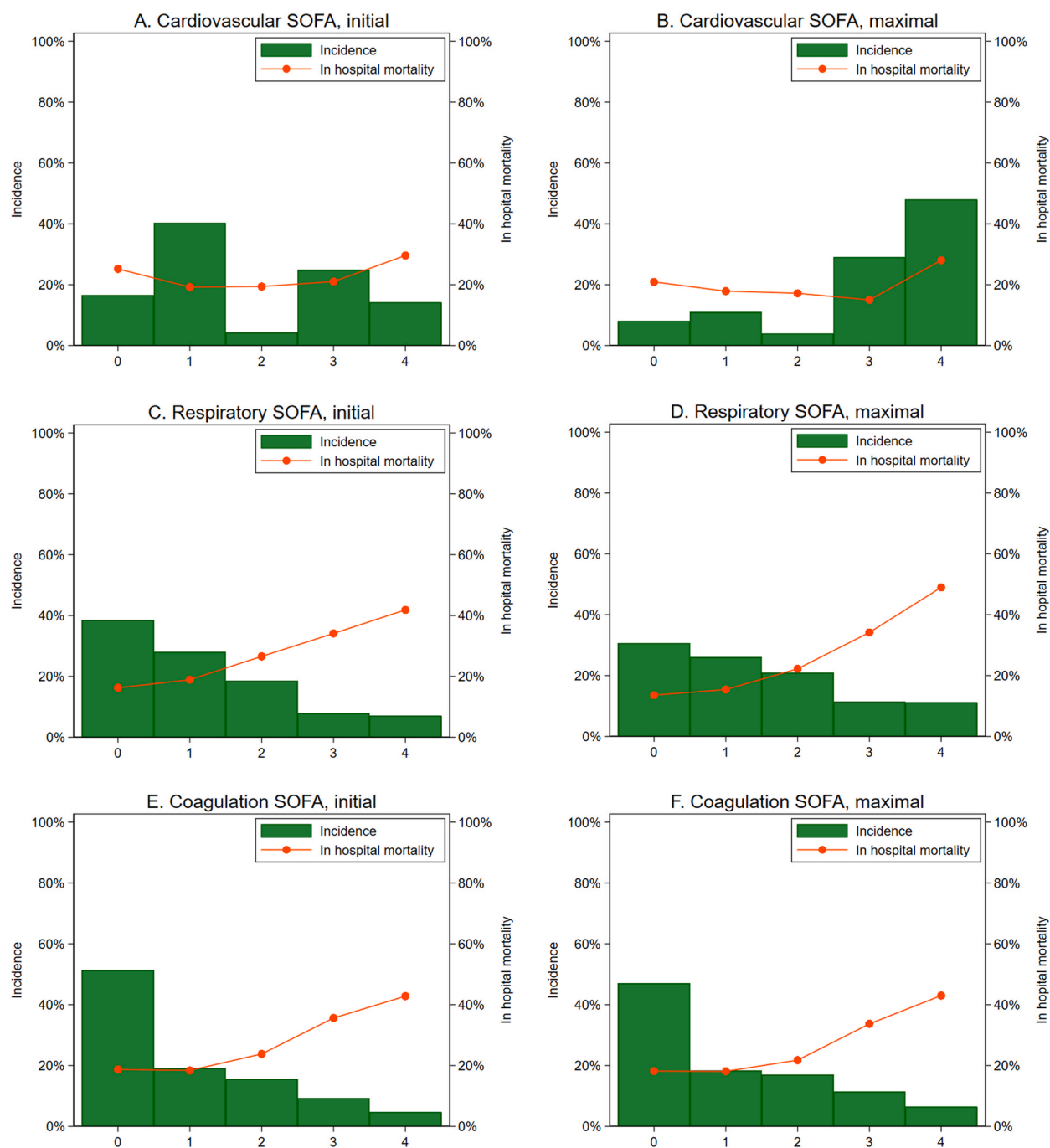


Fig. 2. Incidence and in-hospital mortality according to the score of each SOFA component.

of those 19 were excluded due to missing data. A total of 4860 patients in the septic shock registry was included in this study (Fig. 1). The in-hospital mortality, 28-day mortality, and 90-day mortality were 22.1% (1076/4860), 22.4% (1037/4625), and 34.4% (1514/4405), respectively. The baseline characteristics of this study according to in-hospital mortality are presented in Table 1. The median age was 70.5 (IQR, 61.1–78.5) years, and 57.1% ($n = 2776$) were male. The most frequent infection source was the lungs (32.4%). The median SOFA_{ini} and SOFA_{max} were 6 (IQR, 4–8) and 8 (IQR, 5–11), respectively. There were significant differences both in SOFA_{ini} (median 6 vs. 8) and SOFA_{max} (median 7 vs. 10) between the survivors and non-survivors.

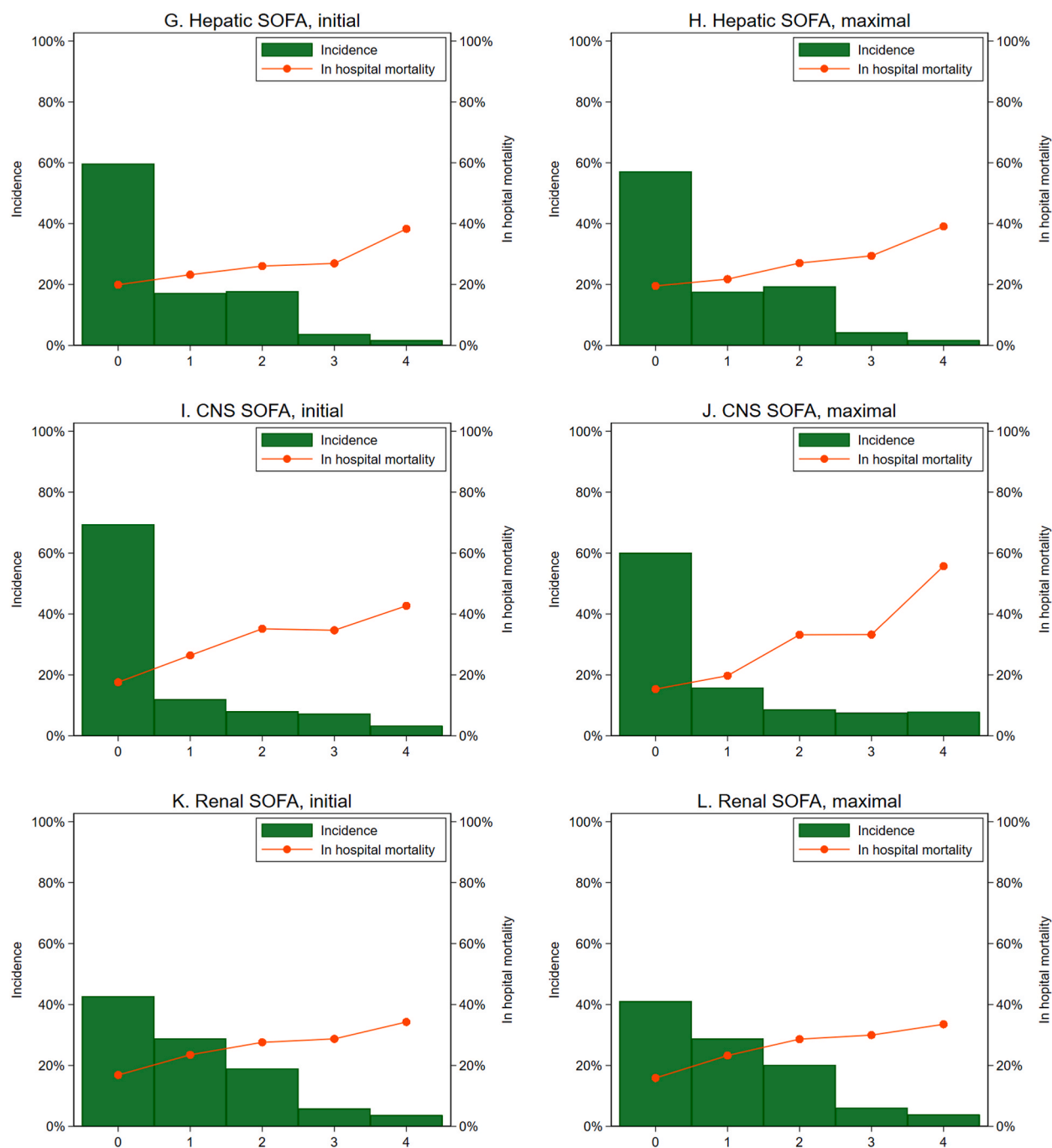


Fig. 2. (continued).

2.2. Changes in SOFA score from initial measurement to the 24-h maximum value

Fig. 2 represents the incidence and in-hospital mortality according to scores of the six SOFA components. In all these components except cardiovascular SOFA, there was an increasing tendency in mortality and a decreasing tendency in incidence. Regarding the cardiovascular SOFA score, there were few patients with a score of 2, and an incremental tendency of mortality was not observed. The trends were similar for SOFA_{ini} and SOFA_{max} .

Changes in SOFA score from initial measurement to the 24-h maximum value, as well as a comparison of the in-hospital mortality are presented in Table 2. In 59.7% of the patients, SOFA_{max} increased compared with SOFA_{ini} , and the mean change of the total SOFA score was 2.0 (SD, 2.3). When the SOFA score increased at 24 h, there was a significant difference in in-hospital mortality according to

Table 2

Changes in SOFA score from initial measurement to the 24-h maximum value and comparison of in-hospital mortality.

	Increase of score in 24-h maximal value (%)	In-hospital mortality in cases with no change (%)	In-hospital mortality in cases with increase in SOFA score (%)	<i>p</i> ^a
Cardiovascular SOFA	50.3	21.7	22.6	0.484
CNS SOFA	13.1	19.4	40.3	<0.001
Respiratory SOFA	19.4	19.2	34.5	<0.001
Renal SOFA	3.6	21.5	40.2	<0.001
Hepatic SOFA	4.6	21.4	36.6	<0.001
Coagulation SOFA	12.5	21.5	26.9	0.003
Total SOFA	59.7	20.7	23.1	0.042

Abbreviations: SOFA, Sequential Organ Failure Assessment; CNS, Central Nervous System.

^a *p*-value is for comparison of in-hospital mortality according to presence of SOFA score change.**Table 3**

Area under the receiver operating characteristic (AUC) for predicting in-hospital mortality.

Initial SOFA	AUC	95% CI	Maximal SOFA	AUC	95% CI	<i>p</i> ^a
All patients						
CNS SOFA	0.60	0.58–0.62	CNS SOFA	0.65	0.63–0.67	<0.001
Respiratory SOFA	0.61	0.59–0.63	Respiratory SOFA	0.66	0.64–0.68	<0.001
Cardiovascular SOFA	0.52	0.50–0.54	Cardiovascular SOFA	0.57	0.56–0.59	<0.001
Renal SOFA	0.58	0.56–0.60	Renal SOFA	0.59	0.57–0.61	<0.001
Hepatic SOFA	0.54	0.53–0.56	Hepatic SOFA	0.55	0.54–0.57	0.001
Coagulation SOFA	0.58	0.56–0.60	Coagulation SOFA	0.59	0.57–0.61	0.008
Total SOFA	0.67	0.66–0.69	Total SOFA	0.71	0.69–0.72	<0.001
Sepsis-3 septic shock patients						
CNS SOFA	0.60	0.57–0.62	CNS SOFA	0.65	0.63–0.67	<0.001
Respiratory SOFA	0.57	0.55–0.60	Respiratory SOFA	0.64	0.62–0.66	<0.001
Cardiovascular SOFA	0.50	0.47–0.52	Cardiovascular SOFA	0.57	0.55–0.59	<0.001
Renal SOFA	0.57	0.54–0.59	Renal SOFA	0.58	0.56–0.60	<0.001
Hepatic SOFA	0.53	0.50–0.55	Hepatic SOFA	0.53	0.51–0.56	0.032
Coagulation SOFA	0.57	0.55–0.60	Coagulation SOFA	0.58	0.56–0.61	0.039
Total SOFA	0.63	0.61–0.66	Total SOFA	0.69	0.67–0.71	<0.001

Abbreviations: SOFA, Sequential Organ Failure Assessment; AUC, Area Under the Receiver Operating Characteristic; CI, Confidence Interval; CNS, Central Nervous System.

^a *p*-value is for comparison of AUCs of the initial and maximum SOFA scores.

total SOFA score and all SOFA component scores except for the cardiovascular component.

2.3. Prognostic accuracy of SOFA_{ini} and SOFA_{max} to predict outcomes

The AUC of SOFA_{max} (0.71; 95% CI, 0.69–0.72) was significantly higher than that of SOFA_{ini} (AUC, 0.67; 95% CI, 0.66–0.69) for predicting in-hospital mortality ($p < 0.001$) (Table 3 and Fig. 3A). The AUCs of all scores of the six components were higher in the maximum values. In patients who met the sepsis-3 criteria for septic shock, the AUCs showed similar trends to entire study subjects. The AUCs of SOFA_{ini} and SOFA_{max} were 0.68 (95% CI, 0.66–0.70) and 0.70 (95% CI, 0.68–0.72) for 28-day mortality ($p < 0.001$) and 0.65 (95% CI, 0.63–0.67) and 0.67 (95% CI, 0.65–0.68) ($p < 0.001$) for 90-day mortality, respectively (Fig. 3B and C). The optimal cut-offs of SOFA_{ini} and SOFA_{max} for predicting in-hospital mortality were 7 and 9, respectively. The prognostic performance data of these cut-off values are shown in Table 4.

4. Discussion

The SOFA score has been widely used for organ failure assessment, prognostication, and clinical sepsis definition in EDs as well as in ICUs. In previous studies based on EDs, the SOFA score was measured at various points in time [10–13,17,18]. The present study showed that SOFA_{ini} is less reliable than SOFA_{max} at predicting mortality among patients with septic shock in EDs. Additionally, a significant portion of study patients, roughly half, demonstrated an increase in SOFA score within 24 h, and this increase was linked to an increase in mortality.

Our findings may have significance from clinical and scientific standpoints because the SOFA score is widely used in both clinical practice and scientific research, including in the clinical definition of sepsis. The results suggest that serial evaluation of the SOFA score rather than a single measurement at a specific time point should be conducted. Also, our results indicate that patients with lower initial SOFA scores require urgent management. Furthermore, in terms of identifying sepsis patients using the SOFA score in clinical practice or research, there may be some differences in the proportion of sepsis patients according to the time points used in measuring the SOFA

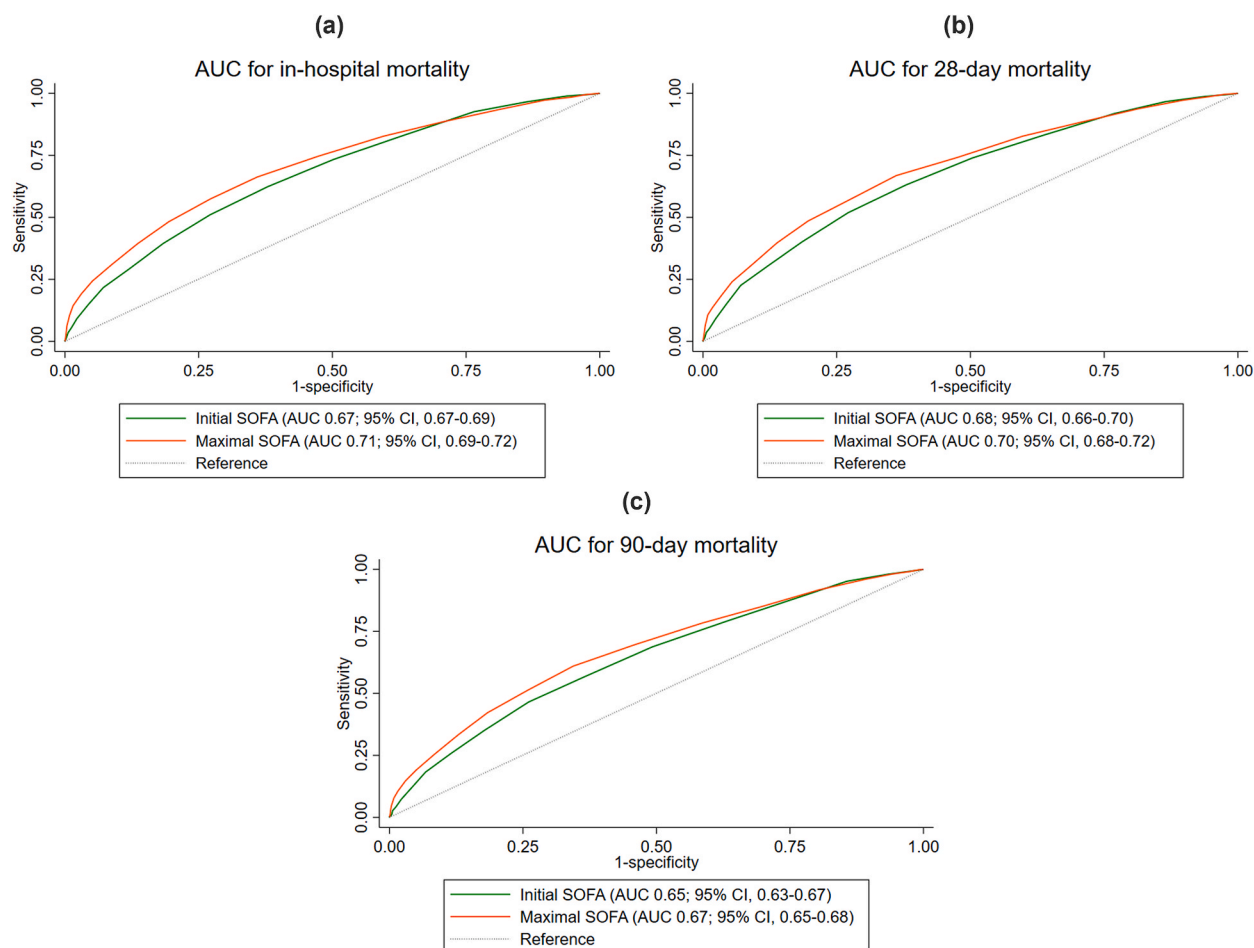


Fig. 3. Area under the receiver operating characteristic (AUC) for predicting in-hospital mortality (A), 28-day mortality (B), and 90-day mortality (C) of the initial SOFA score and the 24-h maximum SOFA score.

Table 4

AUROC and SOFA score cutoff points for in-hospital mortality.

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUROC (95% CI)
SOFA _{ini} ≥ 7	62.4% (59.4–65.3)	62.1% (60.5–63.6)	31.9% (29.9–33.9)	85.3% (83.9–86.6)	0.62 (0.61–0.64)
SOFA _{max} ≥ 9	66.3% (63.4–69.1)	64.0% (62.5–65.6)	34.4% (32.3–36.5)	87.0% (85.7–88.2)	0.65 (0.64–0.67)

Abbreviations: SOFA, Sequential Organ Failure Assessment; AUROC, Area Under the Receiver Operating Characteristic Curve; PPV, Positive Predictive Value; NPV, Negative Predictive Value.

score.

Jones et al. evaluated the prognostic accuracy of the SOFA score measured at the time of ED recognition and resuscitation (T0) and at 72 h after ICU admission (T72) [13]. The AUC of SOFA for predicting in-hospital mortality at T0 was 0.75, and that at T72 was 0.84. The change of SOFA was also associated with in-hospital mortality. Kovach et al. investigated the prognostic accuracy of the SOFA score in ICU and non-ICU settings. They calculated the SOFA score using the parameters showing the greatest change during the 24 h following inclusion. The AUC of SOFA was 0.88 in their study [19]. Freund et al. assessed quick SOFA using the worst value during the ED stay in a multicenter prospective study, but the timing of SOFA score assessment was not clear. The AUROC of SOFA was 0.77 in that study [11]. Direct comparison of AUCs among these studies was not possible, but the trend is consistent with our results that single values from a specific time can be less reliable than measures over time.

Change in SOFA score has been reported as a useful prognostic marker [20]. The change of SOFA score usually is calculated after 2 or 4 days from the initial assessment. Our results are consistent with the utility of change in SOFA score and suggest that very early change of SOFA score has prognostic value.

In addition, when conducting a subgroup analysis in accordance with the components of each SOFA score, cardiovascular SOFA had features distinct from the other components. In cardiovascular SOFA, there was no incremental tendency of mortality as the score

increased, and there were very few patients with a score of 2. Moreover, there was no difference in in-hospital mortality according to the increase in cardiovascular SOFA component scores from the initial value to the 24-h maximum value. These findings suggest that the cardiovascular SOFA score may require modification to reflect current clinical practice and a wider severity range.

This study had certain limitations. First, it was a retrospective study without intervention. Second, this study focused on relatively severe patients with hypoperfusion or refractory hypotension, and the data used were obtained in a university hospital setting. Therefore, it is difficult to generalize the results to all patients with infection or to those with less severe sepsis; additional research is required. Third, we did not evaluate the change of the proportion of clinical sepsis defined by the SOFA score of 2 or higher because non-sepsis patients were not included in this study. Forth, the inclusion criteria of the registry were established before the Sepsis-3 publication. However, the registry criteria are broader than those of Sepsis-3. We found similar results in patients who met the current definition.

5. Conclusion

In sum, the predictive accuracy of the initial SOFA score at the time of sepsis detection was inferior to the maximum SOFA score at 24 h in patients with septic shock in the ED. Follow-up evaluations of organ failure based on patient conditions may enhance the discriminative power of the SOFA score for predicting mortality.

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Ethics approval and consent to participate

The study was approved by the Institutional Review Board of Samsung Medical Center (IRB No.: 2023-01-044). The need for informed consent was waived given the study's retrospective, observational, and anonymous nature.

Author contribution statement

Tae Han Kim: Gun Tak Lee: Tae Gun Shin: Conceived and designed the experiments; Wrote the paper.

Daun Jeong: Jong Eun Park: Performed the experiments.

Sung Yeon Hwang: Gil Joon Suh: Analyzed and interpreted the data.

Sung-Hyuk Choi: Sung Phil Chung: Won Young Kim: Contributed reagents, materials, analysis tools or data.

Data availability statement

The authors do not have permission to share data.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

SOFA	Sequential Organ Failure Assessment
ED	Emergency department
AUC	Area under the receiver operating characteristic
CI	Confidence interval
ICU	Intensive care unit
KoSS	Korean Shock Society

APACHE II Acute Physiology And Chronic Health Evaluation II

IQR Interquartile range

SD Standard deviation

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