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The predictive value of renal vascular resistance index and serum biomarkers for sepsis-associated acute kidney injury: a retrospective study

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Abstract

Background Sepsis-associated acute kidney injury (AKI) presents a significant clinical challenge, necessitating the identification of predictive indicators for early detection and intervention. This retrospective case-control study aimed to investigate the predictive potential of renal vascular resistance index and serum biomarkers in sepsis-associated AKI.

Methods A cohort of 108 patients diagnosed with sepsis was separated into two groups—those with acute kidney injury (AKI) and those without—using the diagnostic criteria established by the kidney disease: Improving Global Outcomes (KDIGO) guidelines. Various demographic, clinical, and laboratory parameters were collected, including renal resistive index, serum biomarkers, disease severity scores, and clinical outcomes. Statistical analyses, including t-tests, correlation analysis, receiver operating characteristic (ROC) analysis, and joint model construction, were conducted to evaluate the predictive value of these parameters.

Results The AKI group exhibited higher APACHE II and SOFA scores compared to the non-AKI group, indicating the association between disease severity scores and the presence of AKI in septic patients. Renal resistive index and several serum biomarkers, including C-reactive protein and procalcitonin, were notably elevated in the AKI group. Correlation analysis demonstrated significant associations between renal vascular resistance index, serological biomarkers, and clinical severity scores. ROC analysis revealed that several parameters, including Renal Resistive Index (AUC = 0.667), C-reactive Protein (CRP, AUC = 0.665), Platelet Count (AUC = 0.666), and Prothrombin Time (AUC = 0.669), demonstrated moderate diagnostic performance for predicting sepsis-associated AKI. These parameters were subsequently incorporated into a joint predictive model, which exhibited robust diagnostic accuracy with an AUC of 0.780, highlighting its potential utility as a reliable predictive tool in clinical practice.

Conclusions The study findings underscore the potential for integrating renal vascular parameters and serum biomarkers in clinical risk stratification and early intervention strategies for sepsis-associated AKI.

Clinical registration Not applicable.

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Keywords Renal vascular resistance index, Serum biomarkers, Sepsis, Acute kidney injury

Introduction

Sepsis, a critical and often deadly condition arising from an abnormal defensive response to infection, represents a substantial load on healthcare systems globally [1–3]. It is a primary cause of morbidity and fatalities, with an approximate annual incidence of approximately 31.5 million cases and 5.3 million deaths worldwide [4–6]. Importantly, sepsis is frequently complicated by acute kidney injury (AKI), further exacerbating the clinical course and outcomes of affected patients. Sepsis-associated AKI is linked to higher mortality rates, extended hospital stays, and grew healthcare costs [7, 8]. Thus, identifying effective predictive indicators for sepsis-associated AKI is critical for early detection, risk stratification, and timely intervention to mitigate the impact of renal dysfunction in septic patients.

The influencing factors of sepsis driving AKI including hemodynamic alterations, microcirculatory dysfunction, immune dysregulation, as well as inflammatory and coagulation cascades [9–11]. The pathophysiology of sepsis-associated AKI involves complex interactions between systemic and renal-specific mechanisms, necessitating a comprehensive understanding of the predictive parameters for early detection and intervention [12, 13]. Recently, efforts have been directed towards elucidating the predictive potential of renal vascular resistance index and serum biomarkers in sepsis-associated AKI [14, 15].

Smoking, alcohol consumption, hypertension, diabetes, and hyperlipidemia were selected as parameters in this study because they are well-documented risk factors for AKI and are commonly associated with poor renal outcomes in patients with sepsis. Smoking has been shown to exacerbate vascular inflammation and endothelial dysfunction, contributing to an increased risk of AKI in critically ill patients [16]. Heavy alcohol consumption, independently or in combination with smoking, is associated with impaired kidney function and an increased incidence of CKD, a precursor to AKI [17]. Hypertension and diabetes, which are components of metabolic syndrome, are recognized as strong predictors of AKI due to their impact on systemic vascular resistance and microvascular damage, leading to impaired renal perfusion and increased susceptibility to injury during sepsis [18]. Hyperlipidemia, through its association with oxidative stress and endothelial dysfunction, has also been implicated in the pathogenesis of kidney injury and contributes to systemic inflammation in sepsis-associated AKI [19].

In this context, understanding the predictive associations between renal vascular resistance index, serum biomarkers, and disease severity scores has the potential to revolutionize risk stratification and early intervention strategies for sepsis-associated AKI. This manuscript aims to synthesize the existing evidence on the predictive value of renal vascular resistance index and serum biomarkers, shedding light on their interplay and potential as integrated predictive indicators in clinical risk stratification.

Materials and methods

Study design

This study utilized a retrospective case-control design, analyzing data from a total of 108 sepsis patients admitted to the internal medicine intensive care unit from October 2021 to October 2022. The patients were classified into AKI and non-AKI groups following the KDIGO diagnostic criteria to determine the occurrence of AKI within 7 days.

Inclusion and exclusion criteria

Inclusion criteria [16]: (1) Patients diagnosed with sepsis according to the Sepsis 3.0 diagnostic criteria [17]; Patients with a SOFA score greater than or equal to 2; (3) Patients aged over 18 years; (4) Patients with normal mental and cognitive function; (5) Patients with complete medical records.

Exclusion criteria: (1) Patients receiving dialysis upon ICU admission, with a history of regular dialysis, or suffering from chronic renal insufficiency [17]; Patients who have undergone kidney transplantation; (3) Patients who developed AKI before ICU admission, while patients with documented CKD or preexisting renal impairment were excluded, some AKI cases may have had undiagnosed baseline kidney dysfunction. To mitigate this, we rigorously reviewed medical histories and baseline serum creatinine levels (obtained within 3 months prior to admission) to differentiate de novo sepsis-associated AKI from AKI superimposed on unrecognized CKD; (4) Hospital stay of less than 1 day and failure to meet the Sepsis-3 criteria for septic shock within 24 h of admission; (5) Presence of confounding factors for shock etiology (such as cardiogenic or hypovolemic shock).

Grouping criteria

According to the 2012 KDIGO (Kidney Disease Improving Global Outcomes) guidelines, the diagnosis of AKI can be established if any of the listed criteria are met: (1) an elevation in serum creatinine level exceeding 26.5 umol/L within 48 h [17]; Serum creatinine levels increased by exceeding 1.5 times the baseline level.; (3) urine output was lower than 0.5 ml/kg/h lasting for over 6 h (when using urine output alone as the diagnostic

criterion, urinary tract obstruction and other causes of decreased urine output should be excluded).

Data collection

Patient demographic information, including age, gender, smoking history, alcohol consumption history, and comorbidities such as hypertension, diabetes, and hyperlipidemia, was collected and recorded from the medical records system. Additionally, APACHE and SOFA scores of the patients were gathered and tabulated. The renal vascular resistance index and serological biomarkers, specifically including renal resistance index (RRI), mean arterial pressure, urine output, and serum creatinine concentration, were also collected and recorded. In addition, the concentrations of inflammatory markers, such as C-reactive protein and procalcitonin (PCT), together with coagulation parameters, including D-dimer, platelet count, prothrombin time, fibrinogen, and international normalized ratio, were statistically compared between the two patient groups.

Methods

APACHE-II score

The APACHE-II score consists of three parts: A, B, and C. Part A includes the Acute Physiology Score [18], comprising 12 physiological parameters. Part B involves the age score, while part C encompasses the chronic health score. This scoring system ranges from 0 to 71 points, allowing for a quantitative assessment of the patient's condition, with higher scores indicating greater severity, poorer prognosis, and higher mortality rates.

SOFA score

The SOFA score is a rating system used to assess patient prognosis by measuring the extent of major organ dysfunction. This scoring system comprises six aspects, including respiratory function, coagulation function, liver function, cardiovascular system, central nervous system, and renal function, with each component scored from 0 to 4 points. A higher SOFA score reflects more severe organ dysfunction and suggests a worse prognosis.

RRI

RRI measurements were conducted using a Sonoscape color Doppler bedside ultrasound machine. A convex array transducer was utilized to obtain a coronal section of the kidney, and Doppler mode was employed to monitor blood flow. A sample volume of 2 mm was selected, and measurements were taken at the proximal, middle, and distal segments of the interlobar artery, with each segment being measured three times to obtain an average value. To ensure measurement consistency, all RRI assessments were performed by the same group of trained sonographers. Interobserver reproducibility was evaluated using the intra-class correlation coefficient (ICC), which demonstrated excellent agreement (ICC = 0.85). Bland-Altman analysis further confirmed minimal bias (mean difference: 0.02; 95% limits of agreement: -0.08 to 0.12), supporting the reliability of the measurements. The formula RRI = (systolic peak velocity - end-diastolic velocity) / systolic peak velocity was used to calculate the renal vascular resistance index, with the normal range of RRI generally considered to be 0.55 to 0.7.

Measurement of Mean Arterial Pressure (MAP)

The Philips MX450 multifunction monitor (Philips, Netherlands) was used for routine continuous monitoring of systolic blood pressure (SBP) and diastolic blood pressure (DBP), from which the mean arterial pressure (MAP) was calculated. The calculation for the MAP level is as follows: MAP = (SBP + 2 * DBP) / 3.

Urinary output

The 24-hour urine volume was collected from 7:00 AM on the day of admission until 7:00 AM the following day, during which time these patients were in a state of catheterization. The total volume of the urine sample was accurately measured and recorded.

Blood parameters

A fasting 5 ml blood sample was collected from the antecubital vein in the morning for blood testing. The sample was centrifuged at a rate of 3000 r/min for 5 min, and the supernatant was used for the analysis of Scr and PCT. Scr was analyzed using the AU5800 automated biochemistry analyzer from Beckman Coulter (Brea, CA, USA) by the scattering method. PCT was analyzed using the iFlash3000 chemiluminescence method from AutoBi Fengxiang Medical Technology Co., Ltd. (Shenzhen, China). C-reactive protein was measured using a nephelometry assay with a Siemens BNII or BN Pro specific protein analyzer (Siemens, Germany) and matched reagents (batch number 16573 C).

Measurements of D-dimer, prothrombin time, fibrinogen, and international standardized ratio were conducted using the magnetic bead method on the Sysmex analyzer (Sysmex, Kobe, Japan). Platelet count was determined using the BC-6800 Plus hematology analyzer from Mindray (Shenzhen, China) by flow cytometric staining.

Statistical methods

The acquired data was processed using SPSS software. Continuous data were expressed as ($x \pm s$) if the normality criterion was met and the variance was homogeneous between the two groups, and intergroup contrasts were conducted using the t-test. Categorical data were depicted as frequencies or rates, and

Table 1 Comparison of baseline characteristics between AKI and Non-AKI groups

Parameter	AKI ($n=51$)	No-AKI ($n=57$)	t/χ^2	P
Age (years)	63.38 ± 7.21	62.94 ± 6.55	0.328	0.743
Gender (M/F)	34 (66.67%) / 17 (33.33%)	41 (71.93%) / 16 (28.07%)	0.147	0.701
Smoking history	10 (19.61%)	8 (14.04%)	0.267	0.605
Drinking history	12 (23.53%)	10 (17.54%)	0.283	0.595
Comorbidities	26 (50.98%)	26 (45.61%)	0.133	0.716
Hypertension [n (%)]				
Diabetes [n (%)]	13 (25.49%)	17 (29.82%)	0.082	0.774
Hyperlipidemia [n (%)]	23 (45.1%)	23 (40.35%)	0.092	0.762

intergroup comparisons were assessed using the χ^2 test. Logistic regression analysis was utilized to determine the risk factors influencing the occurrence of AKI in septic patients. Pearson correlation analysis was performed to investigate the correlation between blood and renal resistance index, and the KDIGO staging in septic patients with concomitant AKI. ROC analysis was used to assess the predictive value of blood, and renal resistance index for AKI in septic patients, with the area under the curve (AUC) indicating the predictive value. ROC analysis was performed to evaluate the diagnostic performance of individual parameters as well as the joint diagnostic model for predicting sepsis-associated AKI. Parameters with significant diagnostic potential (AUC ≥ 0.65) were selected for inclusion in the joint model. Statistical significance was set at $P<0.05$.

Results

Comparison of baseline characteristics between AKI and no-AKI groups

The comparison of baseline characteristics between the AKI and no-AKI groups revealed no statistically significant differences (Table 1). The mean age was 63.38 ± 7.21 years in the AKI group and 62.94 ± 6.55 years in the no-AKI group ($P>0.05$). Gender distribution showed 34 (66.67%) males and 17 (33.33%) females in the AKI group, and 41 (71.93%) males and 16 (28.07%) females in the no-AKI group ($P>0.05$). Similarly, smoking history, drinking history, hypertension, diabetes, and hyperlipidemia failed to show statistically significant distinctions between the two groups ($P>0.05$). These results suggest that baseline characteristics were comparable between the AKI and no-AKI groups.

Analysis of APACHE II and SOFA scores in relation to AKI

The mean APACHE II score was 20.14 ± 3.67 within the AKI group and 18.75 ± 2.91 in the no-AKI group (t = 2.169, $P=0.033$), while the mean SOFA score was 6.03 ± 2.55 within the AKI group and 4.89 ± 2.98 within the no-AKI group (t = 2.139, $P=0.035$), indicating higher scores in the AKI group (Table 2). These results suggest a potential association between higher APACHE II and SOFA scores and the presence of sepsis-associated AKI.

Table 2 APACHE II score and sequential organ failure assessment (SOFA) score

Parameter	AKI ($n=51$)	No-AKI ($n=57$)	t/χ^2	P
APACHE II score	20.14 ± 3.67	18.75 ± 2.91	2.169	0.033
Sequential organ failure assessment (SOFA) score	6.03 ± 2.55	4.89 ± 2.98	2.139	0.035

Table 3 Comparison of renal function indexes between AKI and No-AKI groups

Parameter	AKI ($n=51$)	No-AKI ($n=57$)	t	P
Renal resistive index	0.73 ± 0.14	0.66 ± 0.11	2.739	0.007
Mean arterial pressure (mmHg)	87.24 ± 5.41	89.14 ± 5.68	1.787	0.077
Urine output (mL/day)	1450.32 ± 320.25	1582.19 ± 290.76	2.231	0.028
Serum creatinine (mg/dL)	1.85 ± 0.32	1.72 ± 0.29	2.183	0.031

Evaluation of renal vascular resistance and renal function indices

The renal resistive index was markedly higher in the AKI group relative to the no-AKI group (t = 2.739, $P=0.007$), indicating increased renal vascular resistance in the AKI group (Table 3). Serum creatinine levels were markedly higher in the AKI group relative to the no-AKI group (t = 2.183, $P=0.031$), indicating impaired renal function. Urine output was considerably lower (t = 2.231, $P=0.028$) and serum creatinine levels were significantly higher (t = 2.183, $P=0.031$) in the AKI group versus the no-AKI group. Nevertheless, no statistically significant differences were detected in mean arterial pressure between the two groups. These results indicate the potential utility of renal resistive index as predictive biomarkers for sepsis-associated AKI.

Assessment of inflammatory markers in AKI and no-AKI groups

Relative to the no-AKI group, C-reactive protein levels were notably elevated in the AKI group. (t = 3.039, $P=0.003$), indicating a heightened inflammatory response in the AKI population (Fig. 1). PCT levels were also elevated in the AKI group versus the no-AKI group (t = 2.242, $P=0.027$), suggesting a potential role as a biomarker for sepsis-associated AKI. These findings indicate the potential utility of C-reactive protein and PCT as predictive biomarkers for sepsis-associated AKI.

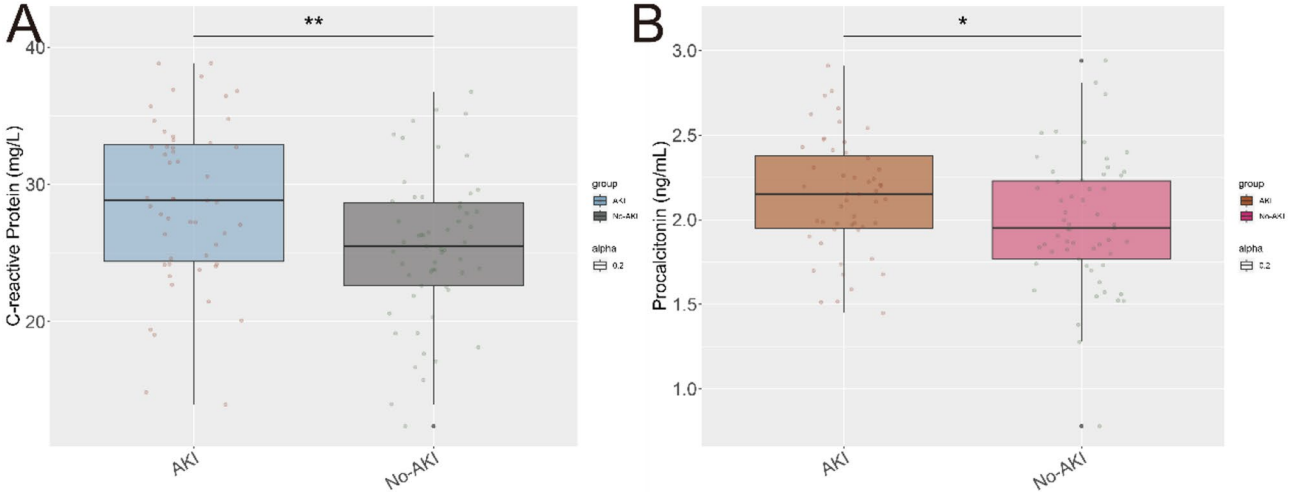

Fig. 1 Comparison of inflammatory markers between AKI and No-AKI groups

Comparison of coagulation parameters between AKI and non-AKI groups

The D-dimer levels were significantly elevated in the AKI group compared to the no-AKI group (t = 2.206, $P = 0.03$), indicating an increased thrombotic risk in patients with sepsis-associated AKI (Fig. 2). Additionally, platelet count was significantly lower (t = 3.11, $P = 0.002$) and prothrombin time was significantly prolonged (t = 3.101, $P = 0.002$) in the AKI group versus the no-AKI group, suggesting a potential coagulopathic state in the AKI population. Furthermore, fibrinogen levels were significantly elevated (t = 2.331, $P = 0.022$) and the international normalized ratio (INR) was higher (t = 2.697, $P = 0.008$) in the AKI group versus the no-AKI group. These findings indicate the potential utility of D-dimer, platelet count, prothrombin time, fibrinogen, and INR as predictive indicators for coagulation abnormalities associated with sepsis-associated AKI.

Analysis of correlations between biomarkers and clinical parameters

For the correlation analysis presented in Table 4, Pearson's correlation coefficient was used to evaluate the strength and orientation of the linear correlation between sets of continuous variables. This method is suitable because the relationships between the variables are expected to be linear, and the data for each variable are assumed to be normally distributed or approximately normal, which is a common assumption for Pearson's correlation. All variables are measured on an interval or ratio scale, making them suitable for Pearson's correlation. Although not strictly required, bivariate normality is often assumed for Pearson's correlation, meaning that the joint distribution of any two variables is bivariate normal. These reasons justify the selection of Pearson's correlation coefficient for the analysis of the data presented in the study. The correlation analysis demonstrated several statistically significant associations between renal vascular resistance index, serological biomarkers, and clinical scores in patients with sepsis complicated by AKI (Table 4). Positive correlations were identified between renal resistive index and C-reactive protein ($r = 0.285$, $P = 0.003$), PCT ($r = 0.211$, $P = 0.028$), and D-dimer ($r = 0.212$, $P = 0.028$). Additionally, significant positive correlations were identified between APACHE II and SOFA scores, as well as serum creatinine levels and APACHE II score, SOFA score, and urine output. Conversely, negative correlations were identified between platelet count and urine output (r=-0.291, $P = 0.002$), suggesting a potential link between thrombocytopenia and reduced urine output in this patient population. These findings highlight the interconnectedness of renal vascular parameters, serological biomarkers, and clinical severity scores in sepsis-associated AKI, underscoring the potential for these parameters to serve as predictive indicators in clinical practice.

ROC analysis of predictive biomarkers for AKI

The predictive value of renal vascular resistance index and serum biomarkers for sepsis-associated AKI was evaluated based on sensitivities, specificities, area under the curve (AUC), Youden index, P, and 95% confidence interval (95% CI) (Table 5). The renal resistive index demonstrated a high sensitivity of 0.93, an AUC of 0.667 (95% CI: 0.565–0.769), and a statistically significant P value of 0.004, highlighting its potential as a valuable predictive indicator for sepsis-associated AKI. The parameters were classified into categories for clarity: disease severity scores (e.g., APACHE II and SOFA scores), renal function parameters (e.g., renal resistive index and serum creatinine), inflammatory markers (e.g., C-reactive protein and procalcitonin), and coagulation parameters (e.g., D-dimer, platelet count, and fibrinogen). While several

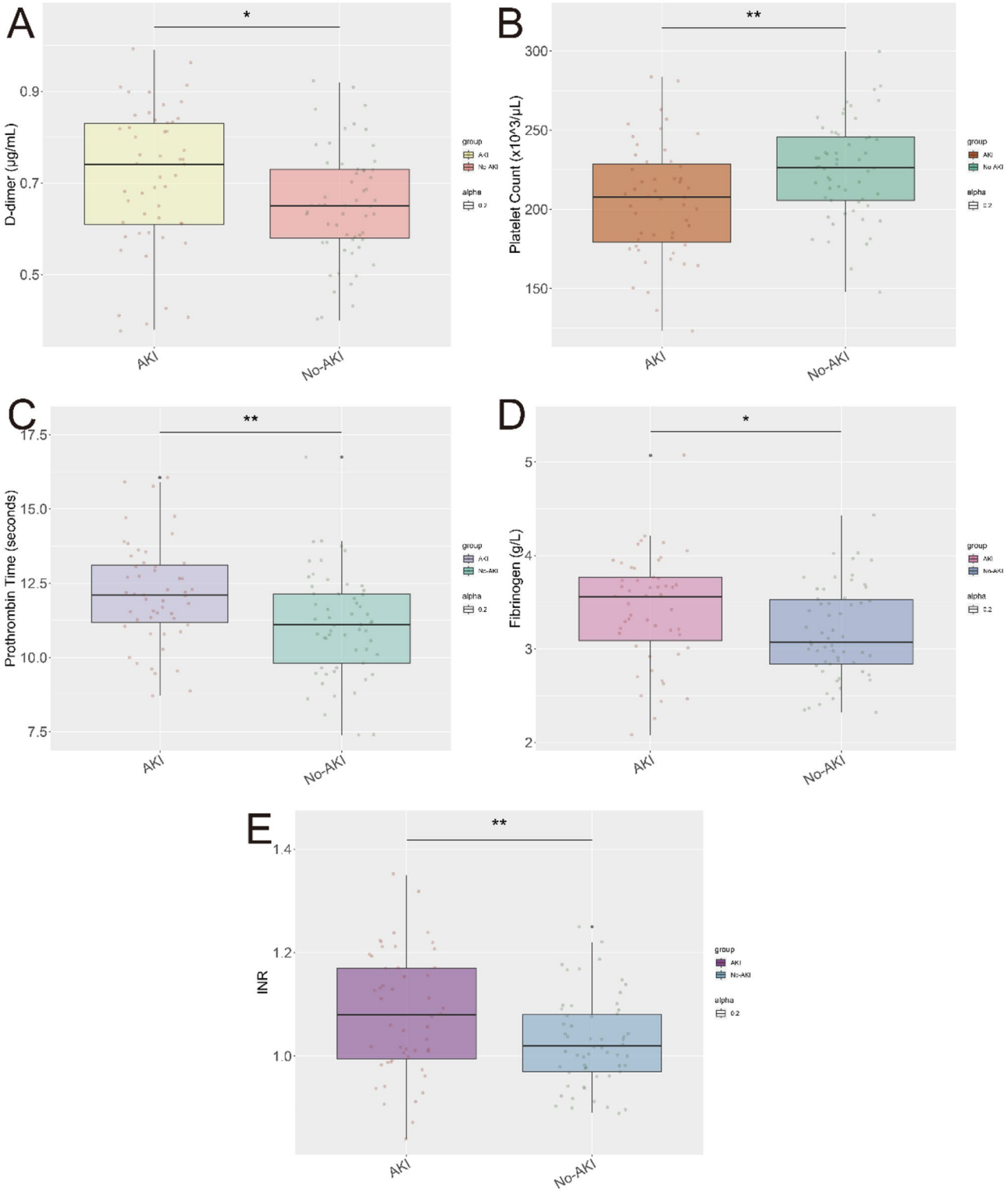

Fig. 2 Comparison of coagulation parameters between AKI and No-AKI groups

Table 4 Correlation analysis of renal vascular resistance index and serological biomarkers with sepsis complicated with AKI

Parameter	*r*	R^2	*P*
APACHE II score	0.209	0.044	0.03
Sequential organ failure assessment (SOFA) score	0.202	0.041	0.036
Renal resistive index	0.261	0.068	0.006
Urine output (mL/day)	-0.213	0.045	0.027
Serum creatinine (mg/dL)	0.209	0.044	0.03
C-reactive protein (mg/L)	0.285	0.081	0.003
Procalcitonin (ng/mL)	0.211	0.045	0.028
D-dimer (μg/mL)	0.212	0.045	0.028
Platelet count (x10^3/μL)	-0.291	0.085	0.002
Prothrombin time (seconds)	0.288	0.083	0.003
Fibrinogen (g/L)	0.223	0.05	0.02

parameters demonstrated moderate AUC values and sensitivities, the specificities varied across categories, indicating the need for further assessment of these biomarkers to enhance their clinical utility for predicting sepsis-associated AKI.

Development and evaluation of a joint predictive model for AKI

A threshold of AUC ≥ 0.65 was used to identify parameters with moderate to high diagnostic accuracy for predicting sepsis-associated AKI. Four parameters met this criterion: Renal Resistive Index (AUC = 0.667), C-reactive Protein (CRP) (AUC = 0.663), Platelet Count (AUC = 0.666), and Prothrombin Time (AUC = 0.669). These parameters were subsequently incorporated into the joint model to evaluate their combined diagnostic value. These parameters were subsequently incorporated into the joint model to evaluate their combined diagnostic value. The joint model demonstrated an AUC of 0.780 (95% CI: 0.710–0.850), with a sensitivity of 81.0% and a specificity of 72.5% (Fig. 3).

Discussion

Sepsis is known to be a major contributor to the development of AKI and is linked to high morbidity and mortality rates [19–21]. Understanding the predictive value of renal vascular resistance index and serum biomarkers for sepsis-associated AKI is crucial for early diagnosis and management of renal dysfunction in septic patients [22–24]. In this retrospective case-control study, we examined a set of sepsis patients hospitalized in the internal medicine intensive care unit and categorized them into AKI and non-AKI groups to investigate the predictive potential of renal vascular resistance index and various serum biomarkers.

The higher APACHE II and SOFA scores observed in the AKI group are consistent with previous studies [25–27] indicating the association between disease severity scores and the presence of AKI in septic patients. These findings highlight the prognostic significance of these scoring systems in identifying patients at higher risk for sepsis-associated AKI.

Our study demonstrated that renal vascular resistance index, and serum biomarkers including C-reactive protein and PCT were notably elevated in the AKI group, in comparison to the non-AKI group. The elevation of renal resistive index in the AKI group indicates increased renal vascular resistance, which may be reflective of renal microcirculatory alterations associated with sepsis-induced renal injury. The increased renal vascular resistance index observed in septic patients with AKI may reflect underlying renal vasoconstriction and microcirculatory dysfunction. These hemodynamic perturbations

Table 5 The predictive value of renal vascular resistance index and serum biomarkers for sepsis-associated AKI

Parameter	Sensitivities	Specificities	AUC (95% CI)	*P*	Youden index
Disease severity scores					
APACHE II score	0.825	0.471	0.628 (0.532–0.724)	0.012	0.296
Sequential organ failure assessment (SOFA) score	0.333	0.922	0.612 (0.504–0.720)	0.031	0.255
Renal parameters					
Renal resistive index	0.93	0.353	0.667 (0.565–0.769)	0.004	0.283
Mean arterial pressure (mmHg)	0.333	0.882	0.606 (0.504–0.708)	0.045	0.215
Urine output (mL/day)	0.789	0.431	0.606 (0.512–0.700)	0.041	0.220
Serum creatinine (mg/dL)	0.789	0.392	0.611 (0.510–0.712)	0.036	0.181
Inflammatory markers					
C-reactive protein (mg/L)	0.649	0.647	0.663 (0.562–0.764)	0.009	0.296
Procalcitonin (ng/mL)	0.526	0.745	0.625 (0.521–0.729)	0.024	0.271
Coagulation parameters					
D-dimer (μg/mL)	0.772	0.510	0.632 (0.531–0.733)	0.018	0.282
Platelet count (x10^3/μL)	0.579	0.706	0.666 (0.567–0.765)	0.008	0.285
Prothrombin time (seconds)	0.614	0.686	0.669 (0.571–0.767)	0.007	0.300
Fibrinogen (g/L)	0.544	0.745	0.637 (0.534–0.740)	0.020	0.289
INR	0.842	0.451	0.638 (0.538–0.738)	0.019	0.293

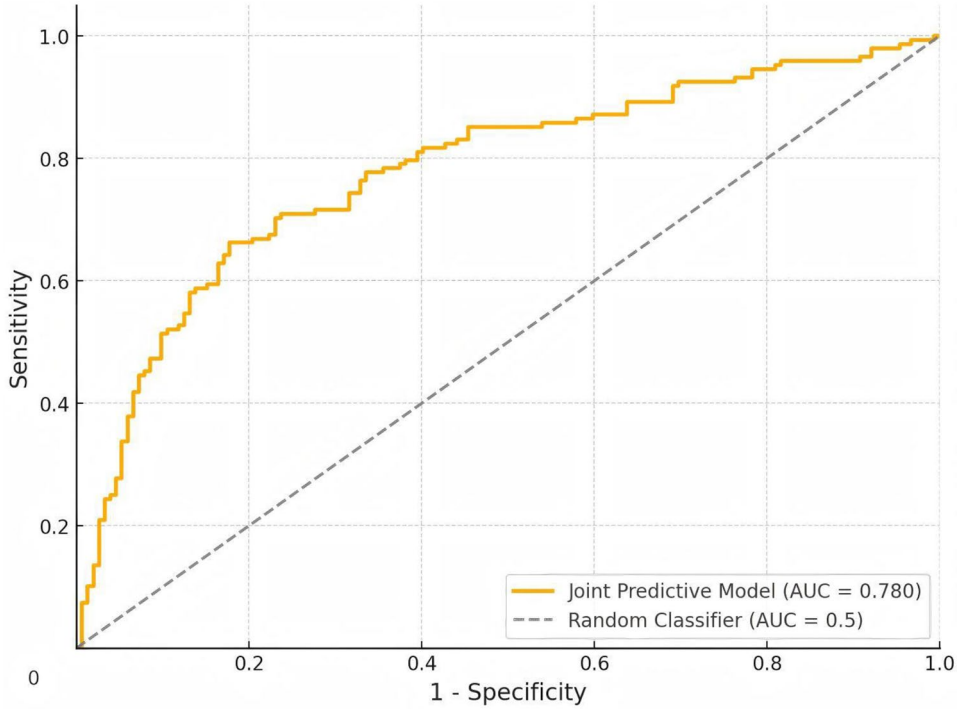

Fig. 3 Joint predictive model of renal vascular resistance index and serological biomarkers

can lead to renal hypoperfusion, impaired oxygen delivery, and subsequent tubular injury, underscoring the prognostic relevance of renal vascular resistance index as a marker of renal microcirculatory dysfunction [28–30].

PCT levels have been shown to correlate with certain parameters, including smoking, hypertension, diabetes, and hyperlipidemia, which are commonly observed in patients with sepsis-associated AKI. Elevated PCT is considered a biomarker of inflammation and bacterial infection but is also linked to chronic low-grade inflammation and metabolic disturbances. For example, studies suggest that smoking and diabetes can amplify the inflammatory response and increase PCT levels due to enhanced oxidative stress and immune activation [31, 32]. Smoking has been identified as a factor that exacerbates vascular damage and inflammation, leading to elevated markers like PCT through direct effects on endothelial cells and immune pathways [33]. Hypertension and hyperlipidemia, both components of metabolic syndrome, are also associated with increased systemic inflammation and higher PCT levels [34]. These conditions contribute to endothelial dysfunction and adipose tissue inflammation, which further elevate PCT levels. In our study, parameters such as smoking history, drinking history, hypertension, diabetes, and hyperlipidemia showed no statistically significant differences between the AKI and non-AKI groups. These findings suggest that the observed elevation in PCT levels in AKI patients is not directly attributable to these baseline characteristics alone but may be driven by the systemic inflammatory response and renal dysfunction associated with sepsis. This highlights the complexity of the interplay between sepsis, inflammatory markers, and clinical outcomes, necessitating further exploration into the specific mechanisms linking these factors to AKI development.

The elevated RRI in the AKI group indicates increased renal vascular resistance, which may be reflective of renal microcirculatory alterations associated with sepsis-induced renal injury. Hemodynamic instability in sepsis triggers sympathetic overactivation and angiotensin II release, exacerbating renal vascular resistance, while endothelial injury and oxidative stress further disrupt microcirculatory flow [35]. Studies have shown that oxidative stress mediated glycocalyx degradation can cause an increase in RRI or postoperative AKI [36]. Meanwhile, RRI is also low-cost, non-invasive and easily reproducible markers of endothelial dysfunction [37]. These mechanisms align with findings from a 2023 cohort study demonstrating that RRI outperformed serum cystatin C and NGAL in predicting SA-AKI, underscoring its sensitivity to early hemodynamic and microvascular perturbations [38]. Furthermore, the significant correlations between renal vascular resistance index, serum biomarkers, and clinical severity scores highlight the interconnectedness of renal vascular parameters and systemic inflammatory and coagulation responses in sepsis-associated AKI, suggesting their potential as integrated predictive indicators in clinical practice.

The evaluation of the predictive value of renal vascular resistance index and serum biomarkers through ROC analysis and the construction of a joint model revealed promising sensitivities and specificities for these parameters, underlining their potential utility as predictive tools for sepsis-associated AKI. The joint model demonstrated a high AUC value, indicating its significant predictive value in identifying septic patients susceptible to developing AKI. These findings emphasize the potential for the integration of renal vascular parameters and serum biomarkers in clinical risk stratification and early intervention strategies for sepsis-associated AKI.

While traditional biomarkers such as NGAL, KIM-1, and IL-18 are well-established for early AKI detection due to their sensitivity to tubular injury, their specificity in SA-AKI is often confounded by systemic inflammation and extrarenal comorbidities [39–41]. In contrast, RRI provides direct insight into renal hemodynamic alterations such as vasoconstriction and microcirculatory dysfunction, which may better reflect the unique pathophysiology of SA-AKI. For instance, a study demonstrated that RRI outperformed NGAL in predicting SA-AKI, highlighting its utility in differentiating sepsis-driven renal hypoperfusion from generalized tubular injury [38]. These findings suggest that RRI complements traditional biomarkers by capturing distinct mechanistic pathways, potentially enhancing risk stratification when integrated with serological markers.

This study has several limitations. First, the retrospective design may introduce selection and information biases inherent to such studies. Second, the relatively small sample size limits the generalizability of the findings and increases the risk of type II errors. These factors underscore the need for validation in larger, prospective multicenter cohorts. Third, while patients with documented CKD or preexisting renal impairment were excluded, some AKI cases may have had undiagnosed baseline kidney dysfunction. To mitigate this, we rigorously reviewed medical histories and baseline serum creatinine levels to differentiate de novo sepsis-associated AKI from AKI superimposed on unrecognized CKD. Nonetheless, residual confounding from subclinical renal impairment cannot be entirely ruled out. Finally, while RRI demonstrated diagnostic potential, its operator-dependent nature necessitates standardized protocols and trained personnel for clinical implementation.

Conclusion

To conclude, our study provides important perspectives into the predictive potential of renal vascular resistance index and serum biomarkers for sepsis-associated AKI. The associations between renal vascular parameters, inflammatory and coagulation markers, and disease severity scores highlight their interplay in the pathophysiology of sepsis-induced renal injury. The findings underscore the potential for these parameters to serve as integrated predictive indicators in the clinical management of septic patients at risk of developing AKI. Future studies should focus on prospective validation of these predictive tools and explore additional biomarkers to enhance risk stratification and facilitate early interventions for sepsis-associated AKI.

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Author contributions
Zhaobin Yang: Investigation, Methodology, Data curation, Formal analysis, Writing - original draft; Luzhen Qiu: Investigation, Methodology, Formal analysis, Software; Jinzhan Lin: Investigation, Methodology, Software; Xiaomei Cheng: Methodology, Formal analysis, Software; Daofeng Huang: Conceptualization, Project administration, Supervision, Funding acquisition, Writing - review and editing.

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Data availability
The dataset generated or analyzed in this study can be provided under reasonable request from corresponding author (Daofeng Huang, hdf2527@163.com).

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Zhangzhou Hospital Affiliated to Fujian Medical University (No. 2020QH1288) in accordance with regulatory and ethical guidelines. Informed consents were obtained from all patients or their representatives prior to enrollment.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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