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Early Identification and Risk Factors for Acute Kidney Injury Progression: A Real-World Study

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Purpose: Acute kidney injury (AKI) is a serious complication in critically ill patients, associated with increased mortality and healthcare burden. Early identification of patients at high risk for disease progression is crucial for timely intervention and improved outcomes. To identify the risk factors for the progression of AKI in critically ill patients.

Patients and Methods: A single-center, retrospective study was conducted involving 341 adult patients diagnosed with AKI stage 1 or 2 according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Univariate and multivariate logistic regression analyses were used to identify independent risk factors for AKI progression. Subgroup analyses were performed based on the initial AKI stage.

Results: Among the 341 enrolled patients, 156 (45.7%) experienced AKI progression. Multivariate analysis identified the following independent risk factors: ischemic heart disease (adjusted Odds Ratio [aOR] = 2.994), sepsis (aOR = 2.644), lower minimum Mean Arterial Pressure (MAP) (aOR = 0.954), higher neutrophil percentage (aOR = 1.029), lower PaO_2/FiO_2 ratio (aOR = 0.997), elevated D-dimer (aOR = 1.097), and increased anion gap (aOR = 1.163). Subgroup analysis revealed that risk factors differed between patients with initial AKI stage 1 and stage 2.

Conclusion: This study identified multiple routinely available clinical factors independently associated with AKI progression. These findings support early risk stratification and targeted interventions—such as infection control, hemodynamic support, and correction of hypoxia and acidosis—to prevent the worsening of AKI and improve patient outcomes.

Keywords: acute kidney injury, disease progression, risk factors, critical illness, logistic models, retrospective studies

Introduction

Acute Kidney Injury (AKI) is a highly prevalent critical condition, affecting approximately 10–15% of hospitalized patients and over 50% of those admitted to the Intensive Care Unit (ICU).[1] The occurrence of AKI significantly impacts patient outcomes, with an associated mortality rate of approximately 24% in adults and 14% in children. In critically ill patients, AKI not only increases in-hospital mortality but also prolongs hospital stays, raises healthcare costs, and is associated with an elevated long-term risk of developing chronic kidney disease and requiring dialysis.[2] AKI can result from various causes, with infections and hypovolemic shock being the most common contributors.[3] Other significant etiologies include drug-induced nephrotoxicity, obstructive uropathy, thrombosis, among others. AKI is characterized by a rapid decline in renal function over a short period, leading to the accumulation of metabolic waste products, as well as disturbances in fluid, electrolyte, and acid-base balance.[4] The diagnostic criteria for AKI have undergone several revisions, and the currently widely accepted standard is based on the 2012 clinical practice guidelines issued by Kidney Disease: Improving Global Outcomes (KDIGO).[5] These guidelines utilize urine output and serum creatinine (SCr) levels as key diagnostic parameters and classify AKI into three stages.

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Research confirms that both the severity and duration of AKI are critical determinants of prognosis: the more severe the injury and the longer its persistence, the poorer the recovery of kidney function and patient survival.[6] Therefore, early intervention to prevent AKI progression is critical, and the early identification of high-risk patients followed by preventive measures can improve outcomes.[7] However, a significant knowledge gap persists. Previous research has predominantly focused on predicting the onset of AKI[8] and the progression from AKI to chronic kidney disease (CKD),[9] while the progression from mild to severe stages of AKI itself has received considerably less attention. This gap is clinically vital, as persistent or worsening AKI is independently associated with substantially increased mortality and healthcare burden.[6,10] In recent years, biomarkers such as urinary C-C motif chemokine ligand 14 (CCL14), Neutrophil Gelatinase-Associated Lipocalin (NGAL), and plasma Cystatin C have been applied to predict AKI progression.[10] Although they demonstrate good predictive performance, their high cost and practical challenges hinder widespread clinical adoption.Therefore, identifying readily available and modifiable risk factors for AKI progression using real-world clinical data is crucial. This approach is grounded in the multifactorial pathophysiology of AKI progression, which involves inflammation, hemodynamic instability, and metabolic disturbances.[11] It not only enables early prediction but also directly points to actionable therapeutic targets (eg, managing sepsis, supporting blood pressure, correcting acidosis). With the development of electronic medical records, the analysis of large-scale clinical data makes this goal achievable.

Therefore, this study aims to identify the risk factors for AKI progression by analyzing real-world clinical data, with the goal of early identification of high-risk patients to inform clinical interventions for improving prognosis.

Materials and Methods

Study Population

This single-center, retrospective study involved a comprehensive review of electronic medical records and nursing documentation systems. Patients diagnosed with AKI and admitted to the ICU of the Fourth Hospital of Hebei Medical University between January 2023 and December 2024 were included. A structured electronic database was constructed to systematically collect clinical data from the enrolled patients. This study was approved by the Ethics Committee of the Fourth Hospital of Hebei Medical University (Ethics Approval No. 2024KS188). AKI was diagnosed and staged in accordance with the KDIGO criteria. The diagnosis required the fulfillment of at least one of the following criteria: a rise in SCr by ≥26.5 μmol/L within 48 hours, an increase in SCr to ≥1.5 times the baseline value within 7 days, or a urine output of less than 0.5 mL/kg/h for 6 hours. Subsequently, AKI was staged as follows: Stage 1 was defined as an SCr level 1.5–1.9 times baseline or an absolute increase of ≥26.5 μmol/L, or urine output <0.5 mL/kg/h for 6–12 hours; Stage 2 was defined as SCr 2.0–2.9 times baseline or urine output <0.5 mL/kg/h for 12 hours or longer; and Stage 3 was characterized by SCr increasing to 3.0 times baseline, an absolute SCr level reaching ≥353.6 μmol/L, the initiation of renal replacement therapy, or urine output dropping below 0.3 mL/kg/h for 24 hours or more.

This study enrolled patients initially diagnosed with AKI at Stage 1 or Stage 2 according to the KDIGO criteria. The exclusion criteria were as follows: (1) age under 18 years; (2) pregnancy; (3) length of ICU stay less than or equal to 24 hours; (4) pre-existing chronic kidney disease (CKD); and (5) incomplete clinical data or loss to follow-up.

Data Collection

This retrospective cohort study consecutively enrolled adult patients with a confirmed diagnosis of AKI. Data collection was performed on the day of AKI diagnosis and included the following domains: (a) patient demographics (sex, age, body mass index [BMI]); (b) comorbidities (hypertension, diabetes mellitus, ischemic heart disease); (c) AKI-specific parameters (initial and maximum AKI stage, and receipt of continuous renal replacement therapy [CRRT]); (d) illness severity (presence of sepsis or multiple organ dysfunction syndrome [MODS], and use of mechanical ventilation or vasopressors); (e) vital signs (maximum and minimum values for mean arterial pressure [MAP], temperature, respiratory rate [RR], and heart rate [HR]); (f) laboratory parameters, including complete blood count, arterial blood gas analysis, coagulation profile, serum electrolytes, markers of liver and renal function, and other metabolic measures; and (g) medication use (diuretics, contrast media, calcium channel blockers [CCBs], and angiotensin-converting enzyme

inhibitors or angiotensin II receptor blockers [ACEIs/ARBs]). All variables were included in the subsequent analysis to examine their association with patient outcomes.

Definitions and End Points

The primary outcome of this study was the progression of AKI, defined as the advancement from AKI stage 1 or 2 to a more severe stage. The secondary outcome was ICU mortality.

Statistical Analysis

Statistical analyses were performed using R software (version 4.5.1). Continuous variables are presented as medians with interquartile ranges (IQRs) and were compared using the Mann–Whitney *U*-test. Categorical variables are expressed as percentages (%) and were compared using the Chi-square test or Fisher's exact test, as appropriate. To identify independent risk factors for AKI progression, a two-step logistic regression approach was employed. First, univariate analyses were conducted for each candidate predictor variable. Variables with a significance level of $P < 0.1$ in the univariate analysis were included in the multivariable logistic regression model to adjust for potential confounders. The results are presented as adjusted odds ratios (ORs) with corresponding 95% confidence intervals (CIs). A two-sided P value < 0.05 was considered statistically significant. The final results of the multivariable analysis are visualized in a forest plot.

Subgroup Analysis

We conducted subgroup analyses stratified by the initial AKI stage (stage 1 or stage 2). A comparative analysis was performed to investigate the differences in adverse outcomes between these two patient groups.

Results

After screening 473 patients with AKI, 132 were excluded based on the criteria, leaving 341 patients for the final analysis. Among them, 156 (45.7%) experienced AKI progression, while 185 (54.3%) did not. The patient enrollment flowchart is presented in Figure 1.

Baseline Characteristics

The baseline characteristics of the 341 enrolled patients, stratified by AKI progression, are summarized in Table 1. Of these, 156 (45.7%) experienced disease progression. The two groups were comparable in terms of sex, age, and comorbidities like hypertension and diabetes (all $p > 0.05$). However, significant differences were observed in several key parameters. Patients with progressive AKI had a significantly higher ICU mortality rate (19.9% vs 2.2%, $p < 0.001$) and a greater prevalence of sepsis (60.9% vs 33.5%, $p < 0.001$). Hemodynamically, the progression group exhibited lower minimum MAP (69.80 vs 76.00 mmHg, $p < 0.001$) and higher maximum HR (114.5 vs 107/min, $p = 0.012$). Critical laboratory findings revealed significantly impaired oxygenation (PaO_2/FiO_2 ratio: 189.00 vs 268.70, $p < 0.001$), higher acidosis (pH: 7.37 vs 7.39, $p < 0.001$), elevated lactate (2.10 vs 1.60 mmol/L, $p = 0.005$), and increased inflammatory markers such as neutrophil percentage (89.45% vs 87.50%, $p = 0.002$). Furthermore, the progression group required more frequent mechanical ventilation (86.5% vs 76.8%, $p = 0.03$) and vasopressor support (78.8% vs 55.1%, $p < 0.001$).

Univariate and Multivariate Logistic Regression for the Primary Outcome (AKI Progression)

To identify independent risk factors for AKI progression, univariate logistic regression analyses were first performed (Table 2). Multiple variables were significantly associated with AKI progression ($P < 0.1$), including BMI, ischemic heart disease, sepsis, MODS, maximum and minimum MAP, maximum RR, maximum HR, RDW, maximum WBC count, neutrophil percentage, PaO_2/FiO_2 ratio, pH, lactate, FiO_2, $AaDO_2$, $PaCO_2$, D-dimer, PT, APTT, anion gap, ALT, AST, total bilirubin, phosphate, magnesium, use of mechanical ventilation, and use of vasopressors.

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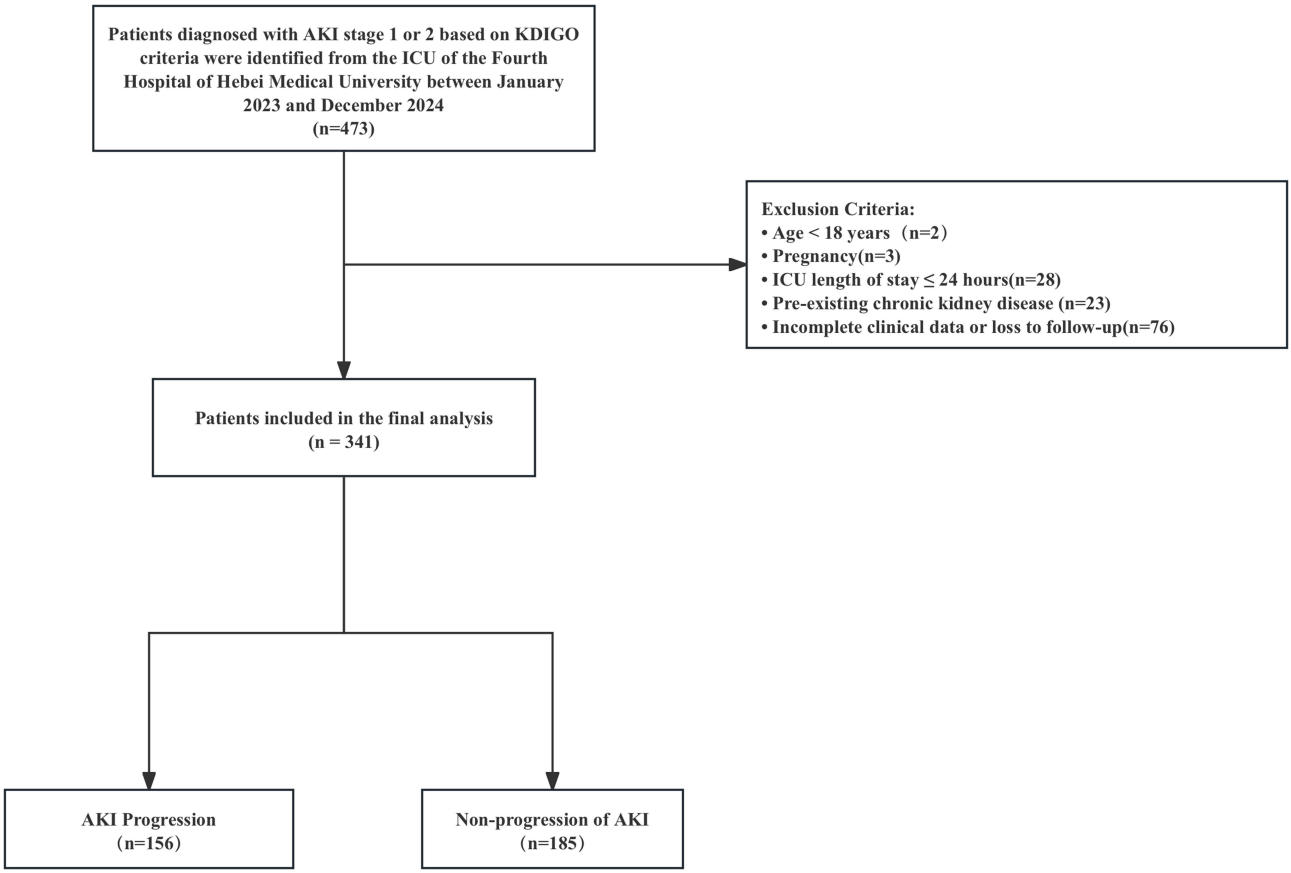

Figure 1 Study protocol flowchart.
Abbreviations: AKI, Acute Kidney Injury; ICU, intensive care unit; KDIGO, Kidney Disease Improving Global Outcomes.

Variables with a P value < 0.1 in the univariate analysis were entered into a multivariate logistic regression model. This analysis identified the following factors as independent predictors of AKI progression: ischemic heart disease (adjusted OR = 2.994, 95% CI: 1.460–6.240; P < 0.01), sepsis (adjusted OR = 2.644, 95% CI: 1.514–4.681; P < 0.01), minimum MAP (adjusted OR = 0.954, 95% CI: 0.927–0.980; P < 0.01), neutrophil percentage (adjusted OR = 1.029, 95% CI: 1.001–1.060; P = 0.049), PaO_2/FiO_2 ratio (adjusted OR = 0.997, 95% CI: 0.994–0.999; P = 0.021), D-dimer (adjusted OR = 1.097, 95% CI: 1.027–1.195; P = 0.015), and anion gap (adjusted OR = 1.163, 95% CI: 1.074–1.266; P < 0.01). BMI showed a trend towards significance but did not reach the statistical threshold (adjusted OR = 0.917, 95% CI: 0.836–1.002; P = 0.059). The results of the multivariate analysis are visually summarized in a forest plot (Figure 2).

Table 1 Baseline Characteristics of Patients Stratified by AKI Progression

Variables	Non-Progression (N=185)	Progression (N=156)	*p* value
Demographics			
Male, n (%)	62 (33.5)	45 (28.8)	0.419
Age, years	67.00 (58.00, 74.00)	68.00 (58.00, 75.00)	0.394
BMI, kg/m^2	24.82 (22.86, 26.99)	23.88 (22.07, 25.68)	0.015
Clinical Outcomes			
ICU Mortality, n (%)	4 (2.2)	31 (19.9)	<0.001
Clinical Characteristics			
MAP_Max, mmHg	102.00 (93.00, 109.00)	96.00 (88.65, 108.00)	0.006

(*Continued*)

Table 1 (Continued).

Variables	Non-Progression (N=185)	Progression (N=156)	*p* value
MAP_Min, mmHg	76.00 (67.00, 83.00)	69.80 (62.00, 78.00)	<0.001
Maximum Temperature, °C	37.40 (36.70, 38.00)	37.50 (36.80, 38.40)	0.291
Minimum Temperature, °C	36.40 (36.10, 36.80)	36.45 (36.10, 36.80)	0.842
RR_Max,/min	22.00 (19.00, 28.00)	24.00 (20.00, 33.00)	0.013
HR_Max,/min	107.00 (86.00, 121.00)	114.50 (85.50, 135.00)	0.012
HR_Min,/min	75.00 (61.00, 94.00)	81.00 (64.00, 97.00)	0.094
Comorbidities			
Hypertension, n (%)	100 (54.1)	80 (51.3)	0.688
Diabetes Mellitus, n (%)	48 (25.9)	36 (23.1)	0.627
Ischemic Heart Disease, n (%)	27 (14.6)	36 (23.1)	0.061
Sepsis, n (%)	62 (33.5)	95 (60.9)	<0.001
MODS, n (%)	19 (10.3)	26 (16.7)	0.115
Laboratory Parameters			
Hematology			
RBC Count, $\times 10^{12}$/L	3.80 (3.20, 4.20)	3.62 (3.00, 4.24)	0.3
Hemoglobin, g/L	107.00 (89.00, 125.00)	104.50 (88.00, 126.50)	0.844
Hematocrit	0.34 (0.30, 0.40)	0.34 (0.29, 0.40)	0.6
RDW, %	13.60 (12.90, 15.10)	14.20 (13.10, 16.15)	0.013
WBC_Max Count, $\times 10^9$/L	12.63 (9.05, 17.42)	13.87 (10.41, 19.70)	0.104
WBC_Min Count, $\times 10^9$/L	10.69 (7.18, 14.32)	10.55 (7.48, 15.34)	0.65
Neutrophil Percentage, %	87.50 (82.90, 90.80)	89.45 (85.05, 92.73)	0.002
Lymphocyte Count, $\times 10^9$/L	0.98 (0.71, 2.24)	0.90 (0.51, 2.02)	0.079
Platelet Count, $\times 10^9$/L	172.00 (130.00, 231.00)	161.00 (107.00, 236.50)	0.178
Blood Gas and Respiratory			
PaO_2/FiO_2 Ratio	268.70 (180.20, 350.30)	189.00 (121.75, 261.40)	<0.001
pH	7.39 (7.35, 7.43)	7.37 (7.30, 7.42)	<0.001
HCO_3^-, mmol/L	20.48 (18.40, 22.70)	20.60 (17.40, 24.35)	0.48
Lactate, mmol/L	1.60 (1.10, 2.50)	2.10 (1.30, 3.20)	0.005
FiO_2, %	41.00 (38.33, 50.00)	50.00 (40.00, 67.50)	<0.001
$AaDO_2$, mmHg	169.30 (120.80, 240.20)	221.45 (145.45, 322.45)	<0.001
PaO_2, mmHg	98.70 (77.60, 132.20)	89.85 (67.90, 126.20)	0.082
$PaCO_2$, mmHg	32.70 (29.40, 37.80)	35.05 (28.95, 42.05)	0.028
Coagulation Profile			
D-dimer, mg/L	1.36 (0.63, 2.62)	1.76 (0.77, 3.95)	0.005
INR	1.21 (1.12, 1.34)	1.24 (1.12, 1.41)	0.235
PT, seconds	13.40 (12.50, 15.00)	13.90 (12.60, 15.65)	0.149
APTT, seconds	30.00 (27.30, 32.60)	32.35 (28.90, 37.40)	<0.001
Fibrinogen, g/L	3.68 (2.91, 4.62)	3.50 (2.62, 4.76)	0.324
Biochemistry			
Anion Gap, mmol/L	13.20 (11.70, 15.40)	15.55 (12.75, 18.40)	<0.001
Maximum Blood Glucose, mmol/L	10.46 (8.09, 13.90)	11.29 (8.88, 14.00)	0.139
Minimum Blood Glucose, mmol/L	7.40 (6.00, 8.90)	7.40 (6.29, 8.75)	0.942
ALT, U/L	24.10 (14.10, 50.10)	29.95 (17.20, 90.25)	0.019
AST, U/L	36.60 (21.60, 64.40)	63.40 (30.85, 145.80)	<0.001
Total Bilirubin, μmol/L	16.10 (9.40, 26.60)	16.40 (10.05, 31.80)	0.366
CO_2 Combining Power, mmol/L	21.80 (19.10, 24.30)	21.30 (18.15, 26.10)	0.974
Sodium, mmol/L	140.00 (137.00, 142.00)	140.00 (136.00, 144.00)	0.599
Potassium, mmol/L	4.30 (3.90, 4.70)	4.45 (4.10, 4.90)	0.004
Calcium, mmol/L	2.04 (1.93, 2.13)	2.04 (1.96, 2.20)	0.474
Phosphate, mmol/L	1.25 (0.95, 1.53)	1.33 (0.99, 1.77)	0.036

(*Continued*)

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Table 1 (Continued).

Variables	Non-Progression (N=185)	Progression (N=156)	*p* value
Magnesium, mmol/L	0.75 (0.67, 0.85)	0.85 (0.73, 0.95)	<0.001
Albumin, g/L	30.10 (27.20, 33.80)	30.10 (26.10, 33.20)	0.639
Treatments and Interventions			
Diuretic Use, n (%)	116 (62.7)	89 (57.1)	0.342
Contrast Media Administration, n (%)	98 (53.0)	69 (44.2)	0.134
Calcium Channel Blocker Use, n (%)	42 (22.7)	28 (17.9)	0.343
Mechanical Ventilation, n (%)	142 (76.8)	135 (86.5)	0.03
Vasopressor Use, n (%)	102 (55.1)	123 (78.8)	<0.001

Abbreviations: AaDO2, Alveolar-arterial Oxygen Gradient; ALT, Alanine Aminotransferase; APTT, Activated Partial Thromboplastin Time; AST, Aspartate Aminotransferase; BMI, Body Mass Index; FIO2, Fraction of Inspired Oxygen; HR_Max, Maximum Heart Rate; HR_Min, Minimum Heart Rate; ICU, Intensive Care Unit; INR, International Normalized Ratio; MAP_Max, Maximum Mean Arterial Pressure; MAP_Min, Minimum Mean Arterial Pressure; MODS, Multiple Organ Dysfunction Syndrome; PaCO2, Partial Pressure of Arterial Carbon Dioxide; PaO2/FIO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio; PT, Prothrombin Time; RBC, Red Blood Cell; RDW, Red Cell Distribution Width; RR_Max, Maximum Respiratory Rate; WBC_Max, Maximum White Blood Cell Count; WBC_Min, Minimum White Blood Cell Count.

Table 2 Univariate and Multivariate Logistic Regression Analysis of Factors Associated with AKI Progression

Variable	P.value	OR_Univariate (95% CI)	P.value	OR_Multivariable (95% CI)
Sex	0.355	0.804 (0.505, 1.274)		
BMI	0.019	0.921 (0.858, 0.986)	0.059	0.917 (0.836, 1.002)
Age	0.378	1.008 (0.991, 1.025)		
Hypertension	0.61	0.895 (0.583, 1.371)		
Diabetes Mellitus	0.54	0.856 (0.519, 1.404)		
Ischemic Heart Disease	**0.046**	**1.756 (1.013, 3.072)**	**<0.01**	**2.994 (1.460, 6.240)**
Sepsis	**<0.01**	**3.090 (1.991, 4.837)**	**<0.01**	**2.644 (1.514, 4.681)**
MODS	0.085	1.747 (0.931, 3.335)	0.775	1.125 (0.500, 2.527)
MAP_Max	0.011	0.982 (0.967, 0.996)	0.55	1.006 (0.987, 1.025)
MAP_Min	**<0.01**	**0.959 (0.940, 0.977)**	**<0.01**	**0.954 (0.927, 0.980)**
Maximum Temperature	0.957	0.998 (0.925, 1.079)		
Minimum Temperature	0.299	1.103 (0.928, 1.365)		
RR_Max	0.096	1.007 (0.999, 1.016)	0.576	0.996 (0.980, 1.011)
HR_Max	0.04	1.006 (1.000, 1.013)	0.209	1.007 (0.996, 1.017)
HR_Min	0.23	1.005 (0.997, 1.013)		
RBC Count	0.844	0.981 (0.804, 1.191)		
Hemoglobin	0.646	1.002 (0.995, 1.009)		
Hematocrit	0.22	0.943 (0.853, 1.032)		
RDW	0.053	1.077 (1.000, 1.163)	0.357	1.051 (0.946, 1.171)
WBC_Max Count	0.084	1.024 (0.997, 1.052)	0.419	0.984 (0.945, 1.023)
WBC_Min Count	0.979	1.000 (0.970, 1.030)		
Neutrophil Percentage	**0.088**	**1.018 (0.999, 1.041)**	**0.049**	**1.029 (1.001, 1.060)**
Lymphocyte Count	0.456	0.974 (0.908, 1.042)		
Platelet Count	0.573	0.999 (0.997, 1.001)		
PaO_2/FiO_2 Ratio	**<0.01**	**0.995 (0.993, 0.997)**	**0.021**	**0.997 (0.994, 0.999)**
pH	<0.01	0.006 (0.000, 0.080)	0.239	0.074 (0.001, 5.363)
HCO_3^-	0.341	1.024 (0.976, 1.074)		
Lactate	0.008	1.129 (1.036, 1.242)	0.327	0.934 (0.813, 1.072)
FiO_2	0.001	1.018 (1.008, 1.028)	0.691	0.995 (0.967, 1.020)
$AaDO_2$	<0.01	1.003 (1.002, 1.005)	0.354	1.002 (0.998, 1.006)
PaO_2	0.121	0.997 (0.993, 1.001)		

(*Continued*)

Table 2 (Continued).

Variable	P.value	OR_Univariate (95% CI)	P.value	OR_Multivariable (95% CI)
$PaCO_2$	0.005	1.035 (1.011, 1.060)	0.194	1.025 (0.988, 1.065)
Ddimer	**<0.01**	**1.127 (1.062, 1.213)**	**0.015**	**1.097 (1.027, 1.195)**
INR	0.349	1.098 (0.910, 1.385)		
PT	0.021	1.064 (1.012, 1.125)	0.275	0.960 (0.893, 1.037)
APTT	0.002	1.045 (1.018, 1.076)	0.383	1.015 (0.981, 1.052)
Fibrinogen	0.692	0.974 (0.855, 1.108)		
Anion Gap	**<0.01**	**1.163 (1.098, 1.239)**	**<0.01**	**1.163 (1.074, 1.266)**
Maximum Blood Glucose	0.108	1.040 (0.992, 1.091)		
Minimum Blood Glucose	0.872	1.007 (0.922, 1.100)		
ALT	0.016	1.001 (1.000, 1.002)	0.644	0.999 (0.997, 1.002)
AST	0.008	1.001 (1.000, 1.002)	0.241	1.001 (0.999, 1.003)
Total Bilirubin	0.02	1.007 (1.002, 1.014)	0.535	1.002 (0.995, 1.010)
CO_2 Combining Power	0.612	1.011 (0.968, 1.056)		
Sodium	0.88	0.999 (0.986, 1.012)		
Potassium	0.438	0.991 (0.961, 1.013)		
Calcium	0.25	0.712 (0.381, 1.241)		
Phosphate	0.005	1.759 (1.189, 2.639)	0.536	0.825 (0.447, 1.514)
Magnesium	<0.01	9.562 (2.914, 33.419)	0.36	2.058 (0.439, 9.808)
Albumin	0.95	0.999 (0.963, 1.036)		
Diuretic Use	0.289	0.790 (0.511, 1.221)		
Contrast Media Administration	0.108	0.704 (0.458, 1.079)		
Calcium Channel Blocker Use	0.28	0.745 (0.433, 1.265)		
Mechanical Ventilation	0.023	1.947 (1.110, 3.505)	0.226	1.603 (0.752, 3.486)
Vasopressor Use	<0.01	3.033 (1.889, 4.955)	0.447	1.291 (0.668, 2.508)

Notes: Variables in bold type indicate statistically significant factors ($P < 0.05$) in the univariate analysis.
Abbreviations: AaDO2, Alveolar-arterial Oxygen Gradient; ALT, Alanine Aminotransferase; APTT, Activated Partial Thromboplastin Time; AST, Aspartate Aminotransferase; BMI, Body Mass Index; CI, Confidence Interval; FIO2, Fraction of Inspired Oxygen; HR_Max, Maximum Heart Rate; HR_Min, Minimum Heart Rate; INR, International Normalized Ratio; MAP_Max, Maximum Mean Arterial Pressure; MAP_Min, Minimum Mean Arterial Pressure; MODS, Multiple Organ Dysfunction Syndrome; OR, Odds Ratio; PaCO2, Partial Pressure of Arterial Carbon Dioxide; PaO2/FIO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio; PT, Prothrombin Time; RBC, Red Blood Cell; RDW, Red Cell Distribution Width; RR_Max, Maximum Respiratory Rate; WBC_Max, Maximum White Blood Cell Count; WBC_Min, Minimum White Blood Cell Count.

Univariate and Multivariate Logistic Regression for the Secondary Outcome (ICU Mortality)

Univariate logistic regression analysis identified several variables significantly associated with ICU mortality ($P < 0.1$), including age, ischemic heart disease, sepsis, MODS, maximum and minimum MAP, maximum and minimum HR, platelet count, PaO_2/FiO_2 ratio, lactate, D-dimer, APTT, anion gap, total bilirubin, magnesium, and albumin (Table 3).

These significant variables from the univariate analysis were subsequently included in a multivariate logistic regression model. After adjustment for potential confounders, four factors emerged as independent risk factors for ICU mortality: age (adjusted OR = 1.051, 95% CI: 1.013–1.096; P = 0.013), maximum HR (adjusted OR = 1.024, 95% CI: 1.002–1.046; P = 0.028), magnesium (adjusted OR = 10.764, 95% CI: 1.370–86.541; P = 0.024), and albumin (adjusted OR = 0.929, 95% CI: 0.849–1.009; P = 0.093). Albumin, with a higher level being a protective factor, showed a strong trend towards significance. The detailed results of the univariate and multivariate analyses for ICU mortality are presented in Table 3, and the results of the multivariate analysis are visualized in a forest plot (Figure 3).

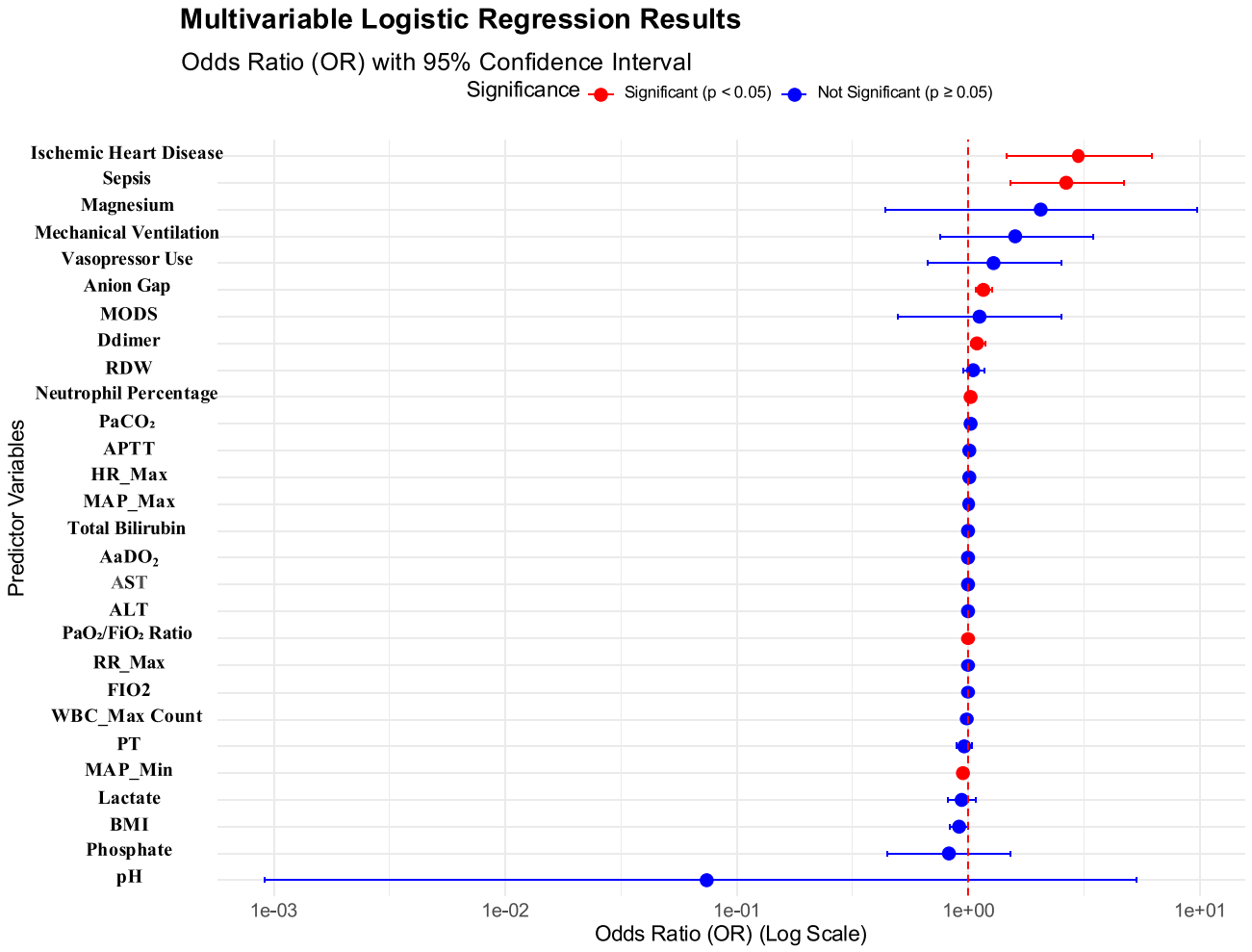

Figure 2 Forest plot of multivariate analysis for AKI progression.

Abbreviations: ALT, Alanine Aminotransferase; APTT, Activated Partial Thromboplastin Time; AST, Aspartate Aminotransferase; AaDO2, Alveolar-arterial Oxygen Gradient; BMI, Body Mass Index; FIO2, Fraction of Inspired Oxygen; HR_Max, Maximum Heart Rate; MAP_Max, Maximum Mean Arterial Pressure; MAP_Min, Minimum Mean Arterial Pressure; MODS, Multiple Organ Dysfunction Syndrome; OR, Odds Ratio; PaCO2, Partial Pressure of Arterial Carbon Dioxide; PaO2/FiO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio; PT, Prothrombin Time; RDW, Red Blood Cell Distribution Width; RR_Max, Maximum Respiratory Rate; WBC_Max, Maximum White Blood Cell Count.

Subgroup Analysis

Subgroup analyses stratified by the initial AKI stage revealed distinct risk factor profiles for disease progression. Among patients initially diagnosed with AKI Stage 1, multivariate analysis identified sepsis (adjusted OR = 3.153, 95% CI:

Table 3 Univariate and Multivariate Logistic Regression Analysis of Factors Associated with ICU Mortality

Variable	P.value	OR_Univariate (95% CI)	P.value	OR_Multivariable (95% CI)
Sex	0.447	0.735 (0.315, 1.573)		
BMI	0.199	0.928 (0.826, 1.038)		
Age	**0.037**	**1.035 (1.003, 1.070)**	**0.013**	**1.051 (1.013, 1.096)**
Hypertension	0.217	0.641 (0.312, 1.293)		
Diabetes Mellitus	0.282	0.605 (0.220, 1.418)		
Ischemic Heart Disease	0.109	1.909 (0.832, 4.108)		
Sepsis	0.038	2.144 (1.055, 4.522)	0.986	0.992 (0.418, 2.374)
MODS	0.025	2.596 (1.077, 5.814)	0.325	1.665 (0.578, 4.494)

(*Continued*)

Table 3 (Continued).

Variable	P.value	OR_Univariate (95% CI)	P.value	OR_Multivariable (95% CI)
MAP_Max	0.039	0.974 (0.948, 0.998)	0.679	0.993 (0.960, 1.025)
MAP_Min	0.011	0.961 (0.931, 0.990)	0.574	0.988 (0.946, 1.031)
Maximum Temperature	0.972	1.002 (0.910, 1.194)		
Minimum Temperature	0.561	0.935 (0.767, 1.245)		
RR_Max	0.955	1.000 (0.984, 1.012)		
HR_Max	**0.001**	**1.022 (1.009, 1.035)**	**0.028**	**1.024 (1.002, 1.046)**
HR_Min	0.014	1.019 (1.004, 1.035)	0.779	0.996 (0.969, 1.024)
RBC Count	0.986	1.003 (0.703, 1.330)		
Hemoglobin	0.958	1.000 (0.988, 1.011)		
Hematocrit	0.453	0.928 (0.703, 1.084)		
RDW	0.130	1.096 (0.974, 1.234)		
WBC_Max Count	0.610	1.011 (0.968, 1.052)		
WBC_Min Count	0.896	1.003 (0.952, 1.051)		
Neutrophil Percentage	0.137	0.983 (0.963, 1.008)		
Lymphocyte Count	0.388	1.043 (0.937, 1.141)		
Platelet Count	0.079	0.996 (0.992, 1.000)	0.260	0.998 (0.993, 1.001)
PaO_2/FiO_2 Ratio	0.031	0.996 (0.993, 0.999)	0.503	0.999 (0.994, 1.003)
pH	0.185	0.072 (0.002, 3.964)		
HCO_3^-	0.324	1.040 (0.962, 1.123)		
Lactate	0.033	1.114 (1.001, 1.227)	0.645	1.033 (0.891, 1.185)
FiO_2	0.269	1.008 (0.993, 1.023)		
$AaDO_2$	0.425	1.001 (0.999, 1.003)		
PaO_2	0.189	0.995 (0.987, 1.002)		
$PaCO_2$	0.186	1.024 (0.988, 1.060)		
Ddimer	0.023	1.047 (1.003, 1.089)	0.269	1.031 (0.975, 1.090)
INR	0.193	1.147 (0.893, 1.397)		
PT	0.270	1.036 (0.965, 1.099)		
APTT	0.028	1.030 (1.001, 1.057)	0.775	1.005 (0.966, 1.041)
Fibrinogen	0.533	0.931 (0.735, 1.151)		
Anion Gap	0.016	1.087 (1.013, 1.162)	0.568	1.027 (0.936, 1.126)
Maximum Blood Glucose	0.438	1.030 (0.953, 1.105)		
Minimum Blood Glucose	0.477	1.051 (0.910, 1.201)		
ALT	0.540	1.000 (0.999, 1.001)		
AST	0.302	1.000 (1.000, 1.001)		
Total Bilirubin	0.009	1.007 (1.002, 1.013)	0.140	1.005 (0.998, 1.012)
CO_2 Combining Power	0.990	1.000 (0.930, 1.073)		
Sodium	0.118	1.046 (0.999, 1.108)		
Potassium	0.688	0.925 (0.552, 1.014)		
Calcium	0.984	0.991 (0.337, 2.142)		
Phosphate	0.791	0.917 (0.473, 1.706)		
Magnesium	**0.017**	**7.618 (1.379, 40.118)**	**0.024**	**10.764 (1.370, 86.541)**
Albumin	0.040	0.930 (0.866, 0.994)	0.093	0.929 (0.849, 1.009)
Diuretic Use	0.270	0.674 (0.333, 1.368)		
Contrast Media Administration	0.143	0.583 (0.277, 1.185)		
Calcium Channel Blocker Use	0.719	1.166 (0.475, 2.587)		
Mechanical Ventilation	0.115	2.656 (0.911, 11.306)		
Vasopressor Use	0.006	4.474 (1.716, 15.332)	0.146	2.488 (0.787, 9.687)

Notes: Variables in bold type indicate statistically significant factors ($P < 0.05$) in the univariate analysis.

Abbreviations: AaDO2, Alveolar-arterial Oxygen Gradient; ALT, Alanine Aminotransferase; APTT, Activated Partial Thromboplastin Time; AST, Aspartate Aminotransferase; BMI, Body Mass Index; CI, Confidence Interval; FIO2, Fraction of Inspired Oxygen; HR_Max, Maximum Heart Rate; HR_Min, Minimum Heart Rate; INR, International Normalized Ratio; MAP_Max, Maximum Mean Arterial Pressure; MAP_Min, Minimum Mean Arterial Pressure; MODS, Multiple Organ Dysfunction Syndrome; OR, Odds Ratio; PaCO2, Partial Pressure of Arterial Carbon Dioxide; PaO2/FIO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio; PT, Prothrombin Time; RBC, Red Blood Cell; RDW, Red Cell Distribution Width; RR_Max, Maximum Respiratory Rate; WBC_Max, Maximum White Blood Cell Count; WBC_Min, Minimum White Blood Cell Count.

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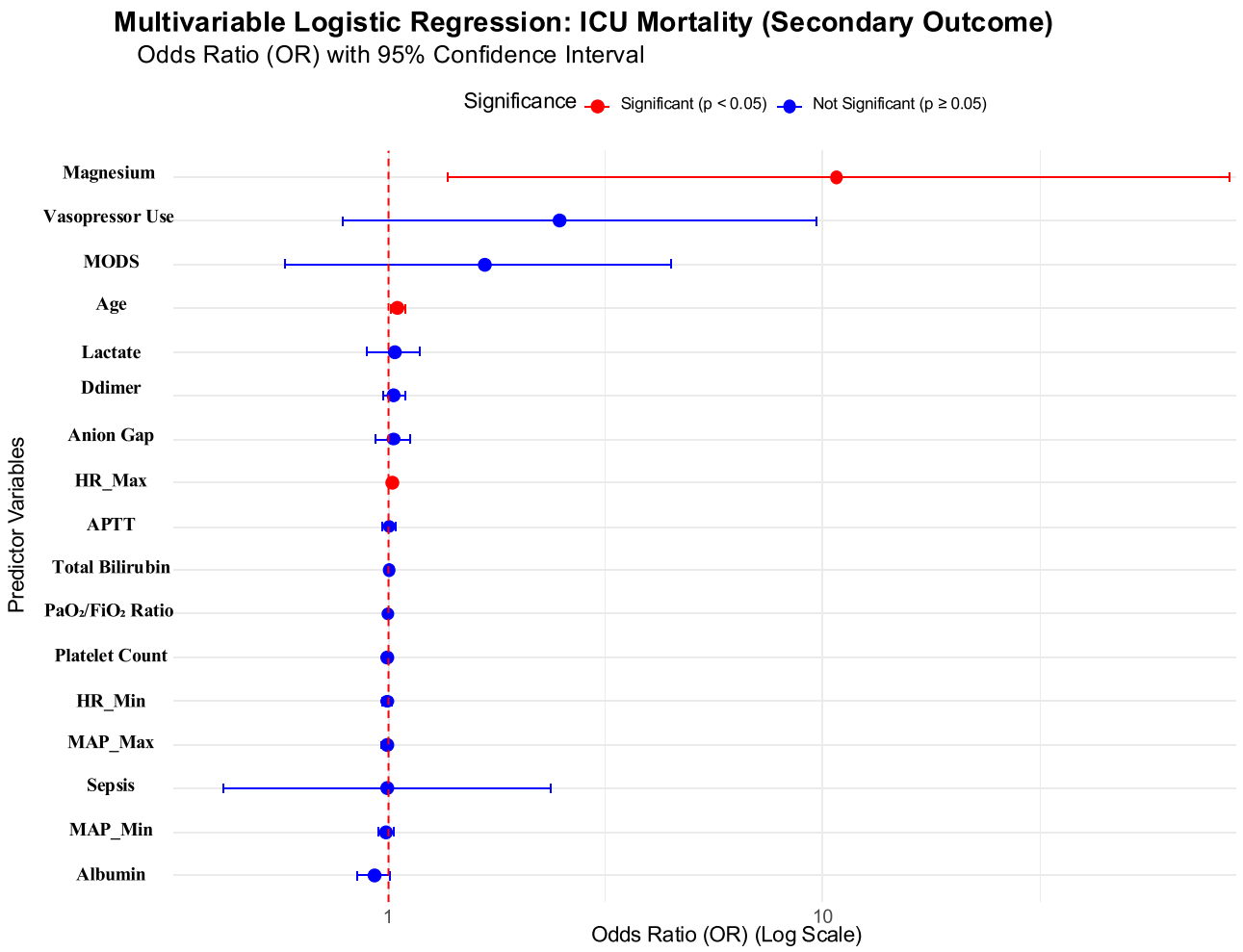

Figure 3 Forest plot of multivariate analysis for ICU mortality.
Abbreviations: APTT, Activated Partial Thromboplastin Time; HR_Max, Maximum Heart Rate; HR_Min, Minimum Heart Rate; ICU, Intensive Care Unit; MAP_Max, Maximum Mean Arterial Pressure; MAP_Min, Minimum Mean Arterial Pressure; MODS, Multiple Organ Dysfunction Syndrome; OR, Odds Ratio; PaO2/FiO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio.

1.616–6.299; P < 0.01), a lower PaO_2/FiO_2 ratio (adjusted OR = 0.996, 95% CI: 0.993–1.000; P = 0.047), and an elevated anion gap (adjusted OR = 1.138, 95% CI: 1.030–1.270; P = 0.015) as independent risk factors (Table 4, Figure 4). In contrast, for patients presenting with AKI Stage 2 (Table 5, Figure 5), a lower minimum white blood cell count (adjusted OR = 0.934, 95% CI: 0.866–0.997; P = 0.055) emerged as a significant independent predictor of progression. These findings suggest that the drivers of AKI progression may differ depending on the initial severity of the injury.

Discussion

This study aimed to identify the risk factors for AKI progression by analyzing real-world clinical data, with the goal of enabling early identification of high-risk patients and informing clinical interventions to improve prognosis. Multivariable logistic regression identified ischemic heart disease, sepsis, a lower minimum MAP, a higher neutrophil percentage, a lower PaO_2/FiO_2 ratio, elevated D-dimer levels, and a greater anion gap as independent risk factors for AKI progression.

The multivariable analysis identified a set of independent risk factors significantly associated with AKI progression. Firstly, the presence of ischemic heart disease nearly tripled the risk of AKI progression (adjusted odds ratio [aOR] = 2.994). Alexander Goldberg et al conducted a prospective study which found that 9.6% of patients with acute myocardial

Table 4 Univariate and Multivariate Logistic Regression Analysis of Factors Associated with AKI Progression in the AKI Stage 1 Subgroup

Variable	P.value	OR_Univariate (95% CI)	P.value	OR_Multivariable (95% CI)
Sex	0.324	0.750 (0.420, 1.322)		
BMI	0.118	0.933 (0.854, 1.017)		
Age	0.123	1.017 (0.996, 1.040)		
Hypertension	0.379	0.790 (0.467, 1.336)		
Diabetes Mellitus	0.154	0.642 (0.344, 1.172)		
Ischemic Heart Disease	0.126	1.699 (0.863, 3.377)		
Sepsis	**<0.01**	**3.719 (2.162, 6.497)**	**<0.01**	**3.153 (1.616, 6.299)**
MODS	0.652	1.194 (0.547, 2.583)		
MAP_Max	0.038	0.982 (0.965, 0.999)	0.644	0.995 (0.972, 1.018)
MAP_Min	0.01	0.971 (0.948, 0.992)	0.061	0.970 (0.939, 1.001)
Maximum Temperature	0.352	0.959 (0.865, 1.045)		
Minimum Temperature	0.98	1.003 (0.803, 1.275)		
RR_Max	0.329	1.005 (0.995, 1.015)		
HR_Max	0.211	1.005 (0.997, 1.013)		
HR_Min	0.468	1.004 (0.994, 1.014)		
RBC Count	0.458	0.902 (0.676, 1.175)		
Hemoglobin	0.666	0.998 (0.990, 1.007)		
Hematocrit	0.455	0.960 (0.854, 1.065)		
RDW	0.335	1.043 (0.958, 1.140)		
WBC_Max Count	0.003	1.062 (1.022, 1.107)	0.291	1.033 (0.973, 1.099)
WBC_Min Count	0.193	1.028 (0.986, 1.073)		
Neutrophil Percentage	0.027	1.043 (1.010, 1.086)	0.075	1.037 (0.997, 1.084)
Lymphocyte Count	0.359	0.962 (0.882, 1.043)		
Platelet Count	0.537	0.999 (0.997, 1.002)		
PaO_2/FiO_2 Ratio	**<0.01**	**0.995 (0.992, 0.997)**	**0.047**	**0.996 (0.993, 1.000)**
pH	0.002	0.005 (0.000, 0.127)	0.907	0.733 (0.004, 135.102)
HCO_3^-	0.443	1.025 (0.963, 1.091)		
Lactate	0.112	1.090 (0.983, 1.219)		
FiO_2	0.019	1.015 (1.003, 1.028)	0.286	0.980 (0.941, 1.014)
$AaDO_2$	0.003	1.003 (1.001, 1.005)	0.17	1.004 (0.999, 1.010)
PaO_2	0.389	0.998 (0.993, 1.003)		
$PaCO_2$	0.007	1.044 (1.013, 1.079)	0.265	1.027 (0.980, 1.079)
Ddimer	0.005	1.138 (1.050, 1.259)	0.16	1.076 (0.985, 1.211)
INR	0.976	0.997 (0.772, 1.253)		
PT	0.398	1.044 (0.945, 1.154)		
APTT	0.04	1.040 (1.005, 1.083)	0.622	1.012 (0.964, 1.061)
Fibrinogen	0.403	0.934 (0.791, 1.095)		
Anion Gap	**<0.01**	**1.172 (1.088, 1.273)**	**0.015**	**1.138 (1.030, 1.270)**
Maximum Blood Glucose	0.435	1.025 (0.964, 1.090)		
Minimum Blood Glucose	0.81	1.013 (0.909, 1.128)		
ALT	0.041	1.001 (1.000, 1.002)	0.213	1.002 (0.999, 1.005)
AST	0.044	1.001 (1.000, 1.002)	0.282	0.999 (0.997, 1.001)
Total Bilirubin	0.016	1.014 (1.005, 1.029)	0.067	1.012 (1.001, 1.029)
CO_2 Combining Power	0.177	1.038 (0.983, 1.098)		
Sodium	0.817	1.003 (0.981, 1.028)		
Potassium	0.698	1.006 (0.973, 1.045)		
Calcium	0.972	1.014 (0.438, 2.267)		
Phosphate	0.022	1.851 (1.103, 3.178)	0.802	1.103 (0.512, 2.387)
Magnesium	<0.01	34.012 (6.441, 207.772)	0.094	6.898 (0.753, 70.306)
Albumin	0.479	0.984 (0.940, 1.028)		

(*Continued*)

Table 4 (Continued).

Variable	P.value	OR_Univariate (95% CI)	P.value	OR_Multivariable (95% CI)
Diuretic Use	0.394	0.794 (0.467, 1.351)		
Contrast Media Administration	0.224	0.723 (0.427, 1.219)		
Calcium Channel Blocker Use	0.138	0.616 (0.319, 1.156)		
Mechanical Ventilation	0.031	2.225 (1.102, 4.753)	0.071	2.596 (0.945, 7.596)
Vasopressor Use	0.001	2.703 (1.546, 4.826)	0.281	1.546 (0.702, 3.455)

Notes: Variables in bold type indicate statistically significant factors (P < 0.05) in the univariate analysis.
Abbreviations: AaDO2, Alveolar-arterial Oxygen Gradient; ALT, Alanine Aminotransferase; APTT, Activated Partial Thromboplastin Time; AST, Aspartate Aminotransferase; BMI, Body Mass Index; CI, Confidence Interval; FIO2, Fraction of Inspired Oxygen; HR_Max, Maximum Heart Rate; HR_Min, Minimum Heart Rate; INR, International Normalized Ratio; MAP_Max, Maximum Mean Arterial Pressure; MAP_Min, Minimum Mean Arterial Pressure; MODS, Multiple Organ Dysfunction Syndrome; OR, Odds Ratio; PaCO2, Partial Pressure of Arterial Carbon Dioxide; PaO2/FIO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio; PT, Prothrombin Time; RBC, Red Blood Cell; RDW, Red Cell Distribution Width; RR_Max, Maximum Respiratory Rate; WBC_Max, Maximum White Blood Cell Count; WBC_Min, Minimum White Blood Cell Count.

infarction experienced renal impairment during hospitalization, and renal dysfunction was associated with an increased risk of mortality.[12] This may be attributed to impaired cardiac function in patients with ischemic heart disease, leading to inadequate organ perfusion and subsequent AKI, a phenomenon referred to as "Cardiorenal Syndrome".[13,14] Cardiorenal

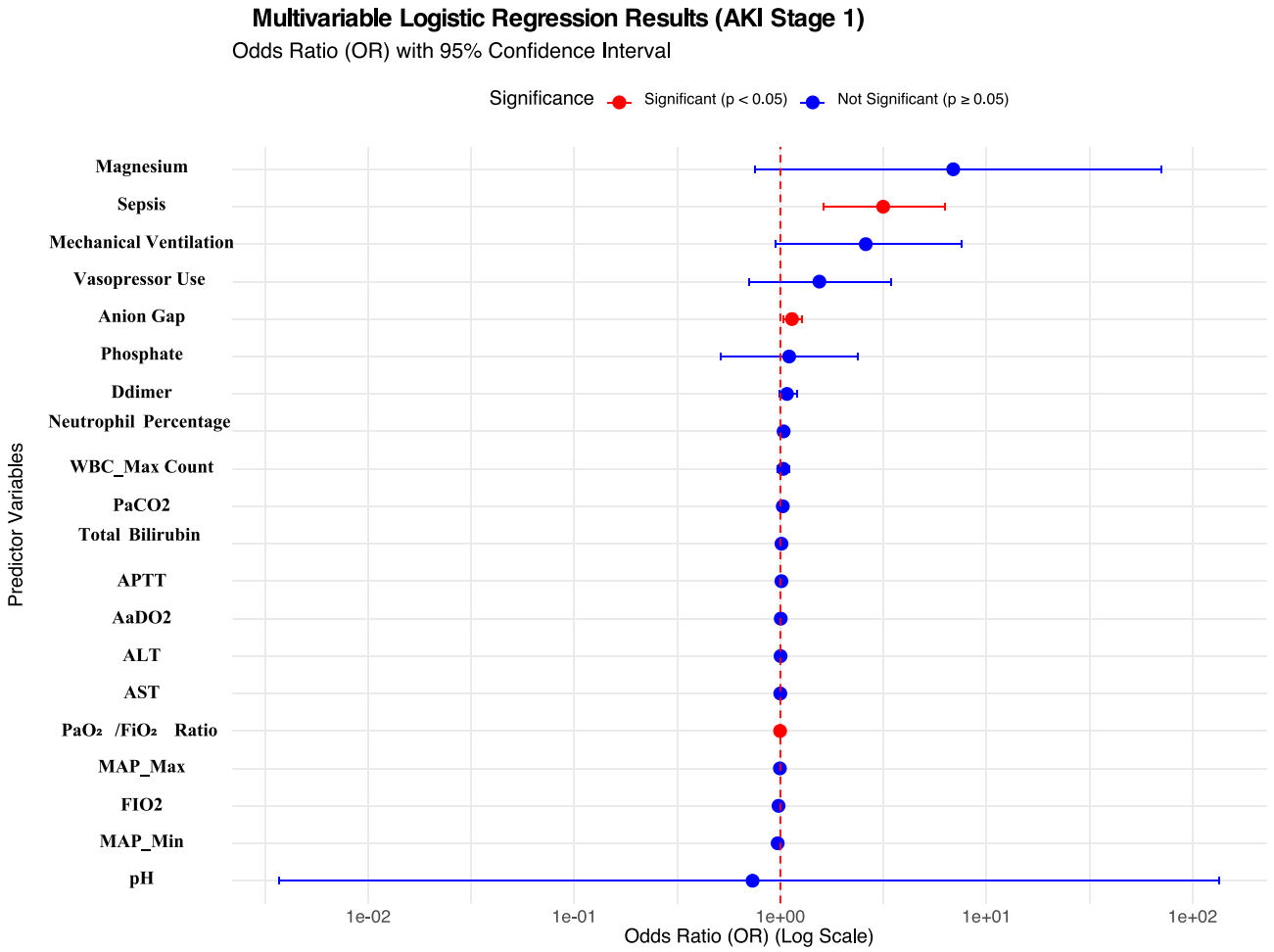

Figure 4 Forest plot of multivariate analysis of independent risk factors for AKI progression in patients with initial AKI stage 1.
Abbreviations: AaDO2, Alveolar-arterial Oxygen Gradient; AKI, Acute Kidney Injury; ALT, Alanine Aminotransferase; APTT, Activated Partial Thromboplastin Time; AST, Aspartate Aminotransferase; FIO2, Fraction of Inspired Oxygen; MAP_Max, Maximum Mean Arterial Pressure; MAP_Min, Minimum Mean Arterial Pressure; OR, Odds Ratio; PaCO2, Partial Pressure of Arterial Carbon Dioxide; PaO2/FiO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio; WBC_Max, Maximum White Blood Cell Count.

Table 5 Univariate and Multivariate Logistic Regression Analysis of Factors Associated with AKI Progression in the AKI Stage 2 Subgroup

Variable	P.value	OR_Univariate (95% CI)	P.value	OR_Multivariable (95% CI)
Sex	0.790	0.897 (0.403, 1.997)		
BMI	0.041	0.884 (0.781, 0.991)	0.453	0.944 (0.809, 1.098)
Age	0.926	0.999 (0.968, 1.030)		
Hypertension	0.548	1.259 (0.594, 2.684)		
Diabetes Mellitus	0.239	1.746 (0.700, 4.563)		
Ischemic Heart Disease	0.219	1.831 (0.711, 4.996)		
Sepsis	0.057	2.095 (0.985, 4.537)	0.347	1.705 (0.562, 5.329)
MODS	0.028	4.444 (1.312, 20.423)	0.135	3.701 (0.722, 23.750)
MAP_Max	0.194	0.982 (0.956, 1.009)		
MAP_Min	<0.01	0.927 (0.887, 0.963)	0.069	0.949 (0.893, 1.002)
Maximum Temperature	0.230	1.199 (0.969, 1.665)		
Minimum Temperature	0.175	1.362 (0.971, 2.384)		
RR_Max	0.160	1.012 (0.996, 1.032)		
HR_Max	0.169	1.008 (0.997, 1.019)		
HR_Min	0.537	1.004 (0.990, 1.019)		
RBC Count	0.712	1.057 (0.788, 1.444)		
Hemoglobin	0.210	1.008 (0.996, 1.022)		
Hematocrit	0.298	0.903 (0.713, 1.080)		
RDW	0.051	1.167 (1.008, 1.381)	0.402	1.090 (0.897, 1.350)
WBC_Max Count	0.280	0.978 (0.939, 1.017)		
WBC_Min Count	**0.067**	**0.956 (0.908, 1.002)**	**0.055**	**0.934 (0.866, 0.997)**
Neutrophil Percentage	0.968	1.001 (0.973, 1.029)		
Lymphocyte Count	0.859	1.012 (0.888, 1.159)		
Platelet Count	0.906	1.000 (0.997, 1.003)		
PaO_2/FiO_2 Ratio	0.004	0.995 (0.991, 0.998)	0.335	0.998 (0.992, 1.002)
pH	0.049	0.009 (0.000, 0.817)	0.120	0.002 (0.000, 3.566)
HCO_3^-	0.481	1.028 (0.952, 1.112)		
Lactate	0.043	1.220 (1.036, 1.537)	0.590	0.921 (0.695, 1.298)
FiO_2	0.018	1.021 (1.004, 1.040)	0.443	1.016 (0.977, 1.060)
$AaDO_2$	0.015	1.003 (1.001, 1.006)	0.590	0.998 (0.991, 1.005)
PaO_2	0.185	0.995 (0.987, 1.002)		
$PaCO_2$	0.255	1.022 (0.985, 1.062)		
Ddimer	0.033	1.105 (1.029, 1.241)	0.077	1.092 (1.007, 1.243)
INR	0.067	2.448 (1.109, 7.354)	0.497	1.315 (0.727, 5.155)
PT	0.063	1.064 (1.002, 1.147)	0.355	0.956 (0.865, 1.053)
APTT	0.032	1.047 (1.009, 1.099)	0.282	1.027 (0.980, 1.082)
Fibrinogen	0.559	1.070 (0.854, 1.354)		
Anion Gap	0.009	1.140 (1.040, 1.266)	0.192	1.099 (0.958, 1.281)
Maximum Blood Glucose	0.121	1.065 (0.986, 1.158)		
Minimum Blood Glucose	0.847	0.985 (0.840, 1.153)		
ALT	0.177	1.001 (1.000, 1.004)		
AST	0.049	1.003 (1.001, 1.006)	0.459	1.001 (0.999, 1.006)
Total Bilirubin	0.796	1.001 (0.994, 1.009)		
CO_2 Combining Power	0.384	0.968 (0.898, 1.041)		
Sodium	0.863	0.999 (0.981, 1.015)		
Potassium	0.321	0.952 (0.765, 1.002)		
Calcium	0.102	0.463 (0.153, 1.054)		
Phosphate	0.180	1.525 (0.831, 2.880)		
Magnesium	0.648	1.525 (0.250, 9.682)		
Albumin	0.311	1.037 (0.969, 1.115)		
Diuretic Use	0.502	0.768 (0.353, 1.655)		

(*Continued*)

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Table 5 (Continued).

Variable	P.value	OR_Univariate (95% CI)	P.value	OR_Multivariable (95% CI)
Contrast Media Administration	0.250	0.643 (0.301, 1.361)		
Calcium Channel Blocker Use	0.531	1.398 (0.495, 4.148)		
Mechanical Ventilation	0.363	1.561 (0.601, 4.180)		
Vasopressor Use	0.006	3.712 (1.508, 9.891)	0.591	1.438 (0.384, 5.637)

Notes: Variables in bold type indicate statistically significant factors (P < 0.05) in the univariate analysis.
Abbreviations: AaDO2, Alveolar-arterial Oxygen Gradient; ALT, Alanine Aminotransferase; APTT, Activated Partial Thromboplastin Time; AST, Aspartate Aminotransferase; BMI, Body Mass Index; CI, Confidence Interval; FIO2, Fraction of Inspired Oxygen; HR_Max, Maximum Heart Rate; HR_Min, Minimum Heart Rate; INR, International Normalized Ratio; MAP_Max, Maximum Mean Arterial Pressure; MAP_Min, Minimum Mean Arterial Pressure; MODS, Multiple Organ Dysfunction Syndrome; OR, Odds Ratio; PaCO2, Partial Pressure of Arterial Carbon Dioxide; PaO2/FIO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio; PT, Prothrombin Time; RBC, Red Blood Cell; RDW, Red Cell Distribution Width; RR_Max, Maximum Respiratory Rate; WBC_Max, Maximum White Blood Cell Count; WBC_Min, Minimum White Blood Cell Count.

Syndrome describes a complex bidirectional pathway between the heart and kidneys, mediated by mechanisms such as reduced arterial perfusion, venous congestion, and neurohormonal activation, creating a vicious cycle that exacerbates injury in both organs. Furthermore, patients with ischemic heart disease often require interventional procedures, and the

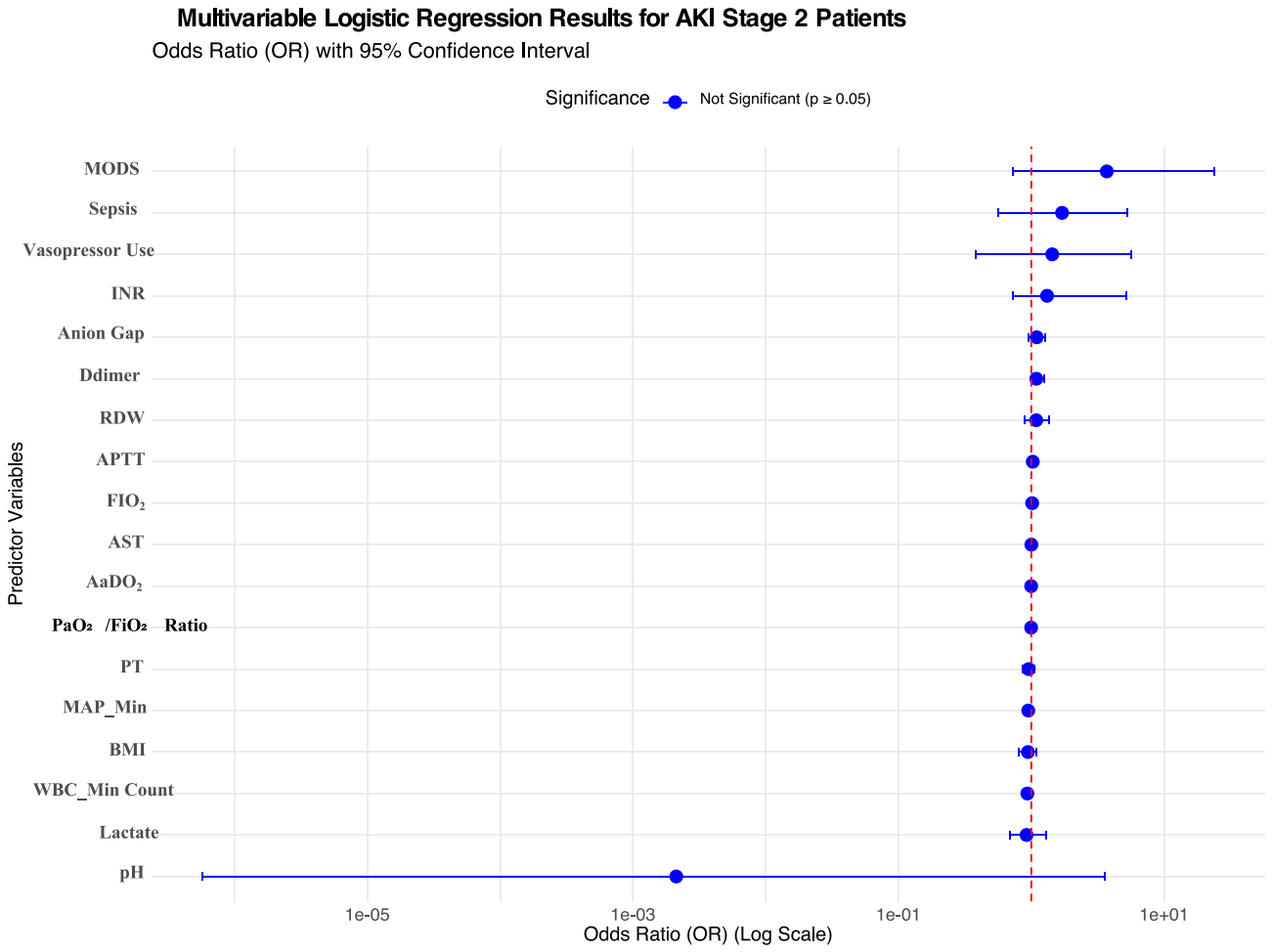

Figure 5 Forest plot of multivariate analysis of independent risk factors for AKI progression in patients with initial AKI stage 2.
Abbreviations: AaDO2, Alveolar-arterial Oxygen Gradient; AKI, Acute Kidney Injury; APTT, Activated Partial Thromboplastin Time; AST, Aspartate Aminotransferase; BMI, Body Mass Index; FIO2, Fraction of Inspired Oxygen; INR, International Normalized Ratio; MAP_Min, Minimum Mean Arterial Pressure; MODS, Multiple Organ Dysfunction Syndrome; OR, Odds Ratio; PaO2/FiO2, Arterial Oxygen Partial Pressure to Fractional Inspired Oxygen Ratio; PT, Prothrombin Time; RDW, Red Cell Distribution Width; WBC_Min, Minimum White Blood Cell Count.

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use of contrast media in such cases may also contribute to the progression of AKI.[15] Secondly, sepsis emerged as another critical driver (aOR = 2.644). Sepsis is a clinical syndrome triggered by an infection that causes a dysregulated host response, leading to life-threatening organ dysfunction, and is associated with an extremely high mortality rate.[16] Sepsis-associated kidney injury is highly prevalent in critically ill patients, significantly increasing both morbidity and mortality rates. Notably, up to 70% of AKI cases may be related to sepsis.[17] The pathogenesis of sepsis-associated kidney injury involves multiple pathophysiological mechanisms, including systemic and renal microcirculatory alterations, mitochondrial dysfunction, and metabolic reprogramming.[18] Early and aggressive fluid resuscitation, judicious use of vasoactive agents, and the timely initiation of renal replacement therapy when indicated can contribute to improving outcomes in these patients.[19] Regarding hemodynamics, our study confirmed that the minimum MAP is an independent protective factor against AKI progression (aOR = 0.954). An odds ratio of less than 1 indicates an inverse correlation between the minimum MAP and the risk of AKI progression, meaning that lower blood pressure is associated with a higher risk. Maintaining an optimal blood pressure is not only a crucial aspect of preventing AKI, but also plays a vital role in preserving renal perfusion and function in critically ill patients who have already developed AKI.[20,21] The use of agents such as norepinephrine, dobutamine, milrinone, and levosimendan to increase MAP can help improve outcomes in these patients.[21] Our findings indicate that the activation of systemic inflammation and the coagulation system is a key pathophysiological pathway in AKI progression.[22] An elevated neutrophil percentage (aOR = 1.029) reflects a significant state of inflammatory response, while increased D-dimer levels (aOR = 1.097) clearly suggest the presence of secondary hyperfibrinolysis and a propensity for microthrombosis. These two mechanisms act in concert, leading to endothelial activation and microcirculatory dysfunction—a process central to sepsis-induced kidney injury, as highlighted by recent research on renal microvascular endothelial responses. This synergy exacerbates renal parenchymal damage.[23,24] This discovery aligns with the cutting-edge focus in AKI research, where the exploration of novel biomarkers (such as NGAL) is precisely targeting inflammation and endothelial injury.[25] Our results confirm that, in clinical practice, these routinely available inflammatory and coagulation parameters can likewise effectively reveal the core mechanisms underlying AKI progression, complementing the limitations of traditional functional markers. Our study identified a lower PaO_2/FiO_2 ratio and a greater anion gap as independent risk factors for AKI progression, which are key markers of impaired systemic oxygenation and metabolic acidosis, respectively. These findings confirm that systemic hypoxia and internal milieu disruption play a pivotal role in the worsening of AKI. The mechanism lies in the fact that the kidneys are highly perfused organs with substantial oxygen consumption; hypoxemia directly compromises energy supply to renal tubular cells, while metabolic acidosis further disrupts intracellular homeostasis.[26,27] This dual assault significantly increases the metabolic burden on the already injured kidneys and is likely to promote the progression of AKI to more severe stages by activating inflammatory pathways and inducing cellular apoptosis, among other mechanisms.[28]

Regarding the secondary outcome of ICU mortality, multivariable analysis identified age, maximum heart rate, and serum magnesium level as independent risk factors, while a higher albumin level showed a protective trend. Advanced age (aOR = 1.051) reflects diminished physiological reserve and a higher burden of comorbidities, rendering patients more vulnerable to critical illness.[29] An elevated maximum heart rate (aOR = 1.024) is a marker of extreme physiological stress and sympathetic nervous system activation, often indicative of cardiovascular decompensation and is closely associated with increased mortality.[30] Notably, an elevated serum magnesium level (aOR = 10.764) emerged as a strong predictor. In critically ill patients, hypermagnesemia is typically not an isolated finding but rather signals severe cellular metabolic dysfunction, renal insufficiency, or iatrogenic overload, warranting high clinical vigilance and investigation into the underlying causes.[31,32] Furthermore, the serum albumin level (aOR = 0.929) is not merely a marker of malnutrition but a comprehensive reflection of persistent inflammation, immunosuppression, and the overall severity of the catabolic state, which is strongly linked to poor outcomes in ICU patients.[33,34]

Subgroup analyses stratified by the initial AKI stage revealed heterogeneity in the risk factors for disease progression. Among patients initially diagnosed with AKI Stage 1, sepsis, a lower PaO_2/FiO_2 ratio, and an elevated anion gap were identified as independent risk factors. This suggests that for early-stage AKI, controlling the primary infection, improving ventilation, and correcting the internal milieu are paramount to preventing progression.In contrast, the risk profile differed for patients presenting with AKI Stage 2. Here, a lower minimum WBC count emerged as a predictor, showing

a trend towards significance (P = 0.055). While this finding did not reach the conventional threshold for statistical significance, it may suggest a potential association with bone marrow suppression or a specific immunoparalytic state in more advanced AKI, warranting further investigation. Collectively, these findings indicate that the drivers of AKI progression may differ depending on the initial severity of the injury, implying that risk prediction and intervention strategies might need to be individualized according to the AKI stage.

This study leverages real-world data to identify actionable, modifiable risk factors for AKI progression. Unlike novel biomarkers such as NGAL, KIM-1, or L-FABP,[35] our predictors—including MAP, neutrophil percentage, and D-dimer—are routinely available and cost-effective. By shifting focus from predicting AKI onset to understanding its progression, we address a key knowledge gap. Our findings enable early risk stratification and support targeted interventions like infection control, blood pressure support, and acidosis correction, offering a practical strategy to improve patient outcomes.

This study has several limitations. Its single-center, retrospective design introduces an inherent risk of selection bias and limits the generalizability of the findings, which require validation in multi-center, prospective cohorts. Furthermore, data on certain potential confounders, such as the precise accuracy of urine output records or detailed medication dosages, were not available and thus not included in the analysis. Additionally, AKI staging was based on serum creatinine according to KDIGO criteria. The interpretation of serum creatinine can be influenced by non-renal factors such as nutritional status, muscle mass, and the specific assay method used, which may introduce misclassification bias in AKI staging. Future prospective studies are needed to validate these risk factors and to investigate the impact of their dynamic changes on patient outcomes.

Conclusion

This study identified key risk factors for AKI progression, including ischemic heart disease, sepsis, hypotension, inflammation, hypoxia, coagulopathy, and acidosis. By leveraging routinely available clinical indicators, it offers a practical and cost-effective strategy for early identification of high-risk patients and timely intervention—such as infection control, blood pressure support, and hypoxia correction—to prevent the worsening of AKI.

AI Statement

The language of this manuscript was polished with the assistance of DeepSeek, an AI tool.

Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of The Fourth Hospital of Hebei Medical University (2024KS188). This study was a retrospective analysis of medical records and did not involve direct intervention with patients. Therefore, the Ethics Committee waived the requirement for obtaining individual patient informed consent. To protect patient privacy, all collected data were de-identified prior to analysis, and any information that could potentially identify individual patients was removed.

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Disclosure

The authors report no conflicts of interest in this work.

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