



# Postoperative organ dysfunction assessed using simplified eSOFA is associated with mortality: a single-center retrospective cohort study

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## Abstract

**Purpose** This study aimed to determine the association between postoperative organ dysfunction evaluated using eSOFA, a simplified measure of organ dysfunction, and postoperative mortality following noncardiac surgery.

**Methods** This study retrospectively analyzed adult patients who underwent noncardiac surgery under general anesthesia between 2009 and 2019. The primary exposure was postoperative organ dysfunction evaluated using eSOFA within 2 postoperative days (positive eSOFA), and the primary outcome was 90-day mortality. Multivariable Cox regression analysis was employed to investigate the association between positive eSOFA and 90-day mortality. In a subanalysis of patients in the surgical intensive care unit (ICU), the predictive performance of the number of eSOFA-positive items for 90-day mortality was compared with those of the Sequential Organ Failure Assessment (SOFA) score and the Acute Physiology And Chronic Health Evaluation (APACHE) II score using Harrell's C-statistic.

**Results** This study included 24,558 patients, of whom 7.5% had positive eSOFA, and the postoperative 90-day mortality was 0.9%. Positive eSOFA was independently associated with the occurrence of 90-day mortality (adjusted hazard ratio [HR]: 3.03, 95% confidence interval: 2.16–4.25,  $P < 0.001$ ). As the number of positive eSOFA items increased, the adjusted HR for 90-day mortality increased. The C-statistics for predicting 90-day mortality in surgical ICU patients using the number of eSOFA-positive items, SOFA score, and APACHE II score were 0.72 (0.65–0.79), 0.73 (0.65–0.80), and 0.74 (0.68–0.81), respectively.

**Conclusion** Postoperative organ dysfunction evaluated using the eSOFA within 2 postoperative days was independently associated with 90-day mortality in patients who underwent noncardiac surgery.

**Keywords** Postoperative organ dysfunction · eSOFA · Postoperative mortality · Noncardiac surgery · General anesthesia

## Introduction

Perioperative organ dysfunction, including the heart, kidneys, and lungs, has been associated with postoperative mortality [1–3]. Thus, early detection of postoperative organ dysfunction is clinically important for early intervention and prediction of patient outcomes.

Several biomarkers for assessing single-organ dysfunction in the perioperative period have been reported and validated. For example, myocardial injury evaluated using blood troponin levels is a predictor of postoperative mortality in noncardiac surgery [2, 4]. The development of postoperative

acute kidney injury, defined by changes in serum creatinine levels, is also known to be associated with postoperative mortality [5]. However, these biomarkers target dysfunction in only a single organ and thus do not reflect dysfunction in other organs.

The Sequential Organ Failure Assessment (SOFA) and Acute Physiology And Chronic Health Evaluation (APACHE) II scores, which are utilized to evaluate illness severity in patients in intensive care units (ICUs), quantify the degree of organ dysfunction and illness severity by combining data reflecting the function of organs, such as the heart, lungs, and kidneys. These scoring systems have been shown to be useful in predicting ICU/in-hospital mortality in surgical patients [6]. Although these scoring systems can be used to evaluate dysfunction across multiple organ systems, they have several drawbacks. Both SOFA and APACHE II score calculations require blood gas analysis, making it

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difficult to calculate scores in non-ICU settings. APACHE II contains many items and requires time for evaluation. The Glasgow Coma Scale (GCS) included in SOFA has been reported to have significant interrater variability [7].

eSOFA is a measure of organ dysfunction proposed by the Centers for Disease Control and Prevention in 2018. It simplifies the SOFA score to be implemented using routine clinical data available in most electronic health record systems. When using eSOFA, lactate  $\geq 2.0$  mmol/L is included instead of GCS, and the respiratory component is assessed based on ventilator initiation instead of the PaO<sub>2</sub>/FiO<sub>2</sub> ratio. eSOFA enables simultaneous evaluation of dysfunction in multiple organ systems and is easier to apply than SOFA or APACHE II. However, there have been no reports of the use of eSOFA to evaluate organ dysfunction in postoperative patients, and the impact of organ dysfunction assessed using eSOFA on patient prognosis is unknown.

This study aimed to determine the association between postoperative organ dysfunction assessed using eSOFA and postoperative mortality in adult patients who underwent noncardiac surgery under general anesthesia. Although eSOFA was originally proposed as a binary measure, this study will examine the usefulness of the number of eSOFA-positive items as well as negative/positive eSOFA.

## Methods

### Study design and participants

This single-center retrospective cohort study was conducted at Kyoto University Hospital. The study protocol was approved by the Ethics Committee of the institution (approval number: R4252). The requirement for informed consent was waived due to the retrospective nature of the study. This study complied with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [8].

This study included patients aged  $\geq 18$  years who underwent noncardiac surgery under general anesthesia at Kyoto University Hospital between April 2009 and December 2019. For patients who underwent multiple surgeries during the study period, only the first surgery was included in the analysis. The Kyoto University Hospital IMProve Anesthesia Care and ouTcomes (Kyoto-IMPACT) database, which was created to elucidate the association between intraoperative respiratory and circulatory parameters and postoperative outcomes [9–11], was utilized to identify eligible patients.

The exclusion criteria were patients judged as not suitable for the evaluation of perioperative organ dysfunction as they already had preoperative severe organ dysfunction. Specifically, patients who had undergone organ transplantation (lung, liver, kidney, or pancreas), preoperative end-stage

renal disease (eGFR  $< 15$  mL/min/1.73 m<sup>2</sup> or patients on hemodialysis), preoperative platelet count  $< 100,000$ , preoperative use of vasopressors or inotropic agents (phenylephrine, dopamine, dobutamine, norepinephrine, or epinephrine), and preoperative ventilator use were excluded. Patients whose postoperative organ dysfunction could not be evaluated due to a lack of preoperative laboratory information (serum creatinine, serum total bilirubin, platelet count) were also excluded.

### Data collection

We collected the following data from the Kyoto-IMPACT database: patient characteristics (age, sex, height, weight, and Charlson Comorbidity Index [CCI]) and operative variables (American Society of Anesthesiologists physical status classification [ASA-PS], emergency, intraoperative blood loss, duration of surgery, and surgery risk). In addition, we collected information on laboratory data, medications, ventilator use, and postoperative course (postoperative survival, in-hospital mortality, and length of hospital stay) from the electronic medical record system. The definitions of the collected variables are presented in Table S1. To collect postoperative survival data, the last day of outpatient visits following discharge from the hospital was used as the last date of survival confirmation.

### eSOFA

The primary exposure was postoperative organ dysfunction, defined as positivity for any of the six components (cardiovascular, respiratory, renal, hepatic, coagulation, and lactate; Table 1) of eSOFA within 2 postoperative days (positive eSOFA). As postoperative patients may be transferred to the ICU with continued intraoperative mechanical ventilation and then ventilation will be terminated, mechanical ventilation completed within 24 h postoperatively was not considered mechanical ventilation in the assessment of the respiratory system. eSOFA was assessed daily, and patients with a positive eSOFA on any of the 0 to 2 postoperative days were judged as having organ dysfunction. For days with missing postoperative laboratory data (serum creatinine, serum total bilirubin, platelet count, or serum lactate), the values from the previous day were utilized. If laboratory data were missing on all days from 0 to 2 postoperative days, the patient was judged as having no organ dysfunction, because these patients were presumed to be patients for whom the clinician has determined there is no need for blood tests. The baseline values for serum creatinine, serum total bilirubin, and platelet count were the most recent preoperative values. The secondary exposures were the occurrence of organ dysfunction in each of the six aforementioned eSOFA components (Table 1) and the number of eSOFA-positive items.

**Table 1** Criteria for the assessment of eSOFA

	Definition
Respiratory system	Mechanical ventilation initiation*
Cardiovascular system	Vasopressor initiation
Kidneys	Doubling in serum creatinine
Liver	Serum total bilirubin to $\geq 2.0$ mg/dL and doubling from baseline
Coagulation	Decrease in platelet count to $< 100$ cells/ $\mu$ L and $\geq 50\%$ decline from baseline (baseline must be $\geq 100$ cells/ $\mu$ L)
Lactate	Serum lactate $\geq 2.0$ mmol/L

\*Mechanical ventilation terminated within 24 h postoperatively was not considered as mechanical ventilation

## Outcomes

The primary outcome was 90-day mortality, whereas the secondary outcomes were 7-day, 30-day, and in-hospital mortalities as well as postoperative hospital stay for patients who were discharged alive.

## Statistical analyses

Continuous variables were expressed as median (interquartile range) and compared using the Mann–Whitney U test. Categorical variables were expressed as numbers (percentages) and compared using Pearson's chi-squared test.

If the data required for the primary analysis was missing, the multiple imputation method was employed. A total of 20 multiply imputed datasets were created using chain equations, and the estimates from the multiple imputation were pooled using Rubin's method.

To examine the association between positive eSOFA and 90-day mortality, survival curves were plotted using the Kaplan–Meier method for patients with and without organ dysfunction and the log-rank test was employed to test for differences between the groups. Cox regression analysis was used to examine the association between positive eSOFA and 90-day mortality after adjustment for potential confounding factors. Based on clinical relevance and a literature search for factors associated with postoperative mortality, nine potential confounding variables (age, sex, body mass index, CCI, ASA-PS, emergency surgery, surgery risk, intraoperative blood loss, duration of surgery) were chosen and forced into the model [1, 12, 13]. Body mass index was categorized as  $< 18.5$ , 18.5–24.9, 25–29.9, and  $\geq 30$  [14]. Meanwhile, surgical procedures were categorized as low, intermediate, or high risk according to the risk of perioperative mortality [13].

Cox regression analysis was conducted to evaluate the association between positive eSOFA and 7-day/30-day mortality. Furthermore, logistic regression analysis was conducted to examine the association between organ dysfunction and in-hospital mortality. The association

between organ dysfunction and length of hospital stay was analyzed via linear regression in only those patients discharged alive. The same variables as those for the primary outcome were adjusted for in the evaluation of the association between positive eSOFA and the secondary outcomes.

To compare the performance of organ dysfunction assessed using eSOFA in predicting 90-day mortality with those of existing scoring systems (SOFA and APACHE II scores), we calculated Harrell's C-statistic for each scoring system. As the calculation of the SOFA and APACHE II scores requires data not readily available outside the ICU (e.g., blood gas analysis and GCS), the C-statistics were compared among the eSOFA, SOFA, and APACHE II scores for patients who postoperatively entered the ICU after 2011, during which the electronic medical records in the ICU were available. To predict 90-day mortality by eSOFA, positive eSOFA and the maximum number of eSOFA-positive items within 2 postoperative days were used; for the SOFA and APACHE II scores, the maximum scores up to 2 and 1 postoperative days were utilized, respectively.

As the association between positive eSOFA and mortality may depend on patient characteristics and surgical variables, subgroup analyses were conducted to evaluate this potential heterogeneity. The patients were divided into subgroups according to the following factors: age ( $\geq 65$  years/ $< 65$  years), sex, emergency surgery, postoperative ICU admission, surgery risk (low/intermediate or high), and surgical procedures (liver and renal surgeries). Using the same model as in the main analysis, the adjusted hazard ratios (HRs) were calculated for each subgroup to evaluate the interaction between the subgroup and positive eSOFA. Two sensitivity analyses were conducted to assess the robustness of the findings. First, a complete analysis was conducted rather than imputing missing data. Second, the association between organ dysfunction evaluated using eSOFA up to 1, 3, and 7 postoperative days and 90-day mortality was examined via Cox regression analysis.

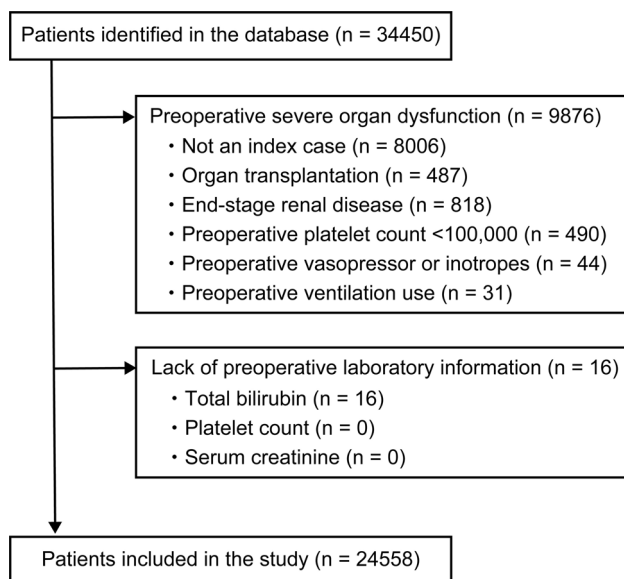
All statistical tests were two-tailed, with a  $P$ -value  $< 0.05$  considered statistically significant. The statistical analyses

were conducted using the statistical program Stata/SE 15.1 (StataCorp LLC®, College Station, TX, USA).

## Results

### Baseline patient characteristics and operative variables

Figure 1 presents the flow diagram of this study. Of the 24,558 eligible patients, 1629 (6.6%) had missing data on the variables needed for the primary analysis. 1832 (7.5%) developed postoperative organ dysfunction assessed using eSOFA during the first 2 postoperative days. Table 2



**Fig. 1** Flow diagram of the study participants

**Table 2** Patient characteristics and operative variables of the study participants

	All patients ( <i>n</i> = 24,558)	Negative eSOFA ( <i>n</i> = 22,726)	Positive eSOFA ( <i>n</i> = 1832)	Standardized difference	<i>P</i> -value
Age (years)	62 [46–72]	62 [46–71]	63 [47–72]	0.05	0.032
Male	11,518 (46.9%)	10,466 (46.1%)	1052 (57.4%)	0.25	<0.001
BMI	22.3 [20.1–24.8]	22.3 [20.1–24.8]	22.2 [20.2–24.5]	0.03	0.913
CCI	2 [0–3]	2 [0–3]	2 [1–3]	0.19	<0.001
ASA-PS [1(1E)/2(2E)/3(3E)/4(4E)/5(5E)]	7709(167)/14354(401)/1552(207)/34(22)/0(1)	7172(153)/13440(340)/1379(120)/26(3)/0(0)	537(14)/914(61)/173(87)/8(19)/0(1)	0.17	0.081
Emergency surgery	798 (3.2%)	616 (2.7%)	182 (9.9%)	0.27	<0.001
Intraoperative blood loss (mL)	50 [0–230]	46 [0–196]	353 [85–1080]	0.53	<0.001
Duration of surgery (min)	183 [109–295]	177 [106–277]	362 [185–518]	0.85	<0.001
Surgery risk (low risk/intermediate risk/high risk)	19,418/1275/3865	18,516/1150/3060	902/125/805	0.78	<0.001

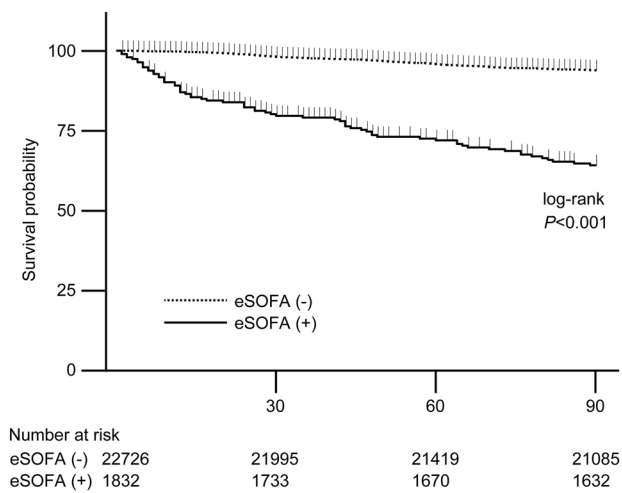
BMI, body mass index; CCI, Charlson Comorbidity Index; ASA-PS, American Society of Anesthesiologists physical status classification

presents the patient characteristics and operative variables stratified according to negative/positive eSOFA. Compared with patients having negative eSOFA, those with positive eSOFA had a significantly higher proportion of men, higher CCI, higher proportion of patients undergoing emergency surgery, longer operating times, greater blood loss, and higher proportion of patients who underwent high-risk surgery. The patient characteristics and operative variables stratified by the number of eSOFA-positive items are shown in Table S2.

### Relationship between positive eSOFA and the primary outcome

Postoperative 90-day mortality occurred in 0.9% of the patients; 3.9% and 0.7% of the patients with positive and negative eSOFA, respectively, died within 90 postoperative days. Kaplan–Meier survival analysis showed a significant difference in survival between patients with negative/positive eSOFA during the 2 postoperative days ( $P < 0.001$ ; Fig. 2). Cox regression analysis, with adjustment for potential confounders, revealed that positive eSOFA was independently associated with the occurrence of 90-day mortality (adjusted HR: 3.03, 95% confidence interval [CI]: 2.16–4.25,  $P < 0.001$ ; Table 3).

We further investigated the association between the number of eSOFA-positive items and 90-day mortality. Cox regression analysis, with adjustment for potential confounders, revealed that the adjusted HR for 90-day mortality increased as the number of positive eSOFA items increased (Fig. 3; Table S3). In addition, the dysfunction of each organ system (cardiovascular, respiratory, renal, liver, coagulation, and lactate) assessed using eSOFA was independently associated with the occurrence of 90-day mortality (Table S3).



**Fig. 2** Kaplan–Meier estimates for the primary outcome by eSOFA until 2 postoperative days

### Relationship between positive eSOFA and secondary outcomes

Postoperative 7- and 30-day mortalities occurred in 0.1% and 0.4% of the patients, respectively. Cox regression

analysis, with adjustment for potential confounders, revealed that positive eSOFA was independently associated with the occurrence of postoperative 7-day mortality (adjusted HR: 22.61, 95% CI: 7.39–69.20,  $P < 0.001$ ) and postoperative 30-day mortality (adjusted HR: 4.49, 95% CI: 2.83–7.11,  $P < 0.001$ ). Similarly, logistic regression analysis, with adjustment for potential confounders, revealed that positive eSOFA was associated with in-hospital mortality (adjusted odds ratio: 4.24; 95% CI: 2.84–6.32;  $P < 0.001$ ). Among patients who were discharged alive, the median (interquartile range) of postoperative hospital stay was 12 (7–21) days in those with negative eSOFA and 22 (12–39) days in those with positive eSOFA. Linear regression analysis, with adjustment for potential confounders, revealed that positive eSOFA was independently associated with longer hospital stays ( $P < 0.001$ ).

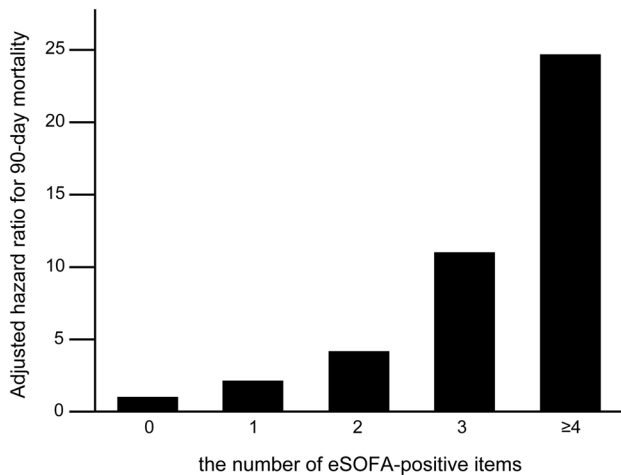
### Predictive performance of the eSOFA, SOFA, and APACHE II scores

We compared the performances of the eSOFA, SOFA, and APACHE II scores in predicting 90-day mortality in 1451 patients who entered the ICU postoperatively. The C-statistics (95% CI) for 90-day mortality with negative/positive

**Table 3** Association between postoperative organ dysfunction assessed using eSOFA and 90-day mortality

	Unadjusted			Adjusted		
	HR	95% CI	<i>P</i> -value	HR	95% CI	<i>P</i> -value
Postoperative organ dysfunction assessed using eSOFA	6.04	4.51–8.07	<0.001	3.03	2.16–4.25	<0.001
Age	1.04	1.03–1.05	<0.001	1.02	1.01–1.03	0.004
Male sex	1.94	1.46–2.57	<0.001	1.45	1.08–1.94	0.013
BMI						
< 18.5	–	–	–	–	–	–
18.5–24.9	0.41	0.29–0.57	<0.001	0.44	0.32–0.62	<0.001
25–29.9	0.20	0.12–0.35	<0.001	0.22	0.13–0.39	<0.001
≥ 30	0.33	0.14–0.76	0.010	0.38	0.16–0.88	0.025
CCI	1.36	1.31–1.41	<0.001	1.26	1.21–1.31	<0.001
ASA-PS						
1	–	–	–	–	–	–
2	6.37	3.34–12.13	<0.001	3.41	1.75–6.65	<0.001
3	31.19	16.08–60.50	<0.001	8.55	4.18–17.36	<0.001
4	33.00	7.26–150.05	<0.001	4.71	0.99–22.33	0.051
Emergency surgery	7.87	5.59–11.10	<0.001	3.38	2.28–5.02	<0.001
Intraoperative blood loss	1.00	1.00–1.00	<0.001	1.00	1.00–1.00	0.039
Duration of surgery	1.00	1.00–1.00	0.001	1.00	1.00–1.00	0.254
Surgery risk						
Low risk	–	–	–	–	–	–
Intermediate risk	0.90	0.44–1.83	0.763	0.68	0.33–1.41	0.301
High risk	2.54	1.90–3.41	<0.001	1.44	1.04–1.99	0.029

Adjusted for age, sex, BMI, CCI, ASA-PS, Emergency, intraoperative blood loss, duration of surgery, surgery risk



**Fig. 3** Association between the number of eSOFA-positive items and 90-day mortality

eSOFA, number of eSOFA-positive items, SOFA score, and APACHE II score were 0.70 (0.63–0.76), 0.72 (0.65–0.79), 0.73 (0.65–0.80), and 0.74 (0.68–0.81), respectively.

### Subgroup and sensitivity analyses

Subgroup analysis based on age, sex, emergency, surgery risk, and surgery site did not significantly affect the association between positive eSOFA and postoperative 90-day mortality (Fig. S1).

The analysis using the complete analysis to treat missing data also revealed that positive eSOFA was independently associated with the occurrence of 90-day mortality (adjusted HR; 2.88, 95% CI: 2.00–4.13,  $P < 0.001$ ). Postoperative organ dysfunction evaluated using eSOFA up to 1, 3, and 7 postoperative days occurred in 1629 (6.6%), 2021 (8.2%), and 2236 (9.1%) patients, respectively, and was found to be independently associated with the occurrence of 90-day mortality (adjusted HR and 95% CI: 2.79 [1.96–3.96], 3.43 [2.47–4.76], and 4.03 [2.93–5.54], respectively).

### Discussion

This retrospective cohort study found that postoperative organ dysfunction assessed using eSOFA within 2 postoperative days was associated with increased 90-day mortality in patients who underwent noncardiac surgery. In a subanalysis of surgical ICU patients, the C-statistic for predicting 90-day mortality using eSOFA was comparable to those of the SOFA and APACHE II scores. These results suggest that eSOFA following noncardiac surgery may serve as a diagnostic tool for convenient detection of patients with poor prognosis.

eSOFA as a prognostic tool for postoperative patients has several advantages. First, the data required for it are mainly objective, such as laboratory data, and are therefore unlikely to vary between assessors. Second, the required data can be easily collected from electronic medical records. Thus, it is a potential candidate for clinically valid outcomes in perioperative studies and can be used in retrospective studies. Third, eSOFA enables simultaneous assessment of the dysfunction of multiple organs and the detection of a wider range of unfavorable conditions compared with measures assessing a single organ, such as myocardial or acute kidney injury. These advantages suggest that eSOFA is a useful tool to easily detect unfavorable conditions in postoperative patients.

This study included a wide range of surgeries, from low- to high-risk noncardiac surgeries. No interaction was observed between intermediate- and high-risk surgeries and low-risk surgeries in the subgroup analysis. These results indicate that organ dysfunction evaluated using eSOFA may be a useful predictor of postoperative mortality in a wide range of noncardiac surgeries, from low to high risk.

In this study, organ dysfunction within 2 postoperative days was considered as the primary exposure. Of the organ dysfunctions that occurred within 7 postoperative days, 83.7% occurred on postoperative day 2; moreover, the sensitivity analyses in which organ dysfunctions that occurred within 3 and 7 postoperative days were used as exposure revealed no substantial increase in the HR compared with the analysis in which organ dysfunction within 2 postoperative days was used. It is clinically reasonable to set the time window for organ dysfunction assessment to 2 postoperative days to enable earlier organ dysfunction assessment and administration of necessary interventions. Sensitivity analysis showed that organ dysfunction occurring within 1 postoperative day was also strongly associated with 90-day mortality. This result suggests that even shorter time windows for assessment enable the detection of clinically significant organ dysfunctions.

Although eSOFA was originally proposed to be used as a binary measure to determine the presence of organ dysfunction when any one of the six organ systems is positive, the present study analyzed the association between the number of eSOFA-positive items and 90-day mortality and observed a trend toward a higher number of deaths in patients with dysfunction in multiple organs. Assessment of the number of positive items instead of a binary measure of the occurrence of postoperative organ dysfunction as “yes” or “no” may improve prognostic stratification.

Postoperative organ dysfunction evaluated using the SOFA or APACHE II scores has been reported to be associated with mortality in surgical ICU patients who underwent noncardiac surgeries [6]. However, its predictive performance is variable, with a wide range of prognostic ability of

0.63–0.79 for mortality in patients admitted to the surgical ICU by the SOFA score [6, 15, 16]. No studies have investigated the association between organ dysfunction assessed using eSOFA and postoperative mortality. We found that the prognostic value of the number of eSOFA-positive items in postoperative ICU patients was comparable to those of the SOFA and APACHE II scores. Considering that eSOFA is easier to assess than SOFA or APACHE II, there may be advantages in the use of eSOFA to predict prognosis in postoperative patients.

The present study had several limitations. The single-center design may limit the generalizability of the results, and external validation is warranted to corroborate our findings. A large amount of missing data was noted for serum lactate levels (97%). It is possible that some patients with unmeasured lactate levels actually have positive lactate levels, in which case the occurrence of organ dysfunction may have been underestimated. This study excluded patients with preoperative severe organ dysfunction (e.g., vasopressor/inotrope use, ventilator use, or end-stage renal disease). Thus, the usefulness of eSOFA in these patient groups needs to be validated in future studies. Finally, the findings are merely associations and cannot imply causation. Therefore, we were unable to determine whether there was a causal relationship between postoperative organ dysfunction evaluated using eSOFA and postoperative mortality.

In conclusion, postoperative organ dysfunction evaluated using eSOFA within 2 postoperative days was independently associated with 90-day mortality in patients who underwent noncardiac surgery.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s00540-025-03492-z>.

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**Data availability** The data used in this work are available upon reasonable request from the corresponding author.

## Declarations

**Conflict of interest** The authors have no conflicts of interest to declare.

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