Clinical and Experimental Medicine (2025) 25:192
https://doi.org/10.1007/s10238-025-01681-4

RESEARCH

A study on the factors influencing mortality risk in sepsis-induced acute kidney injury based on analysis of the MIMIC database

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Received: 15 January 2025 / Accepted: 12 April 2025

Abstract
Sepsis-induced acute kidney injury (SA-AKI) significantly increases mortality and healthcare burdens. Identifying key mortality risk factors is crucial for improving patient outcomes. This study aims to identify the primary factors affecting mortality in SA-AKI patients using the MIMIC-III database. A retrospective analysis was conducted on 4868 SA-AKI patients from the MIMIC-III database. Clinical data from the first 24 h of ICU admission were analyzed using logistic regression to identify mortality predictors. Key mortality predictors included advanced age (OR = 1.015, 95% CI: 1.006–1.024), severe AKI stages (OR = 1.470, 95% CI: 1.285–1.676), low serum albumin (OR = 0.606, 95% CI: 0.506–0.722), delayed antibiotics (OR = 1.001, 95% CI: 1.000–1.002), high AST (OR = 1.035, 95% CI: 1.027–1.083), and bilirubin (OR = 1.055, 95% CI: 1.037–1.083). The area under the curve (AUC) of the combined predictors for mortality risk was 0.796, indicating high predictive accuracy. Conclusions: Early intervention and monitoring of identified risk factors such as age, AKI stage, albumin levels, and antibiotic timeliness can enhance survival rates in SA-AKI patients.

Keywords Sepsis · Acute kidney injury · Mortality risk · MIMIC database · Predictive factors

Introduction

Sepsis is a severe clinical condition characterized by an uncontrolled systemic inflammatory response, which can potentially lead to multiple organ dysfunction syndrome (MODS) [1–3]. Among them, sepsis-induced acute kidney injury (SA-AKI), as a common complication of sepsis, significantly increases patient mortality, extends hospital stay, and raises treatment costs [4, 5]. Sepsis has an acute onset and rapid progression, often accompanied by acute kidney injury (AKI). These characteristics increase the difficulty of patient management and elevate the risk of mortality [6, 7].

Recent studies indicate that among deaths in sepsis patients, approximately 15% are acute, occurring early in the disease course and posing an immediate threat to life. In contrast, up to 85% of patients experience late deaths, which are often closely associated with secondary infections acquired in the ICU [4, 8, 9]. This finding further elucidates the complexity of sepsis and its complications, underscoring the urgency of treatment. Despite numerous studies on sepsis and sepsis-induced acute kidney injury (SA-AKI), there are currently no definitive and universally applicable treatment strategies or medications that effectively reduce their mortality and complication rates. Current treatment methods remain largely supportive, including infection source control, timely use of antibiotics, resuscitation, and supportive care for organ dysfunction [10].

Previous studies using the MIMIC-III database have identified key predictors of mortality in sepsis patients, including advanced age, comorbidities, and laboratory markers. For example, Liu et al. conducted a meta-analysis on sepsis-associated AKI, identifying mortality predictors such as serum albumin, BUN, and age [11]. Additionally, Thongprayoon et al. and Bagshaw et al. [12, 13] have underlined the importance of early antibiotic administration in septic patients with AKI and demonstrated how hypoalbuminemia correlates with worse outcomes in critically ill patients undergoing renal replacement therapy. Legrand et al. and Zarbock et al. [14, 15] also emphasized the importance of large-scale databases like MIMIC in exploring heterogeneity and sub-phenotypes in SA-AKI, which may guide

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Published online: 07 June 2025

future precision therapies. However, these studies primarily focused on individual risk factors and did not incorporate multiple clinical and biochemical parameters into a combined predictive model.

In contrast, our study aims to provide a more integrated approach by using a combination of clinical, biochemical, and time-dependent variables to develop a predictive model for mortality risk in SA-AKI patients. While Zhang et al. developed gene-based predictive models for SA-AKI outcomes using MIMIC data [16], and Yang et al. [17] focused on risk prediction in critically ill patients with sepsis-associated AKI, our study is novel in its focus on the timeliness of antibiotic administration, the severity of AKI stages, and albumin levels, combined with other clinical biomarkers. This multifactorial approach provides a more comprehensive understanding of the factors that influence mortality in SA-AKI, offering new insights into potential therapeutic targets.

Over the past decade, numerous methods for predicting acute kidney injury (AKI) have been explored, with the majority of studies focusing on the discovery of novel biomarkers. Many clinical predictive models have been utilized to forecast acute kidney injury associated with surgery [6, 7, 18]. Despite the abundance of the existing literature that focuses on identifying single biomarkers or isolated clinical variables, studies that integrate these factors into a single, robust predictive model are quite limited. Therefore, an in-depth analysis and study of the factors influencing the mortality risk associated with sepsis-induced acute kidney injury (SA-AKI) are of vital practical significance for optimizing treatment plans, improving patient survival rates, and reducing the burden on the healthcare system. This study aims to utilize data from the MIMIC database, employing a retrospective research method to systematically extract clinical information related to sepsis-associated acute kidney injury (SA-AKI), and to reveal the primary factors influencing the mortality risk in SA-AKI patients through statistical analysis. Our study fills this gap by combining multiple important predictive factors and using logistic regression to assess their performance. This high predictive accuracy indicates that our model can serve as an important tool for clinicians to identify high-risk patients, thereby enabling more targeted and timely interventions.

Methods

Database

The data for this study were derived from the Medical Information Mart for Intensive Care (MIMIC-III v1.4) database, a publicly accessible resource supported by the Laboratory of Computational Physiology at the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. The database documents detailed information on patients who received intensive care treatment at Beth Israel Deaconess Medical Center from 2008 to 2019, encompassing data from over 40,000 patients. All data are available to qualified PhysioNet users without special permission. We conducted a detailed retrospective data analysis based on the MIMIC-III database. The use of data in this study was approved by the appropriate Institutional Review Board and followed all applicable ethical standards and data protection regulations.

Patient admission and data extraction

In this analysis, based on the ICD-9 (International Classification of Diseases, Ninth Revision) diagnostic codes of the database, all patients with SA-AKI who met the Kidney Disease: Improving Global Outcomes (KDIGO) creatinine criteria were included. The following were considered diagnostic criteria: an increase in serum creatinine level by more than 0.3 mg/dL within 48 h or an increase to at least 1.5 times the baseline value within the past 7 days. Patients younger than 18 years of age and those with ICU stays less than 48 h were excluded.

Clinical variables and definitions

Several variables were extracted from the database, including patient demographics, vital signs, comorbidities, laboratory indices, scoring systems, and medical interventions. All data were collected within the first 24 h after admission to the intensive care unit (ICU). The average values of laboratory variables within 24 h after ICU admission were used for analysis and included in the predictive model, taking into account that multiple variables were measured more than once. Persistent AKI was defined as lasting longer than 48 h, in accordance with the KDIGO criteria, based on the consensus report of the Acute Dialysis Quality Initiative (ADQI) workgroup [19]. Transient AKI was defined as AKI with a duration of less than 48 h.

Statistical analysis

All statistical analyses were conducted using SPSS software (version 26, IBM Corp., Armonk, NY, USA). Categorical variables are presented as medians (IQR) and categorical variables as frequencies (n) with absolute numbers and percentages (%). The Mann–Whitney U test, Fisher's exact test, or the Chi-square (χ^2) test was used for intergroup comparisons when appropriate. Initially, a univariate analysis was performed on all variables to identify factors with statistically significant effects on mortality.

Subsequently, only variables that showed significant differences between groups were used in the Cox regression. Data were described by OR (odds ratio) and CI (confidence interval) at 95%, with $P < 0.05$ considered to indicate statistical significance. A clinical predictive model for in-hospital mortality of persistent SA-AKI was established using logistic regression. Variables were selected based on both statistical significance in univariate analysis ($P < 0.05$). Multicollinearity among independent variables was assessed using the variance inflation factor (VIF), confirming that all included variables had VIF values below 5, indicating no significant collinearity. Additionally, interaction terms between key predictors (e.g., AKI severity, albumin, and age) were tested but were not statistically significant and were therefore excluded from the final model. Multiple imputation was performed to fill the missing laboratory data using Bayesian methods in SPSS. The predictive performance of the model was evaluated using the C-statistic and the area under the receiver operating characteristic (ROC) curve (AUC).

Result

Baseline characteristics

According to the ICD-9 diagnostic criteria, we identified a total of 7359 patients diagnosed with sepsis among the admitted patients. To ensure the accuracy of the data and the validity of the analysis, we further meticulously screened these patients based on strict exclusion criteria, ultimately excluding 2491 patients. After this series of screening processes, a total of 4868 patients were included in our analysis. Among the 4868 patients with AKI, there were 2875 males (accounting for 61.4%) and 1993 females (accounting for 38.6%), with a male-to-female ratio of 1.44:1. The average follow-up time was 26.84 ± 5.86 days. There were 956 deaths after admission to the ICU. Figure 1 provides a detailed flowchart of the patient selection process.

Comparison of clinical data between the death and survival groups

As shown in Table 1, the proportions of the following variables are higher in the non-survivor group: age, continuous renal replacement therapy (CRRT), time to antibiotic administration post-admission (antibiotics to admit (h)), time to antibiotic administration post-ICU admission (antibiotics to ICU), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, blood urea nitrogen (BUN), creatinine, heart rate (beats per minute, bpm), white blood cell (WBC) count, neutrophil count, monocyte count, mean corpuscular volume (MCV), red cell distribution width (RDW), international normalized ratio (INR), prothrombin time (PT), partial thromboplastin time (PTT), glucose (measured in mmol/L), magnesium (Mg), phosphorus (P), potassium, Sequential Organ Failure Assessment (SOFA) score, duration of dopamine administration (dopamine time, in minutes), amount of dopamine administered (dopamine amount, in mg), duration of norepinephrine administration (norepinephrine time, in minutes), and amount of norepinephrine administered (norepinephrine amount, in mg). In contrast, the proportions of body weight (Weight, in kg), cerebrovascular disease, mild liver disease, myocardial infarction, peripheral vascular disease, congestive heart failure, malignant cancer, acute respiratory distress syndrome

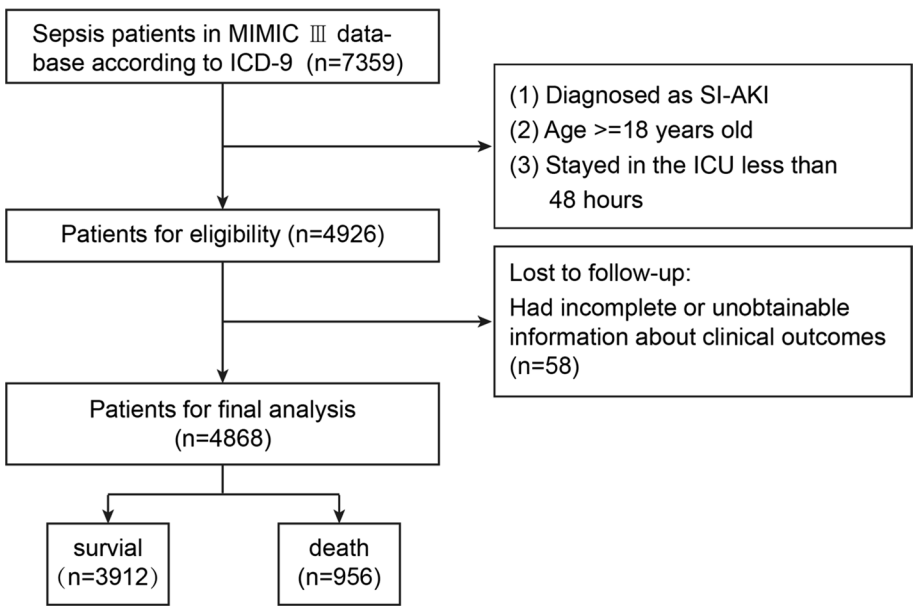


Fig. 1 Patient selection flowchart. MIMIC: medical information mart for intensive care; ICU: intensive care unit; SA-AKI: sepsis-induced acute kidney injury

Table 1 Data comparison between the deceased and surviving groups of patients with acute kidney injury (AKI)

Parameters	Survival group (N = 3912)	Survival group CV	Death group (N = 956)	Death group CV	t/χ2	*P* value
Basic characteristics						
Male/female	2335/1577		540/416		3.26	0.072
Age (year)	61.56 ± 14.90	0.242	65.74 ± 13.36	0.2032	−7.93	**< 0.001**
Weight (kg)	85.91 ± 24.94	0.2189	83.58 ± 28.08	0.336	2.52	0.012
Complications						
AIDS (N = 65)	57 (87.7%)		8 (12.3%)		2.24	0.157
Cerebrovascular Disease (N = 634)	478 (75.4%)		156 (24.6%)		11.40	**0.001**
Dementia (N = 111)	82 (73.9%)		29 (26.1%)		3.03	0.09
Diabetes with Coma (N = 561)	456 (81.3%)		105 (18.7%)		0.341	0.61
Diabetes without Coma (N = 1268)	1027 (81%)		241 (19%)		0.43	0.54
Mild Liver Disease (N = 1036)	754 (72.8%)		282 (27.2%)		47.94	**< 0.001**
Myocardial Infarct (N = 910)	698 (76.7%)		212 (23.3%)		9.50	**0.003**
Peptic Ulcer Disease (N = 152)	120 (78.9%)		32 (21.1%)		0.20	0.678
Peripheral Vascular Disease (N = 569)	424 (74.5%)		145 (25.5%)		13.95	**< 0.001**
COPD (N = 1397)	1108 (79.3%)		289 (20.7%)		1.37	0.248
Congestive Heart Failure (N = 1624)	1260 (77.6%)		364 (22.4%)		11.89	**0.001**
Malignant Cancer (N = 633)	437 (69%)		196 (31%)		59.13	**< 0.001**
Rheumatic Disease (N = 184)	151 (82.1%)		33 (17.9%)		0.352	0.636
Paraplegia (N = 230)	180 (78.3%)		50 (21.7%)		0.68	0.396
ARDS (N = 694)	459 (66.1%)		235 (33.9%)		105.9	**< 0.001**
Peritonitis (N = 57)	39 (68.4%)		18 (31.6%)		5.21	**0.029**
Pneumonia (N = 1148)	857 (74.7%)		291 (25.3%)		31.04	**< 0.001**
Urinary Infection (N = 752)	605 (80.5%)		147 (19.5%)		0.005	1
Mechanical Ventilation (N = 2881)	2230 (77.4%)		651 (22.6%)		39.13	**< 0.001**
CRRT (N = 501)	247 (49.3%)		254 (50.7%)		341.4	**< 0.001**
Use of antibiotics						
Antibiotics to admit (h)	34 (13, 109)		64 (15, 181)		−4.91	**< 0.001**
Antibiotics to culture (h)	24.8 (10.8, 50.5)		29.4 (10, 55.4)		−1.44	0.149
Antibiotics to ICU	15.7 (5.2, 66.5)		33.8 (8, 97)		−6.22	**< 0.001**
Antibiotics to suspect	24.8 (10.8, 50.5)		29.4 (10, 55.4)		−1.44	0.15
Blood and biochemical indicators						
Albumin (g/L)	30.88 ± 6.76	0.1863	27.63 ± 6.76	0.1964	13.32	**< 0.001**
AST	35 (22, 66)		63 (29, 195)		−13.09	**< 0.001**
ALT	26 (16, 54)		38 (19, 128)		−9.50	**< 0.001**
Bilirubin total	10.26 (6.84, 20.52)		18.81 (6.84, 63.27)		−11.39	**< 0.001**
BUN	20 (13, 33)		33 (20, 55)		−15.59	**< 0.001**
Creatinine	79.56 (61.88, 132.6)		132.6 (79.56, 221)		−12.20	**< 0.001**
UO rate 6 h	0.54 (0.4, 2.87)		0.41 (0.2, 0.64)		−15.27	**< 0.001**
SBP (mmHg)	147.08 ± 23.74	0.259	146.04 ± 25.62	0.2963	7.64	**< 0.001**
MBP (mmHg)	76.02 ± 18.58	0.244	74.22 ± 19.19		3.53	**< 0.001**
DBP (mmHg)	46.01 ± 11.17	0.4439	43.08 ± 12.63	0.5	5.16	**< 0.001**
Heart rate (bpm)	88.69 ± 16.52	0.1691	92.51 ± 18.17	0.1776	−6.29	**< 0.001**
WBC	10 (7.2, 13.78)		12.7 (8.8, 18.5)		−12.16	**< 0.001**
Neutrophils count	7.08 (3.07, 11.19)		8.95 (4.09, 11.17)		−7.62	**< 0.001**
Lymphocytes count	1.14 (0.73, 1.76)		0.91 (0.56, 1.43)		−8.89	**< 0.001**
Monocytes count	0.43 (0.18, 0.74)		0.5 (0.19, 0.87)		−3.59	**< 0.001**
Basophils count	0.02 (0, 0.04)		0 (0, 0.03)		−7.74	**< 0.001**
Eosinophils count	0.05 (0, 0.16)		0.01 (0, 0.13)		−8.32	**< 0.001**
RBC	3.33 ± 0.67	0.201	3.19 ± 0.69	0.216	5.89	**< 0.001**

Table 1 (continued)

Parameters	Survival group (N = 3912)	Survival group CV	Death group (N = 956)	Death group CV	t/χ2	*P* value
MCV	91.04 ± 7.05	0.077	92.84 ± 8.23	0.089	−5.46	**< 0.001**
RDW	15.66 ± 2.45	0.157	17.22 ± 3.12	0.181	−16.61	**< 0.001**
PLT	226.50 ± 145.82	0.644	180.11 ± 130.29	0.724	9.0	**< 0.001**
INR	1.43 ± 0.63	0.44	1.83 ± 1.05	0.574	−15.53	**< 0.001**
PT	15.57 ± 6.39	0.404	19.83 ± 10.90	0.55	−15.78	**< 0.001**
PTT	36.28 ± 18.38	0.507	45.78 ± 25.14	0.55	−13.24	**< 0.001**
pH	7.39 ± 0.08	0.011	7.35 ± 0.11	0.015	10.09	**< 0.001**
PO_2	95 (62, 146.75)		88.50 (63, 124)		−3.23	**0.001**
pCO_2	41.50 ± 10.75	0.256	40.84 ± 12.10	0.3	1.66	0.097
Glucose (mmol/L)	7.84 ± 3.48	0.444	8.40 ± 4.20	0.5	−4.21	**< 0.001**
Mg	2.07 ± 0.35	0.164	2.14 ± 0.38	0.178	−5.31	**< 0.001**
P	3.54 ± 1.33	0.379	4.14 ± 1.84	0.444	−11.64	**< 0.001**
Potassium	4.09 ± 0.64	0.155	4.25 ± 0.75	0.177	−6.14	**< 0.001**
Sodium	138.72 ± 5.07	0.037	138.71 ± 6.63	0.048	0.05	0.96
Charlson comorbidity index	6 (3, 8)		5 (3, 7)		−13.12	**< 0.001**
SOFA	2 (0, 4)		3 (1, 6)		−8.18	**< 0.001**
Worsen AKI (N = 901)	667 (74%)		234 (N = 26%)		28.10	**< 0.001**
Vasoactive drug administration						
Dobutamine (N = 203)	114 (56.2%)		89 (43.8%)		78.63	**< 0.001**
Dopamine (N = 293)	184 (62.8%)		109 (37.2%)		60.94	**< 0.001**
Norepinephrine (N = 2116)	1394 (65.9%)		722 (34.1%)		497.45	**< 0.001**
Drug dosage and timing						
Dobutamine time (minute)	2687.5 (696, 5684.75)		1744 (283, 6972)		−0.8	0.423
Dobutamine amount (mg)	731.9 (206.6, 2660.4)		649.9 (86.7, 2483.7)		−1.32	0.187
Dopamine time (minute)	533 (151, 2396, 8)		654 (97.5, 2255)		−0.84	0.402
Dopamine amount (mg)	289.3 (70.9, 1129.3)		400 (55.6, 1210.6)		−0.13	0.899
Norepinephrine time (minute)	1895.5 (660.4114.8)		3750 (1661.5, 7359.5)		−11.7	
Norepinephrine amount (mg)	13.4 (3.8, 37.3)		45.7 (17, 95.7)		−16.05	**< 0.001**

Bold numbers indicate significant *P*-values

Abbreviations: AIDS, Acquired immunodeficiency syndrome; COPD, chronic obstructive pulmonary disease; ARDS, acute respiratory distress syndrome; antibiotics to admit (h), time to antibiotic administration after admission (hours); antibiotics to culture (h), time to antibiotic administration after culture (hours); antibiotics to ICU, time to antibiotic administration after ICU admission; antibiotics to suspect, time to antibiotic administration after suspicion of infection; blood and biochemical indicators, hematological and biochemical parameters; albumin, serum albumin; AST, aspartate transaminase; ALT, alanine transaminase; BUN, blood urea nitrogen; SBP, systolic blood pressure; MBP, mean blood pressure; DBP, diastolic blood pressure; WBC, white blood cell count; RBC, red blood cell count; MCV, mean corpuscular volume; RDW, red cell distribution width; PLT, platelet count; INR, international normalized ratio; PT, prothrombin time; PTT, partial thromboplastin time; PO2, partial pressure of oxygen; pCO2, partial pressure of carbon dioxide; Mg, magnesium; P, phosphate; SOFA, Sequential Organ Failure Assessment (SOFA) score

(ARDS, with a sample size of N = 694), peritonitis, pneumonia, mechanical ventilation, albumin (measured in g/L), urine output rate within 6 h (UO rate 6 h), systolic blood pressure (SBP, in mmHg), mean blood pressure (MBP, in mmHg), diastolic blood pressure (DBP, in mmHg), lymphocyte count, basophil count, eosinophil count, red blood cell (RBC) count, platelet (PLT) count, pH, partial pressure of oxygen (PO2), Charlson comorbidity index, worsening of acute kidney injury (Worsen AKI), and the use of dobutamine, dopamine, and norepinephrine, as well as the duration and amount of dobutamine administered (dobutamine time, dobutamine amount, in mg), are lower in the non-survivor group ($P < 0.05$).

Factors influencing all-cause death and other adverse outcomes

After comparing the clinical data between the mortality and survival groups, Table 1 presents the variables with a *P*-value of less than 0.05, which were included in the univariate Cox regression analysis. The results indicate that age, AKI severity, albumin, delayed antibiotic use, AST,

total bilirubin, blood urea nitrogen (BUN), cerebrovascular disease, eosinophil count, heart rate at maximum diastolic pressure, hemoglobin, lactate, malignancy, MCHC, metastatic solid tumors, magnesium, pH, platelets, PTT, RDW, SOFA score, white blood cell count, body weight, diabetes, and AKI progression were identified as independent risk factors for 28-day all-cause mortality in AKI patients ($P < 0.05$, Table 2).

Through Cox regression analysis, we identified several variables as significant predictors of mortality risk. Specifically, age was a significant risk factor (B = 0.015, $P = 0.001$), with each additional year increasing the mortality risk by 1.5% (HR = 1.015). This finding aligns with previous studies indicating that elderly patients have poorer prognoses in sepsis-associated acute kidney injury (SA-AKI). Similarly, the severity of AKI was also a critical predictor, particularly when AKI progressed to stage 2, where the mortality risk was 28.6% higher compared to patients without progression (B = 0.384, $P < 0.001$; HR = 1.470). These results highlight the strong association between AKI progression and mortality risk, emphasizing the necessity of early monitoring and intervention.

Low albumin levels (B = −0.503, $P = 0.001$) were identified as a strong predictor of mortality risk, suggesting that hypoalbuminemia may reflect malnutrition or a systemic inflammatory response, thereby exacerbating SA-AKI severity and increasing mortality risk (HR = 0.606). Additionally, the timeliness of antibiotic treatment was also a crucial factor influencing mortality risk. Delayed antibiotic administration significantly increased mortality risk (B = 0.001, $P = 0.001$), with each one-hour delay in antibiotic administration leading to a 0.1% increase in mortality risk. This finding underscores the importance of timely antibiotic use in infection control. Elevated total bilirubin levels (B = 0.053, $P < 0.001$; HR = 1.055) were associated with an increased risk of mortality, indicating that liver dysfunction plays a critical role in the mortality risk of SA-AKI patients. Conversely, higher albumin levels

Table 2 Univariate Cox regression analysis of independent risk factors for 28-day all-cause mortality

Parameters	B	SE	Wald	*P* value	95% CI	
					Lower limit	Upper limit
Age	0.021	0.002	70.654	**< 0.001**	1.016	1.026
AKI stage 2 day	0.596	0.094	39.741	**< 0.001**	1.507	2.183
Albumin	−0.311	0.051	36.513	**< 0.001**	0.663	0.811
AST	0	0	345.38	**< 0.001**	1	1
Bilirubin total	0.045	0.005	93.143	**< 0.001**	1.037	1.056
BUN	0.011	0.001	113.75	**< 0.001**	1.009	1.013
Cerebrovascular *Disease*	0.072	0.088	0.683	0.409	0.905	1.277
Eosinophils abs	−0.539	0.155	12.163	**< 0.001**	0.431	0.790
Heart rate time dbp *Max*	0.004	0.001	9.909	**.002**	1.002	1.007
Hemoglobin	0.007	0.018	0.160	0.689	0.973	1.043
LAC	0.181	0.009	412.39	**< 0.001**	1.177	1.219
Malignant cancer	0.514	0.080	41.188	**< 0.001**	1.429	1.957
MCHC	−0.035	0.019	0.304	1.003	0.929	0.069
Metastatic solid tumor	1.023	0.097	112.14	**< 0.001**	2.302	3.363
Mg	0.364	0.086	17.691	**< 0.001**	1.214	1.704
pH	−4.788	0.316	229.86	**< 0.001**	0.004	0.015
Platelet	−0.003	0.000	125.93	**< 0.001**	0.996	0.997
PTT	0.012	0.001	111.49	**< 0.001**	1.01	1.014
RDW	0.098	0.010	99.728	**< 0.001**	1.082	1.125
SOFA 24 h	0.059	0.010	32.32	**< 0.001**	1.039	1.081
WBC	0.013	0.001	76.732	**< 0.001**	1.01	1.016
Weight	−0.004	0.001	10.806	**< 0.001**	0.993	0.998
Worsen AKI	0.046	0.076	0.368	0.544	0.903	1.214

The bold numbers represent the *P* values with significant differences

Abbreviations: 95% CI, 95% confidence interval; AKI, acute kidney injury; B, regression coefficient; BE, standard error; albumin, serum albumin; AST, aspartate aminotransferase; BUN, blood urea nitrogen; heart rate time dbp max, heart rate at maximum diastolic blood pressure hemoglobin; LAC, lactate; MCHC, mean corpuscular hemoglobin concentration; Mg, magnesium; PTT, prothrombin time; RDW, red cell distribution width; SOFA 24 h, Sequential Organ Failure Assessment (SOFA) score at 24 h; WBC, white blood cell (WBC) count; Worsen AKI, worsening acute kidney injury

(B = −0.503, $P = 0.001$) were identified as a protective factor, suggesting that improving patients' nutritional status may help reduce mortality risk.

Table 2 presents the results of the univariate Cox regression analysis, further confirming the impact of these factors on 28-day all-cause mortality. Table 3 displays the results of the

Cox regression analysis after adjusting for multiple variables demonstrates that these factors remain significant predictors of mortality risk despite the influence of other variables.

In summary, age, AKI severity, low albumin levels, delayed antibiotic administration, total bilirubin, BUN, and liver dysfunction are independent risk factors influencing 28-day all-cause mortality in SA-AKI patients.

ROC curve analysis of univariate and combined variables for predicting mortality risk

In the univariate ROC curve analysis, the area under the curve (AUC) for several indicators demonstrated their effectiveness in predicting the risk of death. Notably, the AUC values for AKI stage 2 day, aspartate aminotransferase (AST), total bilirubin (bilirubin total), blood urea nitrogen (BUN), partial thromboplastin time (PTT), red cell distribution width (RDW), and white blood cell count (WBC) were relatively high (Fig. 2), indicating that these indicators possess a good discriminatory power in predicting the risk of mortality.

The area under the curve (AUC) for each variable is as follows: age: AUC = 0.573, AKI stage 2 day: AUC = 0.665, albumin: AUC = 0.358, antibiotic to admit time: AUC = 0.560, AST: AUC = 0.650, bilirubin total: AUC = 0.623, BUN: AUC = 0.674, cerebrovascular disease: AUC = 0.514, eosinophils abs: AUC = 0.398, heart

Table 3 Multivariate Cox regression analysis of independent risk factors for 28-day all-cause mortality

Parameters	B	SE	Wald	*P* value	95% CI	
					Lower limit	Upper limit
Age	0.015	0.004	11.349	**0.001**	1.006	1.024
AKI stage 2 day	0.384	0.068	32.068	**< 0.001**	1.285	1.676
albumin	−0.503	0.090	30.964	**0.001**	0.506	0.722
AST	0.000	0.000	6.710	**0.010**	1.000	1.000
Bilirubin total	0.053	0.014	15.413	**< 0.001**	1.027	1.083
BUN	0.016	0.002	41.806	**< 0.001**	1.011	1.021
Cerebrovascular disease	0.651	0.167	15.222	**< 0.001**	1.383	2.659
Eosinophils abs	−0.567	0.231	6.006	**0.014**	0.360	0.893
Heart rate time dbp max	0.000	0.000	9.264	**0.002**	1.000	1.000
hemoglobin	0.076	0.033	5.277	**0.022**	1.011	1.152
LAC	0.189	0.029	41.418	**< 0.001**	1.141	1.280
Malignant cancer	0.385	0.181	4.539	**0.033**	1.031	2.095
MCHC	−0.129	0.039	10.906	**0.001**	0.814	0.949
Metastatic solid tumor	0.896	0.234	14.705	**< 0.001**	1.550	3.872
Mg	0.332	0.163	4.145	**0.042**	1.012	1.919
pH	−3.391	0.630	28.967	**< 0.001**	0.010	0.116
Platelet	−0.003	0.000	32.218	**< 0.001**	0.996	0.998
PTT	0.010	0.003	15.811	**< 0.001**	1.005	1.015
RDW	0.070	0.024	8.569	**0.003**	1.023	1.124
SOFA 24 h	−0.041	0.021	3.973	**0.046**	0.922	0.999
WBC	0.038	0.007	26.756	**< 0.001**	1.024	1.054
Weight	−0.008	0.002	11.173	**0.001**	0.988	0.997
Worsen AKI	0.687	0.159	18.687	**< 0.001**	1.455	2.713

The bold numbers represent the *P* values with significant differences

Abbreviations: 95% CI, 95% confidence interval; AKI, acute kidney injury; B, regression coefficient; BE, standard error; albumin, serum albumin; AST, aspartate aminotransferase; BUN, blood urea nitrogen; heart rate time dbp max, heart rate at maximum diastolic blood pressure hemoglobin; LAC, lactate; mean corpuscular hemoglobin concentration; Mg, magnesium; PTT, prothrombin time; RDW, red cell distribution width; SOFA 24 h, Sequential Organ Failure Assessment (SOFA) score at 24 h; WBC, white blood cell (WBC) count; Worsen AKI, worsening acute kidney injury

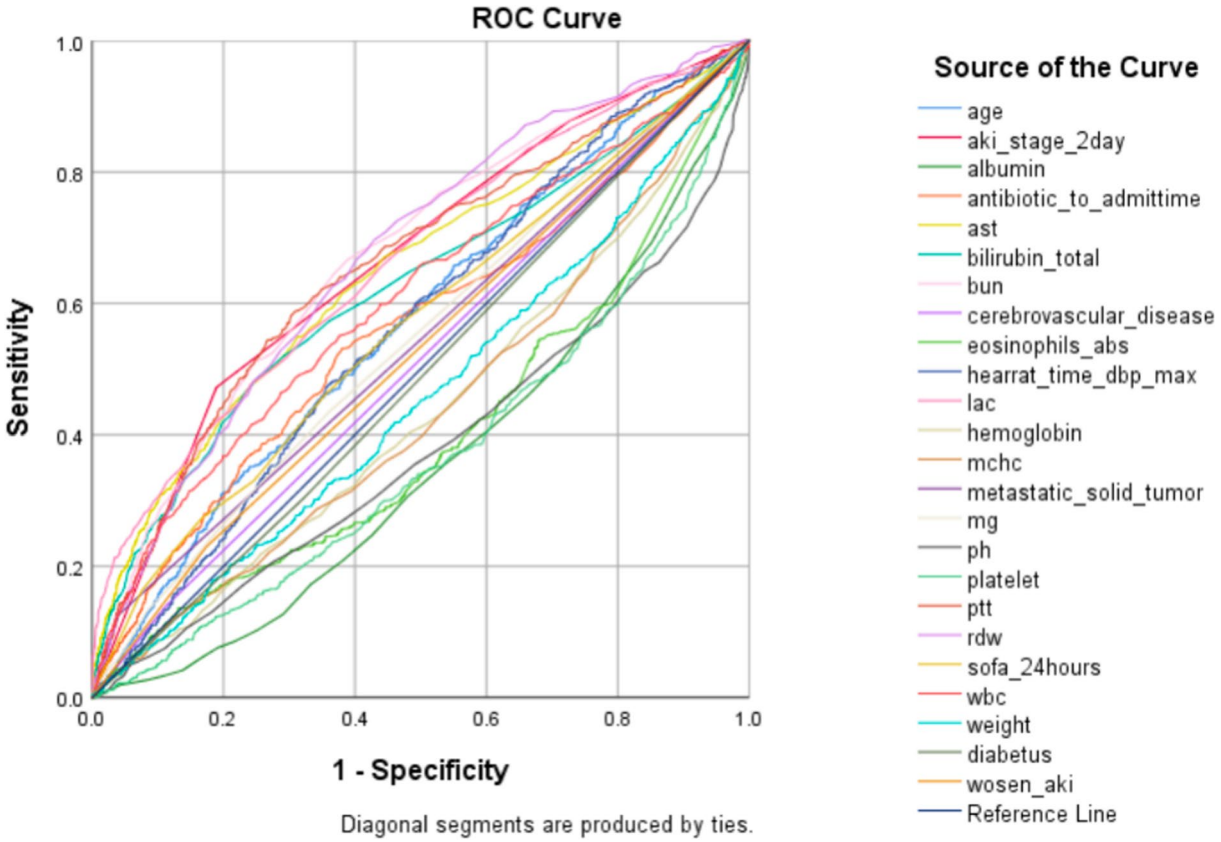


Fig. 2 ROC curves for univariate predictors of mortality in SA-AKI patients. This figure illustrates the predictive performance of individual clinical variables for mortality risk. Higher AUC values indicate stronger predictive power

rate time at DBP max: AUC = 0.566, LAC: AUC = 0.665, hemoglobin: AUC = 0.435, MCHC: AUC = 0.437, metastatic solid tumor: AUC = 0.543, Mg: AUC = 0.546, pH: AUC = 0.380, platelet: AUC = 0.370, PTT: AUC = 0.658, RDW: AUC = 0.673, SOFA 24 h: AUC = 0.565, WBC: AUC = 0.606, Weight: AUC = 0.457, diabetes: AUC = 0.491, Worsen AKI: AUC = 0.528

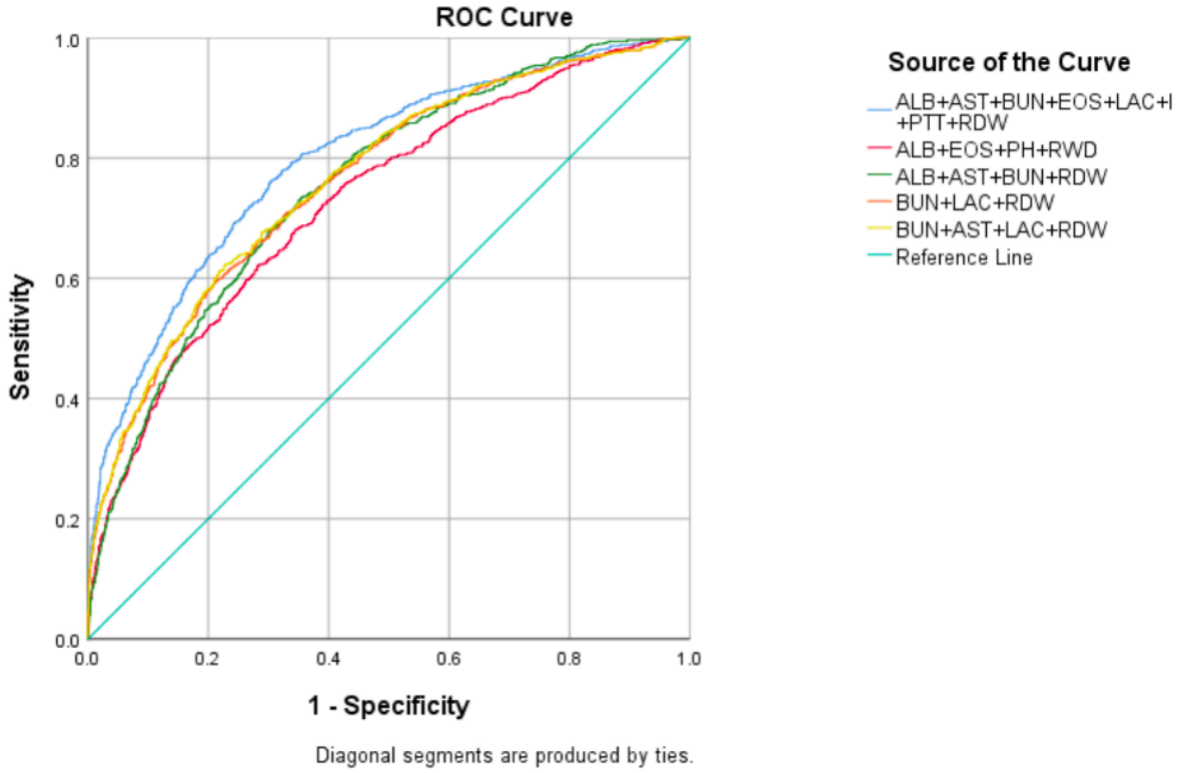
Multivariate Cox regression analysis showed that when using combined indicators such as ALB (albumin), AST (aspartate aminotransferase), BUN (blood urea nitrogen), EOS (absolute eosinophil count), LAC (lactate), pH (pH value), PTT (prothrombin time), and RDW (red cell distribution width), the AUC value reached 0.796 (Fig. 3), indicating that these combined indicators have a high accuracy in predicting the risk of mortality.

Discussion

This study offers a comprehensive examination of the factors influencing mortality risk in patients with SA-AKI using data from the MIMIC-III database. Our findings underscore the complex nature of managing SA-AKI and highlight critical predictors of mortality that can guide clinical practice.

Using univariate and multivariate Cox regression analyses, we assessed the impact of these factors in both unadjusted and adjusted models. Our findings indicate that variables such as age, severity of AKI, albumin levels, timeliness of antibiotic use, total bilirubin, BUN, cerebrovascular disease, eosinophil count, heart rate variability at maximum diastolic pressure, and malignancy are independent risk factors for mortality. Consistent with existing studies, age and AKI progression were confirmed as significant predictors of mortality risk. In the multivariate analysis, after adjusting for potential confounders such as age and sex, the impact of these variables on mortality risk remained significant, highlighting their critical implications for clinical management.

Specifically, age was identified as a significant risk factor, indicating that the risk of mortality increases significantly with advancing patient age. Advanced age emerged as a prominent risk factor, consistent with prior studies that identify age as a critical determinant in sepsis outcomes [17, 20, 21]. The severity of AKI, particularly when it progresses to stage 2, is closely associated with



Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
ALB+AST+BUN+EOS+LAC+PH+PTT+RDW	.796	.010	.000	.777	.816
ALB+EOS+PH+RWD	.730	.011	.000	.709	.752
ALB+AST+BUN+RDW	.755	.010	.000	.735	.775
BUN+LAC+RDW	.762	.011	.000	.742	.783
BUN+AST+LAC+RDW	.765	.011	.000	.744	.786

Fig. 3 ROC curve analysis of multiple clinical indicators (ALB, AST, BUN, etc.) selected by multivariate Cox regression for predicting SA-AKI patient mortality risk. AUC for combined indicators is 0.796, showing high prediction accuracy

an increased risk of mortality. This finding underscores the importance of early diagnosis and intervention, especially in high-risk AKI patients [22, 23]. Additionally, the presence of low albumin levels is recognized as a significant predictor of mortality. Low serum albumin levels indicated poor nutritional status and severe systemic inflammation [24, 25]. Our analysis further demonstrated that delayed antibiotic use significantly increases the risk of mortality, highlighting the critical importance of timely antibiotic administration in controlling infections. Elevated AST and bilirubin levels were indicative of underlying liver dysfunction and systemic severity, contributing to higher mortality risk [26–28].

Notably, elevated total bilirubin was significantly associated with an increased risk of mortality in our analysis, indicating a close relationship between impaired liver function and the severity of systemic infection, which may exacerbate the condition of septic patients. Therefore, monitoring and managing liver function abnormalities are crucial for improving patient survival [29, 30]. Additionally, the presence of cerebrovascular disease and malignancies was associated with increased mortality, highlighting

the need for tailored care strategies for patients with complex medical histories [31]. Additionally, we identified novel influencing factors, such as eosinophil count and malignancy, both of which demonstrated strong predictive power in the multivariate regression analysis, providing new directions for future research. A decrease in eosinophil count was associated with a higher risk of mortality, suggesting potential immune dysfunction, particularly in septic patients. Malignancy, as a known comorbidity, may contribute to increased mortality risk through mechanisms related to immune suppression. Special attention should be given to patients with comorbid conditions like cerebrovascular diseases and malignancies, to develop effective care strategies that address their higher-risk profiles [32, 33].

Our ROC curve analysis further supports the above conclusions. In the univariate analysis, several variables, such as age, AKI stage, AST, BUN, and total bilirubin, exhibited high AUC values, demonstrating their strong discriminatory ability in predicting mortality risk. In the multivariate Cox regression analysis, after incorporating multiple clinical indicators, including albumin, AST, BUN, eosinophils, lactate, pH, PTT, and RDW, the AUC value reached 0.796, indicating a high level of accuracy in predicting mortality risk using these combined indicators.

These findings have significant implications for clinical practice. The study results indicate that delayed antibiotic administration significantly increases the risk of mortality (OR = 1.001, 95% CI: 1.000–1.002). Therefore, clinical practice should adhere to the "golden hour" principle, ensuring that empirical antibiotic therapy is initiated as early as possible when infection is suspected to reduce mortality rates. Low serum albumin levels (OR = 0.606, 95% CI: 0.506–0.722) were identified as an independent risk factor for mortality. Hypoalbuminemia may reflect a systemic inflammatory response and malnutrition. Hence, albumin supplementation should be considered in SA-AKI patients with low albumin levels to improve fluid management and microcirculatory perfusion. Elevated AST (OR = 1.035, 95% CI: 1.027–1.083) and total bilirubin (OR = 1.055, 95% CI: 1.037–1.083) suggest that liver dysfunction is relatively common in SA-AKI patients and may be associated with systemic inflammatory response syndrome (SIRS). Clinically, liver function monitoring should be enhanced, and, if necessary, adjustments to antibiotic, sedative, or nephrotoxic drug dosages should be made to reduce the risk of liver damage. Abnormal magnesium levels (OR = 1.012, 95% CI: 1.002–1.919) and pH values (OR = 0.010, 95% CI: 0.010–0.116) were associated with increased mortality. Therefore, we recommend continuous monitoring of SA-AKI patients and proactive correction of electrolyte imbalances to reduce the incidence of arrhythmias and multiple organ dysfunction syndrome (MODS). Age (OR = 1.015, 95% CI: 1.006–1.024), AKI severity (OR = 1.470, 95% CI: 1.285–1.676), and malignancy (OR = 1.550, 95% CI: 1.031–2.095) were also identified as independent predictors of mortality. Based on these findings, we suggest incorporating these indicators into ICU risk assessment models to identify high-risk patients in advance and develop enhanced treatment strategies, such as close monitoring of fluid balance, early initiation of renal replacement therapy (RRT), or more aggressive anti-infection protocols.

Despite the strengths of this study, there are some limitations associated with the use of the MIMIC-III database that should be acknowledged. First, MIMIC-III is a single-center database, which may limit the generalizability of the findings to broader populations or healthcare settings. Second, the retrospective nature of the database makes it susceptible to information bias, missing data, and unmeasured confounders. Third, the database focuses primarily on ICU patients, which may not fully reflect the characteristics of sepsis or AKI cases in non-ICU settings. Lastly, certain relevant clinical variables—such as fluid management strategies, antimicrobial stewardship interventions, and pre-hospital care data—are either not available or not standardized in the database, which may influence outcome interpretation.

Nonetheless, despite these limitations, our findings provide valuable insights for the early identification of high-risk SA-AKI patients and offer a foundation for optimizing clinical treatment strategies. In the future, these key predictive factors could be integrated into an artificial intelligence-driven clinical decision support system (CDSS) to assist ICU physicians in making more precise and individualized treatment decisions.

Conclusion

In this study, we identified critical factors influencing mortality in patients with sepsis-induced acute kidney injury (SA-AKI) using the MIMIC-III database. The primary findings of our research, including advanced age, severity of AKI, hypoalbuminemia, delayed antibiotic administration, and elevated AST and bilirubin levels, offer substantial insights into the clinical management of these patients.

Our findings have significant implications for clinical practice. The study highlights the importance of early and timely interventions, particularly regarding antibiotic administration, which is shown to reduce mortality risk. The relationship between hypoalbuminemia and increased mortality underscores the need for nutritional support and monitoring of serum albumin levels in critically ill patients. Moreover, the identification of AKI stage severity as a strong predictor of mortality emphasizes the need for early detection and intervention in patients showing signs of progression. These insights could inform more

personalized care strategies, helping clinicians prioritize high-risk patients and adjust therapeutic approaches accordingly. Additionally, our findings suggest that liver dysfunction, indicated by elevated AST and bilirubin levels, plays a critical role in mortality among SA-AKI patients. This highlights the necessity for clinicians to monitor liver function closely, especially in critically ill patients with multiple organ dysfunctions.

This study reinforces the multifactorial nature of SA-AKI and mortality. While the existing literature has identified certain risk factors, the integration of these variables into predictive models with strong discriminative ability (AUC = 0.796) offers a promising approach for future clinical trials and decision-making support tools. By recognizing the combined predictive value of variables such as albumin, AST, and BUN, future studies can refine these findings further, possibly incorporating novel biomarkers for more accurate risk prediction.

Despite these contributions, there are several limitations in this study. Firstly, the retrospective design limits our ability to establish causal relationships. Furthermore, the use of a single-center dataset may reduce the generalizability of the findings, as patients in different settings or regions may present with distinct characteristics. Additionally, the study's reliance on the MIMIC-III database, while comprehensive, may not capture all variables relevant to patient outcomes, such as those related to patient care practices outside the ICU.

Future research should focus on validating these findings in multicenter and prospective studies to improve generalizability. Moreover, incorporating more granular data on treatment protocols, such as the use of novel sepsis therapies or advanced monitoring techniques, could provide further insights into the management of SA-AKI. It would also be valuable to explore the role of immune responses in SA-AKI progression and mortality, particularly in relation to eosinophil counts and other immune markers identified in our study. Additionally, future studies should examine the potential for machine learning algorithms to incorporate these predictors into real-time clinical decision support systems, thereby optimizing patient care.

Acknowledgements We are grateful to everyone who participated in or contributed to this research endeavor.

Author contributions Chongyang Ye and Tianjun Yang designed the study and revised the paper. Chunyan Zhu, Chongyang Ye and Shijing Hu wrote the manuscript.

Funding The work was not funded by any funding.

Data availability No datasets were generated or analyzed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

Ethics approval The data featured in this study were sourced from the MIMIC-III database, which is publicly accessible online. Before their involvement in the research, all participants had provided their consent in written form.

Patient consent for publication Not required

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