Research Article

Association of baseline renal function with mortality in patients with sepsis requiring continuous renal replacement therapy for acute kidney injury: a single-center retrospective study

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Short Title: Association of renal function with mortality in patients with AKI

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Abstract

Introduction

To date, the prognosis of patients with sepsis and underlying chronic kidney disease (CKD) had been poor. However, the impact of preseptic renal function on the short-term prognosis of patients with extremely severe septic shock with acute kidney injury (AKI) that requires renal replacement therapy (RRT) is unclear.

Methods

Of the septic shock cases treated at the intensive care unit for ≥48 hours, 131 adults who were diagnosed as septic AKI and underwent continuous venovenous hemodiafiltration were retrospectively analyzed. The relationships of demographic, clinical, and laboratory data with mortality were evaluated, and the independent risk factors for death were identified.

Results

The median age of the subjects was 73 (range, 63–80) years, and 76 (58%) were men. The rate of mortality was significantly higher among patients with CKD (n = 42) than in those without CKD (n = 89) (43% vs. 22%, $p < 0.016$). On univariate and multivariate logistic regression analyses, the associated factors and independent predictors of death were Sequential Organ Failure Assessment score (Odds ratios [OR] 1.151, 95% confidence intervals [CI] 1.026–1.293, $p = 0.017$ and OR 1.129, 95% CI 1.003–1.271, respectively); baseline estimated glomerular filtration rate (OR 0.986, 95% CI 0.975–0.997, $p = 0.016$ and OR 0.983, 95% CI 0.970–0.996, respectively); and lactic acid (OR 1.094, 95% CI 1.005–1.190, $p = 0.038$ and OR 1.110 CI 1.015–1.215, respectively).

Conclusion

Reduced baseline renal function may be a factor for poor short-term prognosis in severe septic AKI cases requiring RRT.

Introduction

Acute kidney injury (AKI) is a serious complication in critically ill patients, and was reported to occur in more than half of cases in the intensive care unit (ICU) [1]. The complications of AKI not only increase the treatment cost and cause chronic kidney disease (CKD) but can also lead to poor prognosis [2]. AKI secondary to sepsis is particularly severe and increases mortality by five-fold, compared with the rate in patients without sepsis [3, 4]. Septic AKI remains a serious disease, even with modern intensive care and the development of renal replacement therapy (RRT).

In Japan, one in eight adults is estimated to have CKD [2]. In addition, the number of patients with end stage kidney disease (ESKD) continues to increase, with a cumulative incidence as high as 3.14% in men and 1.42% in women [5]. CKD itself is thought to be an important risk factor for AKI onset [6], and there is a close relationship between CKD and AKI. In fact, CKD was estimated to be found in about 30% of patients with AKI in the ICU [7], suggesting that the prognosis for sepsis with underlying CKD is poor [8]. The purpose of this research was to clarify the impact of baseline renal function on the short-term prognosis of patients with septic AKI requiring RRT.

Method and materials

Subjects and setting

Of the patients with septic shock and who were treated for ≥48 hours at the ICU of the Advanced Emergency and Critical Care Center of Kurume University Hospital, Japan from April 2010 to March 2016, those diagnosed as AKI and underwent venovenous hemodiafiltration (CVVHDF) were retrospectively analyzed based on the demographic, clinical, and laboratory data. Patients who were under the age of 18 years, had unknown renal function before the onset of sepsis, had undergone RRT before treatment at our institution, and had undergone maintenance dialysis for ESKD were excluded.

Demographic and clinical data

Sex, age, body mass index, Charlson Comorbidity Index (CCI) [9], smoking history, mean arterial blood pressure, Sequential Organ Failure Assessment (SOFA) score [10], Acute Physiology and Chronic Health Evaluation (APACHE) II score [11], Kidney Disease Improving Global Outcomes (KDIGO) classification [12] of AKI stage, ICU admission days, ICU exit outcome, medication history,

comorbidities, and sepsis-causing diseases were extracted from medical records, fever type tables, and discharge summaries.

Laboratory tests

The following blood test results at the start of ICU treatment were acquired from the electronic medical records: hemoglobin, hematocrit, white blood cell count, platelet count, lactic acid, glycated hemoglobin, total protein, albumin, total bilirubin, blood urea nitrogen (BUN), and creatinine. In order to evaluate the baseline renal function before ICU admission, the values of creatinine and estimated glomerular filtration rate (eGFR) before the onset of sepsis were also extracted.

Definition of baseline renal function and chronic kidney disease

The lowest serum creatinine level (i.e., highest eGFR level) within 12 months before the onset of sepsis was defined as the baseline renal function. eGFR was calculated using the equation suitable for Japanese stature [13]. Moreover, in accordance with the kidney diseases outcome quality initiative clinical practice guidelines for CKD [14], eGFR <60 mL/min/1.73 m^2 was defined as CKD.

Definition of acute kidney injury

The KDIGO criteria [12] were used, and patients were categorized based on serum creatinine and urine volumes. The severity of AKI at the point of RRT initiation was evaluated retrospectively from the medical records and fever type tables.

Criteria and conditions for starting renal replacement therapy

RRT was initiated on patients who were diagnosed as AKI, needed inotropic agents in addition to appropriate fluid loading to maintain a mean arterial pressure of ≥65 mmHg, and had blood lactate level of ≥2 mmol/L. A polymethyl methacrylate (PMMA) membrane hemofilter was used, with the

same conditions as those needed for carrying out CVVHDF, as follows: blood flow rate: 150 mL/minute, dialysate flow rate: 1200 mL/hour, and filtration flow rate: 300 mL/hour).

Statistical analysis

Data were expressed as median and interquartile range (IQR). Proportions were compared by Chi-square test, and quantitative variables were compared by Mann–Whitney U-test or Student's t-test. Survival curves were plotted according to the Kaplan–Meier method and were compared by Cox–Mantel log rank test. The variables that had $p < 0.05$ from the univariate analysis was required were entered into multivariate logistic regression analysis to assess the associations of the clinical and laboratory markers with the clinical outcome of survival. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. A p value < 0.05 was considered statistically significant. All statistical analyses were carried out using JMP Pro Version 15.1 for Microsoft Windows and SPSS Statistics Pack 27.0 for Microsoft Windows.

Results

Of the 131 eligible patients who underwent CVVHDF during the study period, 89 patients had normal renal function (non-CKD group) and 42 patients had CKD (Figure 1). The patient characteristics are presented in Table 1. The median age was 73 years (IQR, 63–80 years), and 76 (58%) were men. The median (IQR) overall APACHE II and SOFA scores were 28 (23–32) and 9 (6–11), respectively, but no significant differences were observed between the two groups. Age, CCI, baseline serum creatinine, BUN at the start of ICU treatment, and creatinine level were significantly higher in the CKD group than in the non-CKD group. Baseline eGFR was significantly lower in the CKD group than in the non-CKD group. In addition, several patients in the CKD group were taking angiotensin II receptor blocker, calcium-channel blocker, β-blocker, and diuretics for their comorbidities, such as hypertension and chronic heart failure. Conversely, the level of lactic acid at the start of ICU treatment was significantly higher in the non-CKD group than in the CKD group. The mortality rate was significantly higher in the CKD group than in the non-CKD group (22% vs. 43%, respectively, $p = 0.016$). As shown in Figure 2, the CKD and non-CKD survival curves differed significantly (log rank test: $X^2 = 4.772$, $p = 0.029$). Compared with survivors, nonsurvivors had higher SOFA score and more patients with baseline CKD. Moreover, pneumonia and pancreatitis were often seen as the causes of septic shock among the nonsurvivors (Table 2). Univariate analysis was performed to identify the variables (Tables 1 and 2) associated with the outcome (survival or death). As shown in Table 3, mortality was significantly

correlated with the SOFA score, baseline eGFR, and lactic acid ($p < 0.05$ for all). The variables in the multivariate logistic regression analysis were selected based on the results of the univariate analysis and previous research. Therefore, SOFA score [15], baseline eGFR, and lactic acid [16] were included as variables in the multivariate model. On multivariate logistic regression analysis (Table 4), the prognosis of patients with septic AKI was highly associated with the SOFA scare, baseline eGFR, and lactic acid. On the receiver operating characteristic (ROC) curve, the optimal baseline eGFR cutoff value to determine the prognosis was 60.5 mL/min/1.73 m^2, with area under the curve value of 0.651, sensitivity of 73.1%, and specificity of 50.0% (Figure 3).

Our results showed that for the prediction of prognosis in patients with septic AKI, a baseline eGFR of 60.5 mL/min/1.73 m^2 was the optimal cutoff value.

Discussion

Among the indications for RRT for AKI in Japan, septic AKI is the most common at 40% and was reported to have an in-hospital mortality rate as high as 60% [17]. Because septic AKI itself is an extremely serious condition, factors that can predict prognosis need to be identified. However, at present, sufficient prediction of the prognosis of patients with septic shock had been difficult. SOFA score and lactate level had been the mainstays, because they had been thought to predict the short-term mortality rate of septic AKI [15, 16]. This study targeted only severe cases that were treated in the ICU for septic shock with AKI that needed CVVHDF. The results showed that in addition to the SOFA score and lactic acid level, baseline eGFR was an independent risk factor for mortality. The cut-off value specifically derived from the ROC curve is 60.5 mL / min / 1.73 m^2, which about the same that of eGFR at which point the risk of death from a cardiovascular event is set to increase or eGFR used in the definition of CKD in K/DOQI clinical practice guidelines for chronic kidney disease. This result suggests that the deterioration of prognosis in severe septic AKI patients may be affected if they also have CKD. The lower the baseline eGFR, the poorer the fetal prognosis; thus, assessing baseline eGFR and presence of CKD as a comorbidity is critical for evaluating the severity of the conditions in ICU patients with severe septic shock and AKI requiring RRT.

Most septic patients were reported to have underlying chronic illnesses [18, 19]. The CCI was evaluated in this study, because various comorbidities may affect the prognosis of sepsis. Although the CCI was not associated with survival, we thought that the presence or absence of CKD may have impacted the prognosis. Similarly, a previous report [20] mentioned that the prognosis after infection was worse in patients with CKD than in those without CKD, although the severity of the cases varied.

The mechanism that links CKD with increased mortality in patients with septic shock and AKI cannot be fully elucidated, but heart disease had been thought to be potentially involved. In patients with CKD without a known heart disease, the coronary flow velocity reserve was reported to be significantly reduced even without a decrease in the left ventricular ejection rate [21]. Moreover, aortic stiffness was reported to increase with decreasing in renal function [22]; therefore, patients with CKD are considered to be at risk for ischemic heart disease. Along with the hemodynamic stress under septic conditions, these cardiovascular abnormalities may have been aggravated and contributed to the increased mortality. However, according to the results of this study, the mortality rates during the period of high hemodynamic stress (i.e., about one month after ICU admission) were the same level between the non-CKD and CKD groups. The increase in the mortality rate among patients with CKD after one month suggested other associated factors, aside from the potential involvement of heart disease. The serious impact of renal failure and uremia on the immune system likely contributed. In uremic patients, although the neutrophil count does not change, there is inhibition of intracellular bactericidal activity [23] and monocyte and monocyte-derived dendritic cell functions, which results in decreased immune function [24]. Moreover, uremia suppresses impaired T cell activation [25] and the differentiation of T lymphocytes into Th1 and Th2 lymphocytes [26] ~~[27]~~. In addition to these immune system abnormalities, the cytokine interleukin 6 (IL 6) induces inflammation as renal function declines; when patients with impaired renal function reaches septic AKI, the level of IL 6 rises [27] and may negatively impact prognosis.

Despite the very high severity of septic AKI cases in this study, the mortality rate was acceptable at 30%. The fact that our facility was a closed ICU may have contributed to the reduction in mortality [28], but the hemofilter used in RRT may have had an impact on prognosis. In Japan, a PMMA membrane hemofilter [29] had been used, and CVVHDF had been implemented at times. In this study, CVVHDF was performed using a PMMA membrane hemofilter in all cases. Recently, the timing of RRT initiation and the prognosis of septic AKI have been reported [30, 31]. In this research, our results on the similar severity of AKI at the start of RRT between survivors and nonsurvivors implied that the timing of RRT initiation did not have an impact on the prognosis of our cases.

Limitations

The retrospective observational nature of this research implied several restrictions. First, there may have been selection bias; the use of baseline eGFR may have led to the exclusion of unclear cases. Next, CKD was evaluated only by eGFR; proteinuria, which could be a risk factor for various diseases [32, 33], could not be evaluated in this study. Because the excretion of urinary protein precedes

decline in eGFR, the incidence of CKD may have been underestimated. In addition, the differences and effects on prognosis of the sepsis treatment strategies were unknown. In addition, because the results were obtained from a relatively small number of cases in a single institution, a multicenter prospective study on a larger sample size would be needed to verify the results.

Conclusions

In cases of septic shock with AKI treated with CVVHDF, low baseline eGFR may be a predictor of poor short-term prognosis. For severe septic AKI cases with CKD, special care should be taken when providing treatment. Future studies should investigate treatment strategies that can improve the prognosis of septic AKI in patients with underlying renal function impairment.

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Statement of Ethics

This study was approved by the Institutional Review Research Committee for Human Subjects of Kurume University Hospital and adhered to the Declaration of Helsinki. This retrospective review of patient data did not require written informed consent from participants in accordance with national guidelines. Protocol summary was publicized on the university Web site clearly informing of the patients' right to refuse participation. The ethics permission number is 20163.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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There was no funding for this study.

Author Contributions

Masafumi Fukuda, Nobuhisa Hirayu and Masakazu Nabeta: research idea and study design; Masafumi Fukuda: data acquisition; Masafumi Fukuda: data analysis/interpretation; Masafumi Fukuda: statistical analysis; Masafumi Fukuda, Masakazu Nabeta and Osamu Takasu: manuscript preparation and drafting; Masafumi Fukuda, Kei Fukami, Masakazu Nabeta, Nobuhisa Hirayu and Osamu Takasu: approval of the final version.

Data Availability Statement

Raw data were generated at Kurume University Hospital. Derived data supporting the findings of this study are available from the corresponding author F.M. on request.

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Figure Legends

Fig. 1. Patient selection scheme

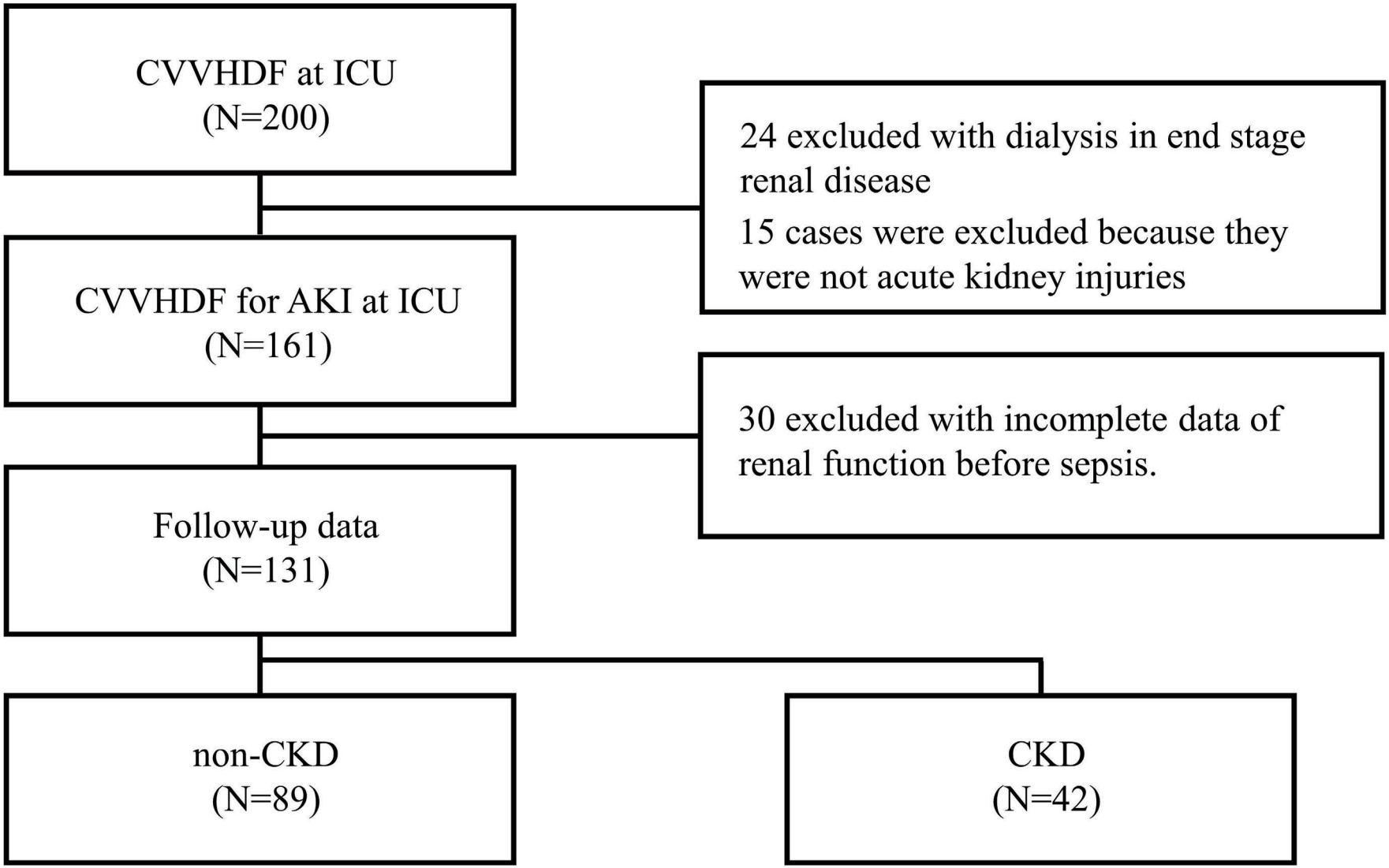
CVVHDF, continuous venovenous hemodiafiltration; AKI, acute kidney injury; ICU, intensive care unit; CKD, chronic kidney disease

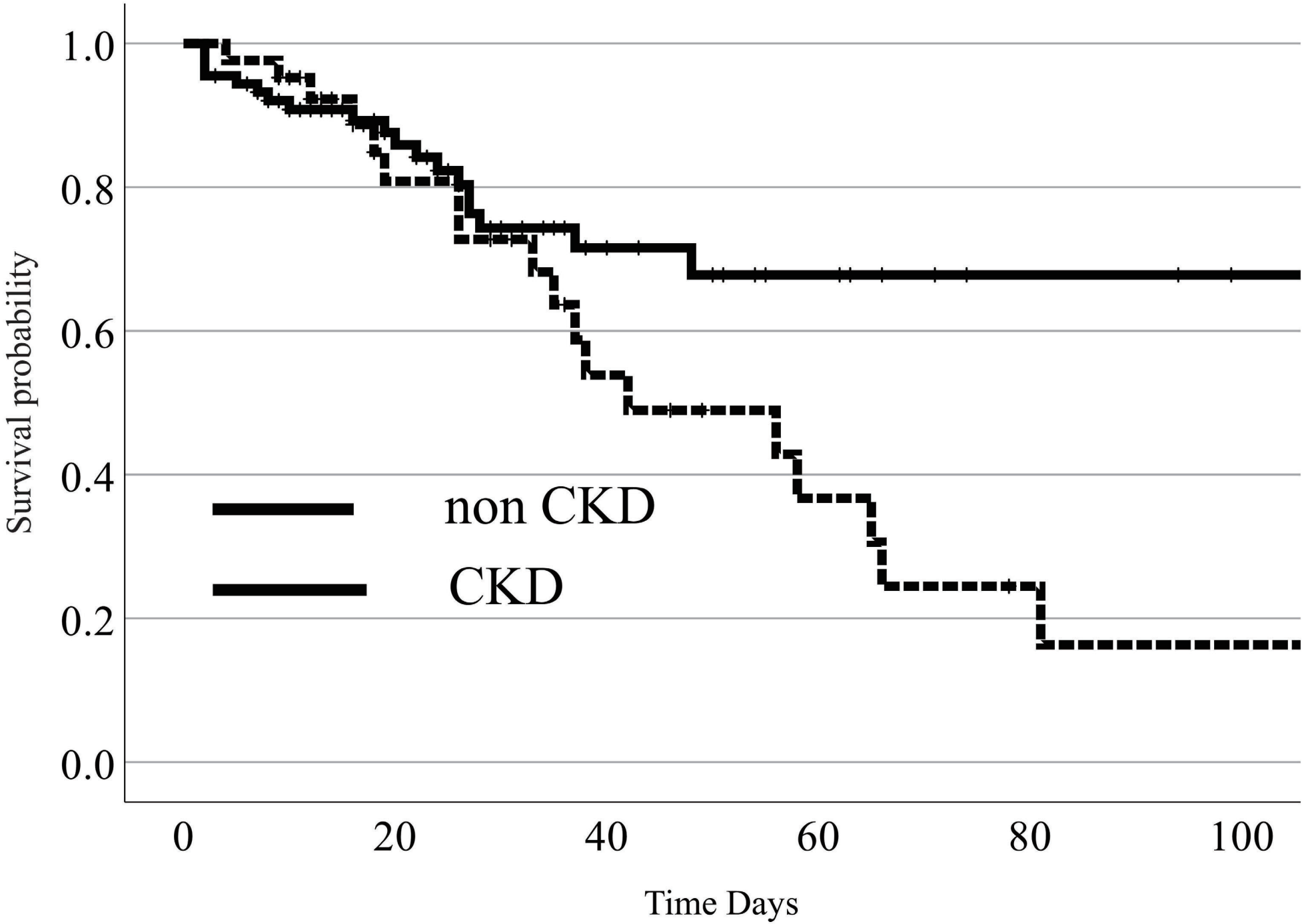
Fig. 2. A Kaplan–Meier survival curve analysis

CKD, chronic kidney disease

Fig. 3. ROC curve of baseline eGFR

ROC, receiver operating characteristic; eGFR, estimated glomerular filtration rate


CVVHDF at ICU
(N=200)
24 excluded with dialysis in end stage renal disease
15 cases were excluded because they were not acute kidney injuries
CVVHDF for AKI at ICU
(N=161)
30 excluded with incomplete data of renal function before sepsis.
Follow-up data
(N=131)
non-CKD
(N=89)
CKD
(N=42)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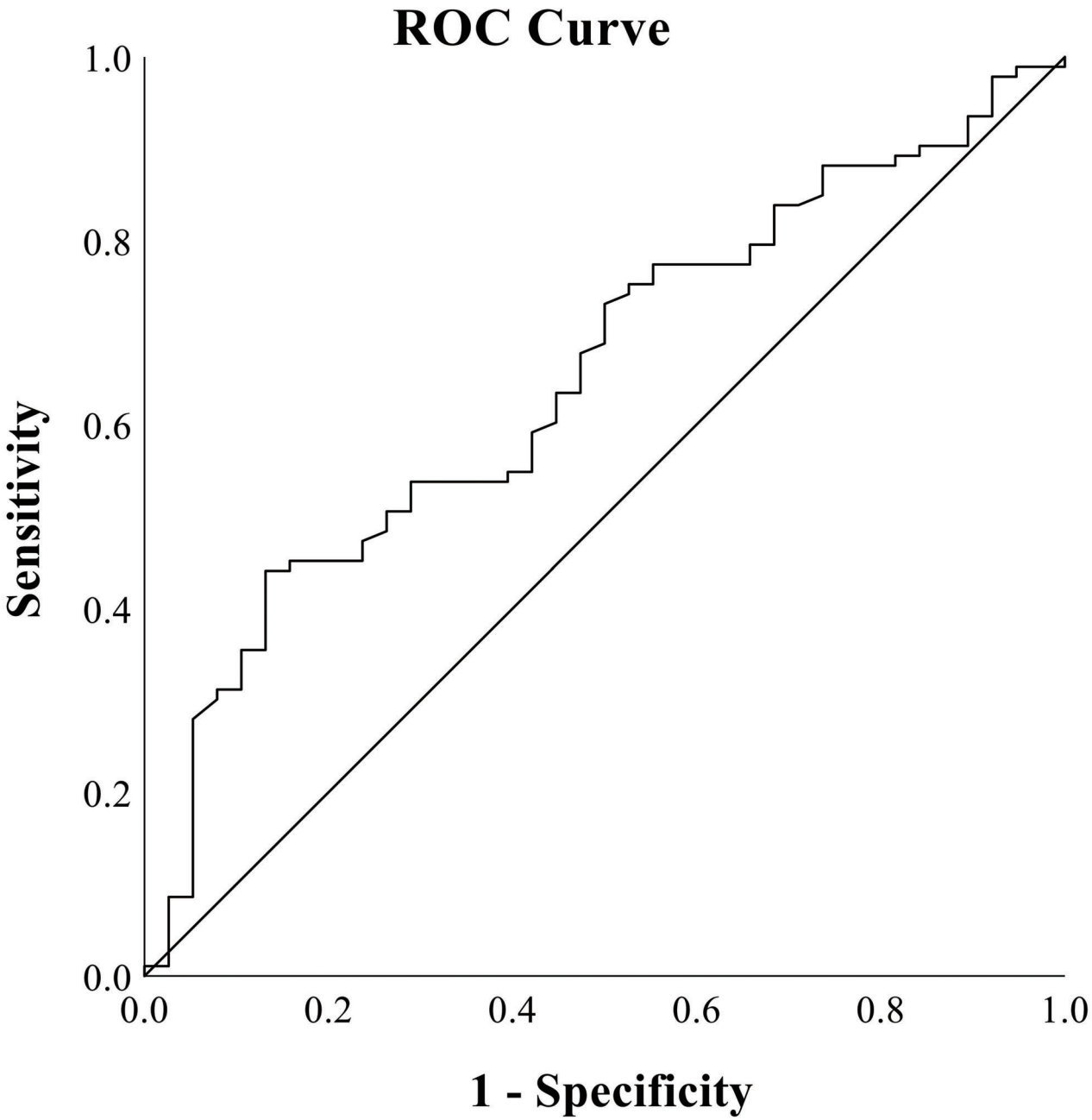
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Table 1: Baseline characteristics of 131 septic AKI patient treated by CVVHDF

variables	Total (N=131)	Non-CKD (N=89)	CKD (N=42)	p value
Male gender	76 (58%)	55 (62%)	21 (50%)	0.202
Age (years)	73 (63–80)	73 (58–79)	74(71–84)	<0.001
Body Mass Index	22 (19–25)	21 (18–25)	22(20–25)	0.489
Charlson Comorbidity Index	2 (1–3)	1 (0–3)	3 (2–4)	<0.001
Smoking	34 (26%)	26 (29%)	8 (19%)	0.215
MAP (mmHg)	68(54–84)	64(53–84)	78 (61–89)	0.052
SOFA score	9 (6–11)	8 (6–10)	10 (5–12)	0.409
APACHE II score	28 (23–32)	28 (23–32)	27 (24–34)	0.336
KDIGO stage				
Stage 1	30 (23%)	21 (24%)	9 (21%)	0.783
Stage 2	34 (26%)	19 (21%)	15 (36%)	0.080
Stage 3	67 (51%)	49 (55%)	18 (43%)	0.192
ICU length of stay (days)	23 (12–40)	24 (12–39)	19 (12–43)	0.491
Mortality	38 (29%)	20 (22%)	18 (43%)	0.016
Beseline eGFR (mL/min/1.73m^2)	71(52–102)	90(72–112)	37 (26–52)	<0.001
Baseline creatinine (mg/dL)	0.72 (0.60–0.98)	0.62 (0.53–0.74)	1.20 (0.98–1.74)	<0.001
Hemoglobin (g/dL)	10.5 (8.7–11.9)	10.5 (9.0–12.0)	10.5 (8.4–12.0)	0.544
Hematocrit (%)	30.9 (26.7–35.9)	30.9 (27.1–36.2)	30.8 (24.9–35.4)	0.435
White blood cell (/mm^3)	7900 (3200–14900)	7800 (3000–14100)	9400 (3300–15800)	0.726
Platelet count (/mm^3)	10.2 (5.3–15.5)	9.7 (5.3–14.7)	12.8 (5.1–12.3)	0.292
Lactic acid (mmol/L)	3.4 (1.6–5.9)	3.9 (2.1–6.8)	2.4 (1.2–5.6)	0.029
Hemoglobin A1c (%)	5.7 (5.3–6.1)	5.7 (5.4–6.0)	5.6 (5.2–6.2)	0.687
Total protein (g/dL)	4.9 (4.3–5.8)	4.8 (4.3–5.5)	5.3 (4.5–6.0)	0.054
Albumin (g/dL)	2.4 (2.0–2.8)	2.4 (1.9–2.8)	2.4 (2.0–2.9)	0.393
Total Bilirubin (mg/dL)	1.0 (0.6–1.5)	1.0 (0.7–1.6)	0.8 (0.4–1.5)	0.440
Blood urea nitrogen (mg/dL)	42(27–71)	37 (24–62)	65 (35–80)	0.004
Creatinine (mg/dL)	1.81 (1.26–2.93)	1.58 (1.02–2.38)	2.40 (1.87–3.65)	<0.001
Previous medications				
Anti platelet drugs	23 (18%)	13 (15%)	10 (24%)	0.196
ACE inhibitor	5 (4%)	3 (3%)	2 (5%)	0.689
ARB	33 (25%)	13 (15%)	20 (48%)	<0.001
Calcium -channel blocker	43 (33%)	21 (24%)	22 (52%)	0.001
β blocker	15 (12%)	8 (9%)	17 (13.2%)	0.198
Diuretics	19(15%)	8 (9%)	11 (26%)	0.009
Statin	13 (10%)	5 (6%)	8 (19%)	0.016
Oral antidiabetic	16 (12%)	13 (15%)	3 (7%)	0.223
Insulin	6 (5%)	4 (4%)	2 (5%)	0.946
Comobidities				
Hypertension	70 (53%)	39 (44%)	31 (74%)	0.001
Diabetes mellitus	39 (30%)	28 (31%)	11 (26%)	0.538
Neurological disease	20 (15%)	12 (13%)	8 (19%)	0.409
Chronic heart failure	17 (13%)	5 (6%)	12 (29%)	<0.001
Liver disease	17 (13%)	14(16%)	3 (7%)	0.172
Neoplasm	11 (8%)	9 (10%)	2 (5%)	0.303
Cardiovascular disease	10 (8%)	6 (7%)	4 (10%)	0.576
Peripheral vascular disease	8 (6%)	3 (3%)	5 (12%)	0.057
Respiratory disease	8 (8%)	6 (7%)	2 (5%)	0.659
Causes of sepsis				
Peritonitis	40 (31%)	25 (28%)	15 (36%)	0.377
Pneumonia	22 (17%)	14 (16%)	8 (19%)	0.635
Urinary tract infection	14 (11%)	11 (12%)	3 (7%)	0.367
Ischemic enteritis	13 (10%)	7 (8%)	6 (14%)	0.251
Any abscss	11 (8%)	7 (8%)	4 (10%)	0.749
Skin and soft tissue infection	10 (8%)	10 (11%)	0 (0%)	0.024
Colitis	4 (3%)	2 (2%)	2 (5%)	0.435
Encephalomyelitis	4 (3%)	3 (3%)	1 (2%)	0.759
Pancreatitis	2 (2%)	0 (0%)	2 (5%)	0.038
Cholecystitis	2 (2%)	2 (2%)	0 (0%)	0.328
Necrotizing fasciitis	2 (2%)	2 (2%)	0 (0%)	0.328
Febrile neutropenia	1 (1%)	1 (1%)	0 (0%)	0.490
Corrosive esophagitis	1 (1%)	1 (1%)	0 (0%)	0.490
Infective endocarditis	1 (1%)	1 (1%)	0 (0%)	0.490
Pericarditis	1 (1%)	1 (1%)	0 (0%)	0.490

Unknown	3 (2%)	2 (2%)	1 (2%)	0.962

Reported as No. (%) or median (IQR).
AKI: acute kidney injury; CVVHDF: continuous venovenous hemodiafiltration; MAP: Mean arterial blood pressure; SOFA: Sepsis-related Organ Failure Assessment; APACHE: acute physiology and chronic health evaluation; KDIGO: Kidney Disease Improving Global Outcomes; ICU: intensive care unit; eGFR: estimated glomerular filtration rate; ACE: Angiotensin converting enzyme; ARB: Angiotensin II receptor blocker

Table 2: Clinical and laboratory characteristics of survivors and non survivors

variables	Survivor (N=93)	Nonsurvivor (N=38)	p value
Male gender	52 (56%)	24 (63%)	0.559
Age (years)	72 (61–80)	74 (66–81)	0.225
Body Mass Index	22 (19–36)	22 (19–25)	0.988
Charlson Comorbidity Index	2 (1–3)	2 (1–3)	0.067
Smoking	26 (28%)	8 (21%)	0.512
MAP (mmHg)	69 (54–87)	65 (56–82)	0.421
SOFA score	8 (6–10)	10 (7–13)	0.014
APACHE II score	27 (24–32)	28 (23–33)	0.472
KDIGO stage			
Stage 1	22 (24%)	8 (21%)	0.747
Stage 2	25 (27%)	9 (24%)	0.704
Stage 3	46 (49%)	21 (55%)	0.546
ICU length of stay (days)	23 (12–42)	25 (10–37)	0.358
Baseline eGFR (mL/min/1.73m^2)	78 (58–110)	61 (35–80)	0.013
Baseline creatinine (mg/dL)	0.68 (0.56–0.91)	0.80 (0.68–1.22)	0.124
Hemoglobin (g/dL)	10.7 (9.3–12.1)	9.4 (8.4–12.1)	0.417
Hematocrit (%)	31.6 (27.9–36.0)	27.3(24.3–35.9)	0.451
White blood cell (/mm^3)	7900 (3100–14400)	9200 (3500–15800)	0.351
Platelet count (/mm^3)	12.1 (5.8–16.4)	8.9 (3.8–14.5)	0.383
Lactic acid (mmol/L)	3.2 (1.6–5.1)	5.4 (1.7–8.5)	0.055
Hemoglobin A1c (%)	5.6 (5.2–6.0)	5.8 (5.5–6.2)	0.931
Total protein (g/dL)	4.9 (4.3–5.8)	5.1 (4.1–5.8)	0.915
Albumin (g/dL)	2.4 (1.9–2.8)	2.4 (2.0–2.8)	0.879
Total Bilirubin (mg/dL)	1.0 (0.6–1.4)	1.0 (0.5–2.0)	0.216
Blood urea nitrogen (mg/dL)	40 (27–67)	42 (27–76)	0.680
Creatinine (mg/dL)	1.81 (1.24–3.03)	1.95 (1.29–2.89)	0.804
Previous medications			
Anti platelet drugs	13 (14%)	10 (26%)	0.092
ACE inhibitor	5 (5%)	0 (0%)	0.145
ARB	22 (24%)	11 (29%)	0.527
Calcium -channel blocker	30 (32%)	13 (34%)	0.840
β blocker	10 (11%)	5 (13%)	0.695
Diuretics	12 (13%)	7 (18%)	0.422
Statin	8 (9%)	5 (13%)	0.429
Oral antidiabetic	13 (14%)	3 (8%)	0.335
Insulin	5 (5%)	1 (3%)	0.495
Comobidities			
Hypertension	46 (50%)	24 (63%)	0.179
Chronic Kidney Disease	24 (26%)	18 (47%)	0.023
Diabetes mellitus	26 (28%)	13 (34%)	0.478
Neurological disease	14 (15%)	6 (15%)	1.000
Chronic heart failure	11 (11%)	6 (15%)	0.572
Liver disease	11 (11%)	6(16%)	0.572
Neoplasm	9 (10%)	3 (8%)	0.748
Cardiovascular disease	6 (7%)	4(11%)	0.475
Peripheral vascular disease	4 (4%)	4 (11%)	0.229
Respiratory disease	7 (8%)	1 (3%)	0.437
Causes of sepsis			
Peritonitis	30 (32%)	10 (26%)	0.502
Pneumonia	11 (12%)	11 (29%)	0.017
Urinary tract infection	12 (13%)	2 (5%)	0.199
Ischemic enteritis	11 (12%)	2 (5%)	0.254
Any abscss	8 (9%)	3 (8%)	0.894
Skin and soft tissue infection	5 (5%)	5 (13%)	0.128
Colitis	3 (3%)	1 (3%)	0.857
Encephalomyelitis	4 (4%)	0 (0%)	0.194
Pancreatitis	0 (0)	2 (5%)	0.048
Cholecystitis	2 (2%)	0 (0%)	0.362
Necrotizing fasciitis	2 (2%)	0 (0%)	0.362
Febrile neutropenia	1 (1%)	0 (0%)	0.521
Corrosive esophagitis	1 (1%)	0 (0%)	0.521
Infective endocarditis	1 (1%)	0 (0%)	0.521
Pericarditis	1 (1%)	0 (0%)	0.521
Unknown	1 (1%)	2 (5%)	0.145

Reported as No. (%) or median (IQR).
MAP: Mean arterial blood pressure; SOFA: Sepsis-related Organ Failure Assessment; APACHE: acute physiology and chronic health evaluation; KDIGO: Kidney Disease Improving Global Outcomes; ICU: intensive care unit; eGFR: estimated glomerular filtration rate; ACE: Angiotensin converting enzyme; ARB: Angiotensin II receptor blocker

Table 3: Univariate analysis of factors associated mortality in septic AKI

variables	OR	OR (95%CI)	p value
Male gender	1.352	(0.622, 2.937)	0.447
Age (years)	1.017	(0.990, 1.045)	0.226
Body Mass Index	0.999	(0.918, 1.091)	0.988
Charlson Comorbidity Index	1.214	(0.983, 1.499)	0.072
Smoking	0.687	(0.279, 1.693)	0.415
MAP (mmHg)	0.993	(0.990, 1.025)	0.418
SOFA score	1.151	(1.026, 1.293)	0.017
APACHE II score	1.024	(0.922, 1.033)	0.406
KDIGO stage	1.138	(0.548, 1.408)	0.592
Baseline eGFR (mL/min/1.73m^2)	0.986	(0.975, 0.997)	0.016
Baseline creatinine (mg/dL)	1.417	(0.874, 2.296)	0.158
Hemoglobin (g/dL)	0.935	(0.910, 1.258)	0.414
Hematocrit (%)	0.978	(0.966, 1.823)	0.448
White blood cell (/mm^3)	1.000	(1.000, 1.000)	0.354
Platelet count (/mm^3)	0.980	(0.975, 1.067)	0.382
Lactic acid (mmol/L)	1.094	(1.005, 1.190)	0.038
Hemoglobin A1c (%)	1.017	(0.753, 1.372)	0.913
Total protein (g/dL)	1.022	(0.686, 1.524)	0.914
Albumin (g/dL)	1.054	(0.538, 2.067)	0.878
Total Bilirubin (mg/dL)	1.146	(0.710, 1.072)	0.194
Blood urea nitrogen (mg/dL)	1.002	(0.986, 1.009)	0.678
Creatinine (mg/dL)	1.032	(0.757, 1.240)	0.803

OR：odds ratio; CI: confidence interval; MAP: Mean arterial blood pressure; SOFA: Sepsis-related Organ Failure Assessment; APACHE: acute physiology and chronic health evaluation; KDIGO: Kidney Disease Improving Global Outcomes; eGFR: estimated glomerular filtration rate

Table 4: Multivariate analysis of factors associated mortality in septic AKI

Factors	OR	OR (95%CI)	p value
SOFA score	1.129	(1.003, 1.271)	0.044
Baseline eGFR (mL/min/1.73m^2)	0.983	(0.970, 0.996)	0.011
Lactic acid (mmol/L)	1.110	(1.015, 1.215)	0.022

OR：odds ratio; CI: confidence interval; SOFA: Sepsis-related Organ Failure Assessment; eGFR: estimated glomerular filtration rate