Clin. Lab. 2026;72:XXX-XXX

ORIGINAL ARTICLE

Prognostic Value of the Blood Urea Nitrogen-to-Albumin Ratio for ICU Mortality in Cardiogenic Shock Patients: Evidence from the MIMIC-IV Database

Hu Liu [1, *], Yan-Bo Zhao [1, *], Can Wang [2], Lin Liu [1], Yang Liu [2], Xing-Guo Peng [1], You-En Zhang [3, 4]

[*] Hu Liu and Yan-Bo Zhao contributed equally to this work
[1] Department of Emergency and Critical Care Center, Renmin Hospital, Hubei University of Medicine, Shiyan, Hubei, China
[2] School of Nursing, Hubei University of Medicine, Shiyan, China
[3] Institute of Clinical Medicine and Department of Cardiology, Renmin Hospital, Hubei University of Medicine, Shiyan, Hubei, China
[4] Arteriosclerosis Cardiovascular Disease Clinical Medical Research Center of Hubei Province, Shiyan, Hubei, China

SUMMARY

Background: **Cardiogenic shock (CS) is a life-threatening condition with high mortality. This study explored the association between the blood urea nitrogen-to-albumin ratio (BAR), a marker of renal function and nutritional status, and mortality in CS, aiming to evaluate its utility as a simple early risk stratification tool.**
Methods: **This study analyzed data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, categorizing participants by BAR quartiles to examine 28-day intensive care unit (ICU) mortality. Least absolute shrinkage and selection operator (LASSO) regression was used to identify key variables associated with BAR and clinical outcomes. Logistic regression, Cox proportional hazards models, and restricted cubic splines were applied to assess the relationship between BAR and mortality. Kaplan–Meier curves illustrated cumulative mortality, while sensitivity and subgroup analyses were conducted to ensure the robustness of the findings. Causal mediation analysis (CMA) was conducted to investigate the indirect effects of BAR on prognosis.**
Results: **This study of 1,474 CS patients found that a higher BAR was linked to a greater risk of 28-day ICU mortality. After adjustments, those in the highest BAR quartile had a significantly increased mortality risk (HR 1.88, 95% CI: 1.30 - 2.71, p = 0.001) compared to those in the lowest quartile. Kaplan-Meier analysis demonstrated significantly reduced 28-day ICU survival probabilities in highest BAR quartile. Hemoglobin partially mediated this relationship, explaining 10.88% of the effect. The association between BAR and prognosis in patients with CS remained consistent across most subgroups, with significant interactions identified in the race and acute kidney injury (AKI) subgroups.**
Conclusions: **This study found that elevated BAR is closely associated with adverse ICU outcomes in patients with CS.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250623)

Correspondence:
Prof. Xing-Guo Peng
Department of Emergency and Critical Care Center
Renmin Hospital
Hubei University of Medicine
Shiyan, Hubei 442000
China
Email: pxg8688@sina.com

Prof. You-En Zhang
Institute of Clinical Medicine and Department of Cardiology
Renmin Hospital
Hubei University of Medicine
Shiyan, Hubei 442000
China
Email: 3855091925@qq.com

Manuscript accepted July 20, 2025

KEYWORDS

blood urea nitrogen-to-albumin ratio, cardiogenic shock, MIMIC-IV database, causal mediation analysis, mortality

LIST OF ABBREVIATIONS

CS - Cardiogenic shock
BAR - Blood urea nitrogen-to-albumin ratio
MIMIC-IV - Medical information mart for intensive care IV
LASSO - Least absolute shrinkage and selection operator
ICU - Intensive care unit
CMA - Causal mediation analysis
AKI - Acute kidney injury
BUN - Blood urea nitrogen
AMI - Acute myocardial infarction
BMI - Body mass index
CVA - Cerebrovascular accident
CKD - Chronic kidney disease
T2DM - Type 2 diabetes mellitus
HF - Heart failure
MI - Myocardial infarction
IHD - Ischemic myocardial disease
SBP - Systolic blood pressure
DBP - Diastolic blood pressure
SpO_2 - Oximetry saturation
WBC - White blood cell count
PLT - Platelet count
PCO2 - Carbon dioxide pressure
PO2 - Arterial oxygen pressure
INR - International normalized ratio
LDH - Lactate dehydrogenase
SOFA - Sequential organ failure assessment
SIRS - Systemic inflammatory response syndrome
OASIS - Oxford acute severity of illness score
APACHE II - Acute physiology and chronic health evaluation II
MV - Mechanical ventilation
CRRT - continuous renal replacement therapy
VIF - variance inflation factors
HR - hazard ratios
OR - odds ratio
RCS - restricted cubic spline

INTRODUCTION

CS is a critical condition characterized by severe cardiac pump failure [1], resulting in inadequate tissue perfusion, life-threatening organ dysfunction, and tissue hypoxia [2]. Despite advancements in medical care and improved survival rates in recent years, the prognosis for CS remains grim [3], with in-hospital mortality reaching 33.6% and short-term mortality ranging between 45% and 70% [4,5]. This condition not only places a substantial strain on national healthcare systems and medical resources but also poses significant health and economic challenges for affected individuals. Given its severe impact, CS remains a major focus of global healthcare efforts. Clinically, the development of CS is attributed to various underlying causes, including severe valvular disease, arrhythmias, and cardiac tamponade [6]. Therefore, there is an urgent need to identify reliable prognostic indicators associated with poor outcomes in CS patients, enabling timely therapeutic interventions and ultimately reducing mortality rates.

Blood urea nitrogen (BUN), a metabolic byproduct synthesized by the liver and excreted by the kidneys, is a widely used biochemical parameter for assessing renal function [7]. Alongside serum creatinine, BUN plays a crucial role in evaluating kidney health [8]. Recent studies have highlighted its prognostic significance in various diseases, including aortic dissection, acute pancreatitis, and cerebral hemorrhage [9-11]. Albumin, a liver-synthesized protein, serves multiple physiological functions, including osmotic regulation, antioxidation, and anti-inflammatory activity [12]. Numerous studies have established albumin as a valuable prognostic marker for critically ill patients with conditions such as acute kidney injury, cirrhosis-related gastrointestinal bleeding, acute heart failure, and sepsis [13–16]. The BAR integrates these two biomarkers. Previous research has demonstrated that BAR is a significant predictor of mortality in various diseases, including ischemic stroke, sepsis, acute respiratory failure, and lung cancer [17–20]. In the realm of cardiovascular diseases, BAR has been identified as an independent predictor of long-term mortality in patients with acute myocardial infarction (AMI) [21]. Notably, cardiogenic shock, a severe complication of AMI, occurs in approximately 10% of cases and is associated with exceptionally high mortality rates [22,23].

Although BAR has been studied in various critical illnesses, its prognostic value in CS remains unclear. This study investigated whether BAR can predict mortality in CS, aiming to support early risk identification and guide treatment strategies.

MATERIALS AND METHODS

Study design and population

This retrospective, observational cohort study utilized data from the MIMIC-IV 3.1 database (https://mimic.mit.edu), a large, single-center, publicly available clinical database that includes comprehensive medical records of 94,458 patients admitted to the Beth Israel Deaconess Medical Center in Boston, Massachusetts, USA, between 2008 and 2022. Access to the database was granted to one of the authors (Hu Liu) after completing the Collaborative Institutional Training Initiative Program (certification number: 68041273). Due to the de-identified nature of the patient health information in this database, the requirement for ethical approval was waived.

Study participants

This study encompassed patients aged 18 years and older who were admitted to the ICU with a diagnosis of CS, as classified by the Ninth and Tenth Revisions of the International Classification of Diseases (ICD-9 code 785.51 and ICD-10 code R57.0). The exclusion criteria were as follows: 1) patients with ICU stays of less than 24 hours were excluded; 2) for patients with multiple ICU admissions, only data from the initial hospitalization were considered; and 3) patients with missing blood urea nitrogen and serum albumin values in their initial laboratory tests were excluded (Figure 1).

Data extraction

Data were extracted from the MIMIC IV database using Structured Query Language in Navicat Premium (version 16.0). Patient characteristics, including age, gender, and body mass index (BMI), were collected. Information on comorbidities, such as hypertension, AKI, cerebrovascular accident (CVA), chronic kidney disease (CKD), type 2 diabetes mellitus (T2DM), heart failure (HF), myocardial infarction (MI), ischemic myocardial disease (IHD), and hyperlipidemia, were extracted based on the International Classification of Diseases coding system. Vital signs [heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate, pulse oximetry saturation (SpO_2), and temperature] and laboratory tests [hemoglobin, white blood cell count (WBC), platelet count, serum sodium, serum potassium, serum calcium, pH, carbon dioxide pressure (PCO_2), arterial oxygen pressure (PO_2), lactate, prothrombin time international normalized ratio (INR), lactate dehydrogenase (LDH), aspartate aminotransferase, alanine aminotransferase, creatinine, BUN, serum albumin, and serum glucose] were extracted. Various scores [such as the sequential organ failure assessment (SOFA) score, systemic inflammatory response syndrome (SIRS) score, Oxford acute severity of illness score (OASIS), acute physiology and chronic health evaluation II (APACHE II) score, Charlson comorbidity index, and Glasgow coma scale score], treatment [mechanical ventilation (MV) and continuous renal replacement therapy (CRRT)], and drug therapies (vasopressors and glucocorticoids) were extracted. All of the laboratory data were extracted from the data collected the first time after the patient was admitted to the ICU. The blood urea nitrogen to BAR is defined as the index calculated using the following formula: BAR = blood urea nitrogen (mg/dL)/serum albumin ratio (g/dL).

Outcome

The main outcome was 28-day all-cause mortality in the ICU, while secondary outcomes included 90-day, 360-day, and overall ICU all-cause mortality.

Statistical analysis

The normality of continuous variables was assessed using Shapiro-Wilk test. Variables with normal distribution were expressed as mean ± standard deviation and compared using *t*-test; variables with non-normal distribution were expressed as median and interquartile range and compared using Wilcoxon test. Categorical variables (expressed as counts and percentages) were compared using chi-squared or Fisher's exact test. Variables exceeding 20% missing data were excluded, and missing values in the remaining variables were imputed through multiple imputation [24]. Detailed missing data patterns are provided in Supplementary Table S1. Multicollinearity was assessed using variance inflation factors (VIF), with variables exceeding a VIF threshold of 5 removed. Detailed VIF values for variables are provided in Supplementary Table S2. LASSO regression combined with 10-fold cross-validation was used for variable selection. The optimal λ value was determined based on the one-standard-error rule [25]. Variables with non-zero coefficients were retained for the subsequent multivariate regression analysis.

To explore the independent impact of BAR on the mortality rate of patients with CS, multivariate Cox analysis or multivariate logistic regression was used with different models being adjusted for potential confounders models. Model 1 was used for crude analysis, without any adjustments for confounders. Model 2 was adjusted for age, OASIS, Charlson comorbidity index, APACHE II score. Based on Model 2, Model 3 was further adjusted for lactate, pH, HF, CRRT, and vasopressors use. The BAR was divided into quartiles, with the first group as the reference. Adjusted hazard ratios (HR) or odds ratio (OR) for primary and secondary endpoints were calculated relative to this group. Kaplan-Meier analysis assessed 28-day, 90-day, and 360-day mortality rates for ICU-admitted, critically ill CS patients.

Restricted cubic spline (RCS) curves evaluated non-linear associations between BAR and mortality, and the log-likelihood ratio test compared non-segmented and segmented regression models to determine any thresholds.

To evaluate the robustness of the findings, a sensitivity analysis was performed using three incremental models. Model 1 included no adjustments. Model 2 was adjusted for age, gender, race, and BMI, whereas Model 3 incorporated comprehensive covariate adjustments.

CMA separates the total effect of a treatment into direct and indirect effects. If an independent variable X affects a dependent variable Y via another variable M, then M is the mediator [26]. This study hypothesized that BAR might impact the prognosis of cardiogenic shock patients by mediating variable changes. CMA average causal mediation effect, average direct effect, and total effect can validate this hypothesis.

The prognostic value of BAR was further examined through comprehensive subgroup analyses, for each subgroup analysis, both p-values and interaction terms were calculated to assess the consistency of the prognostic value of BAR across different patient populartions.

All statistical analyses were performed using R software (version 4.5). Statistical significance was considered

Table 1. Association of BAR with mortality outcomes in patients with cardiogenic shock in ICU.

Outcomes	Model 1			Model 2			Model 3		
	HR/OR (95% CI)	p-value	p-for trend	HR/OR (95% CI)	p-value	p-for trend	HR/OR (95% CI)	p-value	p-for trend
28-day ICU all-cause mortality									
BAR (continuous)	1.03 (1.02 - 1.04)	< 0.001		1.02 (1.01 - 1.03)	< 0.001		1.02 (1.01 - 1.03)	< 0.001	
Q1	Reference			Reference			Reference		
Q2	1.71 (1.27 - 2.29)	< 0.001	< 0.001	1.37 (1.02 - 1.85)	0.037	0.001	1.40 (1.04 - 1.89)	0.026	< 0.001
Q3	2.20 (1.65 - 2.93)	< 0.001		1.49 (1.10 - 2.01)	0.010		1.57 (1.16 - 2.13)	0.003	
Q4	2.68 (2.03 - 3.54)	< 0.001		1.67 (1.24 - 2.26)	0.001		1.76 (1.30 - 2.38)	< 0.001	
90-day ICU all-cause mortality									
BAR (continuous)	1.03 (1.02 - 1.04)	< 0.001		1.02 (1.01 - 1.03)	< 0.001		1.02 (1.01 - 1.03)	< 0.001	
Q1	Reference			Reference			Reference		
Q2	1.66 (1.26 - 2.18)	< 0.001	< 0.001	1.36 (1.03 - 1.80)	0.032	0.001	1.38 (1.04 - 1.82)	0.026	< 0.001
Q3	2.10 (1.60 - 2.75)	< 0.001		1.46 (1.10 - 1.94)	0.009		1.53 (1.15 - 2.04)	0.003	
Q4	2.60 (2.00 - 3.37)	< 0.001		1.67 (1.26 - 2.22)	< 0.001		1.75 (1.31 - 2.33)	< 0.001	
360-day ICU all-cause mortality									
BAR (continuous)	1.03 (1.02 - 1.04)	< 0.001		1.02 (1.01 - 1.03)	< 0.001		1.02 (1.01 - 1.03)	< 0.001	
Q1	Reference			Reference			Reference		
Q2	1.77 (1.35 - 2.32)	< 0.001	< 0.001	1.45 (1.10 - 1.91)	0.008	< 0.001	1.47 (1.12 - 1.94)	0.006	< 0.001
Q3	2.16 (1.66 - 2.83)	< 0.001		1.51 (1.14 - 2.00)	0.004		1.58 (1.20 - 2.10)	0.001	
Q4	2.68 (2.07 - 3.47)	< 0.001		1.73 (1.31 - 2.29)	< 0.001		1.81 (1.36 - 2.40)	< 0.001	
ICU all-cause mortality									
BAR (continuous)	1.04 (1.03 - 1.05)	< 0.001		1.02 (1.01 - 1.04)	< 0.001		1.03 (1.01 - 1.04)	< 0.001	
Q1	Reference			Reference			Reference		
Q2	2.14 (1.54 - 2.99)	< 0.001	< 0.001	1.77 (1.25 - 2.50)	0.001	< 0.001	1.73 (1.21 - 2.48)	0.003	< 0.001
Q3	2.55 (1.83 - 3.58)	< 0.001		1.79 (1.26 - 2.58)	0.001		1.86 (1.28 - 2.70)	0.001	
Q4	3.44 (2.49 - 4.80)	< 0.001		2.21 (1.53 - 3.20)	< 0.001		2.35 (1.60 - 3.45)	< 0.001	

BAR quartiles: Q1 (1.03 - 6.29), Q2 (6.30 - 10.00), Q3 (10.26 - 16.30), Q4 (16.33 - 58.75).
Model 1: No variables were adjusted.
Model 2: Adjusted for age, OASIS, Charlson comorbidity index, APACHE II score.
Model 3: Based on Model 2, further adjusted for lactate, pH, HF, CRRT, and vasopressor use.
BAR blood urea nitrogen-to-albumin ratio, ICU intensive care unit, HR hazard ratio, OR odds ratio, OASIS Oxford acute severity of illness score, APACHE II acute physiology and chronic health evaluation II, pH potential of hydrogen, HF heart failure, CRRT continuous renal replacement therapy.

Table 2. The threshold analysis of the BAR.

Outcome	360-day ICU all-cause mortality		ICU all-cause mortality	
	HR (95% CI)	p-value	OR (95% CI)	p-value
Model I				
One line effect	1.02 (1.01, 1.03)	< 0.001	1.03 (1.01, 1.04)	< 0.001
Model II				
Turning point (K)	31.79		9.68	
< K effect 1	1.03 (1.01, 1.04)	< 0.001	1.14 (1.06, 1.22)	< 0.001
< K effect 2	0.97 (0.93, 1.01)	0.110	1.01 (1.00, 1.03)	0.108
LRT test		0.004		0.003

BAR blood urea nitrogen-to-albumin ratio, ICU intensive care unit, LRT log-likelihood ratio test, HR hazard ratio, OR odds ratio.

when p-value was < 0.05 using two-tailed tests.

RESULTS

Characteristics of patients

As shown in Supplementary Table S3, the median age of the 1,474 patients was 71 years (60.00 - 80.00 years), and men accounted for 60.39% of the total patient population. Compared with patients in the survival group, those in the non-survival group were older and had significantly higher glucose, WBC, INR, lactate, LDH, creatinine, BUN, BAR, and lower temperature, DBP, SBP, hemoglobin, pH, and albumin (all p < 0.05). Disease severity scores, including SOFA score, OASIS, Charlson comorbidity index, and APACHE II score were notably higher in the non-survival group (all p < 0.001). The non-survival group exhibited a higher incidence of complications including acute kidney injury, pneumonia, and chronic kidney disease, whereas heart failure and hyperlipidemia demonstrated a lower incidence compared to the survival group. The non-survival group had significantly higher proportions of patients receiving CRRT, glucocorticoid, and vasopressor support (all p < 0.05).

Association between BAR and clinical outcome in CS patients

LASSO regression identified 10 variables with non-zero coefficients (age, BAR, lactate, pH, OASIS, Charlson comorbidity index, APACHE II, heart failure, CRRT, and vasopressor use) based on the optimal λ value of 0.040 (Figure 2). The relative importance of these features is illustrated in Supplementary Figure S1. These variables were subsequently included in the multivariate regression analysis. As shown in Table 1, multivariable Cox regression analysis revealed a significant association between elevated BAR levels and 28-day ICU all-cause mortality. When BAR was analyzed as a continuous variable, the unadjusted Model 1 demonstrated a strong association (HR 1.03, 95% CI: 1.02 - 1.04, p < 0.001). This association remained statistically significant but attenuated in Model 2 (HR 1.02, 95% CI: 1.01 - 1.03, p < 0.001) and Model 3 (HR 1.02, 95% CI: 1.01 - 1.03, p < 0.001). In quartile-based analyses, compared to the reference Q1 group, progressively higher mortality risks were observed for Q2, Q3, and Q4 in Model 1 (all p < 0.001). These graded risks persisted even after sequential adjustments in Model 2 and Model 3, with a consistent dose-response relationship across all models. Notably, Q4 (highest BAR quartile) exhibited the strongest risk elevation (Model 3 HR 1.76, 95% CI: 1.30 - 2.38, p < 0.001), underscoring the clinical relevance of extreme BAR levels in predicting adverse outcomes. Through multivariable Cox analysis or multivariable logistic regression analysis, elevated BAR was significantly associated with 90-day ICU all-cause mortality, 360-day ICU all-cause mortality, and ICU all-cause mortality, with the higher quartiles (Q3-Q4) predicting mortality risk after multivariable adjustments and demonstrating a clear dose-response relationship.

As shown in Figure 3, Kaplan-Meier analysis demonstrated significantly reduced survival probabilities in Q4 across all time points (28-day, 90-day, and 360-day ICU survival rates).

Restricted cubic spline and threshold effect analysis

According to the RCS analysis results (Figure 4), both 28-day ICU all-cause mortality and 90-day ICU all-cause mortality demonstrated a linear relationship between BAR and mortality risk after adjusting for variables, whereas 360-day ICU all-cause mortality and ICU all-cause mortality exhibited a nonlinear association between BAR and mortality risk following the

Table 3. Sensitivity analysis of associations between BAR and mortality outcomes in patients with cardiogenic shock in ICU.

Outcomes	Model 1			Model 2			Model 3		
	HR/OR (95% CI)	p-value	p-for trend	HR/OR (95% CI)	p-value	p-for trend	HR/OR (95% CI)	p-value	p-for trend
28-day ICU all-cause mortality									
BAR (continuous)	1.03 (1.02 - 1.04)	< 0.001		1.02 (1.02 - 1.04)	< 0.001		1.02 (1.01 - 1.04)	< 0.001	
Q1	Reference			Reference			Reference		
Q2	1.71 (1.27 - 2.29)	< 0.001	< 0.001	1.61 (1.20 - 2.17)	0.002	< 0.001	1.45 (1.06 - 1.98)	0.020	0.001
Q3	2.20 (1.65 - 2.93)	< 0.001		2.04 (1.53 - 2.73)	< 0.001		1.64 (1.19 - 2.27)	0.003	
Q4	2.68 (2.03 - 3.54)	< 0.001		2.35 (1.77 - 3.12)	< 0.001		1.88 (1.30 - 2.71)	0.001	
90-day ICU all-cause mortality									
BAR (continuous)	1.03 (1.02 - 1.04)	< 0.001		1.03 (1.02 - 1.04)	< 0.001		1.02 (1.01 - 1.04)	< 0.001	
Q1	Reference			Reference			Reference		
Q2	1.66 (1.26 - 2.18)	< 0.001	< 0.001	1.59 (1.20 - 2.10)	0.001	< 0.001	1.46 (1.09 - 1.96)	0.010	< 0.001
Q3	2.10 (1.60 - 2.75)	< 0.001		1.99 (1.51 - 2.61)	< 0.001		1.65 (1.22 - 2.24)	0.001	
Q4	2.60 (2.00 - 3.37)	< 0.001		2.33 (1.78 - 3.04)	< 0.001		1.98 (1.40 - 2.79)	< 0.001	
360-day ICU all-cause mortality									
BAR (continuous)	1.03 (1.02 - 1.04)	< 0.001		1.03 (1.02 - 1.04)	< 0.001		1.02 (1.01 - 1.03)	< 0.001	
Q1	Reference			Reference			Reference		
Q2	1.77 (1.35 - 2.32)	< 0.001	< 0.001	1.70 (1.30 - 2.23)	< 0.001	< 0.001	1.56 (1.17 - 2.07)	0.002	< 0.001
Q3	2.16 (1.66 - 2.83)	< 0.001		2.05 (1.56 - 2.69)	< 0.001		1.68 (1.25 - 2.27)	0.001	
Q4	2.68 (2.07 - 3.47)	< 0.001		2.41 (1.85 - 3.14)	< 0.001		1.98 (1.41 - 2.79)	< 0.001	
ICU all-cause mortality									
BAR (continuous)	1.04 (1.03 - 1.05)	< 0.001		1.04 (1.03 - 1.05)	< 0.001		1.04 (1.02 - 1.06)	< 0.001	
Q1	Reference			Reference			Reference		
Q2	2.14 (1.54 - 2.99)	< 0.001	< 0.001	2.07 (1.48 - 2.91)	< 0.001	< 0.001	1.86 (1.27 - 2.73)	0.002	< 0.001
Q3	2.55 (1.83 - 3.58)	< 0.001		2.44 (1.74 - 3.45)	< 0.001		2.03 (1.35 - 3.07)	< 0.001	
Q4	3.44 (2.49 - 4.80)	< 0.001		3.17 (2.27 - 4.47)	< 0.001		2.87 (1.78 - 4.66)	< 0.001	

BAR quartiles: Q1 (1.03 - 6.29), Q2 (6.30 - 10.00), Q3 (10.26 - 16.30), Q4 (16.33 - 58.75).
Model 1: No variables were adjusted.
Model 2: Adjusted for age, gender, race, BMI.
Model 3: Based on Model 2, further adjusted for heart rate, respiratory rate, SpO_2, temperature, diastolic blood pressure, systolic blood pressure, serum glucose, white blood cell count, platelet count, hemoglobin, INR, pH, PCO_2, PaO_2, lactate, serum calcium, serum potassium, serum sodium, ALT, AST, LDH, creatinine, SOFA score, SIRS score, OASIS, GCS score, Charlson comorbidity index, APACHE II score, hypertension, acute kidney injury, cerebral vascular accident, chronic kidney disease, type 2 diabetes mellitus, heart failure, myocardial infarct, ischemic heart disease, hyperlipidemia, mechanical ventilation, CRRT, glucocorticoid, and vasopressor use.
BAR blood urea nitrogen-to-albumin ratio, ICU intensive care unit, HR hazard ratio, OR odds ratio, BMI body mass index, INR prothrombin time international normalized ratio, pH potential of hydrogen, PCO_2 partial pressure of carbon dioxide, PaO_2 partial pressure of oxygen, ALT alanine aminotransferase, AST aspartate aminotransferase, LDH lactate dehydrogenase, SOFA sequential organ failure assessment, SIRS systemic inflammatory response syndrome, OASIS Oxford acute severity of illness score, GCS Glasgow coma scale, APACHE II acute physiology and chronic health evaluation II, CRRT continuous renal replacement therapy.

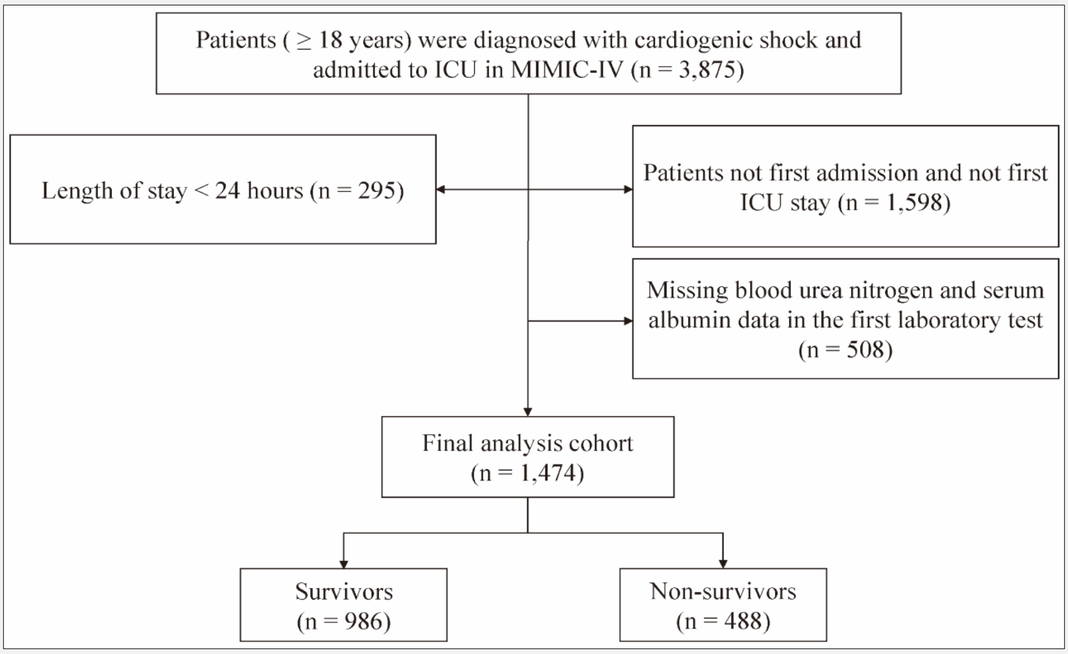


Figure 1. Flow chart of the current study.

MIMIC-IV medical information mart for intensive care IV, ICU intensive care unit.

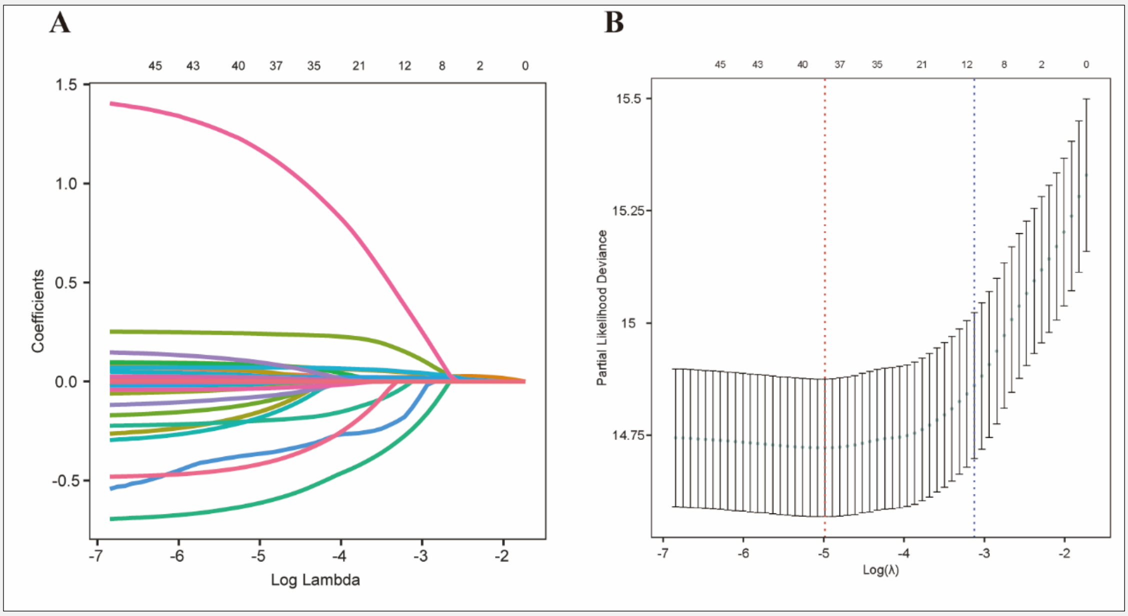


Figure 2. Selection using the LASSO regression model.

A) LASSO regression λ mean squared error plot. B) LASSO regression λ coefficient plot.

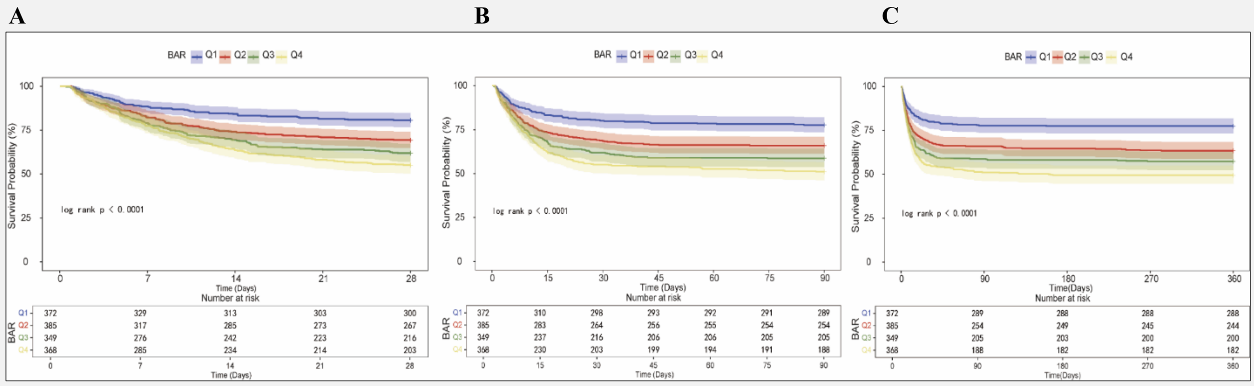


Figure 3. Kaplan-Meier survival curves for 28-day ICU all-cause mortality (A), 90-day ICU all-cause mortality (B), and 360-day ICU all-cause mortality (C) in patients with CS, stratified by quartiles of the BAR.

BAR categories: Q1 (1.03 - 6.29), Q2 (6.30 - 10.00), Q3 (10.26 - 16.30), Q4 (16.33 - 58.75).
ICU intensive care unit, CS cardiogenic shock, BAR blood urea nitrogen-to-albumin ratio.

same adjustment. The threshold effects of BAR on 360-day ICU all-cause mortality and ICU all-cause mortality were further analyzed (Table 2). For 360-day ICU all-cause mortality, the threshold of BAR was 31.79, while for ICU all-cause mortality, the threshold was 9.68. Below the threshold, each unit increase in BAR significantly raised the 360-day ICU all-cause mortality risk (HR = 1.03, 95% CI: 1.02 - 1.04, p < 0.001), as well as the ICU all-cause mortality risk (OR = 1.14, 95% CI: 1.06 - 1.22, p < 0.001). However, when BAR exceeded the threshold, the risk association weakened and became statistically nonsignificant. Likelihood ratio tests indicated that the threshold effect model significantly outperformed the linear model (both p < 0.05).

Sensitivity analysis

Sensitivity analysis (Table 3) confirmed the stability of the association between BAR and outcomes in patients with cardiogenic shock after full adjustment (Model 3). As a continuous variable, BAR was significantly positively associated with 28-day ICU all-cause mortality (HR 1.02, 95% CI: 1.01 - 1.04, p < 0.001), 90-day mortality (HR 1.02, 95% CI: 1.01 - 1.04, p < 0.001), 360-day mortality (HR 1.02, 95% CI: 1.01 - 1.03, p < 0.001), and ICU all-cause mortality (OR 1.04, 95% CI: 1.02 - 1.06, p < 0.001). Grouped by BAR quartiles, patients in Q4 showed significantly increased mortality risks compared with Q1 (reference group) in Model 3: 28-day mortality (HR 1.88, 95% CI: 1.30 - 2.71, p = 0.001), 90-day mortality (HR 1.98, 95% CI: 1.40 - 2.79, p < 0.001), 360-day mortality (HR 1.98, 95% CI: 1.41 - 2.79, p < 0.001), and ICU all-cause mortality (OR 2.87, 95% CI: 1.78 - 4.66, p < 0.001). Additionally, the risk of mortality increased significantly with higher BAR quartiles (all p-for-trend < 0.05). These results were consistent with the primary analysis, supporting a strong association between BAR and adverse outcomes in patients with CS.

Causal mediation analysis

In the CMA, hemoglobin was confirmed to have a mediating effect. Figure 5 shows that in terms of 28-day ICU mortality of CS patients, hemoglobin mediated 10.88% (95% CI: 4.23 - 19.86%; p = 0.002) of the adverse effect of BAR (ACME: p = 0.002)

Subgroup analyses

Subgroup analyses for the relationship between BAR and 28-day ICU all-cause mortality were performed according to gender, race, comorbidities (hypertension, AKI, CVA, CKD, T2DM, MI, IHD, and hyperlipidemia), MV, and glucocorticoid use. The findings consistently showed that a higher BAR was associated with an elevated risk of 28-day ICU all-cause mortality in most of the investigated subgroups (Figure 6). Overall, BAR showed significant associations with 28-day ICU all-cause mortality (HR 1.02, 95% CI: 1.01 - 1.03, p < 0.001). Significant interactions were observed in race subgroups (p for interaction = 0.03) and AKI subgroups (p for interaction = 0.01), indicating that the link between BAR and mortality may vary in these cohorts. Additionally, subgroup analyses of 90-day ICU all-cause mortality and 360-day ICU all-cause mortality demonstrated persistent interaction effects in race subgroups (all p for interaction = 0.02) and AKI subgroups (all p for interaction < 0.001), while ICU all-cause mortality analysis revealed interaction in race subgroups (p for interaction = 0.024), with detailed stratification results visualized in Supplementary Figure S2.

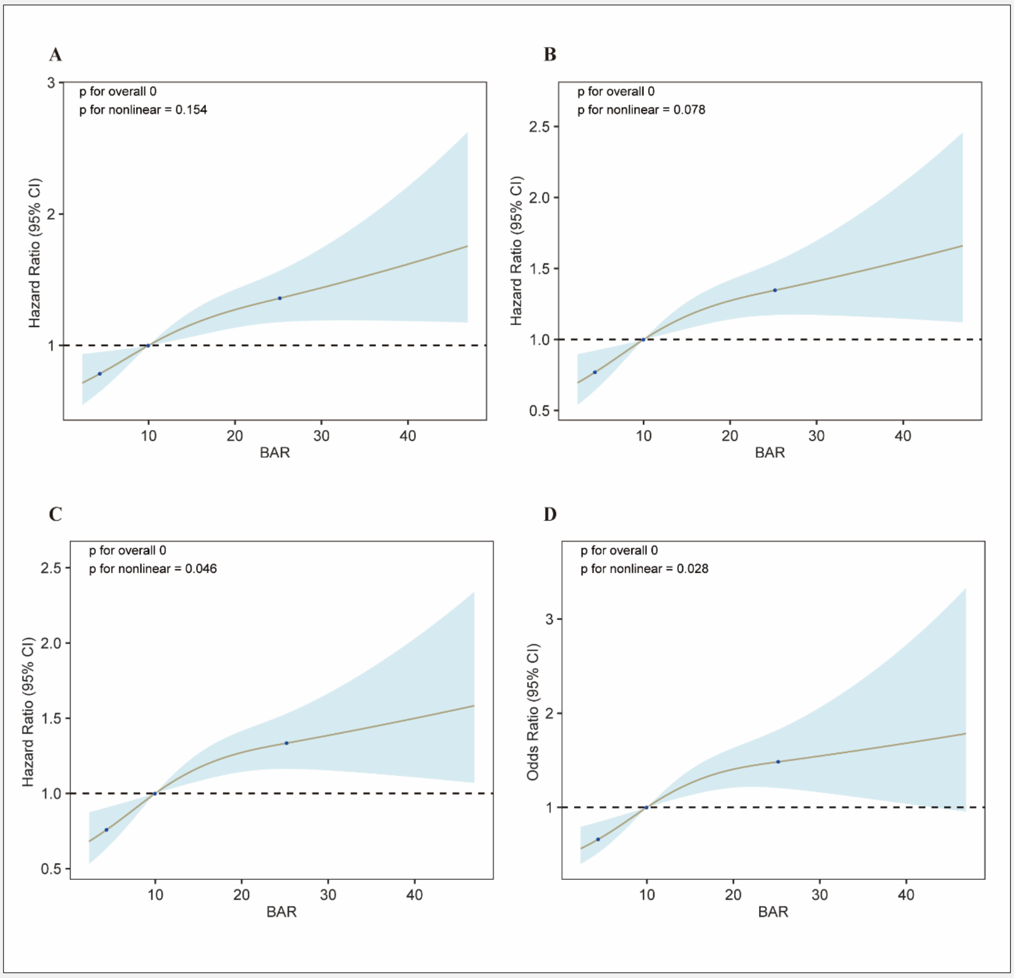


Figure 4. Restricted cubic spline function between BAR and 28-day ICU all-cause mortality (A), 90-day ICU all-cause mortality (B), 360-day ICU all-cause mortality (C), and ICU all-cause mortality (D) in patients with CS, adjusted for age, OASIS, Charlson comorbidity index, APACHE II score; lactate, pH, HF, CRRT, and vasopressor use.

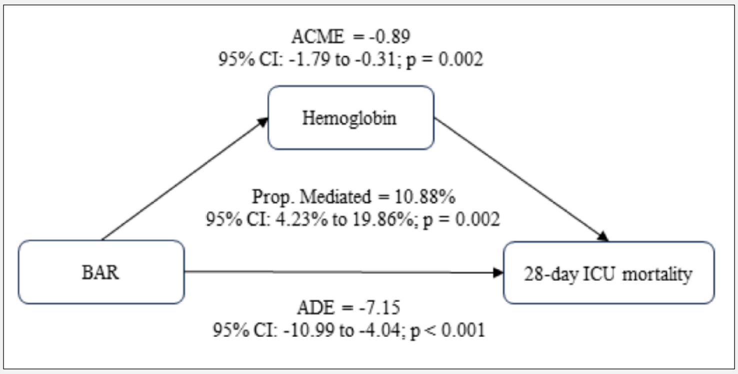
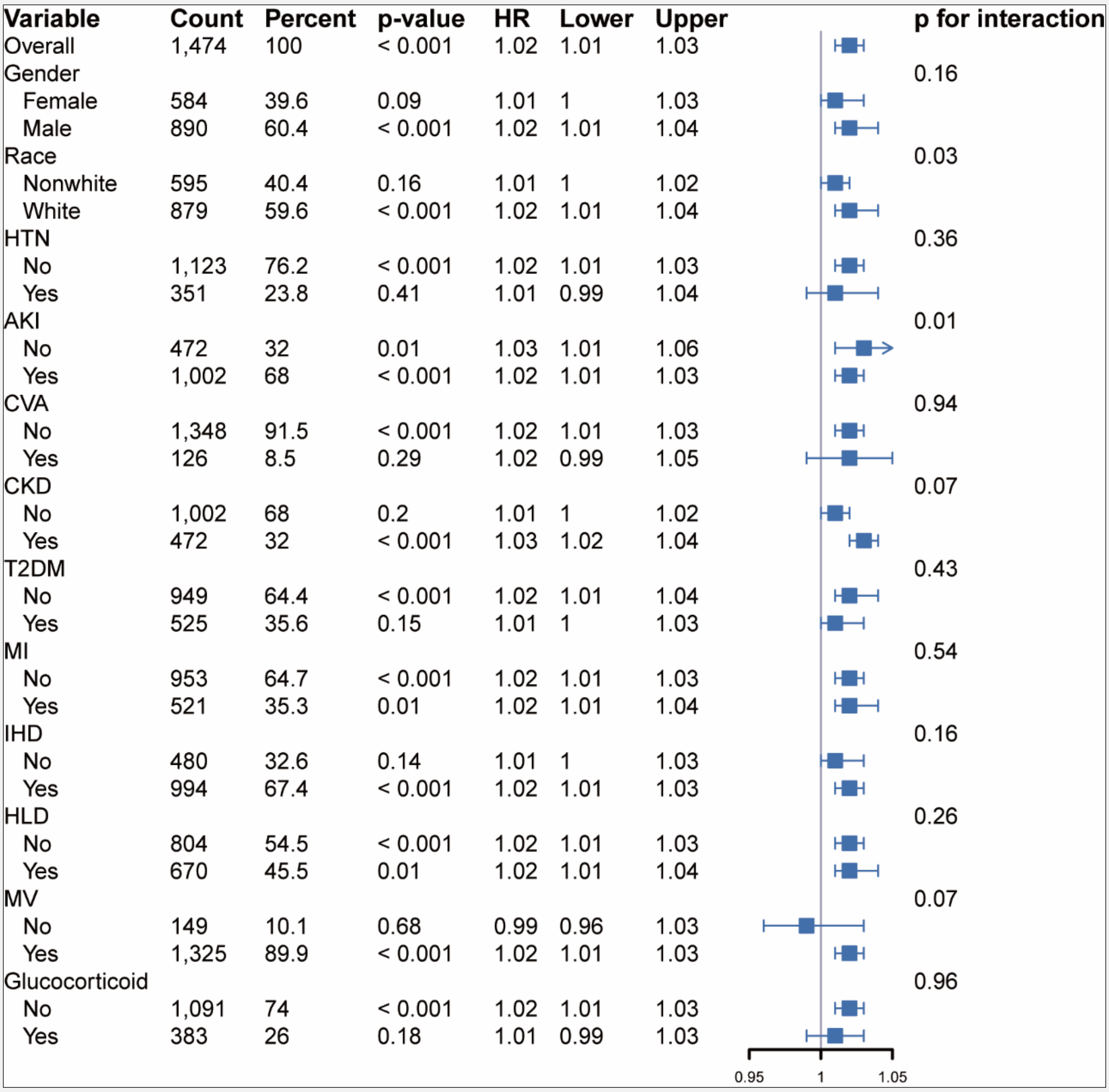


Figure 5. Causal mediation analysis for hemoglobin reduction.



Variable	Count	Percent	p-value	HR	Lower	Upper	p for interaction
Overall	1,474	100	< 0.001	1.02	1.01	1.03	
Gender							0.16
Female	584	39.6	0.09	1.01	1	1.03	
Male	890	60.4	< 0.001	1.02	1.01	1.04	
Race							0.03
Nonwhite	595	40.4	0.16	1.01	1	1.02	
White	879	59.6	< 0.001	1.02	1.01	1.04	
HTN							0.36
No	1,123	76.2	< 0.001	1.02	1.01	1.03	
Yes	351	23.8	0.41	1.01	0.99	1.04	
AKI							0.01
No	472	32	0.01	1.03	1.01	1.06	
Yes	1,002	68	< 0.001	1.02	1.01	1.03	
CVA							0.94
No	1,348	91.5	< 0.001	1.02	1.01	1.03	
Yes	126	8.5	0.29	1.02	0.99	1.05	
CKD							0.07
No	1,002	68	0.2	1.01	1	1.02	
Yes	472	32	< 0.001	1.03	1.02	1.04	
T2DM							0.43
No	949	64.4	< 0.001	1.02	1.01	1.04	
Yes	525	35.6	0.15	1.01	1	1.03	
MI							0.54
No	953	64.7	< 0.001	1.02	1.01	1.03	
Yes	521	35.3	0.01	1.02	1.01	1.04	
IHD							0.16
No	480	32.6	0.14	1.01	1	1.03	
Yes	994	67.4	< 0.001	1.02	1.01	1.03	
HLD							0.26
No	804	54.5	< 0.001	1.02	1.01	1.03	
Yes	670	45.5	0.01	1.02	1.01	1.04	
MV							0.07
No	149	10.1	0.68	0.99	0.96	1.03	
Yes	1,325	89.9	< 0.001	1.02	1.01	1.03	
Glucocorticoid							0.96
No	1,091	74	< 0.001	1.02	1.01	1.03	
Yes	383	26	0.18	1.01	0.99	1.03	

Figure 6. Subgroup analyses for the association of BAR with 28-day ICU all-cause mortality in patients with CS, adjusted for age, OASIS, Charlson comorbidity index, APACHE II score; lactate, pH, HF, CRRT, and vasopressors use.

HR hazard ratio, OR odds ratio, HTN hypertension, AKI acute kidney injury, CVA cerebrovascular accident, CKD chronic kidney disease, T2DM type 2 diabetes mellitus, MI myocardial infarction, IHD ischemic myocardial disease, HLD hyperlipidemia, MV mechanical ventilation.

DISCUSSION

Our study is the first to evaluate the association between BAR and ICU outcomes in patients with CS. The results indicate that patients in the high BAR group had a significantly increased risk of death at 28 days in the ICU. This association remained significant even after adjusting for multiple confounding variables. Kaplan-Meier survival curves demonstrated that higher BAR levels were associated with lower survival rates. Additionally, CMA confirmed that hemoglobin mediated 10.88% of the adverse effects of BAR on 28-day ICU mortality, and subgroup analysis showed that higher BAR was associated with an increased risk of 28-day ICU mortality in most subgroups, with significant interactions observed only in the subgroups defined by race and AKI. The RCS curve reveals a non-linear relationship between BAR and 360-day and overall ICU mortality risk. Further analysis indicates a clear threshold effect. Below the threshold, the risk increases significantly with the rise of BAR, while above the threshold, the risk remains statistically unchanged. This highlights the importance of clinical monitoring, especially focusing on changes below the BAR threshold, to achieve the best assessment of patient prognosis.

Given the high mortality rate of CS [27], recent studies have increasingly focused on novel biomarkers for early prognostic evaluation in CS patients. Wang et al. reported that the albumin-corrected anion gap independently and strongly correlates with clinical outcomes in CS, aiding clinicians in identifying high-risk patients [28]. Xie et al. demonstrated that an elevated stress hyperglycemia ratio is significantly associated with increased 30-day and 360-day all-cause mortality in CS patients, particularly those with concurrent AMI [29]. Similarly, Sun et al. identified that a higher blood urea nitrogen-to-creatinine ratio at admission independently predicts reduced in-hospital mortality in CS [30]. Notably, BAR, a comprehensive indicator reflecting inflammation, metabolic status, and nutritional conditions in critically ill patients, has shown significant prognostic value in cardiovascular diseases such as AMI and chronic heart failure [21,31]. Building on these findings, our study is the first to validate BAR as a predictive marker for ICU mortality in CS using a public database, offering new insights for clinical risk stratification.

In our study, elevated BAR was significantly associated with increased short-term mortality in patients with CS. The potential mechanisms underlying this adverse outcome may be explained through the following pathways: 1) Hypoperfusion-induced metabolic derangements: the abrupt decline in cardiac output during CS leads to systemic hypoperfusion and hypoxia, triggering mitochondrial dysfunction [32]. Compensatory anaerobic metabolism exacerbates metabolic acidosis, which accelerates skeletal muscle proteolysis and elevates serum urea nitrogen levels [33]. Elevated urea nitrogen reflects a hypercatabolic state and protein-energy imbalance, ultimately contributing to nutritional depletion and poor prognosis; 2) reduced renal blood flow in CS lowers the glomerular filtration rate, causing a spike in urea nitrogen. This triggers the sympathetic nervous system and renin-angiotensin-aldosterone system, leading to fluid retention and increased urea reabsorption [34]. These responses further increase cardiac preload, establishing a vicious cycle of "cardio-renal syndrome" and accelerating clinical deterioration [35].

CMA revealed that hemoglobin plays a partial mediating role in the relationship between the BAR and poor outcomes in cardiogenic shock, accounting for approximately 10.88% of the total effect. This suggests that the BAR not only directly influences patient prognosis but may also indirectly affect disease outcomes through hemoglobin as a mediating variable. Anemia is one of the most common complications in the ICU. A prospective study by Thomas et al. [36] found that nearly all patients hospitalized in the intensive care unit for more than seven days experienced a decline in hemoglobin levels. In the context of an elevated BAR, reduced hemoglobin further impairs oxygen delivery and tissue perfusion, diminishing the ability of the injured myocardium and other vital organs to tolerate hypoxia [37]. This exacerbates disease severity and contributes to poorer patient outcomes. This finding offers valuable insight for clinical practice. In the management of CS, maintaining hemoglobin at an appropriate level may be a key factor in improving patient outcomes. It could help mitigate the adverse impact of elevated BAR on 28-day mortality, thereby contributing to the optimization of treatment strategies and enhancing patient survival.

Subgroup analysis revealed significant racial differences: the association between BAR and 28-day ICU mortality was more pronounced in White patients. This disparity may be partly attributed to the smaller sample sizes in other racial groups, potentially leading to reduced effect sizes. Alternatively, it might reflect inherent differences in nutritional metabolism among racial groups. A study by Vong et al. [38] reported that, among hospitalized adults with COVID-19, White patients were more susceptible to malnutrition compared to Asian, Black, or other racial groups. Since hypoalbuminemia may be more prevalent in malnourished individuals, this could partly explain the stronger association observed between BAR and mortality in White patients. Another significant finding was the moderating effect of AKI status on the prognostic value of BAR. Among patients without AKI, the association between BAR and mortality was notably stronger. This could be attributed to the fact that, in these patients, elevated BUN and decreased albumin levels more directly reflect a state of systemic hyper catabolism and nutritional imbalance, rather than azotemia and hypoalbuminemia resulting from impaired renal function. Consequently, BAR may serve as a more precise indicator of overall disease severity in patients without AKI, thereby enhancing its predictive value for mortality.

Limitations

However, this study has several limitations. First, as a single-center retrospective study based on the MIMIC-IV database, the findings are inherently subject to selection bias and may not be generalizable to broader patient populations or healthcare settings. Validation in large-scale, multi-center, prospective cohorts is essential to confirm the robustness and external applicability of our results. Second, although we adjusted for a wide range of potential confounders using commonly accepted statistical methods, the impact of unmeasured or residual confounding factors cannot be entirely excluded. Additionally, due to the retrospective nature of the database, we were limited by the availability and completeness of certain clinical variables, which may have influenced the observed associations. Third, the study population was limited to ICU-admitted patients with cardiogenic shock. As a result, the findings may not reflect the prognostic value of the BAR index in patients managed outside the ICU setting. Future studies incorporating both ICU and non-ICU populations are warranted to provide a more comprehensive assessment. Finally, while this study focused exclusively on cardiogenic shock, the BAR index has shown potential prognostic relevance in various other diseases. Further research is needed to investigate its predictive utility across a broader spectrum of acute and chronic conditions, which may help establish BAR as a versatile biomarker for risk stratification in diverse clinical contexts. Moreover, mechanistic studies are encouraged to explore the underlying biological pathways linking BAR to adverse outcomes.

CONCLUSION

Elevated BAR is significantly correlated with heightened ICU mortality rates in patients experiencing cardiogenic shock. As a prospective early biomarker for mortality risk prediction, BAR could assist clinicians in identifying high-risk patients for targeted interventions. Nonetheless, larger-scale studies are necessary to validate these findings and evaluate the clinical applicability of BAR.

Acknowledgment:
The authors would like to thank all the staff at the MIMIC database, as their contributions have been indispensable to this research.

Ethical Approval and Consent to Participate:
The MIMIC-IV database, accessed with credential number 68041273, contains de-identified, publicly available data, eliminating the need for further ethical approval or informed consent.

Consent for Publication:
All authors concurred with the submission.

Availability of Data and Materials:
The datasets from this study are accessible in the MIMIC-IV database (https://mimic.mit.edu).

Source of Funds:
This study was supported by grants from the National Nature Science Foundation of China (Nos. 81500237 and 81701891), Special Foundation for Knowledge Innovation of Hubei Province (Nature Science Foundation) (No. 2017CFB563), Hubei Provincial Health Science and Technology Project (No. WJ2025M027) and the Shiyan City Guiding Research Project (Nos. 24Y 115 and 24Y092).

Declaration of Interest:
The authors confirm that the study was done without any ties to businesses or money matters that might be seen as a conflict of interest.

References:

1. Tarabichi S, Ikegami H, Russo MJ, Lee LY, Lemaire A. The role of the axillary Impella 5.0 device on patients with acute cardiogenic shock. J Cardiothorac Surg 2020 Aug 14;15:218. (PMID: 32795321)

2. Moghaddam N, Diepen S van, So D, Lawler PR, Fordyce CB. Cardiogenic shock teams and centres: a contemporary review of multidisciplinary care for cardiogenic shock. ESC Heart Fail 2021 Jan 16;8(2):988-98. (PMID: 33452763)

3. Meuwese CL, Ramjankhan FZ, Braithwaite SA, et al. Extracorporeal life support in cardiogenic shock: indications and management in current practice. Neth Heart J 2018 Feb;26(2):58-66. (PMID: 29349674)

4. Yang JH, Choi KH, Ko YG, et al. Clinical characteristics and predictors of In-hospital mortality in patients with cardiogenic shock: results from the RESCUE registry. Circ Heart Fail 2021 Jun;14(6):e008141. (PMID: 34129366)

5. Rathod KS, Koganti S, Iqbal MB, et al. Contemporary trends in cardiogenic shock: incidence, intra-aortic balloon pump utilisation and outcomes from the London heart attack group. Eur Heart J Acute Cardiovasc Care 2018 Feb;7(1):16-27. (PMID: 29111770)

6. Berg DD, Bohula EA, Morrow DA. Epidemiology and causes of cardiogenic shock. Curr Opin Crit Care 2021 Aug;27(4):401-8. (PMID: 34010224)

7. Chen Z, Wang J, Yang H, Li H, Chen R, Yu J. Relationship between the Blood Urea Nitrogen to Creatinine Ratio and In-Hospital Mortality in Non-Traumatic Subarachnoid Hemorrhage Patients: Based on Propensity Score Matching Method. J Clin Med 2022 Nov 28;11(23):7031. (PMID: 36498609)

8. Gheith I, El-Mahmoudy A. Novel and classical renal biomarkers as evidence for the nephroprotective effect of Carica papaya leaf extract. Biosci Rep 2018 Sep 21;38(5):BSR20181187. (PMID: 30206132)

9. Koutroumpakis E, Wu BU, Bakker OJ, et al. Admission Hematocrit and Rise in Blood Urea Nitrogen at 24 h Outperform other Laboratory Markers in Predicting Persistent Organ Failure and Pancreatic Necrosis in Acute Pancreatitis: A Post Hoc Analysis of Three Large Prospective Databases. Am J Gastroenterol 2015 Dec;110(12):1707-16. (PMID: 26553208)

10. Liu J, Sun LL, Wang J, Ji G. Blood urea nitrogen in the prediction of in-hospital mortality of patients with acute aortic dissection. Cardiol J 2018 Jun 28;25(3):371-6. (PMID: 28653311)

11. Rhoney DH, Parker D, Millis SR, Whittaker P. Kidney dysfunction at the time of intracerebral hemorrhage is associated with increased in-hospital mortality: a retrospective observational cohort study. Neurol Res 2012 Jun;34(5):518-21. (PMID: 22664363)

12. Hu Z, Wang J, Xue Y, et al. The Neutrophil-to-Albumin Ratio as a New Predictor of All-Cause Mortality in Patients with Heart Failure. J Inflamm Res 2022 Feb 2;15:701-13. (PMID: 35140500)

13. Guo H, Wang J. Association Between Albumin-Corrected Anion Gap and In-Hospital Mortality and Sepsis-Associated Acute Kidney Injury. Med Sci Monit. 2024 Feb 10;30:e943012. (PMID: 38339777)

14. Wang Z, Xie YW, Lu Q, et al. The impact of albumin infusion on the risk of rebleeding and in-hospital mortality in cirrhotic patients admitted for acute gastrointestinal bleeding: a retrospective study of a single institute. BMC Gastroenterol 2020 Jun;20(1): 198. (PMID: 32576140)

15. Uthamalingam S, Kandala J, Daley M, et al. Serum albumin and mortality in acutely decompensated heart failure. Am Heart J 2010 Dec;160(6):1149-55. (PMID: 21146671)

16. Frenkel A, Novack V, Bichovsky Y, Klein M, Dreiher J. Serum Albumin Levels as a Predictor of Mortality in Patients with Sepsis: A Multicenter Study. Isr Med Assoc J 2022 Jul;24(7):454-9. (PMID: 35819214)

17. Huang Y, Li Z, Wang J, Wang D, Yin X. Association of the blood urea nitrogen to serum albumin ratio and all-cause mortality in critical ill acute ischemic stroke patients: a retrospective cohort study of MIMIC-IV database 3.0. Front Nutr 2025 Jan 7;11: 1509284. (PMID: 39839282)

18. Wang Y, Gao S, Hong L, et al. Prognostic impact of blood urea nitrogen to albumin ratio on patients with sepsis: a retrospective cohort study. Sci Rep 2023 Jun 20;13(1):10013. (PMID: 37340147)

19. Xiao Q, Zhou Q, Shen W, et al. Blood urea nitrogen-to-albumin ratio independently predicts 30-day mortality in acute respiratory failure patients: a retrospective cohort study. J Thorac Dis 2024 Aug 31;16(8):4892-903. (PMID: 39268142)

20. Peng X, Huang Y, Fu H, Zhang Z, He A, Luo R. Prognostic Value of Blood Urea Nitrogen to Serum Albumin Ratio in Intensive Care Unit Patients with Lung Cancer. Int J Gen Med 2021 Oct 28;14:7349-59. (PMID: 34737629)

21. Zhao D, Liu Y, Chen S, et al. Predictive Value of Blood Urea Nitrogen to Albumin Ratio in Long-Term Mortality in Intensive Care Unit Patients with Acute Myocardial Infarction: A Propensity Score Matching Analysis. Int J Gen Med 2022 Mar 1;15:2247-59. (PMID: 35256854)

22. Vojjini R, Patlolla SH, Cheungpasitporn W, et al. Racial Disparities in the Utilization and Outcomes of Temporary Mechanical Circulatory Support for Acute Myocardial Infarction-Cardiogenic Shock. J Clin Med 2021 Apr 2;10(7):1459. (PMID: 33918132)

23. Thiele H, Ohman EM, De Waha-Thiele S, Zeymer U, Desch S. Management of cardiogenic shock complicating myocardial infarction: an update 2019. Eur Heart J 2019 Aug 21;40(32):2671-83. (PMID: 31274157)

24. Yan F, Chen X, Quan X, Wang L, Wei X, Zhu J. Association between the stress hyperglycemia ratio and 28-day all-cause mortality in critically ill patients with sepsis: a retrospective cohort study and predictive model establishment based on machine learning. Cardiovasc Diabetol 2024 May 9;23:163. (PMID: 38725059)

25. Tibshirani R. Regression Shrinkage and Selection Via the Lasso. J R Stat Soc Ser B Methodol. 1996 Jan 1;58(1):267-88. https://doi.org/10.1111/j.2517-6161.1996.tb02080.x

26. Zhang L, Li S, Yuan S, et al. The Association Between Bronchoscopy and the Prognoses of Patients With Ventilator-Associated Pneumonia in Intensive Care Units: A Retrospective Study Based on the MIMIC-IV Database. Front Pharmacol 2022 Jun 8;13: 868920. (PMID: 35754471)

27. Berg DD, Bohula EA, van Diepen S, et al. Epidemiology of Shock in Contemporary Cardiac Intensive Care Units. Circ Cardiovasc Qual Outcomes 2019 Mar;12(3):e005618. (PMID: 30879324)

28. Wang Y, Tao Y, Yuan M, et al. Relationship between the albumin-corrected anion gap and short-term prognosis among patients with cardiogenic shock: a retrospective analysis of the MIMIC-IV and eICU databases. BMJ Open 2024 Oct 2;14(10):e081597. (PMID: 39357986)

29. Xie L, Chen J, Li Y, Huang B, Luo S. The prognostic impact of stress hyperglycemia ratio on mortality in cardiogenic shock: a MIMIC-IV database analysis. Diabetol Metab Syndr 2024 Dec 24;16(1):312. (PMID: 39719644)

30. Sun D, Wei C, Li Z. Blood urea nitrogen to creatinine ratio is associated with in-hospital mortality among critically ill patients with cardiogenic shock. BMC Cardiovasc Disord 2022 Jun 8; 22(1):258. (PMID: 35676647)

31. Lin Z, Zhao Y, Xiao L, Qi C, Chen Q, Li Y. Blood urea nitrogen to serum albumin ratio as a new prognostic indicator in critical patients with chronic heart failure. ESC Heart Fail 2022 Feb 11;9(2):1360-9. (PMID: 35146943)

32. Kang EJ, Cho S, Lim C, Lee B, Kim YK, Kim KM. Effects of the methanol fraction of modified Seonghyangjeongki-san water extract on transient ischaemic brain injury in mice. Pharm Biol 2021 Dec;59(1):840-53. (PMID: 34184969)

33. Mitch WE, Medina R, Grieber S, et al. Metabolic acidosis stimulates muscle protein degradation by activating the adenosine triphosphate-dependent pathway involving ubiquitin and proteasomes. J Clin Invest 1994 May;93(5):2127-33. (PMID: 8182144)

34. Hering D, Winklewski PJ. Autonomic nervous system in acute kidney injury. Clin Exp Pharmacol Physiol 2017 Feb;44(2):162-1. (PMID: 28116780)

35. Ma K, Gao W, Xu H, Liang W, Ma G. Role and Mechanism of the Renin-Angiotensin-Aldosterone System in the Onset and Development of Cardiorenal Syndrome. J Renin Angiotensin Aldosterone Syst 2022 Jan 24;2022:3239057. (PMID: 35111237)

36. Thomas J, Jensen L, Nahirniak S, Gibney RTN. Anemia and blood transfusion practices in the critically ill: a prospective cohort review. Heart Lung 2010 May;39(3):217-25. (PMID: 20457342)

37. Asakawa T, Joki N, Tanaka Y, et al. Association between the hemoglobin level and cardiothoracic ratio in patients on incident dialysis. Cardiorenal Med 2014 Dec;4(3-4):189-200. (PMID: 25737683)

38. Vong T, Yanek LR, Wang L, et al. Malnutrition increases hospital length of stay and mortality among adult inpatients with COVID-19. Nutrients 2022 Mar 21;14(6):1310. (PMID: 35334967)

Additional material can be found online at:
http://supplementary.clin-lab-publications.com/250623/