# ORIGINAL RESEARCH Blood Urea Nitrogen to Serum Albumin Ratio in the Prediction of Acute Kidney Injury of Patients with Rib Fracture in Intensive Care Unit

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Background: We hypothesized that the blood urea nitrogen (BUN) to serum albumin ratio (BAR) could serve as an independent predictor for incident acute kidney injury (AKI) in intensive care unit (ICU) patients with rib fracture.

Methods: Rib fracture patients in ICU were extracted from Medical Information Mart for Intensive Care IV (MIMIC-IV v1.0) database. The primary outcome in this study was the incidence of AKI. Univariate and multivariate logistic regression analyses were used to determine the relationship between BAR and AKI and propensity score matching (PSM) and inverse probability of treatment weighting (IPTW) were also applied to assure the robustness of our results.

Results: The optimal cut-off value for BAR was 5.26 based on receiver operator characteristic curve. Among the 953 patients who diagnosed with rib fracture, 197 high-BAR group (≥5.26) patients and 197 low-BAR group (<5.26) patients who had similar propensity scores were finally included in the matched cohort. High-BAR group patients had a significantly higher incidence of AKI (odds ratio, OR, 3.85, 95% confidence index, 95% CI, 2.58-5.79, P<0.001) in the original cohort, in the matched cohort (OR, 4.47, 95% CI 2.71-7.53, P<0.001), and in the weighted cohort (OR, 4.28, 95% CI 2.80-6.53, P<0.001). Furthermore, BAR was superior to that of acute physiology score III for predicting AKI and could add more net benefit for incident AKI in critical care patients with rib fracture.

Conclusion: As an easily access and cost-effective parameter, BAR could serve as a good diagnostic predictor for AKI in ICU patients with rib fracture.

Keywords: blood urea nitrogen to serum albumin ratio, rib fracture, intensive care unit, acute kidney injury, medical information mart for intensive care

#### Introduction

Acute kidney injury (AKI) is one of the most common disorders in intensive care units (ICU) worldwide and has been demonstrated to be a frustrating disease with high morbidity, mortality, healthcare cost and limited treatment options.<sup>1-4</sup> Increasing evidences advocate that identifying patients with AKI at an early phase may improve the clinical outcomes of AKI patients after appropriate interventions be conducted.<sup>5,6</sup> Therefore, a biomarker with highly accuracy and easily accessible may be crucial for clinicians to immediately and appropriately decision-making. Compared with the common reason for AKI, sepsis and cardiac surgery, for example, patients with fracture may be the rare one.<sup>7,8</sup> However, more and more studies paid their attention to the development of AKI in hip or femoral neck fracture patients following surgery,<sup>9-13</sup> and limited study had been published before to investigate the incident AKI in rib fracture patients in ICU.

Serum albumin is an easily accessible index for nutritional status and has been found to be associated with the prognosis of fractured patients.<sup>14–16</sup> Blood urea nitrogen (BUN) is a simple but important index, combination with serum

creatinine, to reflect kidney function and has also been found to be a prognostic factor for mortality in various diseases.<sup>17,18</sup> Moreover, the BUN to serum albumin ratio (BAR), which is combined BUN and serum albumin, had introduced to be an important predictor for mortality in different types of disease.<sup>19,20</sup> Nevertheless, as far as we can see, no study published before was made to evaluate the relationship between BAR and incident AKI for rib fracture patients. Therefore, in this study, we firstly demonstrated the relationship between BAR and the development of AKI for rib fracture patients from a freely public database, the Medical Information Mart for Intensive Care IV (MIMIC-IV version 1.0) database. Moreover, propensity score matching (PSM) and propensity score-based inverse probability of treatment weighting (IPTW) were also applied to assure the robustness of our findings.

# **Materials and Methods**

#### **Study Population**

All data in this study were extracted from the MIMIC IV database,<sup>21</sup> which consists of the information of more than 70,000 patients in Beth Israel Deaconess Medical Center. After successfully accomplishing the National Institutes of Health's (NIH) online training course and the Protection of Human Research Participants Examination, we had the access to extract data from MIMIC IV database. What is more, the study protocol was approved by the Ethics Committee of Sinopharm Dongfeng General Hospital and was waived to informed consent.

#### Selection of Participants

Adult patients ( $\geq$ 18 years old) who were diagnosed as rib fracture based on the International Classification of Diseases (ICD) code were initially enrolled in this retrospective study. We only included patients who admitted to hospital and ICU firstly and we also excluded patients whose hospital stay less than 48 hours. Moreover, patients with end-stage renal disease (ESRD) or with missing BUN or serum albumin values were also excluded in this study. Finally, there were 953 patients diagnosed with rib fracture were included in the current study (Figure 1).

#### Variable Extraction

Demographic and admission information: age, gender, body mass index (BMI), number of rib fracture, and severity scores and the Charlson comorbidity index were also calculated. Commodities including hypertension, diabetes, chronic kidney disease (CKD), congestive heart failure (CHF), myocardial infarct, chronic obstructive pulmonary disease (COPD), liver disease and malignancy were also extracted based on the ICD codes. Use of mechanical ventilation (MV), vasopressors and renal replacement therapy during their first day of hospital stay were also recorded in this study. Moreover, initial vital signs and laboratory results were also extracted by structured query language with PostgreSQL 9.6.

The BAR was calculated by initial serum BUN (mg/dL)/serum albumin (g/dL).

The primary outcome in this study was the incident of AKI in 48 hours, which was stratified based on its severity, according to the KDIGO Clinical Practice Guidelines for AKI.<sup>22</sup>

#### Statistical Analyses

Continuous variables were expressed as mean (standardized mean difference, SMD), categorical covariates were reported as number (percentage). Receiver operator characteristic curve (ROC) and Youden index were used to identify the best cutoff values of BAR for AKI. PSM and IPTW were also used to adjust the imbalance of the covariates between two groups. Multivariate logistic regression and adjusted odds ratio (OR) were calculated in this study to determine the relationship between BAR and the incident AKI. Discrimination was also assessed by the integrated discrimination index (IDI). Improvement in clinical risk stratification was assessed by calculating net reclassification improvement (NRI). Moreover, the decision curve analysis (DCA) was performed to assess the clinical benefits of the BAR. All analyses were conducted using R (version 4.1.0) and p<0.05 was considered statistically significant.

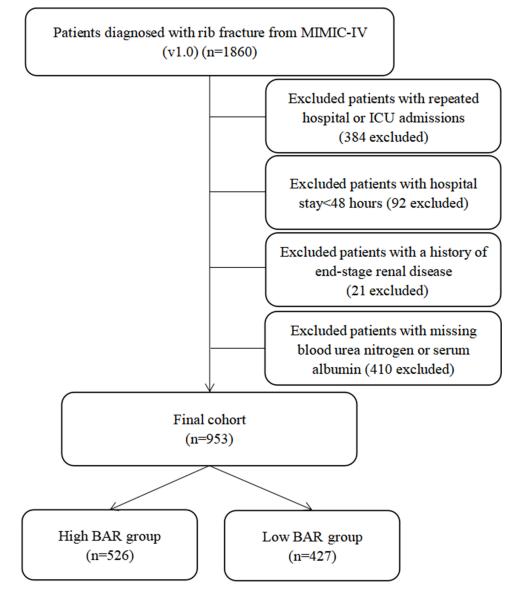


Figure I Study flow diagram in the present study.

## Results

#### Patient Clinical Features

Finally, a total of 953 patients with rib fracture were included in this study (Figure 1). Among them, AKI occurred in 459 (48.2%) patients. According to the KDIGO criteria, 104 (10.9%) patients were AKI stage I, 166 (17.4%) patients were AKI stage II and 89 (9.3%) patients were AKI stage III.

Based on the optimal cut-off value of BAR (5.26), which was determined by ROC analysis, we grouped patients as high BAR group ( $\geq$ 5.26, n=427) and low BAR group (<5.26, n=526). The baseline characteristics of the high BAR group and low BAR group are summarized in Table 1. In original cohort, 25/35 covariates (age, use of MV, CRRT and vasopressors, OASIS score, APSIII score, SOFA score, SAPSII score, Charlson score, hypertension, diabetes, CKD, myocardial infarct, CHF, liver disease, white blood cells, hemoglobin, platelet, total bilirubin, anion gap, creatinine, glucose, potassium, mean arterial pressure, and SpO<sub>2</sub>) were imbalanced between high BAR group and low BAR group. Based on the estimated propensity scores, PSM and IPTW were used to standardize the differences between the two groups. Moreover, the imbalance between the two groups was significantly decreased and all variables were comparable between high BAR group and low BAR group (Table 1 and Supplemental Figure 1).

Low BAR						Weighted Cohort		
	High BAR	Р	Low BAR	High BAR	Ρ	Low BAR	High BAR	Р
526	427		197	197		189.8	192.9	
53.5 (19.5)	70.6 (16.6)	<0.001	66.3 (16.5)	64.7 (17.5)	0.353	64.9 (17.3)	64.5 (17.7)	0.782
334 (63.5)	266 (62.3)	0.753	116 (58.9)	122 (61.9)	0.607	117.5 (61.9)	120.1 (62.3)	0.934
26.8 (6.3)	27.1 (7.5)	0.483			0.409	26.9 (6.3)	26.9 (7.1)	0.969
. ,		0.171			0.972			0.753
106 (20.2)	70 (16.4)		35 (17.8)	33 (16.8)		33.6 (17.7)	28.5 (14.8)	
78 (14.8)	57 (13.3)		26 (13.2)	24 (12.2)		25.8 (13.6)	27.5 (14.3)	
140 (26.6)	107 (25.1)		51 (25.9)	51 (25.9)		53.0 (27.9)	51.2 (26.5)	
202 (38.4)	193 (45.2)		85 (43.I)	89 (45.2)		77.4 (40.8)	85.7 (44.4)	
221 (42.0)	235 (55.0)	<0.001	95 (48.2)	95 (48.2)	1.000	93.1 (49.0)	93.9 (48.7)	0.934
3 (0.6)		<0.001			1.000			0.804
99 (18.8)		<0.001			1.000	61.3 (32.3)		0.999
. ,	. ,		. ,	. ,		. ,	. ,	
3.6 (1.0)	6.2 (2.1)	<0.001	4.7 (1.3)	4.8 (1.6)	0.739	4.7 (2.3)	4.7 (2.5)	0.989
29.9 (8.0)	35.7 (9.0)	<0.001	33.6 (7.6)	33.1 (8.0)	0.558	33.3 (7.9)	33.1 (8.0)	0.792
		<0.001	47.1 (21.9)		0.948	47.0 (22.1)	46.9 (19.5)	0.973
	40.1 (13.6)	<0.001			0.690	33.3 (10.6)		0.809
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176 (33.5)	174 (40.7)	0.024	87 (44.2)	88 (44.7)	1.000	84.5 (44.5)	86.0 (44.6)	0.995
		<0.001			0.604			0.975
	· ,	<0.001			0.321		. ,	0.647
		<0.001			1.000			0.997
								0.883
								0.899
					0.864			0.951
		0.829			0.799			0.988
		<0.001	4.2 (1.3)		0.761			0.962
. ,								
90.7 (17.0)	86.1 (20.2)	<0.001	88.7 (17.0)	88.9 (21.8)	0.910	89.2 (17.4)	88.9 (19.2)	0.835
91.7 (18.6)		0.070			0.834			0.835
19.6 (5.8)		0.346			0.400			0.794
97.3 (3.4)		0.001			0.783	96.9 (4.1)	96.9 (3.9)	0.963
12.2 (5.3)	13.4 (5.6)	0.019	12.2 (5.6)	12.3 (5.4)	0.865	12.4 (5.7)	12.5 (5.8)	0.986
		<0.001	11.3 (2.0)		0.769			0.856
		0.015			0.837	195.2 (78.2)	194.9 (83.0)	0.966
		<0.001			0.684			0.863
		0.032			0.687			0.855
		0.030			0.890			0.881
22.9 (3.9)	22.5 (4.2)	0.192	22.8 (4.3)	22.7 (3.8)	0.802	22.9 (4.2)	22.8 (4.0)	0.942
104.2 (6.0)	104.6 (6.4)	0.421	104.6 (6.5)	104.5 (6.1)	0.861	104.6 (6.3)	104.6 (6.2)	0.929
0.8 (0.3)	1.3 (0.7)	<0.001	0.9 (0.4)	1.0 (0.4)	0.069	1.0 (0.4)	1.0 (0.3)	0.636
4.1 (0.7)	4.4 (0.8)	<0.001	4.3 (0.8)	4.3 (0.8)	0.652	4.3 (0.8)	4.3 (0.7)	0.905
138.6 (4.6)	139.0 (5.0)	0.229	138.9 (5.0)		0.656	138.8 (4.9)		0.996
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		<0.001			<0.001			<0.001
370 (80.3)	124 (29.0)		121 (61.4)	71 (36.0)		119.4 (62.9)	70.9 (36.7)	
	334 (63.5) 26.8 (6.3) 106 (20.2) 78 (14.8) 140 (26.6) 202 (38.4) 221 (42.0) 3 (0.6) 99 (18.8) 3.6 (1.0) 29.9 (8.0) 38.1 (18.7) 25.8 (11.2) 176 (33.5) 65 (12.4) 8 (1.5) 20 (3.8) 31 (5.9) 93 (17.7) 34 (6.5) 22 (4.2) 2.7 (1.3) 90.7 (17.0) 91.7 (18.6) 19.6 (5.8) 97.3 (3.4) 12.2 (5.3) 11.8 (2.0) 20.2.9 (77.3) 136.3 (49.6) 1.1 (0.5) 14.7 (3.6) 22.9 (3.9) 104.2 (6.0) 0.8 (0.3) 4.1 (0.7) 138.6 (4.6)	334 (63.5)   266 (62.3)     26.8 (6.3)   27.1 (7.5)     106 (20.2)   70 (16.4)     78 (14.8)   57 (13.3)     140 (26.6)   107 (25.1)     202 (38.4)   193 (45.2)     221 (42.0)   235 (55.0)     3 (0.6)   23 (5.4)     99 (18.8)   191 (44.7)     3.6 (1.0)   6.2 (2.1)     29.9 (8.0)   35.7 (9.0)     38.1 (18.7)   55.8 (24.1)     25.8 (11.2)   40.1 (13.6)     176 (33.5)   174 (40.7)     65 (12.4)   93 (21.8)     8 (1.5)   63 (14.8)     20 (3.8)   58 (13.6)     31 (5.9)   109 (25.5)     93 (17.7)   74 (17.3)     34 (6.5)   56 (13.1)     22 (4.2)   20 (4.7)     2.7 (1.3)   5.2 (2.7)     90.7 (17.0)   86.1 (20.2)     91.7 (18.6)   89.4 (19.8)     19.6 (5.8)   20.0 (5.5)     97.3 (3.4)   96.5 (4.3)     12.2 (5.3)   13.4 (5.6)     11.8 (2.0)   10.9 (2.1)     202.9 (77.3)   190.0 (66.1) </td <td>334 (63.5)   266 (62.3)   0.753     26.8 (6.3)   27.1 (7.5)   0.483     106 (20.2)   70 (16.4)   17     78 (14.8)   57 (13.3)   140 (26.6)   107 (25.1)     202 (38.4)   193 (45.2)  </td> <td>334 (63.5)     266 (62.3)     0.753     116 (58.9)       26.8 (6.3)     27.1 (7.5)     0.483     26.5 (6.1)       106 (20.2)     70 (16.4)     35 (17.8)       78 (14.8)     57 (13.3)     26 (13.2)       140 (26.6)     107 (25.1)     51 (25.9)       202 (38.4)     193 (45.2)     85 (43.1)       221 (42.0)     23 (5.4)     &lt;0.001</td> 25 (1.0)       3 (0.6)     23 (5.4)     <0.001	334 (63.5)   266 (62.3)   0.753     26.8 (6.3)   27.1 (7.5)   0.483     106 (20.2)   70 (16.4)   17     78 (14.8)   57 (13.3)   140 (26.6)   107 (25.1)     202 (38.4)   193 (45.2)	334 (63.5)     266 (62.3)     0.753     116 (58.9)       26.8 (6.3)     27.1 (7.5)     0.483     26.5 (6.1)       106 (20.2)     70 (16.4)     35 (17.8)       78 (14.8)     57 (13.3)     26 (13.2)       140 (26.6)     107 (25.1)     51 (25.9)       202 (38.4)     193 (45.2)     85 (43.1)       221 (42.0)     23 (5.4)     <0.001	334 (63.5)     266 (62.3)     0.753     116 (58.9)     122 (61.9)       26.8 (6.3)     27.1 (7.5)     0.483     26.5 (6.1)     27.1 (7.3)       106 (20.2)     70 (16.4)     35 (17.8)     33 (16.8)       26 (13.2)     24 (12.2)     51 (25.9)     51 (25.9)       202 (38.4)     193 (45.2)     95 (48.2)     95 (48.2)       21 (42.0)     235 (55.0)     <0.001	334 (63.5)     266 (62.3)     0.753     116 (58.9)     122 (61.9)     0.607       26.8 (6.3)     27.1 (7.5)     0.483     26.5 (6.1)     27.1 (7.3)     0.409       106 (20.2)     70 (16.4)     35 (17.8)     33 (16.8)     24 (12.2)       140 (26.6)     107 (25.1)     15 (25.9)     51 (25.9)     51 (25.9)     51 (25.9)     51 (25.9)     202 (38.4)     193 (45.2)     95 (48.2)     95 (48.2)     1.000       3 (0.6)     23 (5.4)     <0.001	334 (63.5)     266 (62.3)     0.753     116 (58.9)     122 (61.9)     0.607     117.5 (61.9)       26.8 (6.3)     27.1 (7.5)     0.483     26.5 (6.1)     27.1 (7.3)     0.409     26.9 (6.3)       160 (20.2)     70 (16.4)     35 (17.8)     33 (16.8)     33 (16.8)     33.6 (17.7)       202 (38.4)     197 (25.1)     25.1 (25.9)     51 (25.9)     51 (25.9)     53.0 (27.9)       221 (42.0)     233 (5.4)     -0.001     27.1 (7.3)     1.000     22.1 (1.0)       3 (0.6)     23 (5.4)     -0.001     27.1 (7.3)     45.2     1.000     21.1 (4.0)       3 (6.1)     62 (2.1)     -0.001     47.1 (3.9)     48.1 (6.)     0.739     4.7 (2.3)       3.4 (10.7)     55.8 (24.1)     -0.001     3.4 (10.0)     3.37 (1.8)     0.604     3.2.1 (16.9)       2.5 (11.2)     30 (1.8)     -0.001     3.4 (1.0)     3.37 (1.8)     0.694     3.2.1 (16.9)       2.6 (12.4)     93 (21.8)     -0.001     3.4 (1.0)     3.7 (1.8)     0.694     3.2.1 (16.9)       3.1 (5.9)     109 (25.5)	334 (63.5)     266 (62.3)     0.753     116 (58.9)     122 (61.9)     0.607     117.5 (61.9)     120.1 (62.3)       26.8 (6.3)     27.1 (7.5)     0.483     26.5 (6.1)     27.1 (7.3)     0.409     2.6 9 (6.3)     26.9 (7.1)       106 (20.2)     70 (16.4)     35 (17.8)     33 (16.8)     33.6 (17.7)     28.5 (14.8)       78 (14.8)     57 (13.3)     26 (13.2)     24 (12.2)     25.8 (13.6)     27.5 (14.3)       202 (38.4)     193 (45.2)     85 (43.1)     89 (45.2)     1.000     93.1 (49.0)     93.1 (49.0)       21 (42.0)     235 (55.0)     <0.001

Table I Comparisons of Baseline Characteristics Between the Original Cohort, Matched Cohort and Weig	ghted Cohort
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(Continued)

Covariates	Original Co	Original Cohort			ohort	Weighted Cohort			
	Low BAR	High BAR	Р	Low BAR	High BAR	Р	Low BAR	High BAR	Ρ
Stage I	40 (7.6)	64 (15.0)		22 (11.2)	31 (15.7)		19.0 (10.0)	32.7 (17.0)	
Stage II	93 (17.7)	173 (40.5)		41 (20.8)	81 (41.1)		39.1 (20.6)	76.7 (39.8)	
Stage III	23 (4.4)	66 (15.5)		13 (6.6)	14 (7.1)		12.2 (6.4)	12.6 (6.5)	

Notes: For all continuous covariates, the mean values and standard deviations are reported.

Abbreviations: BAR, blood urea nitrogen to serum albumin ratio, BMI, body mass index, MV, mechanical ventilation, CRRT, continuous renal replacement therapy, SOFA, sequential organ failure assessment, OASIS, Oxford Acute Severity of Illness Score, APSIII, Acute Physiology Score III, SAPSII, Simplified Acute Physiology Score II, CKD, chronic kidney disease, CHF, congestive heart failure, COPD, chronic obstructive pulmonary disease, MAP, mean arterial pressure, RR, respiratory rate, WBC, white blood cell, HGB, hemoglobin, PLT, platelet, AKI, acute kidney injury.

Table 2 Univariate and Multivariate Logistic Analysis of BAR for the Development of AKI

	Original Cohort		Matched Cohort		Weighted Cohort	Weighted Cohort		
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value		
Unadjusted	5.80 (4.39–7.69)	<0.001	3.01 (2.01-4.56)	<0.001	2.92 (2.03-4.21)	<0.001		
Model I	5.98 (4.34-8.32)	<0.001	3.18 (2.08-4.92)	<0.001	3.18 (2.17-4.65)	<0.001		
Model 2	5.45 (3.91–7.65)	<0.001	3.22 (2.09-5.02)	<0.001	3.26 (2.22-4.78)	<0.001		
Model 3	3.88 (2.66-5.71)	<0.001	4.20 (2.59-6.95)	<0.001	4.07 (2.71-6.10)	<0.001		
Model 4	3.85 (2.58–5.79)	<0.001	4.47 (2.71–7.53)	<0.001	4.28 (2.80–6.53)	<0.001		

Notes: Model I adjusted for age, gender, body mass index and number of fracture. Model 2 adjusted for model I plus comorbidities. Model 3 adjusted for Model 2 plus score systerm, interventions and Charlson index. Model 4 adjusted for model 3 plus vital signs and laboratory results. Abbreviations: AKI, acute kidney injury, OR, odds ratio, 95% CI, 95% confidence index.

#### BAR as a Predictor for the Primary End Point

Compared patients in low-BAR group, high-BAR group patients had a relatively higher incidence of AKI in original set (71.0% vs 19.7%, P<0.001), in matched set (64.0% vs 38.6%, P<0.001) and in weighted set (63.3% vs 37.1%, P<0.001). Moreover, the Spearman analysis also indicates that BAR was positively correlated with AKI stage in the original cohort (r=0.411, P<0.001) and in the matched cohort (r=0.324, P<0.001).

Univariate logistic analysis showed that patients in high BAR group had increased incident of AKI, with the crude odds ratio (OR) was 5.80 (95% confidence index, 95% CI, 4.39–7.69, P<0.001) and the relationship remained robust after PSM (OR, 3.01, 95% CI 2.01–4.56, P<0.001) and IPTW (OR, 2.92, 95% CI 2.03–4.21, P<0.001) (Table 2). This association was further verified in multivariate analyses. BAR could still serve as a significant predictor for incident AKI in original cohort (OR, 3.85, 95% CI 2.58–5.79, P<0.001), in matched cohort (OR, 4.47, 95% CI 2.71–7.53, P<0.001) as well as in weighted cohort (OR, 4.28, 95% CI 2.80–6.53, P<0.001) after adjustment for confounding features (Table 2). Those results demonstrated that BAR was an independent and robust predictor for AKI in rib fracture patients.

To further confirm whether BAR remained an independent factor for AKI, we also performed subgroup analyses. Forest plot demonstrated that high BAR was associated with high incidence of AKI in most subgroups (Figure 2A). Furthermore, the results in matched cohort also verify our results (Figure 2B).

## Effect of BAR on Risk Reclassification of AKI

NRI and IDI were introduced to verify the hypothesis that BAR could improve the risk reclassification of incident AKI in critical care patients with rib fracture. And not surprisingly, compared with APSIII score, BAR could significantly improve the risk reclassification for incident of AKI in the original set as well as in the matched set (Table 3).

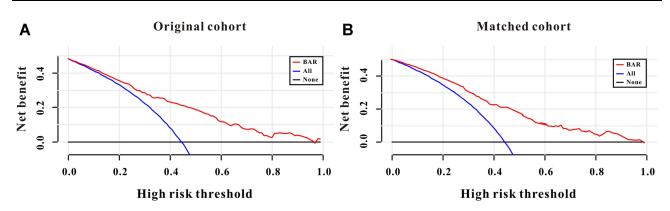


Figure 2 Decision curve analysis of BAR for incident AKI in rib fracture patients to detect its clinical usefulness in the original cohort (A) and in the matched cohort (B).

#### Clinical Usefulness of BAR

DCA curve was also applied to assess the clinical usefulness of BAR for incident of AKI. As described in Figure 3, BAR could add more net benefit than the "treat all" or "treat none" strategies both in the original set and in the matched set (Figure 3A and B). Therefore, these results demonstrated that BAR was clinical usefulness.

## Discussion

In this retrospective study of 953 rib fracture patients from a freely public database and found that patients with high BAR had increased incidence of AKI and demonstrated that initial BAR could serve as a good predictor for incident AKI even after PSM and IPTW were applied to adjust the imbalance of the covariates. Moreover, BAR was superior to that of APSIII score for predicting AKI and could added more net benefit for AKI than treat all or treat none strategies. Therefore, our findings concluded that the initial BAR might have good diagnostic ability for incident AKI in rib fracture patients in ICU.

The incidence of AKI in fracture patients had been described in previous studies, mostly were hip fracture following surgery.<sup>23–26</sup> Rantalaiho et al performed a retrospectively multicenter study of 486 consecutive low-energy trauma hip fracture patients and found that a percent of 8.4% patients were developed AKI and AKI patients had threefold threemonth mortality after surgery compared with patients without AKI.<sup>27</sup> Another retrospective study of 299 patients aged above 65 years who underwent surgery concluded that the incidence of AKI was 28.4% and AKI was associated with longer hospital stay and increased mortality.<sup>25</sup> Moreover, a recent meta-analysis consisting of 11 studies with 16,421 surgical hip fracture patients found the pooled prevalence of AKI was 17% (95% CI 14–21%).<sup>28</sup> Compared with those studies, the incidence of AKI in the current study was much higher (48.2%) and might at least partly explained by differences in patient populations and severity of disease. Furthermore, rib fracture patients especially in ICU occasion-ally require surgical treatment and commonly complain about chest pain, atelectasis, hypoventilation, hypoxemia, respiratory failure and subsequent cardiac complications. Therefore, those subsequent cardiopulmonary complications may be another significant reason why the incidence of AKI is really high.

To the best of our knowledge, we had applied BAR for incident AKI in rib fracture patients in ICU for the first time and observed significant positive correlations between them. More importantly, the initial BAR was superior to that of APSIII score alone for predicting AKI and could add more net benefit for AKI than treat all or treat none. We could explain this as follows: first of all, as a rejected material of protein metabolism manufactured in the liver and evacuated by the kidney, BUN unusually used as one of the most common indexes to assess the renal function in clinical practice and BUN can also be affected by several conditions, such as protein intake, gastrointestinal bleeding, dehydration, inflammation, and so on.<sup>29</sup> Increased BUN level may result from the reduction of water volume in the whole body, leading to higher risk of AKI and while decreased BUN level may be caused by protein deficiency or hepatic failure, both of them can increase the risk of AKI.<sup>30,31</sup> Secondly, ALB maintains the body's nutrition and osmotic pressure as one of the most crucial protein for mankind. Patients with low level of ALB are a sign of malnutrition and has been found to be associated with increased clinical outcomes in patients with different types of disease as well as AKI patients.<sup>32,33</sup> Due to

**NRI**<sup>a</sup>

Outcome				AU	IDI			
	Sensibility (%)	Specificity (%)	Biomarker	Biomarker+	Clinical Model <sup>b</sup>	P value <sup>c</sup>	Value (95% CI)	Р
				Clinical Model				value

Table 3 NRI and IDI Analyses for Risk Reclassification of AKI in the Original Cohort and in the Matched Cohort

	Sensibility (%)	Specificity (%)	Biomarker	Biomarker+	Clinical Model <sup>b</sup>	P value <sup>c</sup>	Value (95% CI)	Р	Value (95% CI)	Р
				Clinical Model				value		value
Original cohort										
BAR	73.0	71.7	0.757	0.854	0.835	< 0.00	0.066 (0.050-0.081)	<0.001	0.134 (0.078–0.191)	<0.001
APSIII	66.0	74.9	0.705	0.839		< 0.00	0.009 (0.003-0.016)	0.045	0.034 (-0.003-0.071)	0.075
BAR+APSIII	71.7	75.3	0.812	0.855		< 0.00	0.075 (0.058-0.092)	<0.001	0.172 (0.111–0.233)	<0.001
Matched cohort										
BAR	71.3	60.2	0.711	0.837	0.789	< 0.00	0.105 (0.071-0.132)	<0.001	0.172 (0.071–0.270)	0.0008
APSIII	69.9	61.5	0.687	0.793		0.0004	0.013 (0.002-0.023)	0.018	0.112 (0.052–0.173)	0.0003
BAR+APSIII	85.4	52.3	0.767	0.841		< 0.001	0.117 (0.085–0.149)	<0.001	0.256 (0.150-0.362)	<0.001

Notes: <sup>a</sup>The NRI is calculated through two-way category by using the event rate of acute kidney injury. <sup>b</sup>The clinical model for predicting AKI are composed of age, gender, BMI, comorbidities, interventions, vital signs, laboratory results and score system except APSIII score. <sup>c</sup>Biomarker+clinical model versus clinical model.

Abbreviations: AUC, area under the receiver-operating characteristic curve; IDI, integrated discrimination improvement; NRI, net reclassification index; BAR, blood urea nitrogen to serum albumin ratio, APSIII, Acute Physiology Score III.

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Characteristics	Ν		OR (95%CI) P value	Characteristics	Ν		OR (95%CI)
All case	953	-	5.80 (4.39-7.69) <0.001	All case	394	*	3.01 (2.00-4.54)
Age				Age			
≥ 60 yr	529	H <b>-</b>	5.47 (3.74-8.01) <0.001	≥ 60 yr	257	HEH .	2.71 (1.64-4.50)
< 60 yr	424		7.16 (4.33-11.86) <0.001	< 60 yr	137	H <b>B</b> 1	3.64 (1.79-7.41)
Gender				Gender			
Male	600	H <b>-</b>	5.41 (3.80-7.68) <0.001	Male	238	H <b>H</b> -1	2.34 (1.39-3.94)
Female	353		6.56 (4.12-10.45) < 0.001	Female	156	H <b>H</b>	4.48 (2.29-8.78)
Number of rib fracture	•			Number of rib fracture			
One	176	<b></b>	4.29 (2.25-8.16) <0.001	One	68	•=	2.30 (0.87-6.08)
Two or three	135	• <b>•</b> •••	5.37 (2.55-11.30) <0.001	Two or three	50	• <b>=</b> •	2.23 (0.72-6.97)
Four or more	247	-	4.89 (2.84-8.43) <0.001	Four or more	102	-	3.09 (1.38-6.92)
Multiple	395	<b></b>	7.43 (4.75-11.62) <0.001	Multiple	174	H <b></b>	3.61 (1.93-6.75)
Hypertension				Hypertension			
Yes	350	-	3.97 (2.55-6.20) <0.001	Yes	175	•	2.15 (1.17-3.92)
No	603	<b></b>	7.30 (5.07-10.51) <0.001	No	219	H <b>H</b> -H	4.00 (2.28-7.02)
Diabetes				Diabetes			
Yes	158	-	3.11 (1.61-6.01) 0.001	Yes	73	-	1.79 (0.70-4.56)
No	795	H <b>-</b>	6.48 (4.74-8.85) <0.001	No	321		3.39 (2.14-5.35)
CKD				CKD			
Yes	71		8.81 (1.61-48.14) 0.012	Yes	17		12.50 (1.61-34.56)
No	882	H <b>-</b>	5.60 (4.18-7.51) <0.001	No	377	<b>111</b>	2.80 (1.85-4.25)
COPD				COPD			
Yes	167		6.53 (3.29-12.98) <0.001	Yes	72	-	2.44 (1.04-6.32)
No	786	H <b>H</b> -1	5.68 (4.17-7.73) <0.001	No	322	HEH .	3.15 (2.00-4.97)
CHF				CHF			
Yes	140		4.80 (2.06-11.21) 0.014	Yes	52	-	2.63 (0.84-8.17)
No	813	+=++	5.26 (3.88-7.15) <0.001	No	342	HE-H	3.09 (1.99-4.81)
Myocardial infarct				Myocardial infarct			
Yes	78	-	2.06 (0.68-6.31) 0.204	Yes	33	-	0.86 (0.21-3.47)
No	875	H <b>8</b> -4	5.83 (4.34-7.82) <0.001	No	361	H	3.40 (2.20-5.23)
Liver disease				Liver disease			
Yes	90		4.09 (1.57-10.68) <0.001	Yes	38	-	1.40 (0.35-5.57)
No	863	-	5.78 (4.30-7.77) <0.001	No	356	-	3.34 (2.16-5.16)
Malignancy				Malignancy			
Yes	42	<b></b>	8.00 (2.01-31.80) 0.003	Yes	16	<b>⊢</b> ∎−-1	7.50 (0.62-90.65)
No	911		5.71 (4.29-7.61) <0.001	No	378		2.96 (1.95-4.50)
		1 3 5 7 9 11				1 3 5 7 9 11 15	
		OR				OR	

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the usage of some instruments or the limits of disease, patients in ICU usually show ALB reduction in serology, leading to the high risk of AKI. BUN and ALB are easily accessible and inexpensive and in the current study, we firstly combined BUN and ALB and found that initial BAR had superior diagnostic ability for AKI to that of APSIII score alone and could added more net benefit for AKI in DCA curve. Hence, BAR, an indicator of inflammation and nutritional status, may act as a new independent predictor for AKI.

However, some limitations also exist in this retrospective study. Firstly, only the initial BAR value was included in this study to access the diagnostic value for AKI while dynamic changes of it did not monitor in this study even those values may be more accurate for AKI. Secondly, due to the limit of the database, we did not obtain levels of serum C-reactive protein and some other inflammatory or nutritional indicators, which may be helpful to investigate the mechanism of the association between BAR and incident AKI for rib fracture patients in ICU. Moreover, serum BUN value might be affected by the diet structure; however, due to the database limit, we did not obtain the information about their diet structure. Finally, this was a retrospective study, and further perspective multicenter studies are proposed to validate the conclusions of our study and to investigate the potential mechanism behind them.

Figure 3 Subgroup analysis for odds ratio of rib fracture patients with BAR  $\geq$  5.26 versus BAR < 5.26 in different groups in the original cohort (A) and in the matched cohort (B).

# Conclusions

In this retrospective study, based on a public database, we firstly concluded that initial BAR was a significant predictor for incident AKI in critical care patients with rib fracture, which was good discrimination and clinical usefulness. Considering that BAR was an easily access and cost-effective parameter, it might provide a helpful method for clinicians to stratify the risk of AKI. Despite the solid statistics of this retrospective study, further studies have been proposed to validate the results of our study.

# **Data Sharing Statement**

All data in our study are available from the corresponding author upon reasonable request.

# **Statement of Ethics**

This study was conducted in accordance with the Helsinki Declaration, and authors had successfully accomplished the National Institutes of Health's (NIH) online training course and the Protection of Human Research Participants Examination and got the permission to extract data from MIMIC IV database. Moreover, the study protocol was reviewed and successfully approved by the Ethics Committee of Sinopharm Dongfeng General Hospital and was waived to informed consent.

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#### Disclosure

The authors declare that they have no competing interests.

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