Research Square

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Association between the blood urea nitrogen to albumin ratio and all-cause mortality in critically ill patients with non-traumatic subarachnoid hemorrhage: a multicenter retrospective study and machine learning with external validation

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Research Article

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Abstract

Background

The blood urea nitrogen to serum albumin ratio (BAR) has been established as a prognostic indicator in critically ill patients. However, its prognostic significance in non-traumatic subarachnoid hemorrhage (NSAH) patients remains uncertain. This study explores the association between BAR and all-cause mortality in NSAH patients in the Intensive Care Unit (ICU).

Methods

Data were derived from the Medical Information Mart for Intensive Care IV (MIMIC-IV), focusing on NSAH patients. The outcomes encompassed all-cause mortality involving 30-, 90-, and 365-day. Cox regression analyses, Kaplan-Meier curves, restricted cubic splines (RCS), receiver operating characteristic (ROC) curve, the Area Under Curve (AUC), and subgroup analyses were applied. Seven machine learning models with incorporated BAR were developed and systematically assessed to predict 30-day all-cause mortality. The interpretability of the models was assessed using the SHapley Additive exPlanations (SHAP) method. External validation was conducted with the eICU-Collaborative Research Database (eICU-CRD) and the Hospital Information System (HIS) of the First Affiliated Hospital of Harbin Medical University to assess the best model's generalizability.

Results

Among 482 patients (52.1% female), higher BAR quartiles were independently associated with higher risk of 30-day (HR = 2.55, 95% CI 1.34,4.87, P = 0.005), 90-day (HR = 2.81, 95% CI 1.55, 5.09, P = 0.001), and 365-day (HR = 2.25, 95%CI 1.30, 3.88, P = 0.004) all-cause mortality. RCS analyses supported a linear association. Subgroup analyses confirmed BAR’s predictive reliability across multiple populations. The best machine learning model achieved an AUC of 0.872 in internal validation. External validations yielded AUC values of 0.839 and 0.790, respectively. SHAP analysis indicated a relationship between elevated BAR scores and an increased predicted all-cause mortality risk.

Conclusion

BAR emerged as an independent predictor for all-cause mortality in critically ill NSAH patients, underscoring its utility as a prognostic indicator for evaluating all-cause mortality risk in this population.

1. Introduction

Non-traumatic subarachnoid hemorrhage (NSAH) is a type of stroke, referring to the rupture of diseased blood vessels at the base or surface of the brain, with blood directly flowing into the subarachnoid

space. It is often associated with the rupture of aneurysms (80%-85%). The incidence of NSAH is second only to ischemic stroke and intracerebral hemorrhage, and the age of onset is significantly lower than that of other types of stroke[1]. In a 2021 study utilizing the GBD database, the incidence of new cases of NSAH was around 0.70 million, with approximately 7.85 million currently affected, and a death toll of about 0.35 million. The Disability-Adjusted Life Years amounted to approximately 10.64 million[2]. One research highlights that within hospitalized cohorts, the 30-day all-cause mortality rate for NSAH sufferers can soar to 30%[3]. Patients with NSAH tend to experience prolonged the Intensive Care Unit (ICU) stays due to the higher incidence of complications, such as re-bleeding, cerebrovascular spasm, hydrocephalus, and delayed cerebral ischemia [4]. In conclusion, non-traumatic subarachnoid hemorrhage is a severe condition characterized by a high all-cause mortality and disability rate, a tendency to affect younger individuals, and significant utilization of medical resources, thereby placing a substantial burden on both the public health system and the social economy. Consequently, there is a pressing requirement for a dependable and readily available clinical marker to assess prognosis.

Blood urea nitrogen (BUN) reflects renal function, hemodynamic status, protein metabolism, and the severity of systemic inflammation[5]. It has been established as a biomarker of disease severity and prognosis in multiple conditions, including acute pancreatitis, ischemic stroke, acute myocardial infarction, and COVID-19[6–9]. In patients with NSAH, pathophysiological processes such as systemic inflammation, renal impairment, renal hypoperfusion, oxidative stress, and malnutrition frequently produce elevated BUN levels. Albumin (ALB), one of the most abundant plasma proteins, is mainly synthesized in the liver[10]. Serum albumin has long served as an alternative marker of malnutrition. Low ALB levels are also associated with platelet activation, thrombosis, and inflammation. Prior studies have established ALB as a reliable, independent predictor of all-cause mortality and prognosis in conditions including acute coronary syndrome, heart failure, and sepsis[11–13]. More recently, the blood urea nitrogen to albumin ratio (BAR) has emerged as a novel prognostic marker that integrates information from BUN and ALB. BAR provides a composite measure reflecting renal and hepatic function, hemodynamic status, nutritional state, and systemic inflammation. To date, elevated BAR has been linked to several critical diseases, including sepsis, acute pancreatitis, and acute kidney injury (AKI)[14–16]. However, the association between BAR and all-cause mortality in NSAH remains unclear. This study, therefore, investigates the relationship between BAR and short-, medium-, and long-term all-cause mortality in NSAH, to inform prognostic assessment in this population. This study aimed to examine the relationship between the BAR and short-, medium-, and long-term all-cause mortality in patients with NSAH. Additionally, it sought to develop BAR-based machine learning models to enhance the early identification of short-term all-cause mortality risk in this patient population, thereby offering evidence for clinical risk stratification and personalized management.

2. Methods

2.1 Data source and participants

Data for this retrospective cohort study were primarily obtained from the Medical Information Mart for Intensive Care IV (MIMIC-IV v3.1) database. MIMIC-IV is a large, publicly available intensive care database that comprehensively captures ICU-specific data and includes 94,458 patients admitted to Beth Israel Deaconess Medical Center (BIDMC) between 2008 and 2022[17]. After completing the Collaborative Institutional Training Initiative program, Yansong Liu, one of the authors, got permission to access the database (Record ID: 59888572). An external validation cohort was established using the eICU-Collaborative Research Database (eICU-CRD v2.0), which includes deidentified health data from over 200,000 ICU admissions across 208 U.S. hospitals during the years 2014 to 2015[18]. A second external validation cohort was obtained from the Hospital Information System (HIS) of the First Affiliated Hospital of Harbin Medical University in China, covering the period from July 2024 to June 2025. The study protocol received approval from the Ethics Committee of the First Affiliated Hospital of Harbin Medical University, and informed consent was obtained from patients or their legal guardians.

We initially extracted 1,502 critically ill patients with NSAH from the MIMIC-IV database. The diagnosis of NSAH was based on the International Classification of Diseases (ICD), 9th Edition (codes beginning with 430) or Tenth Revision (codes beginning with I60). Exclusion criteria were: (1) age under 18 years; (2) patients who were not the first ICU admission; (3) ICU length of stay less than 24 hours; and (4) missing BUN or ALB measurements. Ultimately, 482 patients were included in the study. For external validation, a total of 519 eligible patients with NSAH were identified from the eICU-CRD database, while 268 eligible patients were identified from the HIS dataset, using the same criteria as the MIMIC-IV database. The detailed study flow was shown in Fig. 1.

2.2 Data collection

Data were extracted from the MIMIC-IV database using PostgreSQL (v13.7.2) and Navicat Premium (v16) through structured SQL queries. The exclusion criteria comprised: (1) Demographic Data: age, gender, and race; (2) Laboratory results: red blood cell count (RBC), white blood cell count (WBC), platelets (PLT), Hemoglobin (Hb), Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), International Normalized Ratio (INR), sodium (Na+), potassium (K+), anion gap (AG), serum creatinine (SCr), blood urea nitrogen (BUN), and albumin (ALB); (3) Vital signs: systolic blood pressure (SBP), mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (Spo2), and urine output; (4) Comorbidities: hypertension (HTN), diabetes mellitus (DM), congestive heart failure (CHF), myocardial infarct (MI), acute kidney injury (AKI), atrial fibrillation (AF), malignant cancer, and Charlson Comorbidity Index (CCI); (5) Clinical severity scores: Acute Physiology Score III (APSIII), Oxford Acute Severity of ILLness Score (OASIS), the Sequential Organ-Failure Assessment (SOFA), Simplified Acute Physiology Score II (SAPSII), Systemic Inflammatory Response Syndrome (SIRS), and the Glasgow Coma Scale (GCS); (6) Treaments: dobutamine, dopamine, epinephrine, norepinephrine, vasopressin, furosemide, mannitol, Continuous Renal Replacement Therapy (CRRT), ventilator, and clipping of aneurysm; All laboratory variables and disease severity scores were extracted, from the data generated within the first 24 h after the patient entered the ICU. Additionally, all diagnoses of comorbidities and treatments were based on ICD-9 and ICD-10 codes. The primary endpoints were short-term (30-day), medium-term (90-

day), and long-term (365-day) all-cause mortality following ICU admission. To maintain data integrity and avoid bias, variables with above 20% missing data were excluded. Variables with missing data of less than 20% were processed by multiple imputation using a random forest algorithm by the “mice” package of R software (**Table S1**).

2.3 BAR

The risk factor BAR was calculated by dividing the blood urea nitrogen level by the albumin level. BAR values were stratified based on their distribution into quartiles. To be specific, BAR was categorized into four groups as per the following quartile ranges (Q1: ≤ 3.05; Q2: 3.05–4.28; Q3: 4.28–6.50; Q4: > 6.5).

2.4 Statistical analysis

In our analysis, study participants were divided into four cohorts based on their BAR quartiles. Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed variables, median (Interquartile Range, IQR) for non-normally distributed continuous variables, and their differences were analyzed using the t-test or Mann-Whitney U-test. Categorical variables were reported as frequencies (%) and compared using the Chi-square test or Fisher’s exact test. Subsequently, we used univariate analyses to assess associations between clinical variables and 30-day, 90-day, and 365-day all-cause mortality. Covariates in the final multivariate Cox regression model were determined by the univariable analysis ($P < 0.05$) together with clinical judgment. In the validation cohorts, in-hospital all-cause mortality was assessed using multivariate logistic regression. The results of multivariate regression analyses were reported as hazard ratios (HRs) or odds ratios (ORs) along with 95% confidence intervals (CIs).

In the MIMIC-IV database, three distinct models were formulated: Model 1 was unadjusted, Model 2 was adjusted for age, gender, race, and model 3 was adjusted for age, gender, race, prothrombin time, activated partial thromboplastin time, international normalized ratio, potassium, anion gap, serum creatinine, heart rate, hypertension, atrial fibrillation, OASIS, SOFA, GCS, vasopressin, mannitol, norepinephrine, furosemide and clipping of aneurysm. Details regarding the adjustments for confounding factors in the external validation cohorts were provided in Table 3.

Table 3
Relationship between BAR and all-cause mortality in critically ill patients with NSAH (eICU-CRD and HIS).

Categories	Model 1		Model 2		Model 3	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
In-hospital mortality (eICU-CRD)						
BAR	1.08 [1.04, 1.12]	< 0.001	1.08 [1.04, 1.13]	< 0.001	1.09 [1.04, 1.14]	0.001
BAR quartiles						
Q1	Ref		Ref		Ref	
Q2	1.11 [0.57, 2.16]	0.757	1.13 [0.58, 2.22]	0.719	1.02 [0.47, 2.20]	0.962
Q3	1.43 [0.76, 2.73]	0.273	1.35 [0.71, 2.59]	0.363	1.63 [0.79, 3.41]	0.188
Q4	2.89 [1.61, 5.34]	0.001	2.89 [1.60, 5.38]	0.001	2.74 [1.37, 5.63]	0.005
P for trend		< 0.001		< 0.001		< 0.001
In-hospital mortality (HIS)						
BAR	1.11 [1.04, 1.19]	0.002	1.12 [1.05, 1.21]	0.002	1.11[1.03,1.22]	0.013
BAR quartiles						
Q1	Ref		Ref		Ref	
Model 1: Unadjusted.						
Model 2: adjusted for age, gender, and race.						
Model 3 (eICU-CRD): adjusted for age, gender, race, K+: potassium, AG: anion gap, SCr: serum creatinine, HR: heart rate, HTN: hypertension, AF: atrial fibrillation, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, GCS: the Glasgow Coma Scale, vasopressin, mannitol, norepinephrine, furosemide, and clipping of aneurysm.						
Model 3 (HIS): adjusted for age, gender, race, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, K+: potassium, AG: anion gap, SCr: serum creatinine, HR: heart rate, HTN: hypertension, AF: atrial fibrillation,GCS: the Glasgow Coma Scale, vasopressin, mannitol, norepinephrine, furosemide, lumbar puncture and clipping of aneurysm.						

Categories	Model 1		Model 2		Model 3	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Q2	1.49 [0.43, 5.50]	0.531	1.62 [0.46, 6.06]	0.455	1.48 [0.32, 7.40]	0.619
Q3	3.05 [0.99, 10.60]	0.06	3.63 [1.12, 13.35]	0.039	3.91 [0.94, 19.44]	0.073
Q4	5.34 [1.81, 18.28]	0.004	6.64 [2.03, 25.08]	0.003	6.91 [1.50, 38.17]	0.018
P for trend		< 0.001		< 0.001		< 0.001
Model 1: Unadjusted.						
Model 2: adjusted for age, gender, and race.						
Model 3 (eICU-CRD): adjusted for age, gender, race, K+: potassium, AG: anion gap, SCr: serum creatinine, HR: heart rate, HTN: hypertension, AF: atrial fibrillation, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, GCS: the Glasgow Coma Scale, vasopressin, mannitol, norepinephrine, furosemide, and clipping of aneurysm.						
Model 3 (HIS): adjusted for age, gender, race, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, K+: potassium, AG: anion gap, SCr: serum creatinine, HR: heart rate, HTN: hypertension, AF: atrial fibrillation,GCS: the Glasgow Coma Scale, vasopressin, mannitol, norepinephrine, furosemide, lumbar puncture and clipping of aneurysm.						

Kaplan–Meier survival curves were constructed to visualize the survival probabilities of different BAR quartiles over time, while the log-rank test was used to determine the statistical significance of differences in survival probabilities between groups. Moreover, restricted cubic spline (RCS) was utilized to explore potential non-linear relationships between BAR and all-cause mortality outcomes. Receiver operating characteristic (ROC) curve analysis was used to assess the predictive ability of BAR, BUN, ALB, GCS, SOFA, SIRS, and APSIII for all-cause mortality, as well as to calculate the Area Under Curve (AUC). Additionally, subgroup analyses were also conducted based on age, gender, race, atrial fibrillation, and hypertension, using the same covariate adjustments as Model 3. Interaction tests were used to assess the heterogeneity of associations between different subgroups. Finally, A double-sided $P < 0.05$ was regarded as statistically significant. All statistical analyses were performed by the R software (v4.0.2) and SPSS 22.0.

2.5 Model development and validation

Features were selected based on the intersection of results from the Boruta and LASSO algorithms [19, 20], visualized in Venn diagrams. Boruta, which is based on Random Forest, compares actual variables with permuted "shadow" variables to identify predictors that convey information beyond random noise.

LASSO employs L1 regularization to reduce regression coefficients, with the optimal λ determined through 10-fold cross-validation.

The MIMIC-IV database was split into 70% for training and 30% for internal validation to prevent overfitting. Seven machine learning algorithms were developed: Logistic Regression (LR), Decision Tree (DT), Random Forest (RF), Extreme Gradient Boosting (XGBoost), Light Gradient Boosting Machine (LightGBM), Support Vector Machine (SVM), and Artificial Neural Network (ANN). Model performance was evaluated using the ROC curve and AUC. Model performance was evaluated using the ROC curve and AUC, while accuracy, precision, sensitivity, specificity, and F1-score were also employed to assess model discrimination. The best-performing model from MIMIC-IV was validated externally on the eICU-CRD and HIS cohorts. The interpretability of the final predictive model was examined using the SHapley Additive exPlanations (SHAP).

3. Results

A total of 482 patients with NSAH from the MIMIC-IV database were enrolled in this study. The median age of the included patients was 62 years (IQR: 47–77). The sex distribution was similar: males (47.9%) and females (52.1%). The 30-day, 90-day, and 365-day all-cause mortality after admission were 28.8% (n = 139), 35.3% (n = 170), and 40.2% (n = 194), respectively (Table 1).

Table 1
Baseline characteristics according to BAR quartiles.

Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
Demographic						
Age, years	62 (47–77)	56 (42–70)	61 (46–76)	66 (51–81)	64 (49–79)	**< 0.001**
Gender						**0.024**
Male	231 (47.9)	43 (35.8)	63 (52.5)	62 (51.2)	63 (52.1)	
Female	251 (52.1)	77 (64.2)	57 (47.5)	59 (48.8)	58 (47.9)	
Race						0.554
White	278 (57.7)	72 (60.0)	74 (61.7)	67 (55.4)	65 (53.7)	
Other	204 (42.3)	48 (40.0)	46 (38.3)	54 (44.6)	56 (46.3)	
Laboratory tests						
RBC, K/uL	3.95 (3.2–4.73)	4.05 (3.51–4.59)	4.13 (3.41–4.85)	4.04 (3.36–4.72)	3.57 (2.68–4.46)	**< 0.001**
WBC, K/uL	13.59 (6.70-20.48)	12.00 (6.88–17.12)	13.09 (7.41–18.77)	14.86 (7.01–22.71)	14.38 (6.28–22.48)	**0.005**
PLT, K/uL	218.05 (110.77-325.33)	242.13 (146.68-337.58)	225.32 (133.38-317.26)	223.78 (130.84-316.72)	181.22 (46.89-315.55)	**< 0.001**
Hb, g/L	11.95 (9.78–14.12)	12.38 (10.63–14.13)	12.59 (10.75–14.43)	12.08 (10.11–14.05)	10.74 (8.20-13.28)	**< 0.001**
PT, s	14.25 (7.97–20.53)	12.58 (11.34–13.82)	13.95 (8.34–19.56)	13.67 (9.33–18.01)	16.80 (6.97–26.63)	**< 0.001**

RBC: red blood cell, WBC: white blood cell, PLT: platelet, Hb: Hemoglobin, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, Na+: sodium, K+: potassium, AG: anion gap, SCr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, BAR: blood urea nitrogen to albumin ratio, SBP: systolic blood pressure, MAP: mean arterial pressure, HR: heart rate, Spo2: peripheral oxygen saturation, HTN: hypertension, DM: diabetes mellitus, CHF: congestive heart failure, MI: myocardial infarct, AKI: acute kidney injury, AF: atrial fibrillation, CCI: Charlson Comorbidity Index, APSIII: Acute Physiology Score III, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, SAPSII: Simplified Acute Physiology Score II, SIRS: Systemic Inflammatory Response Syndrome, GCS: the Glasgow Coma Scale, CRRT: Continuous Renal Replacement Therapy.

Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	**n = 120**	**n = 120**	**n = 121**	**n = 121**	
APTT, s	34.34 (13.12–55.56)	33.70 (14.04–53.36)	33.81 (10.59–57.03)	31.39 (15.86–46.92)	38.45 (13.55–63.35)	0.07
INR	1.29 (0.69–1.89)	1.12 (1.00-1.24)	1.27 (0.70–1.84)	1.24 (0.84–1.64)	1.53 (0.62–2.44)	**< 0.001**
Na+, mmol/L	139.29 (134.70-143.88)	139.02 (135.01-143.03)	140.09 (135.85-144.33)	139.02 (135.39-142.65)	139.02 (132.98-145.06)	0.177
K+, mmol/L	4.00 (3.28–4.72)	3.80 (3.35–4.25)	3.88 (3.35–4.41)	4.03 (3.36–4.70)	4.28 (3.28–5.28)	**< 0.001**
AG	14.67 (10.76–18.58)	13.85 (10.81–16.89)	14.25 (10.99–17.51)	14.47 (10.82–18.12)	16.11 (11.09–21.13)	**< 0.001**
SCr, mg/dL	1.11 (0.12–2.10)	0.71 (0.53–0.89)	0.85 (0.58–1.12)	0.94 (0.58–1.30)	1.93 (0.26–3.60)	**< 0.001**
Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
BUN, mmol/L	19.45 (3.94–34.96)	9.26 (7.12–11.40)	13.37 (11.32–15.42)	17.44 (14.31–20.57)	37.60 (15.96–59.24)	**< 0.001**
ALB, mg/dL	3.40 (2.77–4.03)	3.75 (3.28–4.22)	3.63 (3.15–4.11)	3.36 (2.89–3.83)	2.88 (2.19–3.57)	**< 0.001**
BAR	6.37 (-0.45-13.19)	2.47 (1.97–2.97)	3.69 (3.31–4.07)	5.19 (4.59–5.79)	14.05 (3.92–24.18)	**< 0.001**
Vital signs						

RBC: red blood cell, WBC: white blood cell, PLT: platelet, Hb: Hemoglobin, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, Na+: sodium, K+: potassium, AG: anion gap, SCr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, BAR: blood urea nitrogen to albumin ratio, SBP: systolic blood pressure, MAP: mean arterial pressure, HR: heart rate, Spo2: peripheral oxygen saturation, HTN: hypertension, DM: diabetes mellitus, CHF: congestive heart failure, MI: myocardial infarct, AKI: acute kidney injury, AF: atrial fibrillation, CCI: Charlson Comorbidity Index, APSIII: Acute Physiology Score III, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, SAPSII: Simplified Acute Physiology Score II, SIRS: Systemic Inflammatory Response Syndrome, GCS: the Glasgow Coma Scale, CRRT: Continuous Renal Replacement Therapy.

Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
SBP, mmHg	131.71 (107.42–156.00)	136.75 (115.02-158.48)	134.84 (108.43-161.25)	129.81 (107.86-151.76)	125.51 (100.11-150.91)	**0.001**
MAP, mmHg	89.32 (70.76-107.88)	92.40 (74.95-109.85)	91.58 (72.16–111.00)	87.11 (70.28-103.94)	86.23 (66.41-106.05)	**0.017**
HR, times/min	83.73 (64.98-102.48)	80.52 (63.96–97.08)	83.20 (64.63-101.77)	82.05 (64.58–99.52)	89.12 (67.96-110.28)	**0.002**
SpO2, %	97.44 (93.99-100.89)	98.29 (95.99-100.59)	97.53 (94.11-100.95)	97.58 (94.79-100.37)	96.35 (91.77-100.93)	**< 0.001**
urineoutput, ml	2175.23 (838.49-3511.97)	2582.06 (1165.19-3998.93)	2420.57 (985.49-3855.65)	2026.58 (851.45-3201.71)	1677.12 (559.01-2795.23)	**< 0.001**
Comorbidities						
HTN						**0.004**
No	233 (48.3)	60 (50.0)	48 (40.0)	51 (42.1)	74 (61.2)	
Yes	249 (51.7)	60 (50.0)	72 (60.0)	70 (57.9)	47 (38.8)	
DM						**< 0.001**
No	390 (80.9)	109 (90.8)	103 (85.8)	95 (78.5)	83 (68.6)	
Yes	92 (19.1)	11 (9.2)	17 (14.2)	26 (21.5)	38 (31.4)	
CHF						**< 0.001**
No	429 (89.0)	115 (95.8)	114 (95.0)	101 (83.5)	99 (81.8)	
Yes	53 (11.0)	5 (4.2)	6 (5.0)	20 (16.5)	22 (18.2)	

RBC: red blood cell, WBC: white blood cell, PLT: platelet, Hb: Hemoglobin, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, Na+: sodium, K+: potassium, AG: anion gap, SCr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, BAR: blood urea nitrogen to albumin ratio, SBP: systolic blood pressure, MAP: mean arterial pressure, HR: heart rate, Spo2: peripheral oxygen saturation, HTN: hypertension, DM: diabetes mellitus, CHF: congestive heart failure, MI: myocardial infarct, AKI: acute kidney injury, AF: atrial fibrillation, CCI: Charlson Comorbidity Index, APSIII: Acute Physiology Score III, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, SAPSII: Simplified Acute Physiology Score II, SIRS: Systemic Inflammatory Response Syndrome, GCS: the Glasgow Coma Scale, CRRT: Continuous Renal Replacement Therapy.

Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
MI						**0.001**
No	424 (88.0)	115 (95.8)	106 (88.3)	107 (88.4)	96 (79.3)	
Yes	58 (12.0)	5 (4.2)	14 (11.7)	14 (11.6)	25 (20.7)	
Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
AKI						**< 0.001**
No	75 (15.6)	28 (23.3)	26 (21.7)	9 (7.4)	12 (9.9)	
Yes	407 (84.4)	92 (76.7)	94 (78.3)	112 (92.6)	109 (90.1)	
AF						**< 0.001**
No	389 (80.7)	111 (92.5)	102 (85.0)	96 (79.3)	80 (66.1)	
Yes	93 (19.3)	9 (7.5)	18 (15.0)	25 (20.7)	41 (33.9)	
Malignant cancer						0.450
No	450 (93.4)	111 (92.5)	115 (95.8)	114 (94.2)	110 (90.9)	
Yes	32 (6.6)	9 (7.5)	5 (4.2)	7 (5.8)	11 (9.1)	
CCI	4.67 (1.98–7.36)	3.57 (1.10–6.04)	3.97 (1.80–6.14)	5.09 (2.49–7.69)	6.05 (3.25–8.85)	**< 0.001**
Clinical severity scores						

RBC: red blood cell, WBC: white blood cell, PLT: platelet, Hb: Hemoglobin, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, Na+: sodium, K+: potassium, AG: anion gap, SCr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, BAR: blood urea nitrogen to albumin ratio, SBP: systolic blood pressure, MAP: mean arterial pressure, HR: heart rate, Spo2: peripheral oxygen saturation, HTN: hypertension, DM: diabetes mellitus, CHF: congestive heart failure, MI: myocardial infarct, AKI: acute kidney injury, AF: atrial fibrillation, CCI: Charlson Comorbidity Index, APSIII: Acute Physiology Score III, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, SAPSII: Simplified Acute Physiology Score II, SIRS: Systemic Inflammatory Response Syndrome, GCS: the Glasgow Coma Scale, CRRT: Continuous Renal Replacement Therapy.

Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
APSIII	44.59 (21.74–67.44)	34.14 (16.08–52.20)	38.27 (17.42–59.12)	42.97 (25.98–59.96)	62.83 (39.13–86.53)	**< 0.001**
OASIS	33.28 (24.94–41.62)	29.25 (21.63–36.87)	32.27 (23.64–40.90)	34.64 (27.14–42.14)	36.91 (29.28–44.54)	**< 0.001**
SOFA	3.55 (0.58–6.52)	2.13 (0.53–3.73)	2.81 (0.14–5.48)	3.44 (0.86–6.02)	5.82 (2.45–9.19)	**< 0.001**
SAPSII	36.54 (22.37–50.71)	30.32 (18.57–42.07)	33.12 (20.14–46.10)	36.45 (25.17–47.73)	46.18 (31.02–61.34)	**< 0.001**
SIRS	2.70 (1.74–3.66)	2.43 (1.43–3.43)	2.61 (1.64–3.58)	2.79 (1.85–3.73)	2.98 (2.13–3.83)	**< 0.001**
GCS	14.27 (12.96–15.58)	14.46 (13.58–15.34)	14.27 (12.78–15.76)	14.10 (12.60–15.60)	14.24 (12.97–15.51)	0.192
Treatments						
Dobutamine						0.796
No	474 (98.3)	119 (99.2)	117 (97.5)	119 (98.3)	119 (98.3)	
Yes	8 (1.7)	1 (0.8)	3 (2.5)	2 (1.7)	2 (1.7)	
Dopamine						0.571
No	472 (97.9)	119 (99.2)	118 (98.3)	118 (97.5)	117 (96.7)	
Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	

RBC: red blood cell, WBC: white blood cell, PLT: platelet, Hb: Hemoglobin, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, Na+: sodium, K+: potassium, AG: anion gap, SCr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, BAR: blood urea nitrogen to albumin ratio, SBP: systolic blood pressure, MAP: mean arterial pressure, HR: heart rate, Spo2: peripheral oxygen saturation, HTN: hypertension, DM: diabetes mellitus, CHF: congestive heart failure, MI: myocardial infarct, AKI: acute kidney injury, AF: atrial fibrillation, CCI: Charlson Comorbidity Index, APSIII: Acute Physiology Score III, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, SAPSII: Simplified Acute Physiology Score II, SIRS: Systemic Inflammatory Response Syndrome, GCS: the Glasgow Coma Scale, CRRT: Continuous Renal Replacement Therapy.

Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
Yes	10 (2.1)	1 (0.8)	2 (1.7)	3 (2.5)	4 (3.3)	
Epinephrine						**0.027**
No	456 (94.6)	117 (97.5)	117 (97.5)	113 (93.4)	109 (90.1)	
Yes	26 (5.4)	3 (2.5)	3 (2.5)	8 (6.6)	12 (9.9)	
Norepinephrine						**< 0.001**
No	330 (68.5)	91 (75.8)	92 (76.7)	83 (68.6)	64 (52.9)	
Yes	152 (31.5)	29 (24.2)	28 (23.3)	38 (31.4)	57 (47.1)	
Vasopressin						0.127
No	402 (83.4)	105 (87.5)	103 (85.8)	101 (83.5)	93 (76.9)	
Yes	80 (16.6)	15 (12.5)	17 (14.2)	20 (16.5)	28 (23.1)	
Furosemide						**< 0.001**
No	290 (60.2)	91 (75.8)	81 (67.5)	65 (53.7)	53 (43.8)	
Yes	192 (39.8)	29 (24.2)	39 (32.5)	56 (46.3)	68 (56.2)	
Mannitol						0.126
No	403 (83.6)	95 (79.2)	100 (83.3)	99 (81.8)	109 (90.1)	
Yes	79 (16.4)	25 (20.8)	20 (16.7)	22 (18.2)	12 (9.9)	
CRRT						**< 0.001**
No	451 (93.6)	118 (98.3)	117 (97.5)	116 (95.9)	100 (82.6)	
Yes	31 (6.4)	2 (1.7)	3 (2.5)	5 (4.1)	21 (17.4)	

RBC: red blood cell, WBC: white blood cell, PLT: platelet, Hb: Hemoglobin, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, Na+: sodium, K+: potassium, AG: anion gap, SCr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, BAR: blood urea nitrogen to albumin ratio, SBP: systolic blood pressure, MAP: mean arterial pressure, HR: heart rate, Spo2: peripheral oxygen saturation, HTN: hypertension, DM: diabetes mellitus, CHF: congestive heart failure, MI: myocardial infarct, AKI: acute kidney injury, AF: atrial fibrillation, CCI: Charlson Comorbidity Index, APSIII: Acute Physiology Score III, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, SAPSII: Simplified Acute Physiology Score II, SIRS: Systemic Inflammatory Response Syndrome, GCS: the Glasgow Coma Scale, CRRT: Continuous Renal Replacement Therapy.

Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
Ventilator						0.068
No	71 (14.7)	20 (16.7)	25 (20.8)	12 (9.9)	14 (11.6)	
Yes	411 (85.3)	100 (83.3)	95 (79.2)	109 (90.1)	107 (88.4)	
Clipping of aneurysm						0.275
No	468 (97.1)	114 (95.0)	116 (96.7)	118 (97.5)	120 (99.2)	
Characteristic	ALL	Q1	Q2	Q3	Q4	P-value
	n = 482	n = 120	n = 120	n = 121	n = 121	
Yes	14 (2.9)	6 (5.0)	4 (3.3)	3 (2.5)	1 (0.8)	
Outcome						
30-day mortality	139 (28.8)	17 (14.2)	28 (23.3)	35 (28.9)	59 (48.8)	**< 0.001**
90-day mortality	170 (35.3)	19 (15.8)	34 (28.3)	44 (36.4)	73 (60.3)	**< 0.001**
365-day mortality	194 (40.2)	24 (20.0)	36 (30.0)	54 (44.6)	80 (66.1)	**< 0.001**

RBC: red blood cell, WBC: white blood cell, PLT: platelet, Hb: Hemoglobin, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, Na+: sodium, K+: potassium, AG: anion gap, SCr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, BAR: blood urea nitrogen to albumin ratio, SBP: systolic blood pressure, MAP: mean arterial pressure, HR: heart rate, Spo2: peripheral oxygen saturation, HTN: hypertension, DM: diabetes mellitus, CHF: congestive heart failure, MI: myocardial infarct, AKI: acute kidney injury, AF: atrial fibrillation, CCI: Charlson Comorbidity Index, APSIII: Acute Physiology Score III, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, SAPSII: Simplified Acute Physiology Score II, SIRS: Systemic Inflammatory Response Syndrome, GCS: the Glasgow Coma Scale, CRRT: Continuous Renal Replacement Therapy.

3.1 Baseline characteristics

Table 1 presented baseline characteristics of critically ill patients with NSAH stratified by BAR quartile. Patients were divided into four groups by admission BAR [quartile Q1: 1.22–3.07; Q2: 3.07–4.28; Q3: 4.28–6.50; Q4: 6.50-58.75], with median values of 2.62, 3.65, 5.12, and 10.62, respectively. The 30-day all-cause mortality after admission was highest in Q4, followed by Q3, Q2, and Q1 (48.8% vs 28.9% vs 23.3% vs 14.2%). The same pattern held for 90-day and 365-day all-cause mortality. In addition, age and race, laboratory tests (red blood cells, white blood cells, platelets, hemoglobin, PT, APTT, K, AG, SCr), vital

signs (SBP, MAP, HR, SpO2, urine output), comorbidities (HTN, DM, CHF, MI, AKI, AF, CCI), clinical severity scores (APSIII, OASIS, SOFA, SAPSII, SIRS), and treatments (epinephrine, norepinephrine, furosemide, CRRT) differed significantly across the four groups (all $P < 0.05$). Overall, a higher BAR was associated with increased 30-, 90-, and 365-day all-cause mortality; these trends were statistically significant (all $P < 0.001$).

Table S2 summarized the baseline characteristics of the 30-day survival and nonsurvival groups. The 30-day all-cause mortality was 28.8% (139/482). The BAR in the nonsurvival group was higher than in the survival group (9.06 vs 5.28), the median age was older (64 vs 60), and the heart rate was higher (86 vs 82 times/min). Laboratory results showed that white blood cell count (15.61 vs 12.77 KL), K+ (4.11 vs 3.95 mmol/L), PT (16.12 vs 13.51 s), APTT (39.52 vs 32.37 s), AG (16.19 vs 14.06), SCr (1.40 vs 0.99 mg/dL), and BUN (25.77 vs 16.89 mmol/L) were elevated in the nonsurvival group. By contrast, hemoglobin (11.59 vs 12.09 g/dL), platelet count (194.71 vs 227.50 KL), and ALB (3.24 vs 3.47 mg/dL) were lower in the nonsurvival group. Clinical severity scores, including APSIII (55 vs 40), OASIS (37 vs 31), SOFA (5 vs 3), SAPSII (44 vs 33), and SIRS (3 vs 2), were significantly worse in the death group. Atrial fibrillation was more common in nonsurvival patients (27.3% vs 16%), as was a higher Charlson Comorbidity Index (5 vs 4). Patients with higher BAR levels were more likely to receive furosemide (56.2% vs 24.2%) and less likely to receive vasoactive agents, including norepinephrine (55.4% vs 73.8%) and vasopressin (71.2% vs 88.3%). The same pattern appeared for medium-term outcomes (90-day all-cause mortality) and long-term outcomes (365-day all-cause mortality) (**Table S3 and S4**). Although patients with higher BAR levels more often underwent ventilator support, that difference did not reach statistical significance.

3.2 Multivariate Cox regression models of BAR with all-cause mortality in patients with NSAH

Multivariate Cox regression analysis was performed to assess the association between BAR and all-cause mortality in patients with NSAH. Table 2 presented the Cox regression analysis results. When treating BAR as a continuous variable, higher BAR was associated with increased mortality at 30 days (HR = 1.03, 95% CI 1.01, 1.05, P = 0.027), 90 days (HR = 1.02, 95% CI 1.01, 1.04, P = 0.036), and 365 days (HR = 1.03, 95% CI 1.02, 1.04, P = 0.030).

Table 2
Relationship between BAR and all-cause mortality in critically ill patients with NSAH (MIMIC-IV).

Categories	Model 1		Model 2		Model 3	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
30-day mortality						
BAR	1.04 [1.03, 1.06]	< 0.001	1.04 [1.02, 1.05]	< 0.001	1.03 [1.01, 1.05]	0.027
BAR quartiles						
Q1	Ref		Ref		Ref	
Q2	1.73 [0.95, 3.16]	0.075	1.66 [0.90, 3.06]	0.102	1.40 [0.75, 2.62]	0.287
Q3	2.19 [1.23, 3.91]	0.008	1.98 [1.10, 3.59]	0.024	1.47 [0.79, 2.73]	0.222
Q4	4.19 [2.44, 7.20]	< 0.001	3.98 [2.28, 6.94]	< 0.001	2.55 [1.34, 4.87]	0.005
P for trend		< 0.001		< 0.001		0.002
90-day mortality						
BAR	1.04 [1.03, 1.06]	< 0.001	1.04 [1.03, 1.05]	< 0.001	1.02 [1.01, 1.04]	0.036
BAR quartiles						
Q1	Ref		Ref		Ref	
Q2	1.91 [1.09, 3.35]	0.024	1.81 [1.02, 3.19]	0.041	1.52 [0.85, 2.72]	0.154
Q3	2.55 [1.49, 4.37]	0.001	2.25 [1.30,	0.004	1.66 [0.94,	0.082

Model 1: Unadjusted.

Model 2: adjusted for age, gender, and race.

Model 3: adjusted for age, gender, race, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, K+: potassium, AG: anion gap, SCr: serum creatinine, HR: heart rate, HTN: hypertension, AF: atrial fibrillation, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, vasopressin, mannitol, norepinephrine, furosemide, and clipping of aneurysm.

Categories	Model 1		Model 2		Model 3	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
			3.91]		2.94]	
Q4	5.06 [3.05, 8.39]	< 0.001	4.66 [2.77, 7.84]	< 0.001	2.81 [1.55, 5.09]	0.001
P for trend		< 0.001		< 0.001		< 0.001
365-day mortality						
BAR	1.05[1.03, 1.06]	< 0.001	1.04 [1.03, 1.06]	< 0.001	1.03 [1.02, 1.04]	0.03
BAR quartiles						
Q1	Ref		Ref		Ref	
Q2	1.62 [0.97, 2.72]	0.066	1.49 [0.88, 2.51]	0.138	1.27 [0.74, 2.16]	0.385
Q3	2.55 [1.58, 4.12]	< 0.001	2.18 [1.33, 3.58]	0.002	1.56 [0.93, 2.60]	0.091
Q4	4.68 [2.96, 7.40]	< 0.001	4.12 [2.57, 6.61]	< 0.001	2.25 [1.30, 3.88]	0.004
P for trend		< 0.001		< 0.001		0.002
Model 1: Unadjusted.						
Model 2: adjusted for age, gender, and race.						
Model 3: adjusted for age, gender, race, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, K+: potassium, AG: anion gap, SCr: serum creatinine, HR: heart rate, HTN: hypertension, AF: atrial fibrillation, OASIS: Oxford Acute Severity of ILLness Score, SOFA: the Sequential Organ-Failure Assessment, vasopressin, mannitol, norepinephrine, furosemide, and clipping of aneurysm.						

When BAR was treated as a categorical variable in three Cox regression models, patients with NSAH in the highest BAR quartile had significantly higher 30-day all-cause mortality: unadjusted model 1 (Q4 vs Q1: HR = 4.19, 95% CI 2.44, 7.20, P < 0.001), partially adjusted model 2 (Q4 vs Q1: HR = 3.98, 95% CI 2.28, 6.94, P < 0.001), and fully adjusted model 3 (Q4 vs Q1: HR = 2.55, 95% CI 1.34, 4.87, P = 0.005), with a consistent trend across increasing BAR (Table 2). Comparable associations were observed in multivariate Cox models for 90-day and 365-day all-cause mortality. Together, these findings indicate

that BAR is a significant risk factor and that elevated BAR is independently associated with all-cause mortality after NSAH.

3.3 Kaplan–Meier curve and RCS analysis

We constructed Kaplan–Meier survival curves and compared the incidence of the primary outcome across BAR quartiles. A higher BAR at 30 days after ICU admission was associated with a lower survival probability (Q4 < Q3 < Q2 < Q1). The same pattern persisted at 90 days and 365 days (Fig. 2A-C). The relationship between BAR and all-cause mortality at 30, 90, and 365 days in patients with NSAH was examined using a RCS model (Fig. 2D-E). The analysis revealed a linear association between BAR and all-cause mortality (all P for nonlinear > 0.05). The all-cause mortality at 30 days, 90 days, and 365 days increased linearly with rising BAR levels (30-day P = 0.015, 90-day P = 0.019, 365-day P = 0.029).

3.4 ROC curve analysis

Seven indicators—BAR, BUN, ALB, GCS, SOFA, SIRS, and APSIII—were used to construct ROC curves predicting all-cause mortality at 30, 90, and 365 days after ICU admission. The AUC value stands for the predictive advantage. BAR showed a superior predictive advantage compared with BUN and ALB across any follow-up time: BAR 30-day (AUC = 0.68), 90-day (AUC = 0.70), and 365-day (AUC = 0.71) versus BUN 30-day (AUC = 0.66), 90-day (AUC = 0.68), and 365-day (AUC = 0.69), and versus ALB 30-day (AUC = 0.40), 90-day (AUC = 0.39), and 365-day (AUC = 0.37). Compared with traditional clinical severity scores, BAR also exceeded GCS and SIRS in predictive performance. For 365-day all-cause mortality, the predictive advantage of BAR was similar to SOFA and slightly higher than APSIII. Detailed results were shown in Fig. 3.

3.5 Subgroup analysis

We conducted subgroup analyses to examine the association between BAR and outcomes across multiple patient groups (Fig. 4). Stratifying by demographics [age (≥ 65 years vs 65 years), gender, race] and comorbidities (atrial fibrillation, hypertension) showed a consistent effect of BAR across subgroups, with no significant interactions detected (all P for interaction > 0.05).

3.6 Feature selection

Feature selection was conducted in the MIMIC-IV cohort utilizing both Boruta (Fig. 5A) and LASSO algorithms (Fig. 5B-C). Notably, both algorithms identified BAR as a significant predictor of 30-day all-cause mortality in patients with NSAH. The Venn diagrams (Fig. 5D) illustrate the combined results of these methods. Ten features, race, PLT, AG, BAR, OASIS, SAPSII, SIRS, norepinephrine, vasopressin, and CRRT, were finally selected for inclusion in the modelling.

3.7 Machine learning results

Seven machine learning algorithms were developed to predict the 30-day all-cause mortality risk in NSAH patients: LR, DT, RF, XGBoost, LightGBM, SVM, and ANN. Their performance is summarized in **Table S5** and Fig. 6A. LR exhibited the most robust and stable discriminative performance, achieving an AUC of 0.872, a balanced accuracy of 0.813, a precision of 0.725, a sensitivity of 0.532, a specificity of 0.922, and the highest F1 score of 0.613. Calibration curves (Fig. 6B) indicated that LR had the best agreement between predicted and observed outcomes. Furthermore, decision curve analysis in Fig. 6C demonstrated that LR offered a greater net benefit than both the treat-all and treat-none strategies across a wide range of threshold probabilities, particularly excelling between thresholds of 0.1 and 0.8. Ultimately, LR was selected as the optimal model for further interpretation and external validation.

SHAP analysis was employed to interpret the LR model. The SHAP feature importance ranking (Fig. 6D) and beeswarm plot (Fig. 6E) illustrated the magnitude and direction of each variable's influence on model predictions. The primary contributors to the model output included SIRS, race, vasopressin, PLT, OASIS, SAPSII, AG, norepinephrine, and BAR. Notably, elevated levels of BAR significantly increased short-term mortality among NSAH patients, underscoring BAR as a critical adverse factor.

3.8 External validation

External validation was conducted using the eICU-CRD and HIS cohorts. Following full adjustment, the eICU-CRD revealed that patients in the highest BAR group exhibited a significantly increased risk of in-hospital mortality (Q4 vs Q1: OR = 2.74, 95% CI 1.37, 5.63, P = 0.005). Similarly, in the HIS, a higher BAR was consistently associated with elevated in-hospital mortality (Q4 vs Q1: OR = 6.91, 95% CI 1.50, 38.17, P = 0.018). Additional details were provided in Table 3.

The top-performing LR model underwent validation in external cohorts (eICU-CRD and HIS). It demonstrated robust discrimination and superior predictive capacity for in-hospital mortality, with AUC of 0.839 and 0.790, respectively. The calibration curves indicated a strong agreement between predicted and observed outcomes. However, the calibration curve showed a poor fit in the HIS cohort. The decision curve analysis revealed that the LR model consistently offered a higher net benefit compared to both the treat-all and treat-none strategies across clinically relevant thresholds. Detailed data were presented in Fig. 7.

4. Discussion

This retrospective study represented the first systematic investigation of the relationship between BAR and all-cause mortality in patients with NSAH. The findings revealed that elevated BAR levels independently correlate with an increased risk of all-cause mortality at 30, 90, and 365 days. This association remained robust across both the eICU-CRD and HIS. Furthermore, the machine learning model LR, which incorporated BAR, exhibited optimal performance in all-cause mortality risk prediction, achieving an AUC of 0.872. The results of external validation yielded AUC values of 0.839 and 0.790 for the eICU-CRD and HIS, respectively.

BUN is the terminal product of protein metabolism and is primarily used in clinical settings as a marker of renal insufficiency. BUN also reflects changes in the body's hemodynamic state. A meta-analysis found that elevated BUN independently predicts mortality risk in patients with heart failure[21]. Additionally, BUN serves as an indicator of systemic inflammatory status and is negatively correlated with the systemic immune-inflammation index (SII)[22]. BUN further mirrors endocrine activation and metabolic stress. Xie et al. reported an association between BUN and diabetes risk[23]. Urea nitrogen is currently used as a predictor in a range of critical conditions, including acute pancreatitis[6], ischemic stroke[7], acute myocardial infarction[8], COVID-19[9], and acute pulmonary edema[24].

ALB is synthesized primarily in the liver and serves as an indicator of nutritional status and hepatic function. It maintains colloid osmotic pressure in the vasculature and functions as a nonspecific carrier protein that transports diverse endogenous molecules and drugs[10]. ALB also exerts anti-inflammatory and antioxidant effects and helps preserve vascular endothelial integrity. ALB directly lowers inflammatory factor expression[25]. It also reduces inflammatory cell recruitment by blocking tumor necrosis factor-α (TNF-α) induced nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) activation and the expression of inflammatory adhesion molecules[26]. Under pathological conditions, ALB can be neuroprotective by delivering pyruvate to neurons and supporting their metabolism[27]. Chronic or acute inflammation, malnutrition, hypermetabolism from severe stress, and impaired liver function all reduce ALB levels, which are associated with worse outcomes.

BAR is a novel, simple prognostic marker that requires only a venous blood sample at admission. Because BAR combines BUN and ALB, it typically reflects the combined patterns of elevated BUN and reduced ALB and thus provides an integrated index of renal and hepatic function, hemodynamic status, nutritional state, and systemic inflammation, making it superior to either BUN or ALB alone. Prior studies have linked BAR closely with mortality in diverse critical illnesses. Cai et al. reported that BAR was significantly associated with in-hospital mortality in intensive care patients with sepsis[14]. A multicenter retrospective cohort study found that BAR significantly predicts outcomes in biliary acute pancreatitis[15]. Huang et al. showed that BAR reliably predicts mortality after ischemic stroke, with the highest mortality in the T3 group after adjustment for confounders[28]. In a retrospective cohort of 1,994 patients, Chen et al. reported that BAR aids early identification of high-risk AKI among individuals with immunologic and surgical conditions[16]. GUE and his team utilized machine learning techniques to develop prediction models. And it indicated that the BAR is a highly influential factor in predicting mortality in traumatic brain injury (TBI) patients[29]. BAR has also been shown to predict mortality after pneumonia and cardiac surgery[30, 31].

Although the precise mechanism by which elevated BAR contributes to increased mortality remains incompletely understood, several potential pathophysiological mechanisms have been proposed. In cases of non-traumatic subarachnoid hemorrhage, a significant volume of blood enters the subarachnoid space. The components of this blood are identified as damage-associated molecular patterns (DAMPs), which activate inflammatory signaling pathways and stimulate the production of cytokines by inflammatory cells, including microglia and macrophages, within the central nervous

system. Cytokines such as interleukin-6 (IL-6), TNF-α, and interleukin-1β (IL-1β) can partially traverse the compromised blood-brain barrier and enter the bloodstream, resulting in an elevation of inflammatory mediators in plasma and subsequent activation of systemic inflammatory responses[22, 32]. This increase in inflammatory mediators may damage renal tubules and can coincide with the onset of acute AKI[16, 33].Impaired kidney function results in decreased reabsorption of blood urea nitrogen (BUN), leading to elevated plasma BUN levels. During the acute phase of NSAH, bidirectional regulation of the neuro-renal axis causes excessive sympathetic activation[34]. The hypothalamic-pituitary-adrenal axis (HPA) is also stimulated, producing elevated cortisol and catecholamine levels. Cortisol promotes protein catabolism and thus raises plasma BUN. It is important to note that patients with NSAH frequently experience severe vomiting due to elevated intracranial pressure, which causes substantial fluid loss. The subsequent activation of the renin-angiotensin-aldosterone system (RAAS) results in reduced renal blood perfusion. In the intensive care unit, clinicians administer mannitol to decrease intracranial pressure, often leaving patients in a dehydrated state. Collectively, these factors contribute to the rise in BUN levels observed in patients during NSAH. Patients with NSAH commonly present with hypoalbuminemia. Elevated IL-6 during the systemic inflammatory response suppresses hepatic albumin synthesis while stimulating C-reactive protein production (CRP). Inflammatory cascades also injure vascular endothelial cells, inducing apoptosis and capillary leakage that permits albumin to extravasate[35]. Nontraumatic subarachnoid hemorrhage (NSAH) is frequently accompanied by oxidative stress. Degradation of blood components such as iron ions and hemoglobin in the subarachnoid space generates abundant reactive oxygen species (ROS), which induce oxidative damage[36]. A hypermetabolic state in patients with NSAH accelerates albumin catabolism, further lowering serum ALB. These combined processes produce hypoalbuminemia, which correlates with worse clinical outcomes and higher mortality in NSAH patients.

The principal strengths of this study are as follows. (1) Data derived from the MIMIC-IV database, which contains a large number of real patient records, allowed this retrospective cohort design to evaluate the true prognosis of NSAH. (2) Compared with complex scoring systems, BAR offers simplicity, low cost, and ease of calculation, making it applicable across diverse clinical settings, including resource-limited institutions. (3) External validation was also conducted, where machine learning models trained in MIMIC IV were directly applied to the eICU-CRD and HIS cohorts, further enhancing the reliability and generalizability of the findings.

Despite these strengths, several limitations warrant attention. (1) Due to the retrospective cohort study design, selection bias is unavoidable, and prospective studies are needed in the future. (2) Second, although confounding variables were adjusted, there remain unknown variables that could have influenced our results, such as the specific location of aneurysm characteristics (location, shape, and size), grading systems for NSAH (Hunt-Hess score, Fisher score, and WFNS scale). (3) BAR data were collected during the first 24 hours after ICU admission. Longitudinal data on the BAR were unavailable, hindering the investigation of its dynamic changes over the follow-up period. This limitation underscores the necessity for future studies to evaluate the predictive significance of BAR fluctuations over time.

5. Conclusion

In conclusion, NSAH patients in the high BAR group had a greater risk of short-, medium-, and long-term mortality than those in the low BAR group. Machine learning models incorporating BAR and other clinical factors demonstrated robust discrimination, stability, and clinical utility across external multicenter cohorts. These findings collectively indicated that BAR could enhance risk stratification and inform clinical decision-making in the critical care of NSAH.

Declarations

Funding

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Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

Liang Liu designed the study. **Zhilei Huang**, **Binbin Gui**, **Lin Xu**, **Wei Zhang**, and **Yansong Liu** extracted, collected, and analyzed data. **Haowei Luo** prepared tables and figures. **Xiangtong Zhang** reviewed the results, interpreted data, and wrote the manuscript. All authors have contributed equally to the manuscript and approved the submission.

Ethics approval

This research adhered to the principles of the Declaration of Helsinki. Approval for the MIMIC-IV database was granted by the institutional review boards of Beth Israel Deaconess Medical Center (2001-P-001699/14) and Massachusetts Institute of Technology (No. 0403000206), with waived patient consent due to deidentification. The eICU database release was compliant with the Health Insurance Portability and Accountability Act (HIPAA) safe harbor provision (HIPAA Certification No. 1031219-2), thus ethics approval was not required. The Ethics Committee of the First Affiliated Hospital of Harbin Medical University reviewed and approved the research protocol. Informed consent was obtained from patients or their legal representatives.

Consent to participate

Not applicable.

Consent to publish

Not applicable.

Clinical trial number

Not applicable.

Data availability

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

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Supplementary information

Supplementary data to this article can be found in the Supplementary Materials.

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Figures

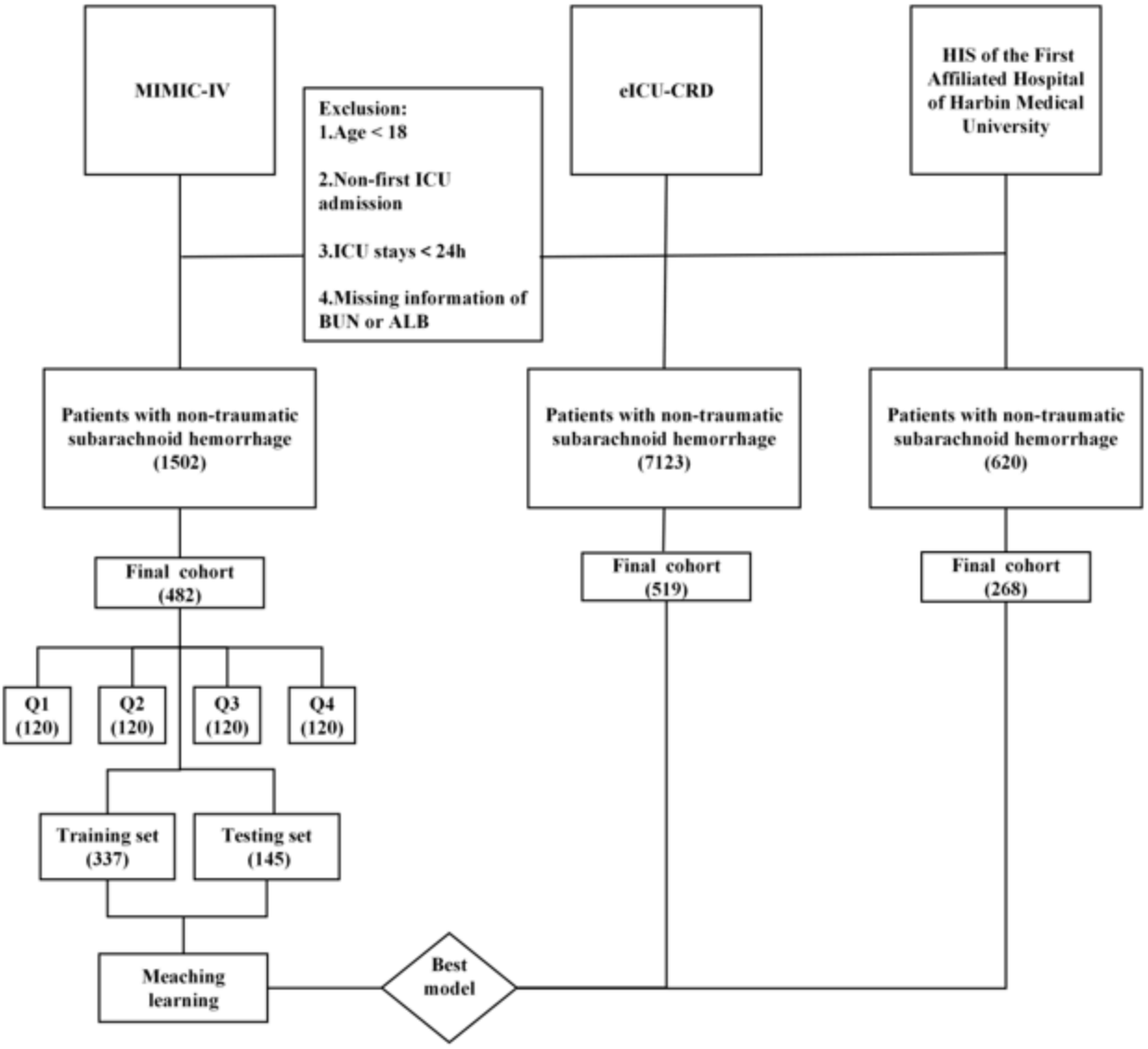


Figure 1

Flowchart of the study process.

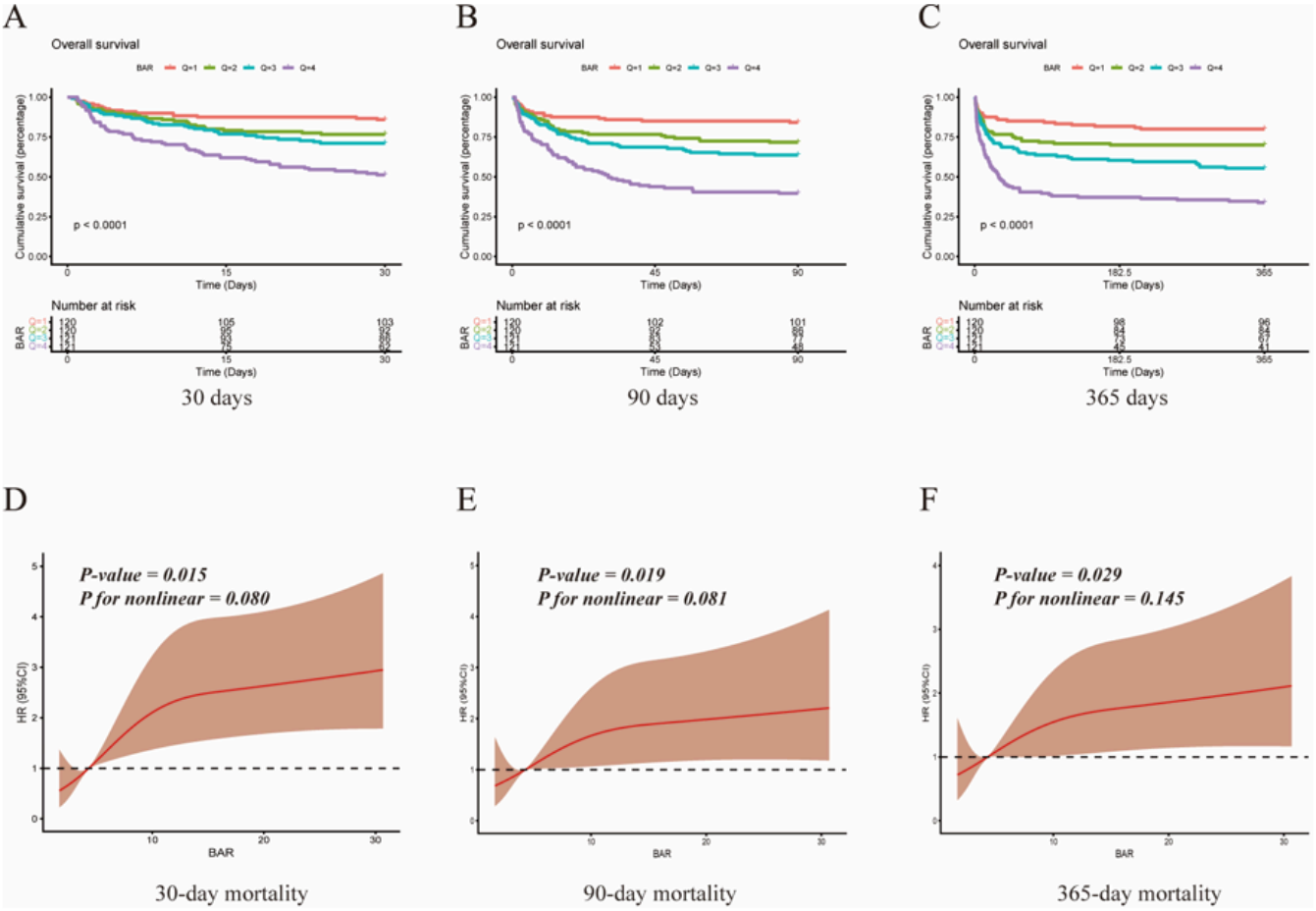


Figure 2

Kaplan–Meier curve and RCS analysis.

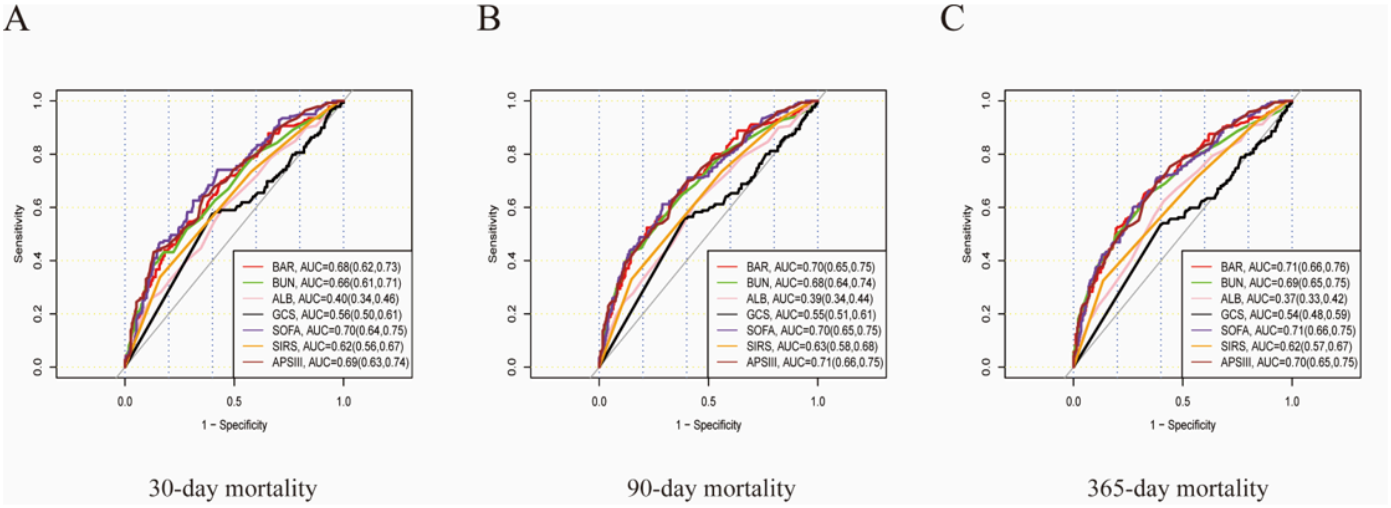


Figure 3

ROC curves for predicting mortality in patients with NSAH.

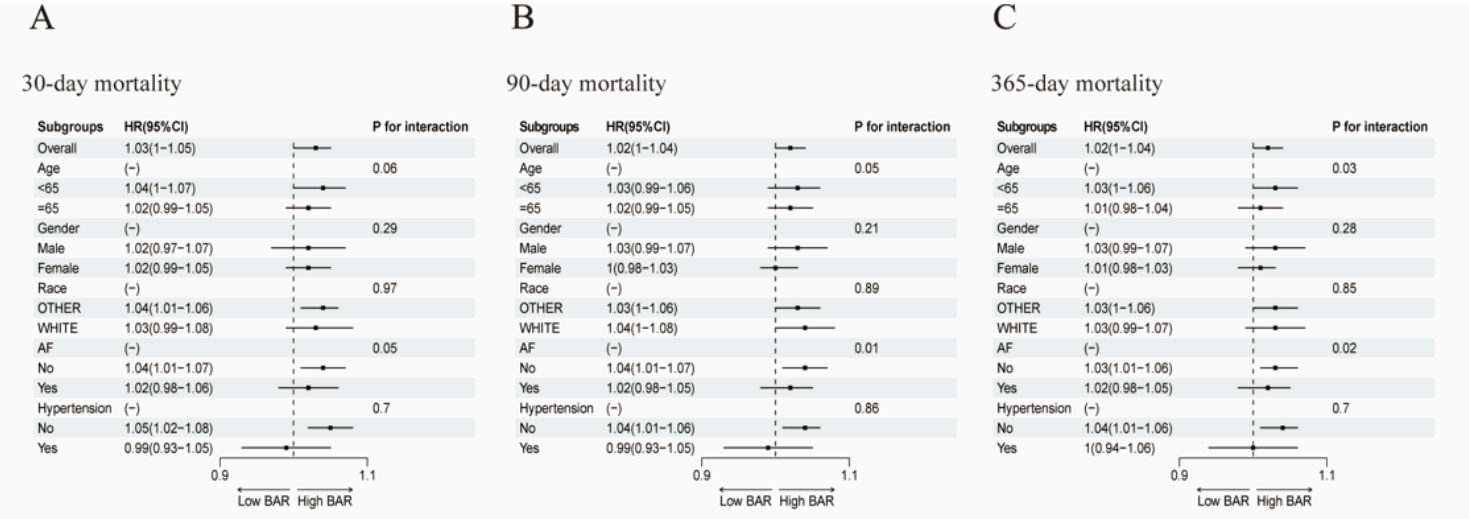


Figure 4

Subgroup analysis for the association of BAR with all-cause mortality.

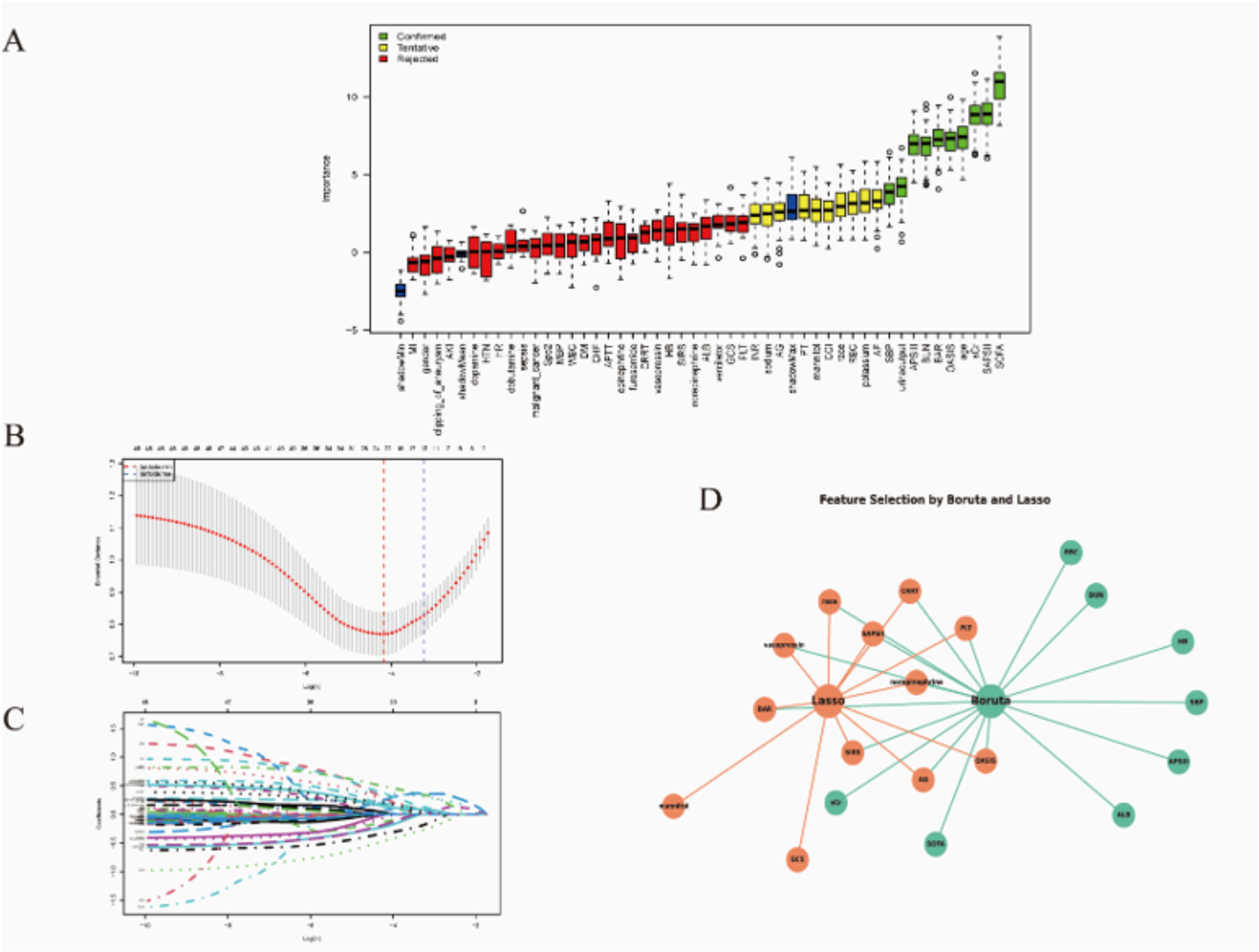


Figure 5

BAR and 30-day all-cause mortality feature selection process. (**A**) Feature selection based on the Boruta algorithm; (**B**, **C**) Path diagrams and cross-validation plots of lasso regression analysis results; (**D**) Venn diagrams for feature selection. The orange section displayed the results of the LASSO regression analysis, and the green section showed the results of the Boruta algorithm. The final features selected were **race**, **PLT**, **AG**, **BAR**, **OASIS**, **SAPSII**, **SIRS**, **norepinephrine**, **vasopressin**, and **CRRT**.

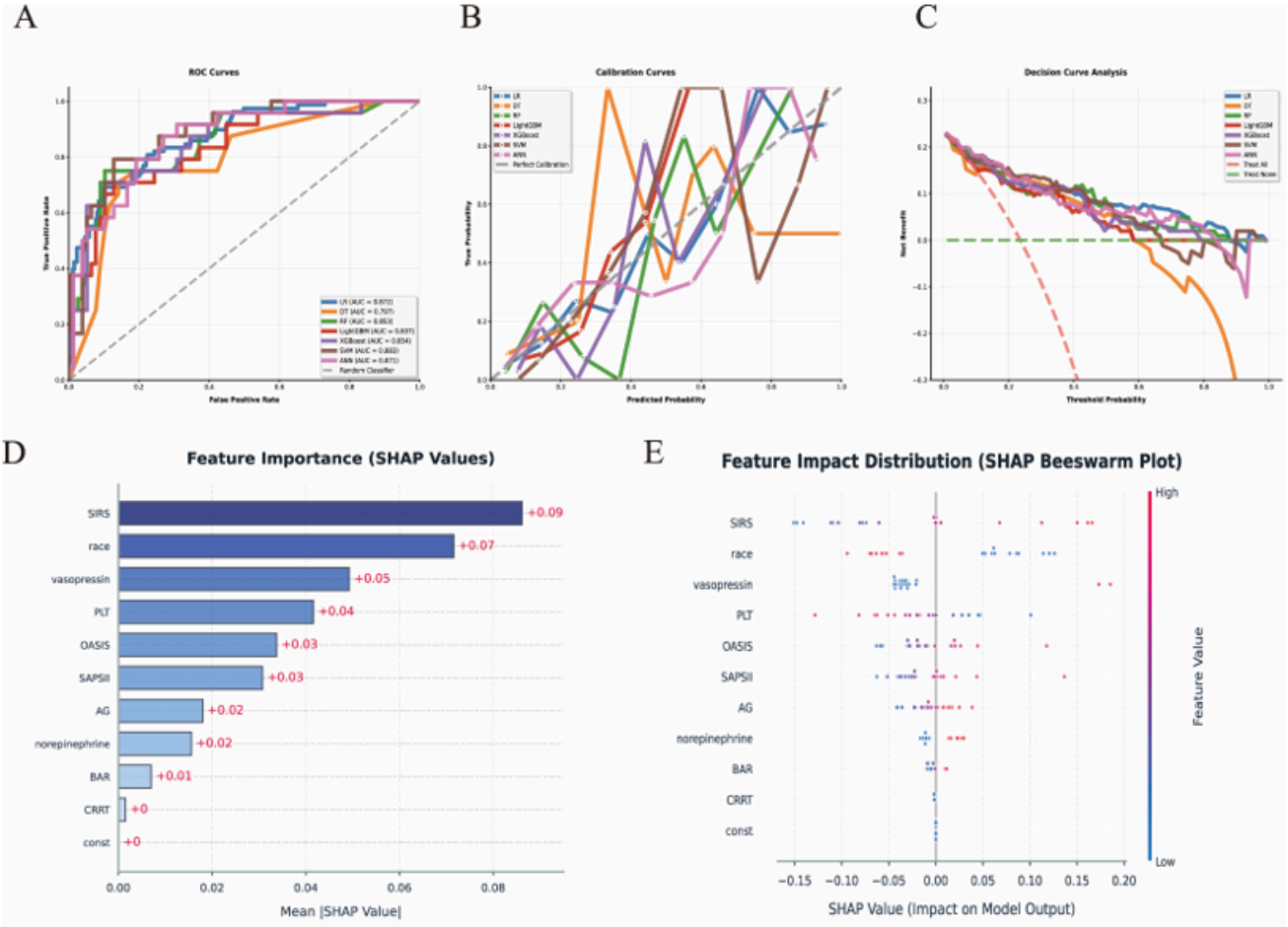


Figure 6

Performance of seven machine learning models in the internal validation cohort (MIMIC-IV) and SHAP analysis. (**A**) ROC Curves; (**B**) Calibration Curves; (**C**) Decision Curves Analysis; (**D**) SHAP bar plot; (**E**) SHAP beeswarm plot.

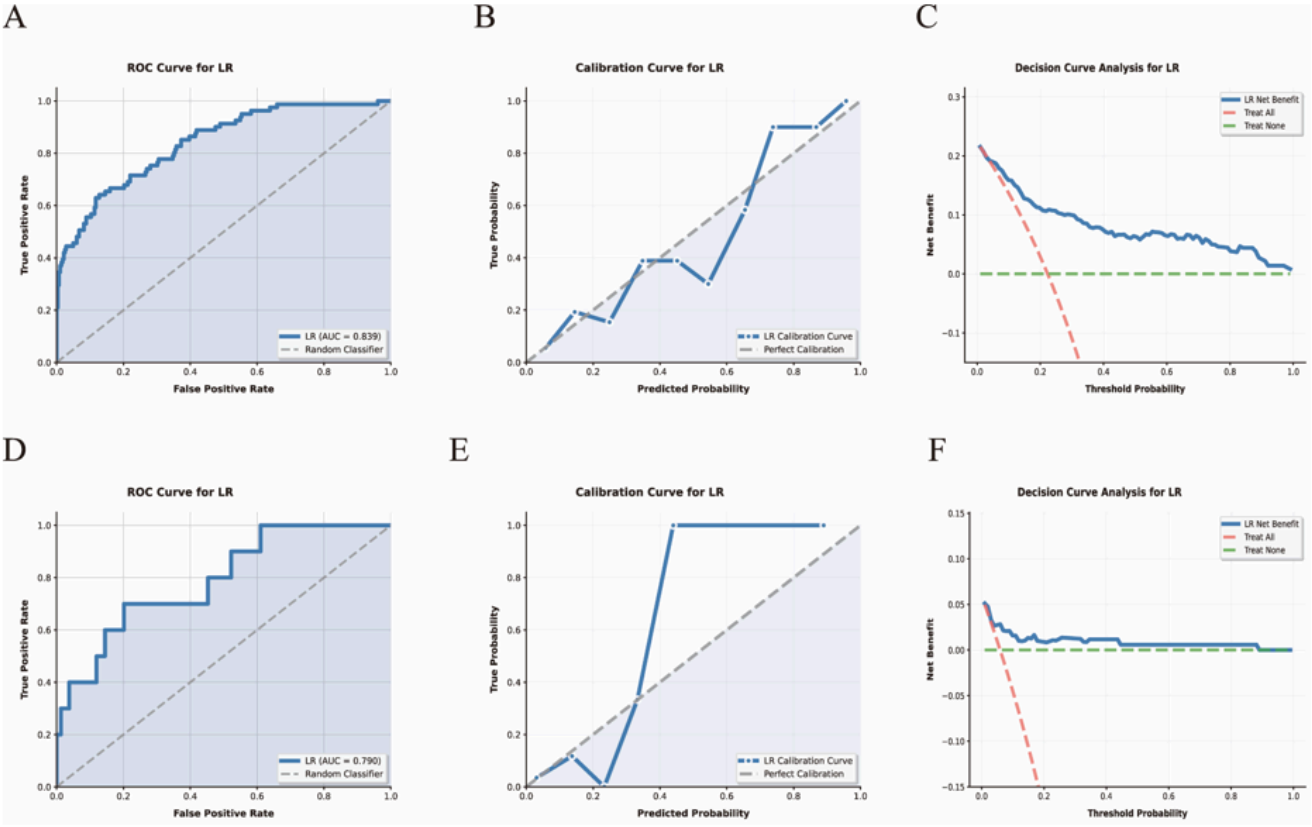


Figure 7

External validation of the LR model. (**A**) ROC Curves for eICU-CRD; (**B**) Calibration Curves for eICU-CRD; (**C**) Decision Curves Analysis for eICU-CRD; (**A**) ROC Curves for HIS; (**B**) Calibration Curves for HIS; (**C**) Decision Curves Analysis for HIS.

Supplementary Files

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