Changes in Sequential Organ Failure Assessment sub-scores as predictors of mortality in patients with septic acute kidney injury requiring continuous renal replacement therapy

Maki Abe, Misa Ikeda-Taniguchi and Hirokazu Honda*

Abstract

Patients with septic acute kidney injury (AKI) often require continuous renal replacement therapy (CRRT), but factors that predict their prognosis have been insufficiently established. Thus, this study aimed to evaluate the associations of the Sequential Organ Failure Assessment (SOFA) score, SOFA-sub scores, and SOFA sub-score components with mortality in patients with AKI on CRRT. A total of 231 patients with AKI who required CRRT were enrolled in this retrospective, cohort study. Associations between the SOFA-sub scores on days 1 or 4 of CRRT and all-cause death within 30 days were assessed. The respiratory SOFA sub-score in patients with sepsis on day 1 was associated with mortality. However, this association disappeared on day 4, and coagulation and renal SOFA-sub scores were significantly associated with mortality in patients with sepsis. These findings differed from patients without septic AKI. The baseline respiratory SOFA sub-score was significantly associated with mortality in patients with septic AKI, whereas the coagulation SOFA sub-score became a prognostic factor on day 4. The evaluation of SOFA-sub scores and changes in the factors after CRRT initiation may be useful for predicting prognosis in patients with septic AKI.

Key words : AKI, CRRT, sepsis, SOFA score, SOFA sub-score

Introduction

Acute kidney injury (AKI) is a severe complication in both patients with and without sepsis. Patients with sepsis frequently develop multiple-organ failure, including AKI, and the in-hospital mortality rate of patients with septic shock is reportedly 40%–60%[1]. Continuous renal replacement therapy (CRRT) is often used to treat AKI in patients with sepsis, but the mortality rate is unacceptably high at 60%–80%[2].

The Sequential Organ Failure Assessment (SOFA) score has been integrated into various aspects of critical care since its development in the early 1990s, and this score is now widely used in the daily monitoring of acute morbidity in critical care units. The SOFA score is based on six sub-scores for respiratory, cardiovascular, hepatic, coagulation, renal, and central nervous system (CNS) functions, scored from 0 to 4, with an increasing score reflecting worsening organ dysfunction[3]. Risk stratification for hospital mortality is primarily determined by the cardiovascular, CNS, renal, and respiratory SOFA-sub scores in patients of the cardiac intensive care unit (CICU) with complete SOFA sub-score data[4]. Several studies identified the SOFA score as a risk factor for mortality in patients with sepsis or critical illness with AKI receiving CRRT[5,6]. The usefulness of the SOFA scoring system and biomarkers for predicting mortality have been evaluated in patients with AKI on CRRT. However, the associations of the SOFA score and sub-scores with mortality in these patients were mainly examined using the scores calculated on a fixed day, such as at baseline[4-8]. A recent systematic review demonstrated that a fixed-day SOFA score was not always associated with mortality due to the effects of treatments on the SOFA score[9]. Moreover, the underlying pathophysiologies requiring

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CRRT differ between patients with and without septic AKI. Patients with sepsis undergo CRRT to remove inflammatory mediators and compensate for decreased urine volume, whereas patients without sepsis, such as those with cardiac failure or hypotension with low cardiac output due to cardiovascular diseases (CVD), start CRRT due to oliguria. Thus, the associations of the SOFA score and sub-scores with mortality might differ between patients with and without septic AKI that require CRRT, and the predictive abilities of these scores might change according to the score assessment timing.

The present study aimed to examine the associations of the SOFA score and sub-scores with 30-day mortality in patients with septic AKI on CRRT compared to those without septic AKI on CRRT, considering the score timing. Furthermore, the predictive ability of lactate levels for mortality was compared with those of SOFA score and sub-scores in these patients because high lactate levels are independently associated with mortality in patients with septic AKI requiring CRRT[10].

Materials and methods

Study design, setting, and participants

This single-center, 3-year, retrospective cohort study was conducted at Showa University Hospital from April 2013 to April 2016. The study was performed according to the 2004 revision of the Declaration of Helsinki. All study protocols were approved by the School of Medicine, Showa University ETHICAL COMMITTEE (Permit Number, 2210). Informed consent was obtained from all participants using the opt-out form on the hospital website. All methods were performed following relevant guidelines and regulations.

A total of 115 patients with septic AKI and 116 patients with non-septic AKI who started CRRT were recruited for this study (Figure 1). Patients treated by maintenance dialysis and those <20 years old were excluded. AKI was defined according to the AKI network classification[11], and sepsis was defined using the diagnostic criteria of Sepsis-2[12].

Patient characteristics, clinical and laboratory data, including components of SOFA and the SOFA-sub scores (Glasgow Coma Scale [GCS], mean arterial pressure [MAP], and PaO_2/FiO_2 (P/F) ratio], biochemical laboratory test results [e.g., hemoglobin, platelet count, albumin, total bilirubin [T-bil], serum creatinine [Cr]), lactate, CRRT indication, and comorbidities on days 1 and 4 of CRRT were recorded.

CRRT protocol

All patients underwent central venous catheterization. CRRT was performed as continuous veno-venous hemodialysis. Blood flow rates were maintained between 80 and 150 ml/min, and dialysis doses were in the range of 10–30 ml/kg/h according to the clinical condition. Continuous nafamostat mesylate infusion was used for anticoagulation of
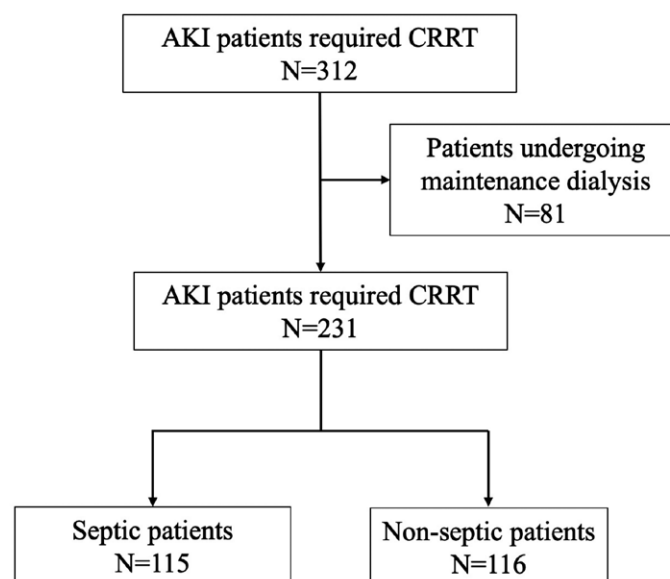
Fig. 1. The flowchart of patient selection in this study. A total of 312 patients required CRRT, excluding patients treated by maintenance dialysis. Finally, a total of 115 patients with septic AKI and 116 patients with non-septic AKI who started CRRT were recruited for this study.

the circuit at an infusion dosage of 5–50 mg/h. The types of the artificial membrane were poly-methylmethacrylate (PMMA), polysulfone, poly-ethersulfone, cellulose triacetate, and acrylonitrile-co-methallyl sulfonate surface-treated. The dialysis membrane was changed every 24 h or earlier if clotting occurred.

Outcome

The primary outcome was all-cause mortality within the 30-day observation period. Secondary outcomes were all-cause mortality within 4 days (early mortality) or after 4 days (late mortality). Changes in the SOFA score and sub-scores within 4 days were assessed in patients with and without sepsis.

Statistics

Categorical variables are reported as numbers (%) and continuous variables as means ± standard deviation or as medians and interquartile range (25th to 75th percentile). The student's t-test or the Wilcoxon rank-sum test was used for group comparison. The paired t-test or Wilcoxon signed-rank test was used to assess SOFA score and sub-score changes over 4 days. Two-tailed p-values of $<$ 0.05 were considered significant.

Cox proportional hazard models were used to assess relationships between mortality and SOFA-sub scores and lactate. To confirm the diagnostic ability of the SOFA score, SOFA-sub scores, and lactate for mortality, the receiver-operating characteristic curves (AUCs) were used. Statistical analyses were performed using JMP version 15.0 Pro (SAS Institute, Cary, NC) and GraphPad Prism 9 (GraphPad Software, LLC, San Diego, CA).

Results

Baseline characteristics of patients

Table 1 shows the baseline characteristics and baseline laboratory data of patients with and without sepsis. For the overall cohort, the mean age was 74 years, and 65.4% were males (patients with sepsis : 70.4% ; patients without sepsis : 60.3% ; p=0.13). The main causes of sepsis were pneumonia (25.2%), gastrointestinal perforation (19.1%), and acute pancreatitis (12.1%). The 30-day mortality rate was 51.3% for all patients, with no significant difference between patient with (n=59, 51.3%) and without sepsis (n=52, 44.8%, p=0.36).

The SOFA score and sub-score components and the CRRT prescriptions of patients with and without

sepsis are shown in Table 2. CRRT for patients without sepsis was required due to AKI with concomitant oliguria and/or overhydration caused by decreased cardiac function post-cardiopulmonary arrest, myocardial infarction, and heart failure, whereas CRRT was performed in patients with sepsis to remove sepsis-related inflammatory mediators, as well as for low urine volume. Comparing the patients with and without sepsis, the CVD history prevalence was lower (29.6% vs. 56.0%, $p < 0.0001$), the treatment rate of endotoxin absorption using polymyxin B-immobilized fiber (PMX) was higher (64.0% vs. 6.1%, $p < 0.0001$), and the use of PMMA for CRRT was more frequent (81.7% vs. 20.7%, $p < 0.0001$). Laboratory data showed that patients with sepsis demonstrated lower albumin levels and platelet counts (Table 2). The SOFA score was higher in patients with sepsis than in patients without sepsis (Table 2).

Spearman's rank correlation coefficient (rho) values for survival days and potential predictors are shown in Table S1. Systolic blood pressure (rho=0.40, $p < 0.0001$) and MAP (rho=0.39, $p < 0.0001$) positively correlated with survival in patients with sepsis, but not in patients without sepsis.

Associations of the SOFA score and sub-scores with early and late mortality

In this study, 37 patients died by day 4 (patients with septic AKI, n=14 vs. patients with non-septic AKI, n=23). The characteristics and the CRRT prescriptions of patients with and without sepsis with early mortality and those surviving >4 days are listed in Tables S2 and S3. Patients with sepsis with early mortality more frequently showed severe acute respiratory distress syndrome (ARDS), lower blood pressure, and oliguria than patients with sepsis surviving >4 days. Patients without sepsis with early mortality more frequently showed low blood pressure and oliguria than patients without sepsis surviving > 4 days. The main causes of death were septic shock and multiple-organ dysfunction syndromes with ARDS in patients with sepsis and cardiac shock, myocardial infarction, arrhythmia, and heart failure in patients without sepsis.

Patients with sepsis who died by day 4 exhibited a higher respiratory SOFA sub-score than patients with sepsis who survived >4 days : SOFA score 12 (IQR, 10–14) vs. 11 (7–13), p=0.17 ; respiratory SOFA score 4 (3–4) vs. 3 (1, 3), p=0.0004 ; PaO_2/FiO_2 ratio 88 (74–229) vs. 268 (171–466), p=0.0003. The cardiovascular SOFA sub-score was not associated with mortality in patients with sepsis who died by

Table 1. Baseline characteristics and laboratory data in all patients and grouped according to the presence of sepsis.

	All （N＝231）	Septic patients （N＝115）	Non-septic patients （N＝116）	p-value
Age （year）	74 （65–80）	74 （61–81）	74 （66–80）	0.78
Gender （% of men）	151 （65.4）	81 （70.4）	70 （60.3）	0.13
BMI （kg/m^2） （SD）	23.3 （4.5）	23.1 （4.7）	23.5 （4.3）	0.43
Diabetes mellitus （%）	79 （34.2）	34 （29.6）	45 （38.8）	0.17
CVD （%）	**99 （42.9）**	**34 （29.6）**	**65 （56.0）**	**＜ 0.0001**
Chronic kidney disease （%）	59 （25.5）	24 （20.9）	35 （30.2）	0.11
Hypertension （%）	113 （48.9）	50 （43.5）	63 （54.3）	0.11
White blood cell （×10^2/μl）	117 （161–77）	119 （78–213）	108.5 （76–145）	0.18
Hemoglobin （g/dl）	10 （8.5–11.9）	10.1 （8.6–12.1）	9.95 （8.4–11.6）	0.52
Albumin （g/dl）	**2.7 （2.2–3.1）**	**2.5 （2.1–3）**	**2.85 （2.3–3.2）**	**0.0010**
C-reactive protein （mg/dl）	**10 （3.09–22.95）**	**20.9 （8.1–27）**	**4.2 （0.98–10.8）**	**＜ 0.0001**
Potassium （mEq/l）	**4.5 （3.9–5.2）**	**4.2 （3.7–5）**	**4.65 （4–5.4）**	**0.0051**
Lactate （mmol/l）	2.79 （1.7–5.5）	2.9 （1.7–4.7）	2.7 （1.6–6.5）	0.84
eGFR （ml/min/1.73 m^2）	17.2 （11.7–29.5）	17.5 （12–29.5）	17.15 （10.7–30.8）	0.90
Urine volume （ml/day）	570 （135–1190）	616 （201–1314）	498 （101–1040）	0.08
Ratio of using catecholamine （%）	161 （69.7）	83 （72.2）	78 （67.2）	0.41
SBP/DBP （mmHg）	119 （27) / 62 （16）	120 （30) / 62 （18）	117 （23) / 63 （14）	0.53 / 0.69
Primary disease （n, ［%］）		Pneumonia 24 （21.1） Gastrointestinal tract perforation 22 （19.3） Acute pancreatitis 14 （12.3） Acute urinary tract infection 10 （8.8）	Acute decompensated heart failure 25 （21.6） Post-cardiac arrest 19 （16.4） Acute myocardial infarction 11 （9.5） Rhabdomyolysis 7 （6.0）	
AKIN score （% of stage 1, 2, and 3）	19, 36, 45	22, 35, 43	15, 37, 48	0.29
Mortality （%）	111 （48.1）	59 （51.3）	52 （44.8）	0.36

Each datum was expressed as mean （interquartile range） or the number of patients （%）, BMI : body mass index, CVD : cardiovascular disease, SBP : systolic blood pressure, DBP : diastolic blood pressure, eGFR : estimated glomerular filtration rate, AKIN : acute kidney injury network.

day 4, but the MAP was significantly lower in these patients （MAP : 69.5 ［59.5–77.8］ vs. 88 （70–94.5）, $p=$ 0.005） （Table S4）. Patients without sepsis who died by day 4 showed significantly higher SOFA scores and CNS and coagulation SOFA-sub scores than those who survived ＞ 4 days : SOFA score 12 （IQR, 10–13） vs. 10 （6–12）, $p=$0.003 ; cardiovascular SOFA score 4 （2–4） vs. 3 （0–4）, $p=$0.03 ; CNS SOFA sub-score 4 （1–4） vs. 2 （0–3）, $p=$0.02 ; and coagulation SOFA score 1 （0–2） vs. 0 （0–1）, $p=$0.02 （Table S4）. Lactate level （6.9 ± 0.9 mg/dl vs. 3.7 ± 0.4 mg/dl, $p=$0.002 ; 9.3 ± 1.0 vs. 3.9 ± 0.5, $p ＜ 0.0001$） and urine volume （157 ± 270 ml vs. 1,020 ± 100 ml, $p=$ 0.004 ; 330 ± 170 ml vs. 820 ± 84 ml, $p=$0.01） in both

patients with and without sepsis who died by day 4 were significantly higher and lower, respectively, than in those who survived ＞4 days. No significant differences were found in age, body mass index, medical history, or albumin level between patients with and without sepsis.

Changes in the SOFA score and sub-scores 4 days after CRRT initiation

Changes in the SOFA score, sub-scores, sub-score components, and lactate for 4 days after starting CRRT were assessed in patients who survived ＞4 days （n＝194 ; Figures 2, 3, S1, S2）. The coagulation SOFA sub-score was significantly increased at 4 days

Table 2.　Baseline SOFA score and components of SOFA-sub scores and CRRT prescription in all patients and grouped according to sepsis or not.

			All (N＝231)	Septic patients (N＝115)	Non-septic patients (N＝116)	p-value
SOFA score			**11 (7–13)**	**11 (8–11)**	**10 (6–12)**	**0.0424**
SOFA-sub scores	Central nervous system	Glasgow Coma Scale	10 (6–15)	11 (6–14)	10 (3.75–15)	0.89
	Respiratory	PaO$_2$/FiO$_2$ ratio	261 (164–366)	236 (157–350)	272 (167–378)	0.17
	Cardiovascular	MAP (mmHg)	81 (70–92)	81 (68–93)	80.5 (71–90)	0.99
	Liver	Total bilirubin (mg/dl)	1.0 (0.6–1.8)	1.1 (0.7–2.1)	0.8 (0.6–1.6)	0.06
	Coagulation	**Platelets (10^4/μl)**	**12.9 (6.8–18.6)**	**9.7 (5.8–18.3)**	**15.3 (9.4–19.2)**	**0.0053**
	Renal	Creatinine (mg/dl)	2.75 (1.7–3.88)	2.75 (1.68–3.88)	2.76 (1.72–3.9)	0.57
PMX and CRRT						
Implementation of PMX (%)			**80 (34.9)**	**73 (64.0)**	**7 (6.1)**	**＜0.0001**
CRRT prescription	Duration for starting CRRT (hours)		24 (0–48)	24 (0–48)	24 (0–72)	0.38
	Implementation time of CRRT (hours)		96 (48–168)	96 (48–168)	72 (48–192)	0.70
	Modality of CRRT (n- (%))	CHDF	199 (86.1)	98 (85.2)	101 (87.1)	0.30
		CHD	25 (10.8)	15 (13.0)	10 (8.6)	
		CHF	7 (3.0)	2 (1.7)	5 (4.3)	
	Qd (ml/h) (interquartile range)		300 (300–300)	300 (300–300)	300 (300–300)	0.71
	Qf (ml/h) (interquartile range)		300 (300–300)	300 (300–300)	300 (300–300)	0.08
	Qb (ml/min) (interquartile range)		100 (100–120)	100 (100–120)	100 (100–120)	0.59
	Dialyzer (n, (%))	PS	85 (36.8)	17 (14.8)	68 (58.6)	＜0.0001
		PES	1 (0.4)	0 (0)	1 (0.9)	
		PMMA	118 (51.1)	94 (81.7)	24 (20.7)	
		CTA	26 (11.3)	3 (2.6)	23 (19.8)	
		AN69-ST	1 (0.4)	1 (0.9)	0 (0)	

SOFA: the Sequential Organ Failure Assessment, MAP: mean arterial pressure, PMX-DHP: polymyxin B-immobilized fiber direct hemoperfusion, CRRT: continuous renal replacement therapy, CHDF: continuous hemodiafiltration, CHD: continuous hemodialysis, CHF: continuous hemofiltration, Qd: quantity of dialysate, Qf: quantity of filtration, Qb: quantity of blood flow, PS: polysulfone, PES: polyethersulfone, PMMA: polymethylmethacrylate, CTA: cellulose triacetate, AN69-ST: acrylonitrile-co-methallyl sulfonate surface-treated.

in non-surviving patients with and without sepsis (Figure 2), but the magnitude of change in the coagulation SOFA sub-score was much higher in patients with sepsis than those without (Figures 2, 3). Platelet counts on day 4 were lower in non-surviving patients with sepsis than in those who survived (6.1 ± 5.2 /mm^3 vs. 8.5 ± 5.2 /mm^3) (Figures S1, S2). Lactate levels on day 4 were decreased by CRRT in both patients with and without sepsis (Figures S1, S2).

Associations of SOFA-sub scores, SOFA sub-score components, and lactate on days 1 and 4 with mortality
The Kaplan-Meier curve that evaluates the difference in 30-day all-cause mortality according to

tertiles of the SOFA-sub scores on days 1 or 4 is presented in Figure S3. Higher SOFA scores in both patients with and without sepsis were independently associated with mortality.

Cox proportional hazard models for 30-day survival after CRRT initiation is shown in Table 3. Cardiovascular, CNS, and respiratory SOFA-sub scores were significantly associated with survival on day 1 in patients with sepsis on univariate modeling, but the respiratory SOFA sub-score was only associated after adjusting all SOFA-sub scores (Table 3, model 2). However, the association of the respiratory SOFA sub-score on day 1 disappeared on day 4, and the coagulation SOFA sub-score and the renal SOFA sub-

Table S1.   Spearman's rank correlation analysis at baseline of sepsis or non-sepsis patients

Sepsis patients	GCS	SBP	MAP	P/F ratio	SCr	U-volume	platelet	lactate	albumin	T-bil	Duration until starting CRRT	Implement-ation time of CRRT
Survival days	**0.43******	**0.40******	**0.39******	**0.39******	−0.13	**0.51******	0.093	**−0.24***	−0.038	**−0.22***	−0.042	0.13
GCS		0.14	0.11	**0.31*****	−0.095	**0.28****	0.053	**−0.26****	0.12	−0.027	−0.035	−0.070
SBP			**0.90******	**0.22***	−0.15	**0.35*****	**0.26****	−0.15	0.15	−0.054	0.013	0.092
MAP				**0.20***	−0.16	**0.36******	**0.25****	−0.13	0.16	−0.12	−0.010	0.062
P/F ratio					0.029	**0.29****	0.094	**−0.19***	0.10	−0.088	−0.17	−0.14
Serum Cr						**−0.26****	0.0098	−0.16	**−0.20***	0.034	−0.17	0.17
U-volume							0.0247	**−0.22***	0.087	−0.045	0.11	−0.093
platelet								−0.18	**0.23***	**−0.21***	**−0.24***	−0.067
lactate									0.080	**0.21***	**−0.21***	0.27
albumin										0.062	−0.14	−0.11
T-bil											**0.19***	−0.033
Implementation time of CRRT												−0.097
Non-sepsis group												
Survival days	**0.25****	0.14	0.15	**0.31*****	0.12	**0.28****	0.15	**−0.40******	0.15	−0.15	0.032	**0.26****
GCS		−0.0007	0.0014	**0.27****	**0.31*****	0.015	0.041	**−0.38******	0.18	0.081	0.14	−0.0052
SBP			**0.82******	−0.019	0.037	**0.25****	0.12	−0.059	0.058	−0.035	0.052	0.11
MAP				−0.010	0.011	**0.30****	0.13	0.0011	0.053	0.056	0.054	0.14
P/F ratio					0.069	0.092	−0.020	0.31	**0.38******	0.017	−0.18	−0.065
Serum Cr						**−0.32*****	0.053	**−0.32*****	−0.017	−0.15	−0.013	0.049
U-volume							0.037	−0.11	0.099	0.048	0.038	−0.016
platelet								−0.18	0.0042	**−0.31*****	0.10	0.095
lactate									**0.20***	**0.28****	**−0.38******	**−0.24***
albumin										**0.23***	−0.022	−0.13
T-bil											0.049	−0.083
Implementation time of CRRT												0.16

* : $p < 0.05$, ** : $p < 0.01$, *** : $p < 0.001$, **** : $p < 0.0001$.   GCS : Glasgow coma scale, SBP : systolic blood pressure, MAP : mean arterial pressure, P/F ratio : PaO_2/FiO_2 ratio, SCr : serum creatinine, U-volume : urine volume. T-bil : total bilirubin, CRRT : continuous renal replacement therapy

score were independently associated with mortality in patients with sepsis (Table 3, model 4). All SOFA-sub scores were not associated with mortality on multivariate modeling in patients without sepsis (Table 3, model 6) ; however, the cardiovascular SOFA sub-score was associated with survival as of day 4 (Table 3, model 8).

The hazard ratio for mortality using the SOFA sub-score components and lactate is shown in Table 4. MAP, GCS, and the P/F ratio on day 1 were significant predictors of prognosis in patients with sepsis (Table 4, models 1 and 2). However, these associations disappeared on day 4 (Table 4, model 4), and the platelet count and Cr and lactate levels were significant factors for mortality (Table 4, models 3 and 4). Whereas lactate, as well as MAP and the P/F ratio, on day 1 was

Table S2. Patient characteristics and laboratory data at baseline in patients with and without sepsis grouped by who survived by day 4 or not.

	Septic				Non-septic			
	All patients (N=115)	Non-survived patients (N=14)	Survived patients (N=101)	p-value	All patients (N=116)	Non-survived patients (N=23)	Survived patients (N=93)	p-value
Age (year) (interquartile range)	74 (61-81)	76 (63-82)	74 (58-81)	0.59	74 (66-80)	71 (60-78)	75 (68-80)	0.12
Gender (% of men)	81 (70.4)	11 (78.6)	70 (69.3)	0.48	70 (60.3)	13 (56.5)	57 (61.3)	0.68
BMI (kg/m^2)	23.2 (19.5-26.3)	20.9 (18.4-24.4)	23.3 (19.7-26.3)	0.23	23.4 (20.4-26.0)	23.5 (20.2-27.0)	23.2 (20.4-26.0)	0.58
Diabetes mellitus (%)	34 (29.6)	3 (21.4)	31 (30.7)	0.48	**45 (38.8)**	**2 (8.7)**	**43 (46.2)**	**0.0009**
CVD (%)	34 (29.6)	3 (21.4)	31 (30.7)	0.47	65 (56.0)	13 (56.5)	52 (55.9)	0.96
Hypertension (%)	50 (43.5)	5 (35.7)	45 (44.6)	0.52	63 (54.3)	12 (52.2)	51 (54.8)	0.81
Systolic Blood Pressure (mmHg)	**118 (100-140)**	**100 (85-109)**	**121 (104-144)**	**0.002**	**119 (99-130)**	**106 (94-123)**	**120 (103-132)**	**0.01**
Diastolic Blood Pressure (mmHg)	**61 (51-74)**	**61 (51-74)**	**62 (52-75)**	**0.03**	62 (55-71)	59 (52-67)	62 (55-71)	0.33
Ratio of using catecholamine (%)	83 (72.2)	12 (85.7)	71 (70.3)	0.23	78 (67.2)	18 (78.3)	60 (64.5)	0.21
Hemoglobin (g/dl)	10.1 (8.6-12.1)	10.6 (8.7-13.1)	10.1 (8.6-12.1)	0.53	10.0 (8.4-11.6)	9.7 (7.6-11.5)	10 (8.5-11.7)	0.46
Albumin (g/dl)	2.5 (2.1-3.0)	2.6 (2.2-3.2)	2.5 (2.1-3.0)	0.21	2.9 (2.3-3.2)	2.8 (2.5-3.2)	2.9 (2.3-3.2)	0.58
Lactate	**2.9 (1.7-4.7)**	**5.5 (2.3-11.6)**	**2.8 (1.7-4.4)**	**0.001**	**2.7 (1.6-6.5)**	**6.4 (3.6-16.1)**	**2.3 (1.5-4.9)**	**< .0001**
Urine volume (ml/day)	**616 (201-1,314)**	**63 (31-248)**	**702 (287-1,383)**	**< .0001**	**498 (100-1,040)**	**113 (45-310)**	**608 (140-1,178)**	**0.001**
Implementation of PMX (%)	73 (64.0)	7 (50.0)	66 (66.0)	0.24	7 (6.1)	1 (4.3)	6 (6.5)	0.70

BMI : body mass index, CVD : cardiovascular disease, PMX-DHP : polymyxin B-immobilized fiber direct hemoperfusion.

significantly associated with mortality in patients without sepsis (Table 4, model 6), only lactate was associated with mortality on day 4 (Table 4, model 8).

Cut-off values and AUCs of the SOFA score and sub-scores on days 1 and 4 for 30-day survival are shown in Table S5. Factors on day 1 that are significantly associated with 30-day survival were the cardiovascular, respiratory, and CNS SOFA-sub scores in both patients with and without sepsis, and the cut-off values of these scores were higher in patients without sepsis than patients with sepsis. The AUCs of the SOFA score on day 1 in both patients with and without sepsis and the CNS SOFA sub-score on day 1 in patients with sepsis showed fair accuracy, whereas those of other SOFA-sub scores showed poor accuracy in both patient groups. The AUCs of the SOFA score on day 4 for mortality showed fair accuracy in patients with and without sepsis. Cardiovascular and CNS SOFA-sub scores

on day 4 were significantly associated with mortality in patients with and without sepsis ; however, the AUCs of these factors showed poor accuracy. The AUC of the coagulation SOFA sub-score on day 4 was more closely associated with 30-day survival in patients with sepsis compared with the sub-score on day 1. The AUCs of SOFA sub-score components and lactate for predicting mortality are listed in Table S6. Lactate on day 1 showed fair accuracy for mortality in patients without sepsis. Additionally, factors on day 1 that were significantly associated with 30-day survival were the MAP and the P/F ratio in patients with sepsis, and the cut-off values of these scores were fair compared with those patients without sepsis. However, these associations disappeared on day 4, and the platelet count and lactate level were significant factors for mortality. Based on their AUCs, the accuracies of these factors on day 4 were similar to patients without sepsis.

Table S3. Setting of continuous renal replacement therapy in patients with and without sepsis grouped by who survived by day 4 or not.

CRRT		Septic				Non-septic			
		All patients (N=115)	Non-survived patients (N=14)	Survived patients (N=101)	p-value	All patients (N=116)	Non-survived patients (N=23)	Survived patients (N=93)	p-value
Duration for starting CRRT (hours)		24 (0–48)	24 (0–60)	24 (0–48)	0.52	24 (0–72)	24 (0–72)	24 (0–72)	0.62
Implementation time of CRRT (hours)		96 (48–168)	24 (24–54)	120 (72–168)	< .0001	72 (48–192)	48 (24–72)	120 (72–192)	< .0001
Modality of CRRT (n, %)	CHDF	98 (85.2)	11 (78.6)	87 (86.1)		101 (87.1)	20 (87.0)	81 (87.1)	
	CHD	15 (13.0)	1 (7.1)	14 (13.9)	0.0006	10 (8.6)	2 (8.7)	8 (8.6)	1.0
	CHF	2 (1.74)	2 (14.3)	0 (0)		5 (4.3)	1 (4.3)	4 (4.3)	
Qd (ml/h) (interquartile range)		300 (300–300)	300 (300–300)	300 (300–300)	0.20	300 (300–300)	300 (300–300)	300 (300–300)	0.47
Qf (ml/h) (interquartile range)		300 (300–300)	300 (300–300)	300 (300–300)	0.11	300 (300–300)	300 (300–300)	300 (300–300)	0.99
Qb (ml/min) (interquartile range)		100 (100–120)	100 (80–120)	100 (100–120)	0.27	100 (100–120)	100 (100–120)	100 (100–120)	0.56
Dialyzer (n, %)	PS	17 (14.8)	6 (42.9)	11 (10.9)		68 (58.7)	14 (60.9)	54 (58.1)	
	PES	0 (0)	0 (0)	0 (0)		1 (0.9)	0 (0)	1 (1.1)	
	PMMA	94 (81.7)	8 (57.1)	86 (85.2)	0.02	24 (20.6)	7 (30.4)	17 (18.3)	0.34
	CTA	3 (2.6)	0 (0)	3 (3.0)		23 (19.8)	2 (8.7)	21 (22.6)	
	AN69-ST	1 (0.9)	0 (0)	1 (1.0)		0 (0)	0 (0)	0 (0)	

CRRT : continuous renal replacement therapy, CHDF : continuous hemodiafiltration, CHD : continuous hemodialysis, CHF : continuous hemofiltration, Qd : quantity of dialysate, Qf : quantity of filtration, Qb : quantity of blood flow, PS : polysulfone, PES : polyethersulfone, PMMA : polymethylmethacrylate, CTA : cellulose triacetate. AN69-ST : acrylonitrile-co-methallyl sulfonate surface-treated.

Discussion

This study evaluated the prognostic factors for mortality using the SOFA-sub scores and SOFA sub-score components and lactate at baseline and day 4 in a retrospective cohort study of 231 patients who were not on maintenance hemodialysis and required CRRT for AKI.

The present study revealed an association of the respiratory SOFA sub-score on day 1 in patients with septic AKI with mortality on multivariate Cox proportional hazard modeling, and the P/F ratio, MAP, and the GCS score, as components of the SOFA-sub scores on day 1, were independent predictors of mortality. The value of the respiratory SOFA sub-score was higher in patients with early mortality than in those with late mortality. These findings were expected because the main causes of early death in patients were ARDS and septic shock. Additionally, the MAP and P/F ratio, as components of SOFA-sub scores and lactate on day 1, were significantly associated with mortality in patients without sepsis. A previous study of a cohort of patients in the CICU reported that cardiovascular, respiratory, CNS, and renal SOFA-sub scores were significant predictors of hospital mortality within 30 days[4]. The predictive ability of the SOFA-sub scores for mortality in the present study differed from the findings of that previous study because the present study assessed patients with and without sepsis who were treated using CRRT. Thus, associations of the SOFA score and SOFA-sub scores with 30-day mortality differed between patients with and without sepsis.

Interestingly, the coagulation SOFA sub-score and platelet counts on day 4 were significantly associated with increased hazard ratios in patients with septic AKI, and associations between the SOFA sub-score and mortality changed 4 days from CRRT initiation in those patients. Next, changes in the coagulation SOFA sub-score and platelet counts after CRRT initiation were observed in both patients with and without sepsis ; however, these changes were greater in patients with sepsis than those without. Associations of the coagulation SOFA sub-score and platelet counts with mortality were supported by previous studies in patients with sepsis[13, 14]. However, several concerning points regarding decreased platelet counts warrant attention ; PMX decreases the platelet count more than other dialysis membranes[15, 16] and CRRT tends to lead to lower platelet counts[17]. In the present study, >60% of patients with sepsis used PMX, and platelet counts decreased in 4 days in both

Table S4. SOFA, SOFA-sub score, and mortality at baseline according to all patients grouped by who survived by day 4 or not.

		Septic				Non-septic			
		All patients (N=115)	Non-survived patients (N=14)	Survived patients (N=101)	p-value	All patients (N=116)	Non-survived patients (N=23)	Survived patients (N=93)	p-value
SOFA score		11 (8–14)	12 (10–14)	11 (7–13)	0.17	**10 (6–12)**	**12 (10–13)**	**10 (6–12)**	**0.003**
SOFA sub score	Central venous system	2 (1–3)	3 (1–4)	2 (1–3)	0.19	**2 (0–4)**	**4 (1–4)**	**2 (0–3)**	**0.02**
	Glasgow Coma Scale	11 (6–14)	6.5 (3–14)	11 (6–14.5)	0.13	**10 (4–15)**	**3 (3–13)**	**11 (6–15)**	**0.02**
	Respiratory system	**3 (2–3)**	**4 (3–4)**	**3 (1–3)**	**0.0004**	3 (1–3)	3 (2–3)	3 (1–3)	0.065
	PaO$_2$/FiO$_2$ ratio	**236 (157–350)**	**88 (74–229)**	**268 (171–466)**	**0.0003**	**272 (167–378)**	**234 (114–310)**	**290 (182–379)**	**0.049**
	Cardiovascular System	3 (1–4)	4 (3–4)	3 (0–4)	0.079	**3 (0–4)**	**4 (2–4)**	**3 (0–4)**	**0.03**
	MAP (mmHg)	**81 (68–93)**	**69.5 (59.5–77.8)**	**88 (70–94.5)**	**0.005**	81 (71–90)	72 (66–88)	82 (73–91)	0.06
	Liver	0 (0–2)	0.5 (0–2)	0 (0–1)	0.67	0 (0–1)	0 (0–2)	0 (0–1)	0.21
	Total bilirubin (mg/dl)	1.1 (0.7–2.1)	1.2 (0.8–2.5)	1.1 (0.6–1.9)	0.47	0.8 (0.6–1.6)	1.1 (0.8–2.1)	0.8 (0.6–1.5)	0.20
	Coagulation	2 (0–2)	1 (0–2)	2 (0–2)	0.41	**0 (0–2)**	**1 (0–2)**	**0 (0–1)**	**0.02**
	Platelets (10^4/µl)	9.7 (5.8–18.3)	12.5 (6.1–19.7)	9.5 (5.7–17.7)	0.40	**15.3 (9.4–19.2)**	**11.5 (6.2–15.3)**	**16.2 (10–19.8)**	**0.009**
	Kidneys	2 (1–3)	1.5 (1–2)	2 (1–3)	0.28	2 (1–3)	2 (1–3)	2 (1–3)	0.39
	Creatinine (mg/dl)	2.75 (1.68–3.88)	2.36 (1.7–3.2)	2.75 (1.67–4.18)	0.45	2.76 (1.72–3.91)	2.06 (1.42–4.07)	2.86 (1.82–3.90)	0.11
Survival days		**30 (11–30)**	**1 (1.0–2.3)**	**30 (15–30)**	**< .0001**	**30 (7–30)**	**2 (1–2)**	**30 (20.5–30)**	**< .0001**
Mortality by 30 days (%)		**59 (51.3)**	**14 (100)**	**45 (44.6)**	**0.0001**	**52 (44.8)**	**23 (100)**	**29 (31.2)**	**< .0001**

SOFA : the Sequential Organ Failure Assessment, MAP : mean arterial pressure.

groups. Thus, the effects of PMX and CRRT on the coagulation system in terms of lowering platelet counts could not be excluded. During infection, platelets are involved in leukocyte migration and activation, thereby promoting immune regulation[18], and the platelet-leukocyte complex (PLC) is increased in sepsis, with a decreased PLC reportedly associated with the progression of multiple-organ failure[19, 20]. Platelets have also been reported to act on endothelial cells in sepsis[21-23], and they may be involved in organ damage[24]. Moreover, platelets are also involved in neutrophil extracellular traps (NETs)[23, 25] and microparticles (MPs)[26], which are related to the severity of sepsis[27-29]. The platelets in the blood vessels might have been consumed as sepsis progressed

in the present study, which may have correlated with disease severity. To validate the importance of the coagulation SOFA sub-score as an assessment of prognosis in patients with sepsis on CRRT, further elucidation of these mechanisms is needed.

In the present study, lactate levels more significantly appeared to be associated with mortality in patients without sepsis. Elevated lactate levels reflect peripheral circulation failure and systemic inflammation with vascular endothelial damage[30], thus offering an independent predictor of mortality in patients with sepsis[5, 31] and patients with cardiac shock[32]. A decrease in systolic and diastolic blood pressures is reportedly predicted for in-hospital mortality after CRRT in a study of critically ill
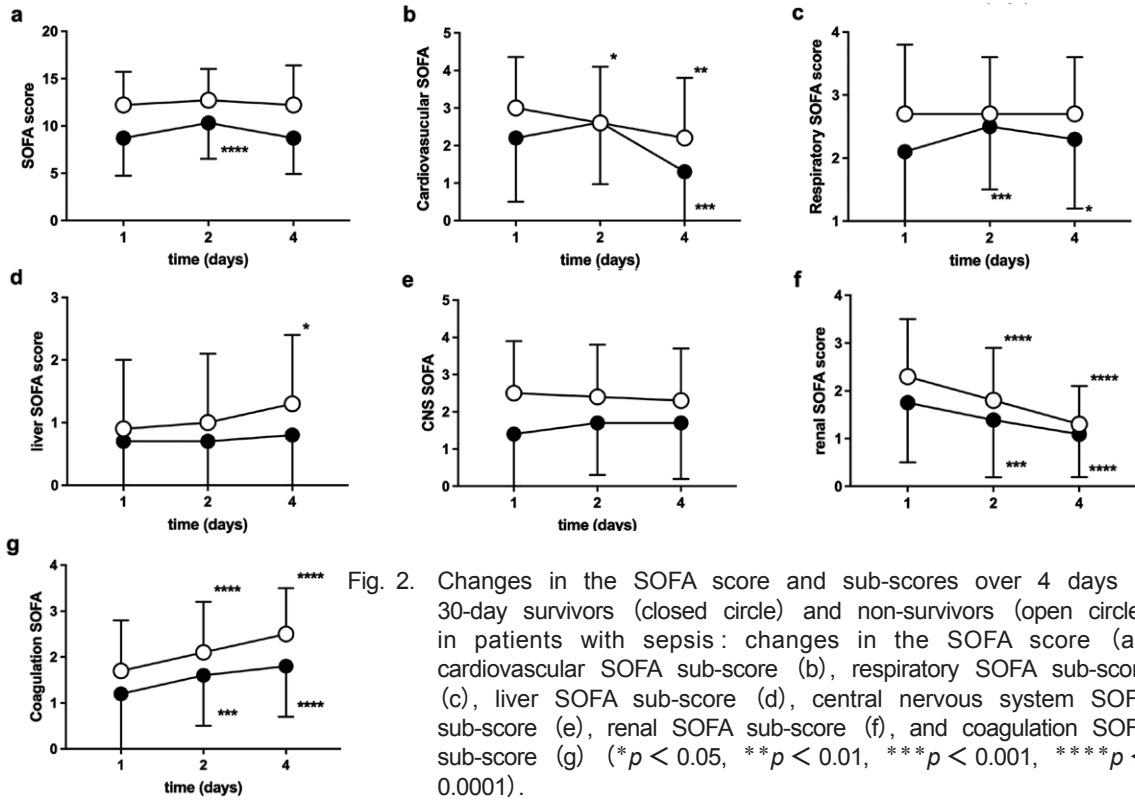
Fig. 2. Changes in the SOFA score and sub-scores over 4 days in 30-day survivors (closed circle) and non-survivors (open circle) in patients with sepsis : changes in the SOFA score (a), cardiovascular SOFA sub-score (b), respiratory SOFA sub-score (c), liver SOFA sub-score (d), central nervous system SOFA sub-score (e), renal SOFA sub-score (f), and coagulation SOFA sub-score (g) ($*p < 0.05$, $**p < 0.01$, $***p < 0.001$, $****p < 0.0001$).
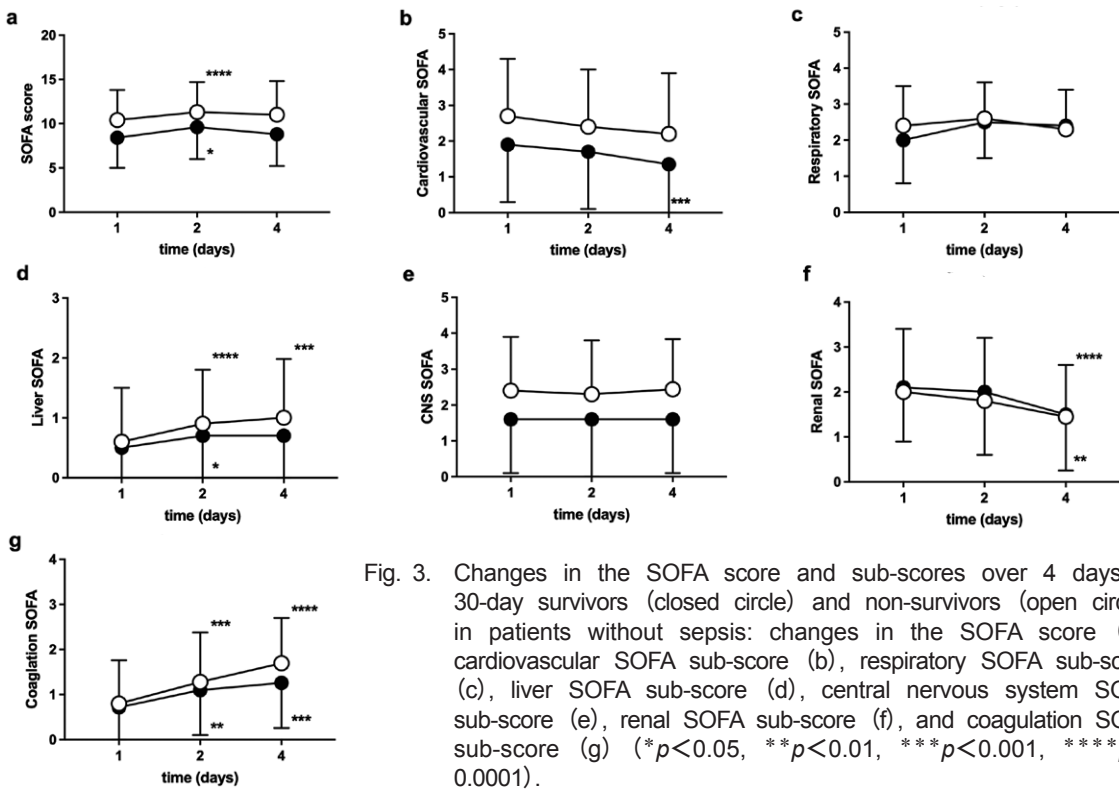

Fig. 3. Changes in the SOFA score and sub-scores over 4 days in 30-day survivors (closed circle) and non-survivors (open circle) in patients without sepsis: changes in the SOFA score (a), cardiovascular SOFA sub-score (b), respiratory SOFA sub-score (c), liver SOFA sub-score (d), central nervous system SOFA sub-score (e), renal SOFA sub-score (f), and coagulation SOFA sub-score (g) ($*p<0.05$, $**p<0.01$, $***p<0.001$, $****p<0.0001$).

Fig. S1.   Changes in SOFA sub-score components and lactate over 4 days between 30-day survivors (closed circle) and non-survivors (open circle) in patients with sepsis: changes in the mean arterial pressure (a), PaO₂/FiO₂ ratio (b), total bilirubin (c), Glasgow Coma Scale score (d), serum creatinine (e), platelet counts (f), and lactate (g). Data were analyzed by the paired t-test or the Wilcoxon rank-sum test. (*$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$)
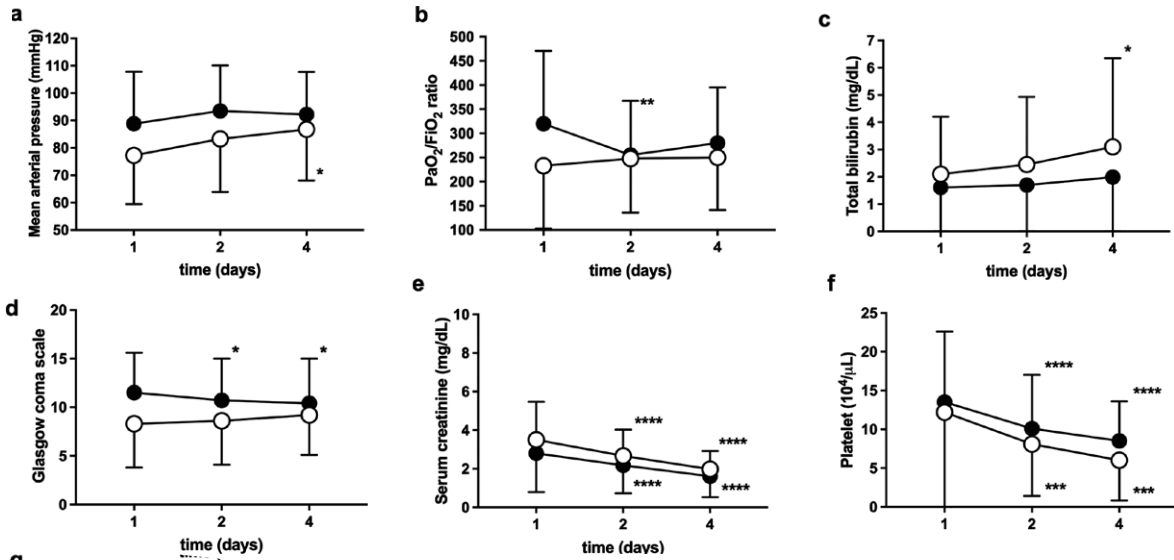

Fig. S2.   Changes in SOFA sub-score components and lactate over 4 days between 30-day survivors (closed circle) and non-survivors (open circle) in patients without sepsis: changes in the mean arterial pressure (a), PaO₂/FiO₂ ratio (b), total bilirubin (c), Glasgow Coma Scale score (d), serum creatinine (e), platelet counts (f), and lactate (g). Data were analyzed by the paired t-test or Wilcoxon rank-sum test. (*$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$)
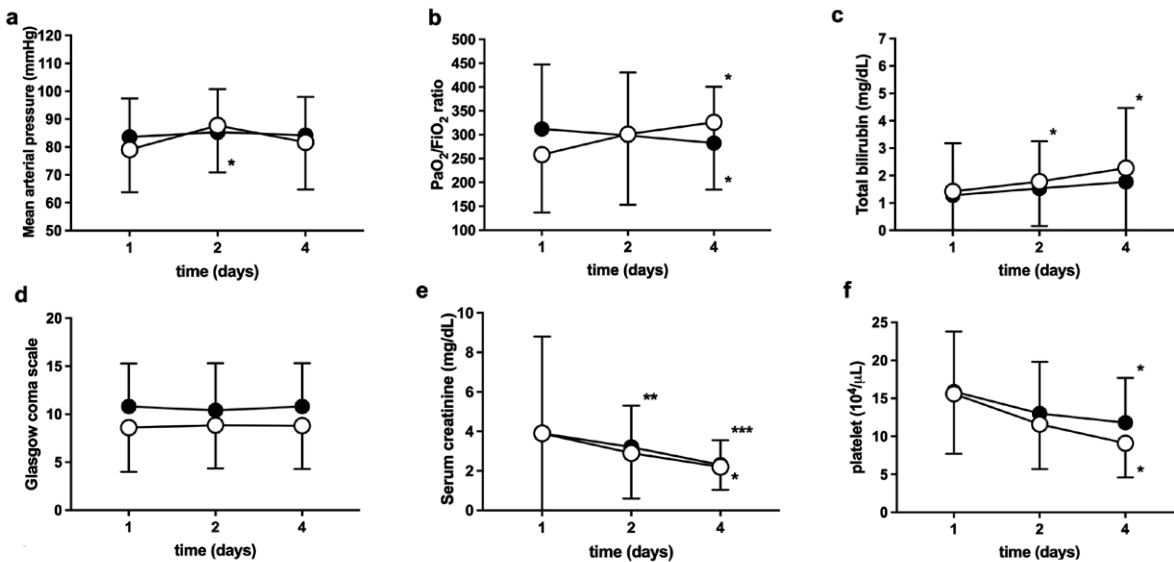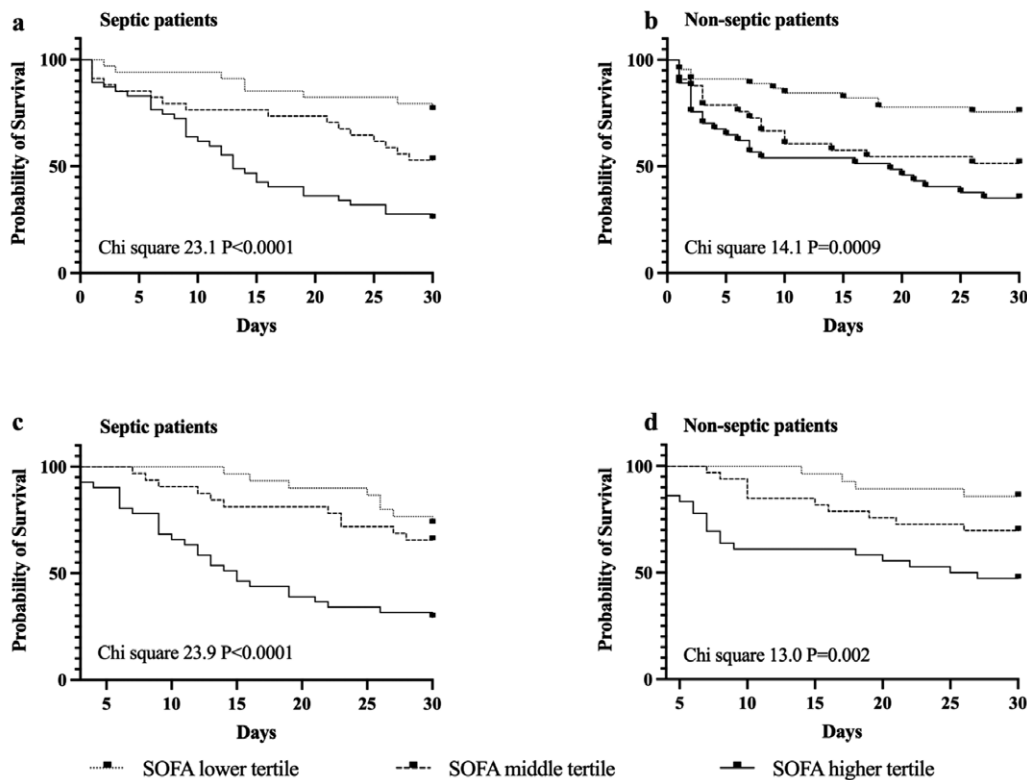
Fig. S3. The Kaplan-Meier curves evaluating the difference in 30-day all-cause mortality according to the SOFA tertiles on days 1 and 4 of patients with (a and c) and without sepsis (b and d), respectively.

patients[33]. Lower blood pressure was significantly associated with mortality in septic and non-septic patients. However, the predictive ability of lactate might be superior to that of the cardiovascular SOFA sub-score and MAP. Organ injury could be improved by auxiliary therapy comprising mechanical ventilation, CRRT, and medications, such as vasopressors, potentially resulting in cardiovascular and respiratory SOFA sub-score and lactate level changes in response to these therapies[5]. However, the predictive ability of lactate levels for mortality might remain, particularly in patients with non-septic AKI.

A previous study reported that the association of the CNS SOFA sub-score with mortality first failed at 0.8 days, and then, the predictive abilities of the respiratory, cardiovascular, renal, coagulation, and hepatic SOFA-sub scores subsequently disappeared[34]. However, the CNS SOFA sub-score on day 1 in the present study was not associated with mortality in patients with septic AKI. The CNS SOFA sub-score uses the GCS score for neurological assessment[35], and evaluation of the GCS score is very difficult or impossible in sedated patients and is prone to be erroneously determined during data collection[34]. Thus, the possibility of errors in these findings could not be ruled out.

Several limitations need to be considered when interpreting this study. This study was undertaken at a single center, and the number of patients was small; moreover, >60% of patients with sepsis used PMX, and several types of hemofilter during CRRT were used in patients in the present study. The timing of CRRT initiation was determined based on the clinical status of each patient, which included factors, such as severe shock, increased serum Cr level, and decreased urine output. Thus, no clear criteria were identified for CRRT initiation, and the intervention status varied depending on the attending physician. Additionally, the GCS score was included in the SOFA assessment, which may lead to data errors, particularly in evaluating comatose patients. Furthermore, the original renal function of the included patients was unknown. Finally, the evaluation criteria of the renal SOFA sub-score and Cr levels after CRRT initiation were not defined, and the meaning of those scores and measurements in patients undergoing CRRT for renal outcome and mortality has not been fully evaluated.

In conclusion, the respiratory SOFA sub-score on day 1 was significantly associated with mortality, and an increased coagulation SOFA sub-score became

Table 3. Association of SOFA-sub scores with all-cause mortality by Cox hazard models.

Septic patients						
	Univariate model			Multivariate model		
SOFA-sub score	HR	95% CI	p	HR	95% CI	*P*-value
Day 1	Model 1			Model 2 (R^2＝0.14)		
CNS	**1.42**	**1.18−1.72**	**0.0001**	1.15	0.93−1.43	0.21
Cardiovascular	**1.31**	**1.09−1.59**	**0.002**	1.17	0.96−1.44	0.12
Respiratory	**1.62**	**1.24−2.20**	**0.0001**	**1.46**	**1.06−2.05**	**0.02**
Liver	1.18	0.69−1.49	0.20	1.14	0.88−1.44	0.31
Renal	1.16	0.95−1.43	0.14	1.20	0.96−1.49	0.11
Coagulation	1.20	0.97−1.48	0.09	1.14	0.92−1.41	0.23
Day 4	Model 3			Model 4 (R^2＝0.089)		
CNS	**1.29**	**1.07−1.58**	**0.01**	0.94	0.71−1.24	0.66
Cardiovascular	**1.33**	**1.13−1.59**	**0.0006**	1.19	0.97−1.47	0.10
Respiratory	**1.42**	**1.04−2.02**	**0.02**	1.31	0.83−2.05	0.22
Liver	**1.42**	**1.09−1.84**	**0.009**	1.21	0.91−1.58	0.18
Renal	**1.61**	**1.20−2.16**	**0.003**	**1.87**	**1.34−2.61**	**0.0002**
Coagulation	**1.56**	**1.16−2.12**	**0.004**	**1.62**	**1.19−2.25**	**0.002**
Non-septic patients						
Day 1	Model 5			Model 6 (R^2＝0.089)		
CNS	**1.37**	**1.14−1.66**	**0.0008**	1.23	0.95−1.60	0.12
Cardiovascular	**1.32**	**1.10−1.61**	**0.004**	1.18	0.95−1.50	0.15
Respiratory	**1.38**	**1.06−1.88**	**0.02**	1.18	0.95−1.50	0.15
Liver	1.16	0.85−1.53	0.33	1.77	0.59−5.05	0.29
Renal	0.91	0.73−1.65	0.40	1.04	0.83−1.30	0.75
Coagulation	1.27	0.99−1.16	0.06	1.21	0.92−1.60	0.15
Day 4	Model 7			Model 8 (R^2＝0.012)		
CNS	**1.40**	**1.12−1.79**	**0.003**	1.36	0.99−1.91	0.06
Cardiovascular	**1.46**	**1.18−1.85**	**0.0006**	**1.33**	**1.04−1.74**	**0.02**
Respiratory	1.14	0.84−1.66	0.41	0.78	0.50−1.24	0.29
Liver	1.42	**1.05−1.92**	0.02	2.24	0.91−1.88	0.14
Renal	0.96	0.70−1.30	0.76	1.26	0.89−1.79	0.19
Coagulation	**1.65**	**1.17−2.35**	**0.005**	1.23	0.84−1.84	0.28

Models 1, 3, 5, and 7 are univariate models. Models 2, 4, 6, and 8 are adjusted with all SOFA-sub scores (central nervous system（CNS）, cardiovascular, respiratory, liver, renal, and coagulation）.

a prognostic factor on day 4 in patients with septic AKI. The predictive ability of respiratory and coagulation SOFA-sub scores and platelet counts, GCS score, MAP, and PaO_2/FiO_2 ratio, as components of SOFA-sub scores, changed according to the timing of scoring during septic AKI in patients requiring CRRT. Therefore, the evaluation of SOFA-sub scores and SOFA sub-score components and changes in these factors after the CRRT initiation may be useful in predicting the prognosis of patients with septic AKI.

Table 4. Associations between components of SOFA-sub scores, lactate, and all-cause mortality.

	HR	95% CI	p	HR	95% CI	P
Septic patients						
Day 1		Model 1			Model 2	
Glasgow coma scale	**0.92**	**0.87−0.98**	**0.01**	**0.91**	**0.87−0.99**	**0.02**
Mean atrial pressure (mmHg)	**0.97**	**0.96−0.99**	**0.0005**	**0.98**	**0.96−0.99**	**0.002**
PaO$_2$/FiO$_2$ ratio	**0.99**	**0.99−0.99**	**0.002**	**0.99**	**0.99−0.99**	**0.01**
T-bilirubin (mg/dl)	1.03	0.94−1.13	0.50	1.03	0.94−1.13	0.45
Serum creatinine (mg/dl)	1.03	0.91−1.18	0.62	1.05	0.91−1.20	0.46
Platelets (10^4/µl)	1.00	0.97−1.03	0.91	1.00	0.97−1.02	0.89
Lactate (mmol/l)	−	−	−	1.03	0.96−1.12	0.35
Day 4		Model 3			Model 4	
Glasgow coma scale	0.98	0.92−1.06	0.73	1.02	0.95−1.11	0.60
Mean atrial pressure (mmHg)	0.99	0.97−1.00	0.26	0.99	0.95−1.01	0.36
PaO$_2$/FiO$_2$ ratio	**0.99**	**0.99−0.99**	**0.03**	0.99	0.99−1.00	0.30
T-bilirubin (mg/dl)	1.10	0.99−1.19	0.06	1.06	0.95−1.16	0.26
Serum creatinine (mg/dl)	**1.52**	**1,12 2.04**	**0.007**	**1.51**	**1.09−2.10**	**0.01**
Platelets (10^4/µl)	**0.92**	**0.86−0.99**	**0.03**	**0.92**	**0.84−0.99**	**0.049**
Lactate (mmol/l)	−	−	−	**1.20**	**1.01−1.40**	**0.04**
Non-septic patients						
Day 1		Model 5			Model 6	
Glasgow coma scale	**0.92**	**0.86−0.98**	**0.009**	0.98	0.91−1.05	0.58
Mean atrial pressure (mmHg)	**0.98**	**0.96−0.99**	**0.04**	**0.98**	**0.95−0.99**	**0.04**
PaO$_2$/FiO$_2$ ratio	**0.99**	**0.99−0.99**	**0.02**	**0.99**	**0.99−0.99**	**0.001**
T-bilirubin (mg/dl)	1.10	0.90−1.30	0.32	1.05	0.83−1.25	0.66
Serum creatinine (mg/dl)	0.99	0.90−1.07	0.92	1.02	0.92−1.10	0.59
Platelets (10^4/µl)	0.97	0.93−1.00	0.08	0.97	0.92−1.01	0.10
Lactate (mmol/l)	−	−	−	**1.12**	**1.06−1.18**	**< 0.001**
Day 4		Model 7			Model 8	
Glasgow coma scale	**0.90**	**0.93−0.97**	**0.009**	0.92	0.84−1.01	0.08
Mean atrial pressure (mmHg)	**0.97**	**0.95−0.99**	**0.03**	0.99	0.97−1.02	0.71
PaO$_2$/FiO$_2$ ratio	1.00	0.99−1.00	0.35	1.00	0.99−1.01	0.06
T-bilirubin (mg/dl)	1.11	0.92−1.31	0.27	1.00	0.79−1.22	0.99
Serum creatinine (mg/dl)	1.12	0.83−1.16	0.43	1.02	0.71−1.40	0.90
Platelets (10^4/µl)	0.93	0.86−1.00	0.07	0.96	0.87−1.04	0.90
Lactate (mmol/l)	−	−	−	**1.38**	**1.15−1.71**	**0.0003**

Models 1, 3, 5, and 7 are adjusted with all components of SOFA-sub scores. Models 2, 4, 6, and 8 are adjusted with all components of SOFA-sub scores and lactate.

Disclosures

No authors have any conflicts of interest to declare.

Ethics

Competing interests
The authors declare no competing interests.

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Table S5. Area under curves and cut-off values of SOFA-sub scores for 30-day survival by ROC curves.

Septic patients					
Day 1	AUC	sensitivity	specificity	cut-off value	p-value
SOFA score	**0.75**	**0.81**	**0.58**	**10**	**＜ 0.0001**
Cardiovascular	**0.63**	**0.85**	**0.40**	**2**	**0.006**
Respiration	**0.67**	**0.88**	**0.34**	**2**	**0.002**
Liver	0.56	0.34	0.84	2	0.19
Renal	0.58	0.93	0.20	1	0.10
Coagulation	0.59	0.61	0.59	2	0.08
Central nervous system	**0.70**	**0.59**	**0.73**	**3**	**0.0003**
Day 4					
SOFA score	**0.72**	**0.58**	**0.88**	**12**	**0.0002**
Cardiovascular	**0.64**	**0.69**	**0.61**	**1**	**0.01**
Respiration	0.60	0.78	0.38	3	0.11
Liver	**0.62**	**0.69**	**0.50**	**1**	**0.03**
Renal	**0.64**	**0.82**	**0.45**	**1**	**0.02**
Coagulation	**0.68**	**0.53**	**0.73**	**3**	**0.003**
Central nervous system	**0.62**	**0.58**	**0.70**	**3**	**0.04**
Non-sepsis group					
Day 1	AUC	sensitivity	specificity	cut-off value	p-value
SOFA score	**0.71**	**0.79**	**0.53**	**9**	**0.0003**
Cardiovascular	**0.67**	**0.50**	**0.81**	**4**	**0.005**
Respiration	**0.61**	**0.71**	**0.44**	**3**	**0.03**
Liver	0.54	0.40	0.77	1	0.38
Renal	0.54	0.37	0.70	1	0.52
Coagulation	0.59	0.58	0.59	1	0.09
Central nervous system	**0.67**	**0.40**	**0.87**	**4**	**0.002**
Day 4					
SOFA score	**0.67**	**0.45**	**0.87**	**13**	**0.008**
Cardiovascular	**0.65**	**0.38**	**0.89**	**4**	**0.02**
Respiration	0.51	0.28	0.88	1	0.85
Liver	0.59	0.59	0.62	1	0.19
Renal	0.51	0.28	0.88	0	0.89
Coagulation	0.65	0.58	0.61	2	0.07
Central nervous system	**0.66**	**0.76**	**0.53**	**2**	**0.02**

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Table S6. Area under curves and cut-off values of components of SOFA-sub scores and lactate for 30-day survival by ROC curves.

Septic patients					
Day 1	AUC	sensitivity	specificity	cut-off value	p-value
Mean arterial pressure (mmHg)	**0.70**	**0.51**	**0.86**	**73**	**0.0004**
PaO$_2$/FiO$_2$ ratio	**0.72**	**0.80**	**0.56**	**291.4**	**0.0005**
Total bilirubin	0.56	0.34	0.84	2	0.19
Serum creatinine	0.60	0.61	0.59	2.6	0.23
Platelet count	0.57	0.59	0.61	9.5	0.67
Glasgow come scale	0.58	0.76	0.46	13	0.15
Lactate	0.59	0.31	0.88	5	0.05
Day 4					
Mean arterial pressure	0.59	0.49	0.77	81	0.12
PaO$_2$/FiO$_2$ ratio	0.57	0.27	0.89	142	0.18
Total bilirubin	0.64	0.67	0.59	1.3	0.03
Serum creatinine	0.64	0.80	0.52	1.29	0.07
Platelet count	**0.67**	**0.48**	**0.73**	**7.6**	**0.03**
Glasgow come scale	0.58	0.76	0.45	13	0.15
Lactate	**0.66**	**0.92**	**0.40**	**2.3**	**0.01**
Non-sepsis group					
Day 1	AUC	sensitivity	specificity	cut-off value	p-value
Mean arterial pressure	**0.62**	**0.67**	**0.56**	**82**	**0.03**
PaO$_2$/FiO$_2$ ratio	**0.63**	**0.38**	**0.86**	**165.6**	**0.003**
Total bilirubin	0.58	0.75	0.50	0.8	0.58
Serum creatinine	0.57	0.63	0.56	2.8	0.48
Platelet count	0.60	0.71	0.55	16.6	0.15
Glasgow come scale	**0.66**	**0.40**	**0.88**	**3**	**0.003**
Lactate	**0.73**	**0.67**	**078**	**2.5**	**0.001**
Day 4					
Mean arterial pressure	0.58	0.38	0.89	70	0.16
PaO$_2$/FiO$_2$ ratio	0.60	0.59	0.77	319	0.12
Total bilirubin	0.56	0.65	0.56	1.1	0.27
Serum creatinine	0.52	0.14	0.98	0.66	0.78
Platelet count	**0.63**	**0.72**	**0.58**	**11.0**	**0.04**
Glasgow come scale	0.64	0.90	0.40	14	0.05
Lactate	**0.61**	**0.94**	**0.31**	**2.7**	**0.02**

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