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The blood urea nitrogen-to-creatinine ratio is associated with acute kidney injury among COVID-19 patients

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ABSTRACT

Introduction: To explore the associations between the blood urea nitrogen-to-creatinine ratio (BCR), acute kidney injury (AKI), and in-hospital mortality in coronavirus disease 2019 (COVID-19) patients.

Methods: COVID-19 patients from Ruijin Hospital LuWan Branch, Shanghai Jiao Tong University School of Medicine were enrolled in this study. Clinical data and laboratory parameters were collected. AKI was defined using two serum creatinine tests according to KDIGO guidelines. Cox regression and receiver operating characteristic (ROC) curve analyses were performed.

Results: Five hundred and sixty-seven COVID-19 patients were enrolled, 44.1% of whom were male. The mean age was 75 years. Among all patients, 17 patients developed AKI, and 30 patients died during hospitalization. Compared to non-AKI patients, the BCR in AKI patients was significantly greater. BCR was significantly associated with AKI (unadjusted HR 1.04, 95% CI: 1.02–1.05, $p<0.001$; adjusted HR 1.06, 95% CI 1.02–1.10, $p=0.001$). BCR was also a risk factor of in-hospital mortality (unadjusted HR 1.03, 95% CI: 1.02–1.05, $p<0.001$; adjusted HR 1.04, 95% CI: 1.01–1.08, $p=0.019$). The BCR threshold was 38.9, with 70.6% sensitivity and 87.1% specificity for predicting AKI, while a threshold of 33.0 predicted mortality. Subgroup analysis revealed that BCR could predict AKI and mortality in different subgroups according to sex, age, diabetes mellitus, and estimated glomerular filtration rate.

Conclusions: The BCR, a simple index, is associated with AKI onset and mortality in COVID-19 patients. The BCR possesses certain specificity for AKI screening, which indicates an effective clinical indicator for screening patients at high risk of AKI.

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Introduction

Since the novel coronavirus infection outbreak began in Wuhan in 2019, more than 770 million cases have been confirmed worldwide, among which more than 6.97 million deaths have occurred [1]. Kidney damage is relatively common in patients with severe coronavirus disease 2019 (COVID-19) infection. A relevant study reported that the incidence of acute kidney injury (AKI) in patients with COVID-19 varies from 5.4–22.2% [2–4], indicating a worse prognosis after the occurrence of AKI. The pathological damage of AKI correlated with COVID-19 may include acute renal tubular injury and glomerulopathy; however, whether the virus causes kidney damage directly remains to be elucidated [5]. Despite the use of AKI indicators such as eGFR and serum creatinine level [6], less is known about the early diagnosis of AKI in COVID-19 patients and the corresponding indicators guiding renal replacement therapy (RRT).

Several studies have aimed to determine the risk factors for AKI in COVID-19 patients. Risk factors such as male sex, black race, and older age are associated with the development of AKI but are not unique to patients with COVID-19 [7]. Other studies have focused on abnormal pathophysiological status and laboratory parameters, such as chronic kidney disease (CKD), hyperkalemia [6], hypophosphatemia [4], lymphopenia, cystatin C levels, and levels of numerous inflammatory indicators [8,9]; however, the reliability of several predictive factors of AKI, especially COVID-19 related AKI remains to be improved. However, in emergent public health situations, some laboratory results are not easy to obtain, and more convenient biomarkers or clinical indices must be investigated to predict AKI occurrence.

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Blood urea nitrogen (BUN) and serum creatinine (Scr) levels are widely used in the clinical evaluation of renal function. However, the BUN-to-creatinine ratio (BCR) is rarely utilized in evaluating renal dysfunction or worse outcomes in different pathological states. A higher BCR reflects a relatively insufficient blood volume and enhanced catabolism and is a commonly used indicator for evaluating hospitalized patients [10,11]. The superiority of BCR as an indicator is also due to a greater AKI mortality rate and a greater possibility of RRT [11,12].

Concerning COVID-19, the first study focusing on kidney disease and COVID-19 in 2020 demonstrated that elevated BUN levels led to greater in-hospital mortality than elevated Scr levels [13]. In addition, research has shown that the SARS-CoV-2 cycle threshold (Ct) is positively correlated with worse outcomes of AKI in ICU patients infected with COVID-19 [14], but less research has investigated the relationship between BCR and AKI in COVID-19 patients. Accordingly, this study elucidates the clinical utility of the BCR as a predictor of AKI incidence and in-hospital mortality in a large-scale study of COVID-19 patients.

Methods

Study design and patients

The study enrolled COVID-19 patients who were hospitalized at Ruijin Hospital LuWan Branch, affiliated with Shanghai Jiao Tong University School of Medicine, between April and June 2022. All patients were diagnosed with COVID-19 infection according to the standards provided by the Chinese National Health Commission (7th Edition) with a cycle threshold (Ct) less than 35 for SARS-CoV-2 nucleic acids (ORF or N gene). Patients who underwent two serum creatinine (Scr) tests during their hospital stay were included in the study. Exclusion criteria ruled out patients with an estimated glomerular filtration rate (eGFR) of less than 15 mL/min/1.73 m^2 at admission, those undergoing dialysis, or those with a history of renal transplantation. Patients with missing essential data—such as serum creatinine levels, admission date, or outcome information—were also excluded from the study. The flowchart illustrating our study design is provided in Figure 1.

Data collection

Data on patient demographics, biochemical indicators, comorbidities (including diabetes mellitus, hypertension, chronic obstructive pulmonary disease [COPD], cerebrovascular accident, heart failure, atherosclerotic coronary vascular disease [ASCVD], and chronic liver disease), and clinical outcomes were collected from medical records. The primary endpoints were acute kidney injury (AKI) and in-hospital mortality. The dates of AKI onset, mortality, and discharge were recorded. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula was utilized to calculate the eGFR [15]. The BCR was calculated by dividing the BUN level in mg/dl by the Scr level in mg/dl.

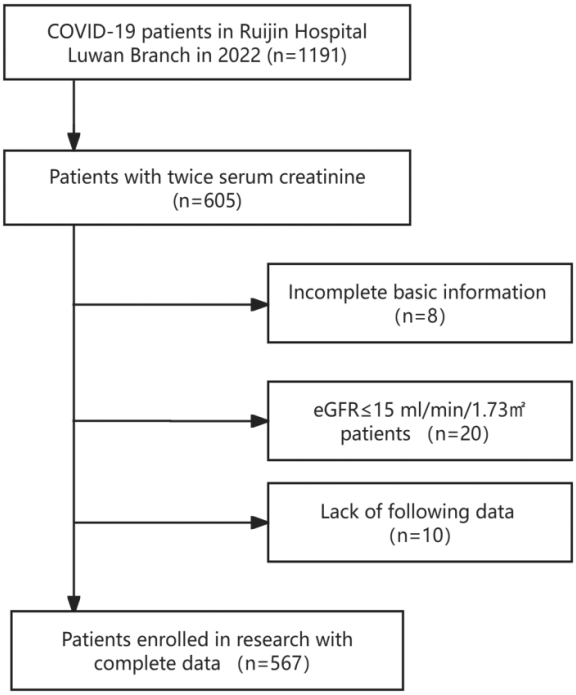


FIGURE 1. Flowchart of COVID-19 patients enrollment.

AKI definition

AKI was defined using KDIGO criteria in which the Scr level increases by ≥26.5 μmol/L (≥0.3 mg/dL) within 48 h or by ≥1.5 times the baseline value within 7 days [16]. Patients whose Scr levels decreased by more than 50% during hospitalization were also categorized as AKI [17]. In the sensitivity analyses, AKI was defined strictly by an increase in Scr levels.

Statistical methods

Normally distributed data are represented as the means ± standard deviations (SDs), and intergroup comparisons were conducted using two-tailed independent sample t-tests. Non-normally distributed data are presented as medians and interquartile ranges [M (Q1, Q3)]. Wilcoxon rank-sum tests were employed for intergroup comparison, and Spearman correlation analysis was used to examine the correlation between BCR and urea nitrogen as well as creatinine levels. Categorical variables are presented as frequencies (%), and comparisons between groups were conducted using the chi-square test. The cumulative survival rate of patients who reached endpoint events was calculated and compared *via* the Kaplan–Meier method and log-rank test. A Cox regression model was used to analyze the correlation between BCR and AKI, and between BCR and in-hospital mortality. BCR was analyzed as a categorical variable (categorized into two groups based on the median 23.75) in the Kaplan-Meier curve, and as a continuous variable in the Cox regression analysis. Parameters with $p < 0.05$ in univariate Cox regression were included in the multivariate Cox regression model. Stepwise forward regression was utilized in the multivariate Cox regression analysis to determine multicollinearity.

Table 1. Clinical characteristics of COVID-19 patients.

	Non-AKI	AKI	Total	*P* value
	(*n* = 550)	(*n* = 17)	(*n* = 567)	
Male, n	242	8	250	0.803
Comorbidities				
Diabetes mellitus, n	118	5	123	0.442
Hypertension, n	241	6	247	0.544
COPD, n	13	0	13	0.998
Cerebrovascular accident, n	141	6	147	0.453
Heart failure, n	28	2	30	0.331
ASCVD, n	124	5	129	0.661
Chronic liver disease, n	16	1	17	0.636
Laboratory examination				
Neutrophils, $\times 10^9$/L	3.8 (2.7, 5.2)	6.3 (3.9, 7.7)	3.8 (2.7, 5.4)	0.003
Lymphocytes, $\times 10^9$/L	1.4 ± 0.7	1.1 ± 0.6	1.4 ± 0.7	0.05
Platelets, $\times 10^9$/L	217.1 ± 91.0	215.1 ± 113.4	217.1 ± 91.7	0.929
ALT, IU/L	19.0 (13.0, 30.0)	18.0 (13.0, 36.0)	19.0 (13.0, 30.0)	0.655
AST, IU/L	22.0 (18.0, 30.0)	27.0 (22.0, 37.0)	22.0 (18.0, 30.0)	0.177
Albumin, g/L	36.9 ± 6.3	31.8 ± 5.6	36.7 ± 6.3	<0.001
Uric acid, μmol/L	292.0 (227.0, 376.0)	316.0 (285.0, 463.0)	294.0 (228.5, 376.5)	0.123
Creatinine, μmol/L	62.0 (49.0, 78.0)	63.0 (44.0, 109.0)	62.0 (49.0, 79.0)	0.634
eGFR, ml/min/1.73m^2	83.7 ± 24.8	72.0 ± 28.3	83.4 ± 24.9	0.062
Urea nitrogen, mmol/L	6.0 (4.4, 8.5)	12.8 (8.6, 17.7)	6.1 (4.5, 8.6)	<0.001
APTT, s	29.7 ± 4.8	31.7 ± 4.5	29.8 ± 4.8	0.1
PT, s	9.6 (9.2, 10.2)	10.3 (9.9, 11.3)	9.6 (9.2, 10.2)	<0.001
D-dimer, μg/mL	0.7 (0.4, 1.6)	2.6 (1.0, 5.5)	0.7 (0.4, 1.7)	<0.001
BCR	23.7 (18.8, 30.9)	58.0 (21.4, 66.0)	23.8 (18.8, 31.5)	<0.001
Outcome				
Transferred, n (%)	24	1	25	0.945
Deceased, n (%)	22	8	30	<0.001

COPD, chronic obstructive pulmonary disease; ASCVD, atherosclerotic coronary vascular disease; ALT, alanine aminotransferase; AST, alanine aminotransferase; eGFR, estimated glomerular filtration rate; APTT, activated partial thromboplastin time; PT, prothrombin time; BCR, blood urea nitrogen-to-serum creatinine ratio.

Moreover, a receiver operating characteristic (ROC) curve analysis was performed to identify the cutoff value of the BCR for AKI. $p < 0.05$ was considered to indicate statistical significance. SPSS version 26.0 software (IBM Corp., Armonk, NY, USA) and R Studio, version 4.4.1 (The R Foundation for Statistical Computing), were used for the statistical analysis.

Results

Study cohort and clinical characteristics of patients with COVID-19

Five hundred and sixty-seven COVID-19 patients with a mean age of 75.0 ± 16.9 years were enrolled, 44.1% of whom were male. Among these patients, 123 patients (21.7%) were diagnosed with diabetes, 247 patients (43.6%) with hypertension, 13 patients (2.3%) with COPD, 147 patients (25.9%) with cerebrovascular accident, 30 patients (5.3%) with heart failure, 129 patients (22.8%) with ASCVD, and 17 patients (3.0%) with chronic liver disease. The laboratory results are presented in Table 1. Patients with AKI exhibited higher neutrophil counts, lower lymphocyte counts, reduced albumin levels, elevated BUN levels, and increased prothrombin time (PT) and D-dimer levels (Table 1).

BCR and AKI

During hospitalization, 17 patients had AKI. The median AKI onset after admission was 10 (7–16) days. The BCR level was 58.0 (21.4, 66.0) in patients with AKI (Table 1), while it was 23.7 (18.8, 30.9) in patients without AKI (Table 1). The Kaplan-Meier curve demonstrates a borderline significant association between higher BCR (≥23.75) and the onset of AKI in COVID-19 patients[log-rank test $\chi 2 = 2.9$, $p = 0.09$; hazard ratio (HR), 95% confidence interval (CI): 2.4, 0.8–6.9, $p = 0.09$, Figure 2A]. Univariate and multivariate Cox regression models were employed to analyze the associations between BCR and AKI. BCR was significantly associated with AKI, with an unadjusted hazard ratio of 1.04 (95% CI: 1.02–1.05, $p < 0.001$, Table 2). In the multivariate Cox regression model, BCR remained significantly associated with AKI after adjusting for albumin level, uric acid level, urea nitrogen level, PT, and D-dimer level (adjusted HR 1.06, 95% CI: 1.02–1.10, $p = 0.001$, Table 2).

In the subgroup analysis, BCR was consistently associated with the onset of AKI in females (HR 1.04, 95% CI: 1.02–1.06, $p < 0.001$), in males (HR 1.06, 95% CI: 1.02–1.11, $p = 0.004$), individuals over 70 years of age (HR 1.07, 95% CI: 1.04–1.09, $p < 0.001$), individuals without diabetes mellitus (HR 1.04, 95% CI: 1.03–1.06, $p < 0.001$) and individuals with an eGFR of at least 60 mL/min/1.73 m^2 (HR 1.04, 95% CI: 1.02–1.06, $p < 0.001$, Figure 3A).

BCR and in-hospital mortality

Thirty patients (5.3%) died during hospitalization, with a median hospitalization duration of 11 (7–16) days. The Kaplan-Meier curve demonstrated patients with higher BCR

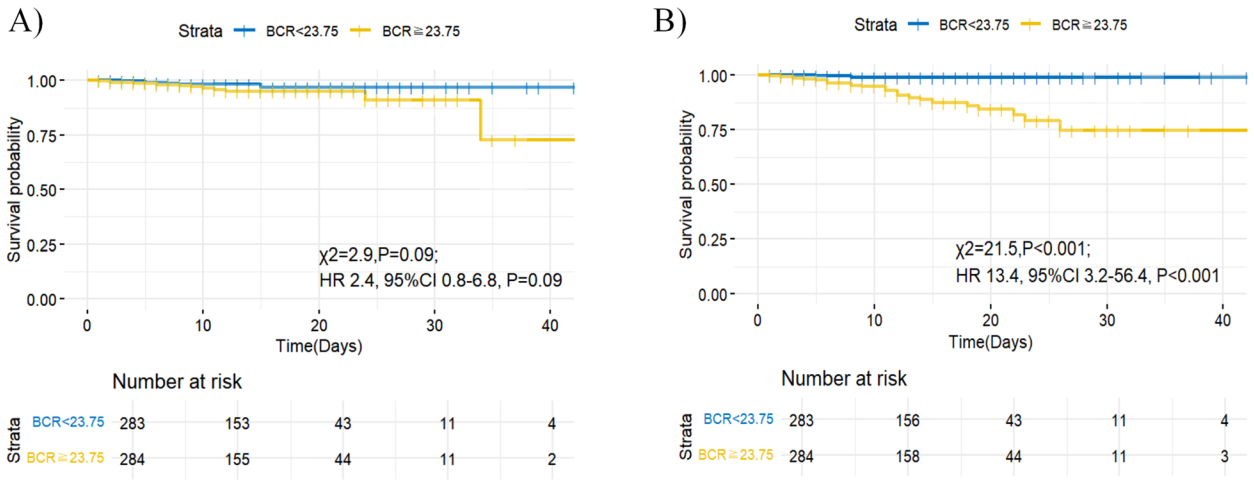


FIGURE 2. Kaplan-Meier curves for acute kidney injury and mortality according to BCR category. (A) Acute kidney injury; (B) Mortality.

Table 2. Cox regression analyses of BCR and acute kidney injury.

	Univariate		Multivariate	
Laboratory examination	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Neutrophils, $\times10^9$/L	1.02 (0.99–1.04)	0.215		
Lymphocytes, $\times10^9$/L	0.43 (0.16–1.15)	0.093		
Platelets, $\times10^9$/L	1.00 (1.00–1.01)	0.782		
ALT, IU/L	0.99 (0.97–1.02)	0.445		
AST, IU/L	1.00 (0.99–1.01)	0.972		
Albumin, g/L	0.89 (0.82–0.96)	0.003	0.85 (0.76–0.96)	0.009
Uric acid, μmol/L	1.00 (1.00–1.01)	0.049	1.00 (1.00–1.01)	0.734
Creatinine, μmol/L	1.01 (1.00–1.02)	0.069		
Urea nitrogen, mmol/L	1.09 (1.05–1.13)	<0.001	0.92 (0.81–1.04)	0.19
APTT, s	1.05 (0.96–1.14)	0.309		
PT, s	1.66 (1.33–2.06)	<0.001	1.46 (1.03–2.06)	0.033
D-dimer, μg/mL	1.14 (1.07–1.22)	<0.001	1.05 (0.94–1.17)	0.399
BCR	1.04 (1.02–1.05)	<0.001	1.06 (1.02–1.10)	0.001

ALT, alanine aminotransferase; AST, alanine aminotransferase; APTT, activated partial thromboplastin time; PT, prothrombin time; BCR, blood urea nitrogen-to-serum creatinine ratio; HR, hazard ratio; CI, confidence Interval.

(≥23.75) had a higher hazard ratio of death, which remained significant during follow-up (log-rank test $\chi2=21.5$, $p<0.001$; HR 13.4, 95% CI: 3.2–56.4, $p<0.001$, Figure 2B). According to the univariate Cox regression, BCR was associated with in-hospital mortality (unadjusted HR 1.03, 95% CI: 1.02–1.05, $p<0.001$). In the multivariate analysis, a significant correlation existed between BCR and in-hospital mortality after adjustment for neutrophil count, lymphocyte count, ALT level, AST level, albumin level, uric acid level, creatinine level, urea nitrogen level, PT, or D-dimer level (HR 1.04, 95% CI: 1.01–1.08, $p=0.019$; Table 3).

In the subgroup analysis, BCR was stably correlated with in-hospital mortality incidence in all subgroups, in female (HR 1.03, 95% CI: 1.01–1.05, $p<0.001$), male (HR 1.07, 95% CI: 1.03–1.10, $p<0.001$), individuals over 70 years (HR 1.05, 95% CI: 1.03–1.07, $p<0.001$), individuals under 70 years (HR 1.04, 95% CI: 1.01–1.06, $p=0.006$), those without diabetes (HR 1.03, 95% CI: 1.02–1.05, $p<0.001$), those with diabetes (HR 1.04, 95% CI: 1.01–1.06, $p=0.012$), individuals with an eGFR of at least 60 mL/min/1.73 m^2 (HR 1.04, 95% CI: 1.02–1.05, $p<0.001$), individuals with an eGFR of below 60 mL/min/1.73 m^2 (HR 1.05, 95% CI: 1.02–1.07, $p<0.001$, Figure 3B).

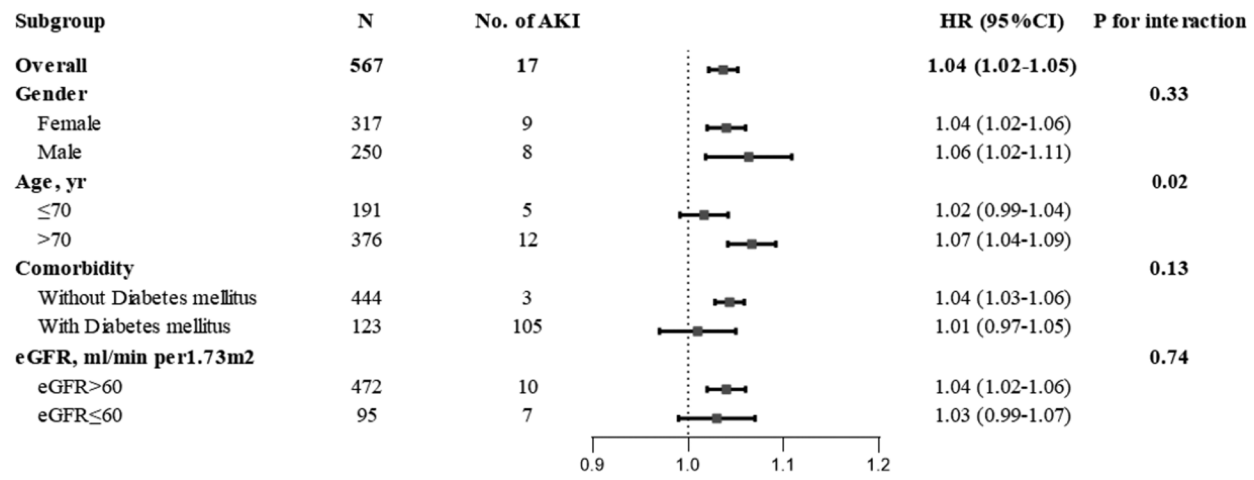
The BCR threshold for AKI and mortality

We determined the best BCR threshold for AKI onset and mortality using ROC curve. The area under the receiver operating characteristic curve (AUROC) of the BCR was 0.745, and the threshold value of 38.9, with a sensitivity of 70.6% and specificity of 87.1% ($p<0.001$, Figure 4A). For in-hospital mortality, the AUROC was 0.812, with a threshold value of 33.0. This yielded a sensitivity of 70.0% and a specificity of 80.4% ($p<0.001$; Figure 4B).

Sensitivity analysis for AKI

For the sensitivity analysis, we used a strict AKI definition, which only included an Scr increase ≥26.5 μmol/L (≥0.3 mg/

(A)



(B)

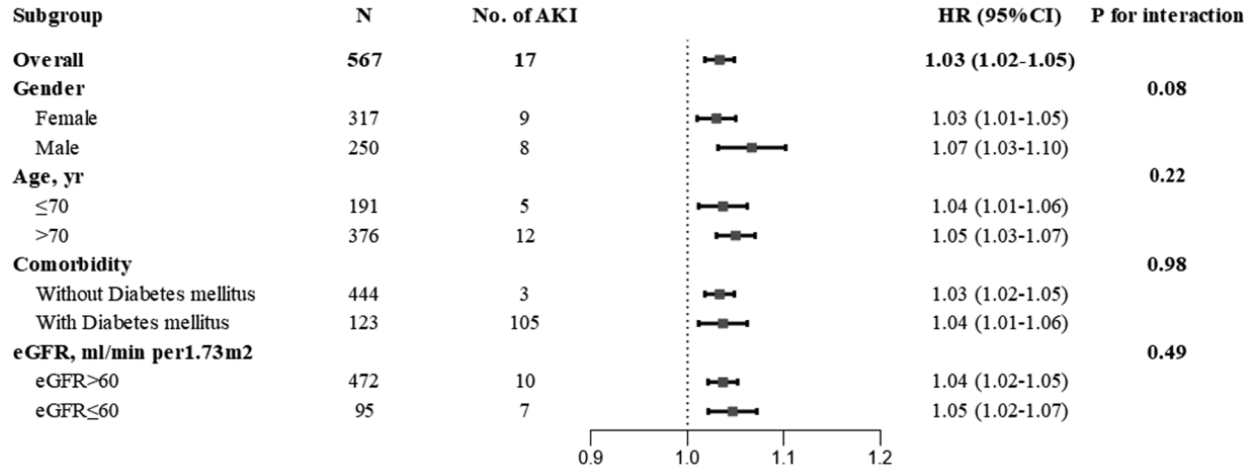


FIGURE 3. Forest plot of BCR association with acute kidney injury and mortality in subgroup analysis. (A) unadjusted hazard ratios of BCR for acute kidney injury; (B) unadjusted hazard ratios of BCR for mortality. eGFR, estimated glomerular filtration rate; HR, hazard ratio; CI, confidence interval.

Table 3. Cox regression analysis of BCR and in-hospital mortality.

	Univariate		Multivariate	
Laboratory examination	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Neutrophils, $\times 10^9$/L	1.03 (1.02–1.04)	<0.001	1.02 (1.01–1.04)	0.011
Lymphocytes, $\times 10^9$/L	0.33 (0.14–0.75)	0.008	1.00 (0.46–2.17)	0.998
Platelets, $\times 10^9$/L	1.00 (0.99–1.00)	0.585		
ALT, IU/L	1.00 (1.00–1.01)	0.003	1.00 (0.99–1.00)	0.369
AST, IU/L	1.00 (1.00–1.01)	<0.001	1.00 (1.00–1.01)	0.296
Albumin, g/L	0.87 (0.82–0.93)	<0.001	0.89 (0.82–0.96)	0.005
Uric acid, μmol/L	1.01 (1.00–1.01)	<0.001	1.00 (1.00–1.00)	0.683
Creatinine, μmol/L	1.02 (1.01–1.02)	<0.001	1.02 (1.00–1.04)	0.016
Urea nitrogen, mmol/L	1.12 (1.09–1.15)	<0.001	0.97 (0.89–1.06)	0.518
APTT, s	1.03 (0.96–1.1)	0.388		
PT, s	1.68 (1.44–1.97)	<0.001	1.50 (1.17–1.93)	0.001
D-dimer, μg/mL	1.11 (1.05–1.17)	<0.001	1.02 (0.93–1.13)	0.629
BCR	1.03 (1.02–1.05)	<0.001	1.04 (1.01–1.08)	0.019

ALT, alanine aminotransferase; AST, alanine aminotransferase; APTT, activated partial thromboplastin time; PT, prothrombin time; BCR, blood urea nitrogen-to-serum creatinine ratio; HR, hazard ratio; CI, confidence Interval.

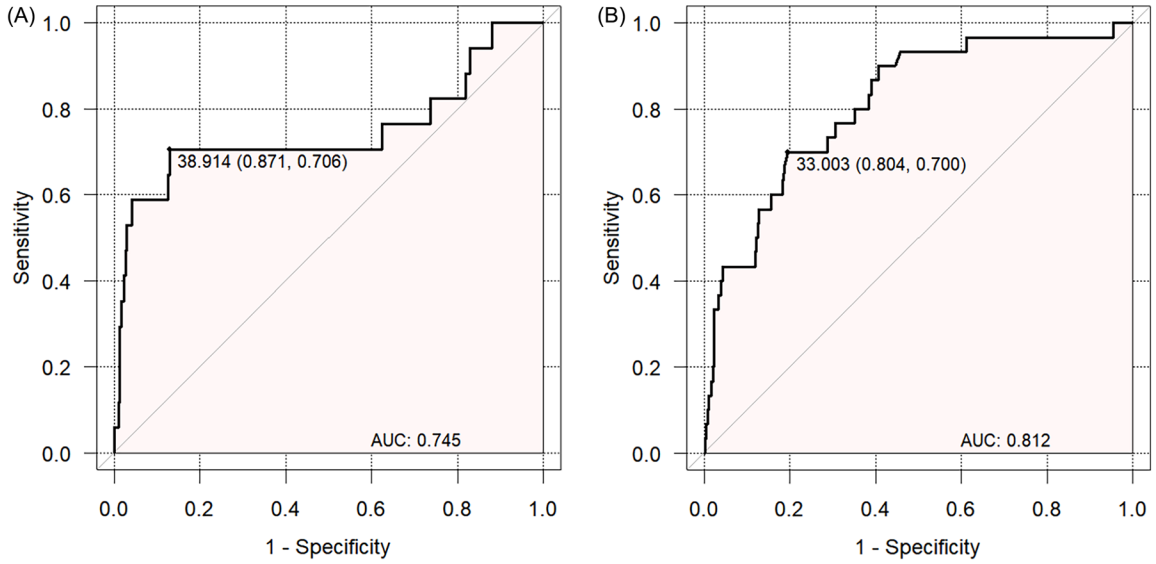


FIGURE 4. (A) AUC for AKI according to the BCR; (B) AUC for mortality according to the BCR.

dL) within 48 h or ≥1.5 times the baseline value within 7 days. Fifteen patients were diagnosed with AKI. BCR and AKI univariate and multivariate Cox regression analyses both revealed statistical significance (unadjusted HR 1.03, 95% CI: 1.02–1.05, $p < 0.001$; adjusted HR 1.06, 95% CI 1.03–1.10, $p = 0.001$).

Discussion

A high occurrence of AKI in patients has become common; 8.3% of ambulatory patients and 10–15% of in-hospital patients are affect by AKI, while more than 50% of patients in the intensive care unit (ICU) experience AKI, which increases mortality and the need for RRT [18,19]. The consequences of AKI, such as lung injury, heart failure, and encephalopathy, are associated with a worse prognosis [19]. Thus, timely identification of potential AKI patients by convenient indicators is vital for improving survival probability. As routine laboratory tests, both BUN and creatinine are common laboratory indicators, while the BCR is used as a kidney health indicator and is widely used in clinical practice. Our results showed that a higher BCR is associated with AKI onset in COVID-19 patients. Furthermore, our results showed that the BCR had a certain sensitivity and high specificity for AKI screening, and the ideal threshold value of the BCR was 38.9. Our research revealed that the BCR can serve as an effective clinical indicator for screening patients at high risk for AKI.

Previous studies have reported that the incidence of COVID-19-related AKI varied from 8% to 46% [3,20], which may be due to the rapid progression of the COVID-19 pandemic and primary diseases such as diabetes mellitus and hypertension [6]. In our research, the incidence of COVID-19-related AKI was 3.0%, which concurs with the results of a meta-analysis in which 5.5% of inpatients experienced AKI [20]. The pathological manifestations of AKI in COVID-19 patients include both renal glomerular and tubular injury [21]. With respect to laboratory findings, proteinuria and an abnormally elevated urine albumin-to-creatinine ratio are the earliest manifestations of AKI occurrence and have previously been utilized to predict AKI [22]. Furthermore, several AKI biomarkers are useful for predicting, diagnosing, and determining the severity of AKI. Expression of both urinary tissue inhibitors of metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein-7 (IGFBP-7), two cell cycle arrest proteins, can be used to determine the occurrence and severity of AKI [23]. In addition, expression of the urinary inflammatory indicator interleukin-18 (IL-18) and the tubular damage indicator kidney injury molecule-1 (KIM-1) can also predict early AKI-related damage *via* different mechanisms [24]. As the measurement of these biomarkers was not available during the COVID-19 pandemic, other simple markers that are convenient to obtain require to be investigated.

The BCR, a common clinical indicator that is widely used, can be used to calculate renal function in an assay that requires only one blood sample; this ratio is simpler than other biomarkers. Urea nitrogen is generated by the metabolism of amino acids, and amino acids are hydrolyzed by the liver and excreted by the kidney [25], 40% of which can be reabsorbed in the proximal tubules by the regulation of renin–angiotensin–aldosterone system (RAAS) [26]. Moreover, serum creatinine is produced by skeletal muscle, and its value is associated with the catabolism of muscle regardless of other renal factors due to its free filtration in the tubules [25,27]. Thus, the activation of RAAS, the accumulation of urea nitrogen, and the reduction of creatinine level may lead to an increase in the BCR, which is associated with a poor prognosis in several pathophysiological states such as chronic heart failure [28], and coronary artery disease in type 2 diabetes mellitus [29]. BCR has also been regarded as a biomarker for insufficient volume in AKI; however, several studies have demonstrated that it is not reliable for distinguishing the causes of AKI, such as prerenal injury and

intrinsic AKI [30]. Since BCR can be readily obtained, it is valuable and useful in emergency situations where medical resources are limited. In our study, we found a remarkable increase in the BCR in patients with AKI. Additionally, we observed that BCR was an independent risk factor for both AKI and mortality, demonstrating good predictive value. Therefore, BCR could serve as an important indicator for physicians in identifying patients with AKI.

In our study, we observed that a higher BCR was correlated with AKI onset. We speculate that both relative plasma volume deficiency in COVID-19 patients with fever and increased metabolic breakdown lead to an increase in the BCR. Considering the high incidence of AKI-related comorbidities, the BCR has a certain ability to predict AKI in both men and women, elderly individuals (aged ≥70 years), patients without diabetes mellitus, and patients with an eGFR of no less than 60 mL/min/1.73 m^2 in COVID-19 patients. This conclusion may not concur with other findings, especially for inpatients with diabetes mellitus. The most common comorbidities, such as diabetes mellitus, hypertension, and cardiovascular disease (CVD), have been implicated as important risk factors for AKI development [22]. We also found that the BCR threshold value of 38.9 had the best AUROC (0.745), with a sensitivity of 70.6% and a specificity of 87.1% for AKI. The BCR threshold showed good calibration, with perfect specificity in the early prediction of AKI, which can be extended to a general population of inpatients in different primary diseases and pathophysiological states.

A previous study showed that the BCR was correlated with COVID-19 severity and mortality [31]. However, in the published study, the multivariate model was adjusted only for age, gender, and comorbidities (such as diabetes mellitus) rather than for laboratory parameters. In our study, the mortality rate of the high-BCR group was 13.4 times greater than the low-BCR group. After adjusting for clinical and laboratory parameters, the significance between BCR and mortality still existed, possibly because another laboratory test revealed a strong effect on mortality. In our study, the best BCR cutoff value is 33.0, while another study showed that the best BCR threshold for predicting in-hospital mortality in COVID-19 patients was 59.8 [32], which concurs with our conclusion.

Our study has several strengths. The enrolled COVID-19 patients were from a large in-hospital COVID-19 cohort during the lockdown period in Shanghai. Then, we defined AKI using two measures of renal function according to the KDIGO definition. Lastly, we identified the optimal cutoff point for BCR in predicting AKI and mortality. This threshold can be utilized in emergency situations where medical resources are limited. There are also several limitations in this study. First, the lack of early AKI detection leads to time-related bias, which may be unavoidable in clinical research. Additionally, the number of patients with COVID-19-related AKI and the number of deaths included in this study is relatively insufficient, which makes it impossible to analyze the associations between BCR and different AKI stages in patients. Thirdly, the study used creatinine criteria for AKI definition without including urine output criteria. Since the study population did not include ICU patients and accurately measuring urine output was challenging, the absence of urine output criteria may have led to underdiagnosis of AKI. Finally, there was a selection bias in our study and our study could not represent the broader COVID-19 patients in Shanghai.

In summary, our results showed that the BCR, a simple index, is a risk factor associated with AKI occurrence in COVID-19 patients and can be widely utilized in clinical practice. The BCR threshold of 38.9 is optimal for determining the onset of AKI as early as possible. Although this finding needs to be confirmed by prospective studies, it reminds clinicians to pay attention to AKI occurrence and timely identify relative AKI risk factors.

Ethics statement

This study was approved by the ethics committee of the hospital (1.0/20200201), and informed consent was obtained from each patient (LWEC2022036).

Disclosure statement

No potential conflict of interest was reported by the author(s).

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