

Original Article

Predictive value of renal resistive index and urinary neutrophil gelatinase-associated lipocalin for acute pancreatitis-associated renal injury and renal replacement therapy efficacy

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Abstract: Objective: To evaluate the predictive value of Renal Resistive Index (RRI) and urinary neutrophil gelatinase-associated lipocalin (uNGAL) for acute pancreatitis (AP)-associated acute kidney injury (AKI) and the efficacy of continuous renal replacement therapy (CRRT). Methods: A retrospective analysis was conducted on 251 patients with AP treated between July 2022 and May 2024. The patients were divided into an AKI group (145 cases) and a non-AKI group (106 cases) based on the occurrence of AKI. Clinical data and laboratory indicators, including RRI, uNGAL, serum creatinine (SCr), and blood urea nitrogen (BUN) were collected and compared between the two groups. Independent risk factors for AKI were identified using multivariate logistic regression, and receiver operating characteristic (ROC) curves were generated to assess predictive performance. Among the AKI patients who received CRRT, treatment response was evaluated by reductions in SCr, BUN, and Cystatin C (CysC), dividing patients into an effective group (74 cases) and an ineffective group (71 cases). Logistic regression model was used to identify independent predictors of CRRT efficacy, and ROC curves were applied to evaluate the predictive performance of relevant factors. Results: Compared with the non-AKI group, the AKI group exhibited significantly higher RRI (0.83 vs. 0.61, $P<0.001$), uNGAL (110.32 ng/mL vs. 77.89 ng/mL, $P<0.001$), and SCr (84.15 $\mu\text{mol/L}$ vs. 72.99 $\mu\text{mol/L}$, $P<0.001$). C-reactive protein (CRP) also showed a statistically significant difference ($P=0.010$). High uNGAL (OR=13.378, $P<0.001$), RRI (OR=16.246, $P<0.001$), and SCr (OR=3.138, $P=0.002$) levels were protective factors against AKI in AP patients. In patients undergoing CRRT, diabetes (OR=5.464, $P=0.014$), elevated uNGAL (OR=7.824, $P=0.001$), RRI (OR=11.556, $P<0.001$), and white blood cell count (WBC, OR=9.682, $P<0.001$) were independent risk factors for poor treatment response. ROC curve analysis showed that RRI (AUC=0.855) and uNGAL (AUC=0.804) had high predictive values for CRRT efficacy. Conclusion: RRI, uNGAL, SCr, and CRP are valuable predictors of AP-associated AKI. Among patients receiving CRRT, diabetes, elevated uNGAL, high RRI, and elevated WBC are associated with reduced treatment efficacy.

Keywords: Acute pancreatitis, renal injury, renal resistance index (RRI), urinary neutrophil gelatinase-associated lipocalin (uNGAL), renal replacement therapy

Introduction

Acute pancreatitis (AP) is a common acute abdominal condition characterized by remarkable heterogeneity in clinical presentation. While mild cases may resolve spontaneously, severe cases can progress to multiple organ dysfunction syndrome, posing serious threat to patient health and survival [1, 2]. Epidemiological data show that the global incidence of AP is

on the rise, with approximately 13 to 45 cases per 100,000 individuals [3].

Acute kidney injury (AKI), a common and severe complication of AP, significantly increases both mortality and length of hospital stay [4]. The incidence of AKI is particularly high in patients with severe AP (SAP), reaching 25%-45% [5]. Once AKI occurs, especially in severe cases, mortality increases significantly. Among

patients requiring continuous renal replacement therapy (CRRT), treatment response varies widely. While some patients recover well, those with poor outcomes experience mortality rates as high as 50%-80% [6]. CRRT remains a key therapeutic option for AP-associated AKI. However, timely and accurate evaluation of therapeutic efficacy is crucial for improving patient outcomes. Conventional renal function indices such as serum creatinine (SCr) and blood urea nitrogen (BUN) provide limited value in assessing CRRT efficacy and fail to meet clinical needs [7]. Moreover, there is currently no gold standard for evaluating CRRT efficacy in clinical practice, necessitating comprehensive judgment combining laboratory tests, imaging examinations, and organ function evaluations. Therefore, identifying more sensitive and specific markers for the early prediction of AP-related AKI and for evaluating post-treatment efficacy, remains a major focus of clinical research.

The renal resistive index (RRI) is a hemodynamic parameter derived from Doppler ultrasound assessment of intrarenal blood flow [8]. Renal injury can lead to increased intrarenal vascular resistance, thereby increasing the RRI value [9]. Existing studies have shown that in conditions such as sepsis and hepatorenal syndrome, RRI correlates closely with the severity of renal injury and patient prognosis [10]. For example, in septic patients, an elevated RRI not only predicts the occurrence of renal injury but also correlates with increased patient mortality [11]. Although RRI may reflect renal hemodynamic changes and the degree of renal injury in AP patients, relevant studies are currently limited. Its utility in predicting the occurrence of AP-related AKI and treatment efficacy evaluation remains to be further clarified [12].

Urinary neutrophil gelatinase-associated lipocalin (uNGAL) is a protein highly expressed in renal tubular epithelial cells [13]. Upon tubular injury, uNGAL is rapidly released into the urine, with urinary concentrations rising significantly within 2-4 hours - much earlier than changes observed in traditional indices such as SCr [14]. Numerous studies have confirmed that uNGAL exhibits high sensitivity and specificity in the early diagnosis of AKI from various causes, including cardiac surgery and trauma [15, 16]. However, in the field of AP-related AKI, although progress has been made, controversies remain

regarding the diagnostic and prognostic value of uNGAL. The value of uNGAL, when used alone or in combination with other indices, for predicting AKI occurrence and evaluating post-treatment efficacy requires further exploration [17]. This study aims to systematically explore the predictive value of RRI and uNGAL for AP-related AKI and evaluating treatment efficacy of CRRT, so as to provide a scientific basis for early diagnosis and optimized clinical decision-making.

Materials and methods

General data

A total of 251 patients with AP admitted to Dingxi People's Hospital from July 2022 to May 2024 were retrospectively included as research subjects. They were divided into the AKI group and non-AKI group according to the occurrence of AKI. This study was approved by the Medical Ethics Committee of Dingxi People's Hospital. Inclusion criteria: (1) aged ≥ 18 years; (2) diagnosis of AP in accordance with established criteria [18] (3) time from onset to admission < 72 hours. Exclusion criteria: (1) death within 48 hours after admission; (2) pre-existing AKI before AP onset; (3) mental illness or communication disorders; (4) history of kidney transplantation; (5) comorbid autoimmune diseases or malignant tumors; (6) pregnancy or lactation.

Sample size calculation was based on the formula for predictive models, $N = EPV \times X/P$, where the EPV (Events Per Variable) was set to at least 10; X represents the number of predictive factors to be included in the model (estimated at 6-8 for pre-treatment AKI risk factors and 5-7 for post-treatment efficacy predictors); and P denotes the incidence of the outcome event. Previous studies reported that the 48-hour comprehensive response rate (renal function + inflammatory improvement) in AP patients with AKI undergoing CRRT ranged from 55% to 68%. The calculation showed that a minimum of 208 patients were required, and finally 251 cases were enrolled according to actual recruitment.

Treatment protocols

Patients in the non-AKI group received conservative management, including fasting, correction of electrolyte disorders, gastrointestinal decompression, routine use of antibiotics for

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infection prophylaxis, administration of H₂ receptor antagonists, somatostatin and other drugs to inhibit pancreatic secretion and reduce pancreatic enzyme activity. Analgesic and antispasmodics therapy were administered for severe pain as needed.

Patients in the AKI group received CRRT in addition to the above-mentioned treatments, using a Prismaflex blood purification machine and Prismaflex M150 filter. The specific procedures were as follows: (1) The circuit and filter were rinsed with 4,000 mL of normal saline. (2) Anticoagulation was achieved with low-molecular-weight heparin sodium at a loading dose of 10-20 U/kg followed by a maintenance dose of 3-15 U/kg/h. (3) The extracorporeal circulation blood flow was maintained at 200-300 mL/min, adjustable according to the patient's blood pressure. (4) The ultrafiltration rate was set at 300-600 mL/h and adjusted based on the degree of edema and hemodynamic status. (5) The replacement fluid contained 143 mmol/L sodium, 116 mmol/L chloride, 2.1 mmol/L calcium, 1.57 mmol/L magnesium, and 12 mmol/L glucose, packaged in a 3 L/bag. (6) Replacement fluid was infused in a pre-dilution mode at a rate of 2,000-3,000 mL/h and replaced every 24 hours.

Diagnostic criteria and index detection methods

The diagnostic criteria for AKI [19] were as follows: (1) a sudden decline in renal function within 48 hours; (2) urine output ≤ 0.5 mL/(kg·h) for at least 6 hours; (3) an increase in serum creatinine (SCr) level ≥ 26.5 μ mol/L. Hypertension was defined as a history of clinic blood pressure $\geq 140/90$ mmHg (1 mmHg=0.133 kPa). Diabetes mellitus was diagnosed according to the World Health Organization (WHO) 1999 criteria for diabetes mellitus and impaired fasting glucose [20]. Smoking was defined as current smoking at admission or smoking cessation ≤ 1 year prior to admission. Alcohol consumption was defined as alcohol intake ≥ 40 g/d for men and ≥ 20 g/d for women, or a history of heavy drinking within the previous 2 weeks (equivalent to >80 g/d of alcohol).

RRI measurement

RRI was measured using a Philips CX50 color Doppler bedside ultrasound machine (frequency:

2-5 MHz). A convex probe was applied to obtain a renal coronal section, and blood flow was monitored in Doppler mode with a 2-mm sampling volume. Measurements were taken at the proximal, middle, and distal segments of the interlobar artery, with 3 repeated measurements at each segment for calculating the mean value. The RRI was defined as $1 - (\text{end-diastolic peak velocity} / \text{systolic peak velocity})$ [21].

uNGAL detection

uNGAL was measured using an enzyme-linked immunosorbent assay (ELISA) kit (Shanghai Jimian Industrial Co., Ltd.) following the manufacturer's instructions.

Detection of SCr, CysC, BUN, and CRP

SCr, CysC, BUN, and CRP levels were measured using a Beckman Coulter AU680 automated biochemical analyzer. White Blood Cell (WBC) count was determined by a SYSMEX XS-500i automated five-differential hematology analyzer. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were measured using a Behnk Elektronik Thrombolyzer XRM automated coagulation analyzer.

Efficacy evaluation of CRRT

Given the lack of a unified gold standard for evaluating CRRT efficacy in AP-associated AKI, three representative indices (SCr, BUN, and CysC) were used for comprehensive assessment. Treatment was considered effective if SCr decreased by $\geq 25\%$ and both BUN and CysC decreased by $\geq 30\%$ within 48 hours after CRRT initiation. Failure to meet these criteria, including minimal reductions or increases in the indices, was classified as poor efficacy [22].

Results evaluation indicators

(1) The levels of RRI and uNGAL were compared between groups; independent influencing factors for AP-associated AKI were identified. (2) The changes in laboratory and physiological indices after treatment were compared between the two groups, as well as the incidence of adverse reactions. (3) The clinical efficacy of CRRT in the AKI group was assessed, and the patients were categorized into effective group and ineffective group. Logistic regression analysis was used to identify risk factors associated with poor treatment response. (4) Receiver

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Table 1. Comparison of general data between the two groups

Variables	Non-AKI Group (n=106)	AKI Group (n=145)	t/ χ^2 /Z	P
Age (years)	49.50 [40.00, 59.00]	48.00 [38.00, 57.00]	1.369	0.171
Gender			0.079	0.779
Male	56 (52.83%)	74 (51.03%)		
Female	50 (47.17%)	71 (48.97%)		
Diabetes			5.880	0.015
No	88 (83.02%)	101 (69.66%)		
Yes	18 (16.98%)	44 (30.34%)		
Hypertension			0.050	0.823
No	86 (81.13%)	116 (80.00%)		
Yes	20 (18.87%)	29 (20.00%)		
Smoking history			0.124	0.724
No	92 (86.79%)	128 (88.28%)		
Yes	14 (13.21%)	17 (11.72%)		
Alcohol consumption history			1.708	0.191
No	94 (88.68%)	120 (82.76%)		
Yes	12 (11.32%)	25 (17.24%)		
APACHE II	11.26 [9.09, 13.71]	12.98 [11.05, 14.60]	4.160	<0.001
Urine output (mL/24 h)	1269.44 [1107.25, 1521.43]	1200.31 [1031.34, 1343.78]	3.791	<0.001
Heart rate (beats/min)	91.84 [83.35, 106.58]	96.63 [87.56, 111.25]	2.548	0.011
Respiratory rate (times/min)	26.48±2.01	27.37±1.94	-3.529	<0.001

Note: APACHE II (Acute physiology and chronic health Evaluation II).

operator characteristic (ROC) curve analysis was performed to evaluate the predictive value of identified independent risk factors for CRRT efficacy.

Statistical methods

Statistical analysis was performed using SPSS 22.0 statistical software. Measurement data conforming to normal distribution were expressed as mean $\pm$ standard deviation (SD), and independent sample t-test was used for comparison between two groups. Enumeration data were expressed as rate, and chi-square test was used for intergroup comparison. Ranked data were analyzed by rank sum test, expressed as Z value. ROC curves were drawn to calculate the area under the curve (AUC), 95% confidence interval (CI), and standard error (SE). A P value <0.05 was considered statistically significant.

Results

General patient data

Statistical analysis showed no significant differences in age, gender, smoking history, alcohol consumption, or history of hypertension

between the non-AKI and AKI groups ($P>0.05$), while significant differences were observed in diabetes, heart rate, respiratory rate, urine output, and APACHE II score ($P<0.05$), as shown in **Table 1**.

Comparison of laboratory indicators between the AKI and non-AKI groups before treatment

Comparisons between the non-AKI and AKI groups revealed that the AKI group had significantly higher levels of RRI (0.83 vs. 0.61), uNGAL (110.32 vs. 77.89), SCr (84.15 vs. 72.99), Cysc (0.82 vs. 0.69), WBC (16.80 vs. 15.78), PT (16.43 vs. 15.09), BUN (7.24 vs. 6.08), and APTT (44.78 vs. 42.83) compared to the non-AKI group (all $P<0.001$). CRP also showed a statistically significant difference between groups, though less pronounced ($P=0.010$). Detailed results as shown in **Table 2**.

Multivariate analysis of independent risk factors for AKI in patients before treatment

Logistic regression analysis showed that lower levels of uNGAL (OR=13.378, 95% CI=4.692-38.142, $P<0.001$), RRI (OR=16.248, 95% CI=6.265-42.138, $P<0.001$), SCr (OR=3.138, 95%

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Table 2. Comparison of laboratory indicators between the two groups before treatment

Indicator	Non-AKI Group (n=106)	AKI Group (n=145)	t/Z	P
RRI	0.61±0.15	0.83±0.17	10.058	<0.001
uNGAL (ng/mL)	77.89±22.58	110.32±27.00	10.596	<0.001
SCr (μmol/L)	72.99±13.47	84.15±9.62	7.656	<0.001
Cysc (mg/L)	0.69±0.25	0.82±0.21	4.230	<0.001
BUN (mmol/L)	6.08 [4.99, 7.95]	7.24 [6.32, 8.09]	3.810	<0.001
WBC (×10 ⁹ /L)	15.78±2.06	16.80±1.41	4.672	<0.001
CRP (mg/L)	178.85±28.60	189.00±31.64	2.612	0.010
PT(s)	15.09±2.15	16.43±1.89	5.237	<0.001
APTT(s)	42.83 [40.02, 45.95]	44.78 [42.28, 46.74]	2.631	0.009

Note: uNGAL: urinary Neutrophil Gelatinase-Associated Lipocalin, RRI: Renal Resistive Index, SCr: Serum Creatinine, BUN: Blood Urea Nitrogen, Cysc: Cystatin C, WBC: White Blood Cell, CRP: C-reactive protein, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time.

Table 3. Multivariate analysis of factors associated with AKI occurrence

Variable	β	S.E.	P	OR	95% CI	
					Lower Limit	Upper Limit
uNGAL	2.594	0.535	<0.001	13.378	4.692	38.142
RRI	2.788	0.486	<0.001	16.248	6.265	42.138
SCr	1.144	0.462	0.002	3.138	1.269	7.762
Cysc	1.062	0.495	0.007	2.891	1.096	7.630
BUN	1.603	0.467	0.003	4.966	1.987	12.413
WBC	1.737	0.581	0.005	5.679	1.818	17.747
CRP	0.557	0.495	0.197	1.745	0.661	4.605
PT	1.133	0.471	0.011	3.104	1.232	7.820
APTT	0.855	0.454	0.141	2.351	0.966	5.722
Constant	-6.683	0.969	0	0.001		

Note: uNGAL: urinary Neutrophil Gelatinase-Associated Lipocalin, RRI: Renal Resistive Index, SCr: Serum Creatinine, BUN: Blood Urea Nitrogen, Cysc: Cystatin C, WBC: White Blood Cell, CRP: C-reactive protein, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time.

CI=1.269-7.762, P=0.002), Cysc (OR=2.891, 95% CI=1.096-7.630, P=0.007), BUN (OR=4.966, 95% CI=1.987-12.413, P=0.003), WBC (OR=5.679, 95% CI=1.818-17.747, P=0.005), and PT (OR=3.104, 95% CI=1.232-7.820, P=0.011) were independent risk factors for AKI status, as shown in **Table 3**.

Predictive value of independent influencing factors for AKI occurrence

The predictive value of the above independent risk factors for AKI occurrence was evaluated using ROC curve analysis. The AUC values for uNGAL, RRI, SCr, Cysc, BUN, WBC, and PT were 0.815, 0.836, 0.749, 0.853, 0.641, 0.663, and 0.675, respectively (**Figure 1**).

Changes in laboratory indicators of before and after treatment

As shown in **Figure 2**, compared with baseline values, patients in the non-AKI group showed significant improvements in uNGAL (77.89 ng/mL vs. 55.28 ng/mL), SCr (72.99 μmol/L vs. 44.83 μmol/L), BUN (6.08 mmol/L vs. 4.47 mmol/L), Cysc (0.69 μg/mL vs. 0.48 μg/mL), WBC (15.78×10⁹/L vs. 11.72×10⁹/L), and CRP (178.85 mg/L vs. 32.53 mg/L) after conventional treatment (all P<0.001). Similarly, patients in the AP-related AKI group treated with CRRT

showed significant reductions in uNGAL (111.91 ng/mL vs. 88.34 ng/mL), SCr (84.15 μmol/L vs. 59.47 μmol/L), BUN (7.21 mmol/L vs. 5.18 mmol/L), Cysc (0.82 μg/mL vs. 0.59 μg/mL), WBC (18.8×10⁹/L vs. 13.52×10⁹/L), and CRP (189 mg/L vs. 61.45 mg/L) (all P<0.001). These results indicate that CRRT also exerts significant therapeutic benefits in patients with AP-related AKI.

Comparison of physiological indicators between the AKI and non-AKI groups after treatment

After corresponding treatments, both groups showed improvements in physiological indicators compared with baseline. However, com-

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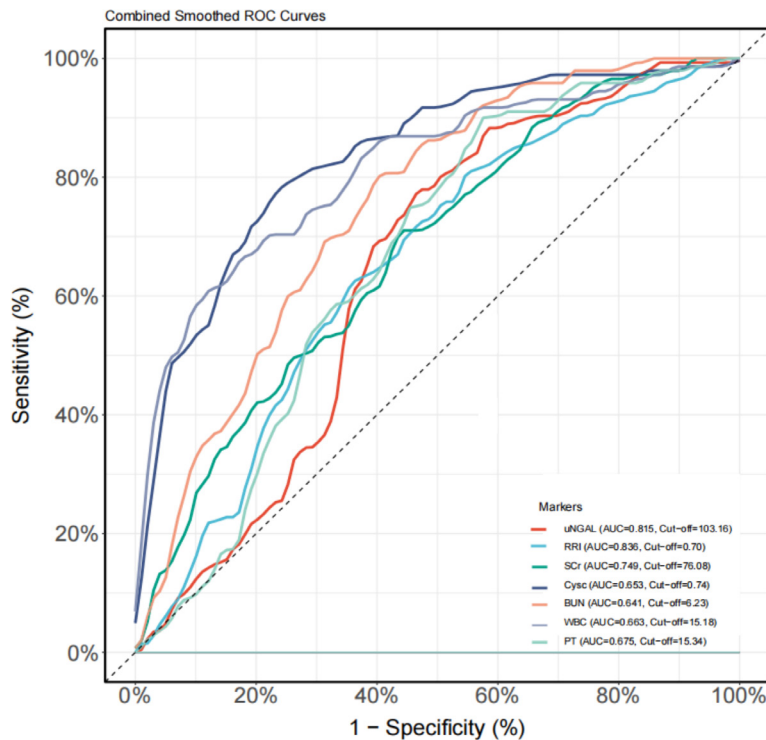


Figure 1. ROC curves for independent influencing factors in predicting AKI occurrence. Note: uNGAL (urinary Neutrophil Gelatinase-Associated Lipocalin), RRI (Renal Resistive Index), SCr (Serum Creatinine), BUN (Blood Urea Nitrogen), Cysc (Cystatin C), WBC (White Blood Cell), CRP (C-reactive protein), PT (Prothrombin Time), APTT (Activated Partial Thromboplastin Time).

parison of post-treatment data between the non-AKI group and AKI group revealed that the AKI group had significantly higher values of RRI (0.79 ± 0.16 vs. 0.59 ± 0.15), PT (14.46 ± 1.66 s vs. 11.55 ± 1.68 s), APTT (32.24 ± 3.64 s vs. 26.13 ± 3.58 s), respiratory rate (23.54 ± 1.72 breaths/min vs. 19.18 ± 1.50 breaths/min), and heart rate (88.00 ± 13.42 beats/min vs. 82.22 ± 13.36 beats/min) (all $P < 0.05$). Urine output was lower in the AKI group than in the non-AKI group (1371.21 ± 275.70 mL/day vs. 1457.34 ± 281.69 mL/day; $P < 0.05$). The details are shown in **Table 4**.

Comparison of adverse reactions between the non-AKI and AKI groups after treatment

As shown in **Table 5**, no significant difference was observed between the non-AKI and AKI groups in the incidence of gastrointestinal adverse symptoms (27/30) and bleeding tendency (3/12) ($P > 0.05$). However, the non-AKI group showed significantly lower incidences of fever and skin reactions compared to the AKI group ($P < 0.05$).

Univariate analysis of factors associated with ineffective treatment response

At 48 hours post-treatment, laboratory indicators such as SCr, BUN, and Cysc-s were detected in patients. Based on comprehensive analysis of the detection results, patients in the AP-related AKI group were further divided into an effective group (74 cases) and an ineffective group (71 cases). Univariate analysis showed that age, gender, smoking history, hypertension, heart rate, PT, APTT, and urine output were not associated with treatment efficacy. However, diabetes, CRP, WBC, respiratory rate, RRI, uNGAL and alcohol consumption history may be influencing factors for efficacy (**Table 6**).

Multivariate analysis of independent risk factors for treatment efficacy

Logistic regression analysis showed that alcohol consumption and respiratory rate were not independent predictors of treatment efficacy. However, elevated CRP (OR=0.225, 95% CI=0.067-0.716, $P=0.016$) was an independent protective factor for treatment efficacy, while diabetes (OR=5.464, 95% CI=1.416-21.086, $P=0.014$), higher WBC (OR=9.682, 95% CI=2.817-33.278, $P < 0.001$), higher uNGAL (OR=7.824, 95% CI=2.413-25.373, $P=0.001$), and higher RRI (OR=11.556, 95% CI=3.406-39.212, $P < 0.001$) were independent risk factors for ineffective treatment response, as shown in **Table 7**.

Predictive value of independent risk factors for treatment efficacy

The predictive performance of the identified independent risk factors for treatment efficacy was evaluated using ROC curve analysis. Results showed that the AUC values for CRP, diabetes, WBC, uNGAL, and RRI were 0.731, 0.812, 0.794, 0.804, and 0.855, respectively (**Figure 3**; **Table 8**).

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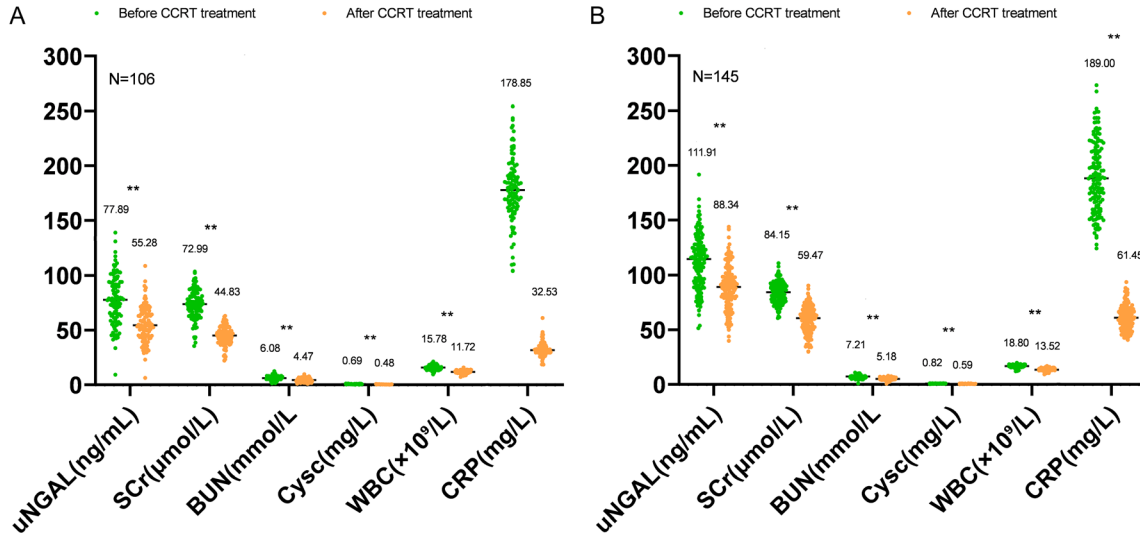


Figure 2. Comparison of laboratory indicators before and after treatment in both AKI and non-AKI groups. A: Comparison of Indicators Before and After Treatment in Non-AKI Group. B: Comparison of Indicators Before and After Treatment in AP-Related AKI Group. **P<0.001. Note: uNGAL (urinary Neutrophil Gelatinase-Associated Lipocalin), SCr (Serum Creatinine), BUN (Blood Urea Nitrogen), Cysc (Cystatin C), WBC (White Blood Cell), CRP (C-reactive protein).

Table 4. Comparison of physiological indicators between the AKI and non-AKI groups after treatment

	RRI	PT (s)	APTT (s)	Respiratory Rate (breaths/min)	Heart Rate (beats/min)	Urine Output (mL/day)
Non-AKI Group (n=106)	0.59±0.15	11.55±1.68	26.13±3.58	19.18±1.50	82.22±13.36	1457.34±281.69
AKI Group (n=145)	0.79±0.16	14.46±1.66	32.24±3.64	23.54±1.72	88.00±13.42	1371.21±275.70
t	10.007	13.622	11.086	11.369	3.337	2.243
P	<0.001	<0.001	<0.001	<0.001	<0.001	0.016

Note: RRI: Renal Resistive Index, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time

Table 5. Adverse reactions in the AKI and non-AKI groups

	Gastrointestinal Symptoms	Fever	Bleeding Tendency	Skin Reactions
Non-AKI Group (n=106)	27 (25.14)	2 (1.25)	3 (2.83)	8 (7.55)
AKI Group (n=145)	30 (20.69)	11 (7.59)	12 (8.28)	23 (15.86)
χ ²	0.798	4.050	3.232	3.911
P	0.229	0.038	0.060	0.035

Discussion

This study evaluated multiple clinical and laboratory indicators in acute pancreatitis (AP) patients with and without acute kidney injury (AKI), and found significant differences in diabetes, heart rate, respiratory rate, urine output, APACHE II score, uNGAL, RRI, SCr, BUN, CysC, WBC, CRP, PT, and APTT. These indicators were used to predict PA-related AKI before treatment, and independent influencing factors were analyzed. Logistic regression of variables

significant in univariate analysis showed that uNGAL, RRI, SCr, Cysc, BUN, WBC, and PT were independent risk factors for AKI occurrence in AP patients. This indicates that elevations in renal function-related indicators (e.g., uNGAL, RRI) and inflammatory indicators (WBC) are risk factors for AKI occurrence. Previous studies have confirmed the value of SCr, BUN, and Cysc in assessing renal injury in acute pancreatitis. Among them, SCr level can intuitively reflect renal function. An increase indicates impaired creatinine excretion, suggesting renal function

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Table 6. Univariate analysis of factors associated with treatment efficacy

Variable	Effective Group (n=74)	Ineffective Group (n=71)	$\chi^2/t/Z$	P
Age	49.00 [38.00, 59.00]	46.50 [38.75, 54.00]	1.199	0.23
Gender			1.17	0.279
Male	34 (46.58%)	40 (55.56%)		
Female	39 (53.42%)	32 (44.44%)		
Diabetes			8.673	0.003
Yes	59 (80.82%)	42 (58.33%)		
No	14 (19.18%)	30 (41.67%)		
Hypertension			3.648	0.056
Yes	63 (86.30%)	53 (73.61%)		
No	10 (13.70%)	19 (26.39%)		
Smoking History			0.083	0.773
Yes	65 (89.04%)	63 (87.50%)		
No	8 (10.96%)	9 (12.50%)		
Alcohol consumption			14.254	<0.001
Yes	69 (94.52%)	51 (70.83%)		
No	4 (5.48%)	21 (29.17%)		
uNGAL	84.44±19.01	93.23±20.17	2.699	0.008
RRI	0.67±0.13	0.81±0.17	5.72	<0.001
Heart Rate	71.10 [64.79, 84.05]	73.22 [65.88, 82.33]	0.208	0.835
WBC	12.90±0.99	14.15±1.29	6.542	<0.001
CRP	66.09±11.49	56.75±9.18	5.405	<0.001
PT	16.38±1.83	16.49±1.96	0.357	0.721
APTT	32.07±2.35	31.80±2.70	0.654	0.514
Urine Output	1507.88±280.49	1536.62±273.93	0.624	0.533
Respiratory Rate	23.10±1.68	23.98±1.66	3.16	0.002

Note: uNGAL: urinary Neutrophil Gelatinase-Associated Lipocalin, RRI: Renal Resistive Index, WBC: White Blood Cell, CRP: C-reactive protein, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time.

Table 7. Multivariate analysis of independent risk factors for treatment efficacy

Variable	β	S.E.	P	OR	95% CI	
					Lower Limit	Upper Limit
uNGAL	2.057	0.6	0.001	7.824	2.413	25.373
RRI	2.447	0.623	<0.001	11.556	3.406	39.212
WBC	2.27	0.63	<0.001	9.682	2.817	33.278
CRP	-1.491	0.622	0.016	0.225	0.067	0.761
Respiratory Rate	0.601	0.607	0.322	1.824	0.555	5.991
Diabetes	1.698	0.689	0.014	5.464	1.416	21.086
Alcohol consumption	1.645	1.038	0.113	5.182	0.678	39.611

Note: uNGAL: urinary Neutrophil Gelatinase-Associated Lipocalin, RRI: Renal Resistive Index, WBC: White Blood Cell, CRP: C-reactive protein.

impairment [23]. As the end product of protein metabolism, BUN level is affected by both glomerular filtration and extrarenal factors. With renal impairment, glomerular filtration rate decreases, leading to reduced BUN excretion and increased blood concentration. Meanwhile,

acute pancreatitis-induced hypercatabolism and massive protein breakdown can also increase BUN production, jointly contributing to its elevation [24, 25]. Cys-c is a more sensitive and earlier marker of glomerular filtration decline, unaffected by factors such as gender,

The predictive value of RRI and uNGAL for AP-related AKI and efficacy of CRRT

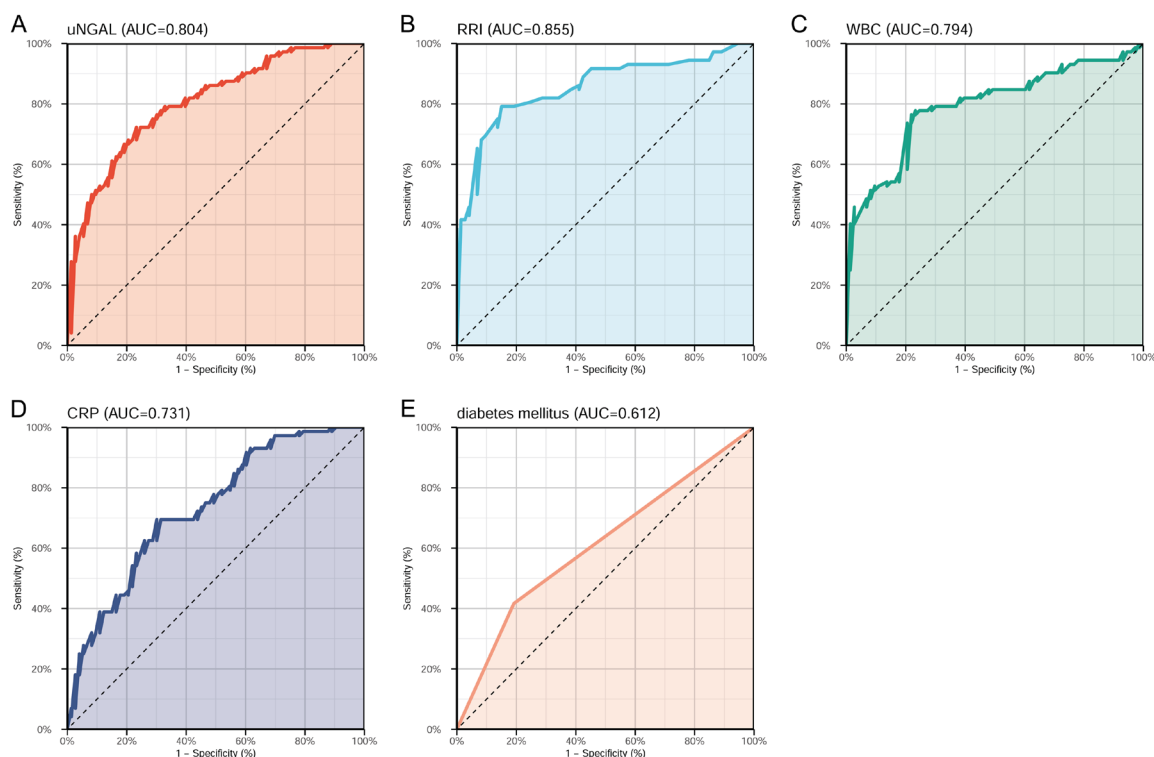


Figure 3. ROC Curves of Independent risk Factors in predicting treatment efficacy. A. ROC curve for uNGAL in predicting treatment efficacy. B. ROC curve for RRI in predicting treatment efficacy. C. ROC curve for WBC in predicting treatment efficacy. D. ROC curve for CRP in predicting treatment efficacy. E. ROC curve for diabetes in predicting treatment efficacy. Note: uNGAL (urinary Neutrophil Gelatinase-Associated Lipocalin), RRI (Renal Resistive Index), WBC (White Blood Cell), CRP (C-reactive protein).

Table 8. Parameters of ROC curve analysis

	AUC	95% CI	Specificity	Sensitivity	Cutoff
uNGAL	0.804	0.733 -0.874	76.71%	72.22%	94.88
RRI	0.855	0.792 -0.919	84.93%	79.17%	0.715
WBC	0.794	0.719 -0.869	76.71%	77.78%	13.52
CRP	0.731	0.650 -0.812	69.86%	69.44%	60.82
Diabetes	0.612	0.539 -0.686	80.82%	41.67%	0.5

Note: uNGAL: urinary Neutrophil Gelatinase-Associated Lipocalin, RRI: Renal Resistive Index, WBC: White Blood Cell, CRP: C-reactive protein.

age, muscle mass, or inflammatory status, with changes strongly correlating to glomerular filtration rate (GFR) [26]. Our results show that uNGAL, SCr, and RRI have high predictive value for identifying AKI in AP patients, providing a basis for early clinical identification of renal injury risk in acute pancreatitis patients and guiding evaluation of CRRT requirements.

By comparing physiological and biochemical indices between AP patients without AKI receiving conventional treatment and AKI patients receiving CRRT treatment at 48 hours post-

treatment, it was found that although physiological indices including RRI, PT, APTT, respiratory rate, and urine output were improved in the AKI group, these improvements were significantly less pronounced than those observed in non-AKI group. Clinical studies have shown that dynamic changes in PT and APTT are closely associated with the severity of AP and progression of renal injury. During renal injury, the kidney's ability to clear procoagulant and anticoagulant substances decreases. PT primarily reflects the function of the extrinsic coagulation pathway, while APTT assesses the

status of the intrinsic coagulation pathway. Prolongation of both often indicates reduced synthesis or excessive consumption of coagulation factors II, V, VII, and X [27-29]. Our results show that except for heart rate, post-treatment indices in the non-AKI group were significantly better than those in the AKI group, indicating that even with CRRT treatment, the physiological status of AKI patients does not normalize or approach that of non-AKI patients within 48 hours. This further highlights the importance of early prediction of AKI and CRRT needs, providing references for subsequent treatment strategies.

A comparison of adverse reactions between AKI and non-AKI patients revealed significantly higher incidences of fever and skin reactions in the AKI group. This may be attributed to the incomplete clearance of toxins and inflammatory mediators by CRRT in AKI patients, as well as suboptimal anticoagulant dosing and adjustments [30, 31].

Univariate analysis showed that diabetes, uNGAL, RRI, WBC, CRP, respiratory rate, and history of alcohol consumption may affect the therapeutic effect of CRRT. Multivariate logistic regression identified diabetes, uNGAL, RRI, and WBC as independent risk factors for poor efficacy, while CRP served as an independent protective factor. ROC curve analysis revealed that among these factors, RRI had the highest AUC (0.855), indicating that elevated RRI may not only reflect renal ischemia associated with AP but also independently suggest the presence of renal microvascular lesions. In this study, the correlation between RRI and AKI severity might be partially driven by the inflammatory response intrinsic to AP. However, existing studies have shown that in patients with diabetic nephropathy or hypertension, RRI can independently predict tubulointerstitial fibrosis and renal function deterioration [32]. Future studies should control AP-related factors such as inflammatory markers and blood volume status to clarify whether RRI is an independent predictor of renal function prognosis in AP patients. Following RRI, uNGAL (AUC=0.804), WBC (AUC=0.794), CRP (AUC=0.731), and diabetes (AUC=0.612) also showed high predictive value for CRRT efficacy. Clinically, monitoring these indicators can facilitate early evaluation of treatment response and timely adjustment of treatment strategy.

This study has limitations. It is a single-center retrospective study with a limited sample size, potentially introducing selection bias. AKI diagnosis relied on serum creatinine and urine output criteria, which may have missed some cases. Moreover, efficacy evaluation was based on declines in SCr, BUN, and Cysc without a unified gold standard. Future multi-center prospective studies incorporating more biomarkers and renal function assessment methods are warranted to further elucidate the pathogenesis of AP-associated AKI and optimize treatment strategies.

Conclusion

In conclusion, RRI and uNGAL are valuable markers for early identification of acute pancreatitis-associated renal injury and prediction of renal replacement therapy (CRRT) efficacy. They provide important clinical references for clinical assessment of patients' renal injury risk and CRRT treatment decisions.

Disclosure of conflict of interest

None.

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