BMC Gastroenterology

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Lactate-to-albumin ratio as an independent predictor of mortality in critically ill patients with gastrointestinal bleeding: a retrospective cohort study

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Abstract

Background The lactate-to-albumin ratio (LAR) is an established prognostic marker in various critical illnesses; However, its association with gastrointestinal bleeding (GIB) in patients has not been thoroughly investigated. This study evaluates the prognostic role of LAR in critically ill patients with GIB.

Methods Data were extracted from the publicly available MIMIC-IV database (v3.1). We assessed the prognostic value of the LAR for both short- and long-term mortality using multivariable Cox proportional hazards regression. Survival differences were analyzed using Kaplan-Meier (K-M) curves with log-rank tests. Discrimination ability was evaluated using receiver operating characteristic (ROC) curve analysis, while nonlinear associations were examined using restricted cubic splines (RCS). Subgroup analyses were conducted to test for potential effect modification. Finally, a Boruta algorithm-based nomogram was developed to integrate key predictors.

Result This retrospective cohort study enrolled 1,210 critically ill patients with gastrointestinal bleeding, demonstrating an ICU mortality rate of 21.7%. Using X-tile analysis, we stratified patients into tertiles (Q1-Q3) based on LAR and 28-day mortality. Multivariable Cox regression confirmed LAR as an independent predictor of mortality ($P < 0.001$), with K-M analysis revealing significantly worse survival in higher LAR groups ($P < 0.001$). ROC analysis showed moderate predictive accuracy, while integrating LAR with SOFA score enhanced performance compared to either parameter alone. Decision curve analysis (DCA) demonstrated clinical utility, and RCS regression indicated a linear dose-response relationship between LAR and mortality risk. Subgroup analyses revealed no significant effect modification. A Boruta-optimized nomogram incorporating LAR achieved robust predictive performance for 28-day (AUC 0.780, 95% CI 0.750–0.811), 90-day (0.777, 0.749–0.805), and 365-day mortality (0.773, 0.745–0.800).

Conclusion The LAR independently predicts short- and long-term mortality in critically ill gastrointestinal bleeding patients.

Keywords Lactate, All-cause mortality, Gastrointestinal bleeding, Prognosis, MIMIC-IV

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Introduction

Severe GIB is a life-threatening clinical emergency associated with significant therapeutic challenges [1–3]. Epidemiological data indicate a global incidence of 55–175 cases per 100,000 individuals annually, with mortality rates varying by bleeding site: 5–10% for upper GIB and 2–5% for lower GIB [4–6]. While advancements in endoscopic management and critical care have improved treatment outcomes [7, 8], complex pathophysiological mechanisms continue to contribute to adverse clinical outcomes in certain patients [1]. Consequently, the identification of reliable and clinically practical prognostic biomarkers remains essential for timely intervention and improved patient survival.

In critically ill patients with gastrointestinal disorders, lactate and albumin levels play pivotal roles in the pathogenesis of organ dysfunction. Elevated lactate, a well-established metabolic marker of tissue hypoxia [9, 10], reflects sustained hypoperfusion that can compromise the intestinal mucosal barrier, facilitating bacterial translocation and secondary infections. Concurrently, hyperlactatemia impairs mitochondrial function and disrupts tissue oxygen utilization [11]. Hypoalbuminemia contributes to pathophysiology through multiple mechanisms: by diminishing colloid osmotic pressure, it exacerbates tissue edema and worsens existing hypoxia [12]. Furthermore, depleted albumin reserves impair endogenous antioxidant and anti-inflammatory capacities, leading to unchecked accumulation of reactive oxygen species and pro-inflammatory mediators that collectively promote multi-organ dysfunction syndrome (MODS) [13].

The LAR is a well-established prognostic marker in critical illnesses such as sepsis [14], cirrhosis [15], and acute pancreatitis [16], yet its utility in critically ill patients with GIB remains unexplored. Using real-world data from the MIMIC-IV database, this study investigates LAR's association with mortality risk and evaluates its potential as a prognostic biomarker in GIB. Given the pathophysiological links between lactate-driven hypoxia and albumin's anti-inflammatory effects in gastrointestinal injury, clarifying LAR's predictive value could refine risk stratification and guide tailored interventions for this vulnerable population.

Database and methods

Database introduction

Researchers utilized the publicly accessible MIMIC-IV database (version 3.1). This database encompasses extensive clinical information from over 90,000 individuals admitted to the ICU at Beth Israel Deaconess Medical Center between 2012 and 2022. The BIDMC Institutional Review Board approved the database (approval no. 2001P-001699/14). All sensitive information was anonymized by substituting original identifiers with randomized codes. Consequently, no additional ethical approval or patient consent was required for this study. After completing the CITI Research Ethics Program, the researchers obtained access to the database (certificate no. 67058598).

Inclusion and exclusion criteria

In this retrospective cohort study, we identified patients with GIB using ICD codes and included them in our analysis. Our initial cohort comprised 4,576 inpatients admitted to the intensive care unit (ICU) due to their condition. Our dataset underwent a rigorous filtration process based on specific exclusion criteria to eliminate irrelevant data, including patients with prior ICU admissions, those whose ICU stay was shorter than 24 h, and cases where ALB or lactate levels were not recorded within the first 24 h of admission. After applying these criteria, our final analysis was based on 1,210 patients. For details of the study design and outcomes, refer to Fig. 1.

Data collection and monitoring

Clinical data were systematically extracted from an intensive care database, covering demographics, laboratory tests, comorbidities, and prognostic outcomes. The collected variables were categorized into five main categories. Category 1 encompassed vital signs, namely blood pressure, heart rate, respiratory rate, and temperature. Category 2 involved laboratory biomarkers such as white blood cell (WBC) count, red blood cell count, platelet count, glucose, blood urea nitrogen, creatinine, total bilirubin (TB), albumin (ALB), activated partial thromboplastin time (APTT), international normalized ratio (INR), anion gap (AG), red cell distribution width (RDW), and Sequential Organ Failure Assessment (SOFA) score. Category 3 covered comorbidities, including diabetes, cirrhosis, acute kidney injury (AKI), sepsis, heart failure (HF), myocardial infarction (MI), and ischemic heart disease (IHD). Category 4 comprised key therapeutic interventions, specifically continuous renal replacement therapy (CRRT) and mechanical ventilation (MV). Category 5 pertained to short - and long - term prognostic outcomes. LAR was identified as the primary variable of interest. All laboratory values were derived from mean measurements obtained within the first 24 h of ICU admission. Participants in the study had to meet the diagnostic criteria for GIB and were followed for one Year to monitor survival status. The primary endpoint was all-cause mortality at predetermined time points following admission, specifically at 28, 90, and 365 days.

Statistical analyses

Continuous variables were first tested for normality using Shapiro-Wilk criteria. Normally distributed measures

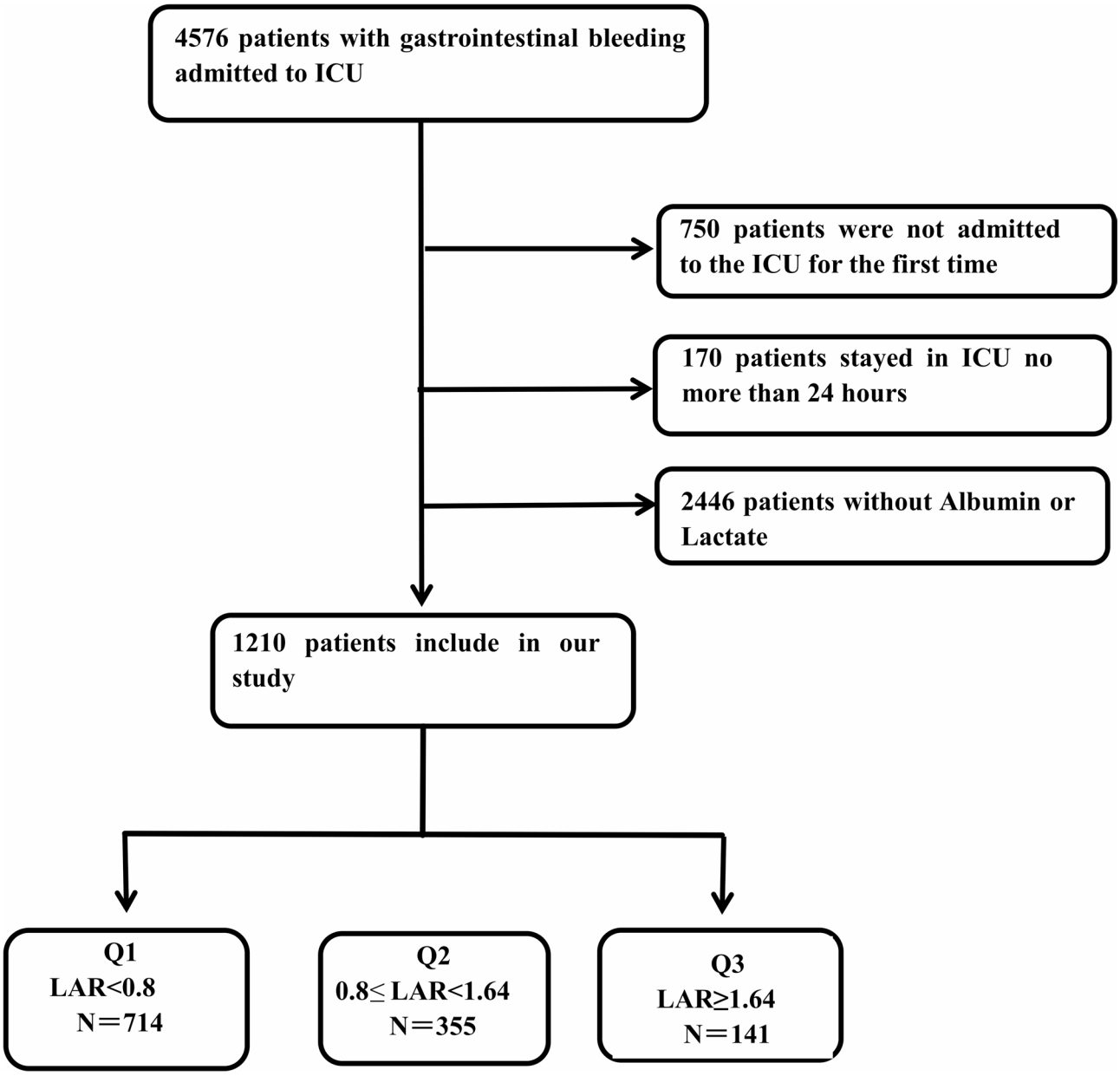

Fig. 1 A flow diagram of study participants

were presented as mean ± SD and analyzed by t-tests; non-normal data were presented as median (IQR) values and examined via Mann-Whitney U tests. Missing data were handled as follows: Variables exhibiting more than 20% missing data were excluded, whereas those with 20% or less missing data were imputed using a random forest algorithm.

Subsequently, optimal LAR cutoffs for 28-day mortality were identified using X-tile software (v3.6.1, Yale University), stratifying patients into three groups: Q1 (LAR < 0.8), Q2 (0.8 ≤ LAR < 1.64), and Q3 (LAR ≥ 1.64). To reduce the confounding effects between LAR and outcomes, multiple models were developed to calculate hazard ratios (HR) and 95% confidence intervals (CI) for all-cause mortality. Survival differences were evaluated via K-M curves and log-rank tests. The predictive performance was assessed using ROC analysis, estimating sensitivity, specificity, and area under the curve (AUC) for LAR, lactate, albumin, SOFA score, and their combination (SOFA + LAR). To better evaluate prognosis in patients with gastrointestinal bleeding, the AIMS65 score—a validated risk assessment tool—was also included in the analysis. Its predictive value, along with that of LAR and their combination (AIMS65 + LAR), was assessed using ROC analysis. Furthermore, nonlinear

associations between LAR and outcomes were examined with RCS regression.

Additionally, subgroup analyses were performed to test interaction effects across prespecified variables. A prognostic nomogram integrating LAR and other risk factors was developed using the Boruta algorithm for feature selection. To account for multiple testing, significance thresholds were adjusted via Bonferroni correction: $P < 0.005$ (0.05/9) for Cox regressions and $P < 0.006$ (0.05/8) for subgroup analyses. All analyses were performed in R (v4.2.2; R Foundation).

Results

Characteristics of patients at baseline

Table 1 presents baseline characteristics of patients stratified by LAR tertiles (tertile 1 [Q1], tertile 2 [Q2], tertile 3 [Q3]). Significant intergroup differences were observed across most clinical variables (all p-values were less than 0.001). Patients in higher LAR tertiles demonstrated younger median age (67 years [Q1], 65 years [Q2], 61 years [Q3], respectively), with the Kruskal-Wallis test confirming age gradients ($p < 0.001$). Physiological parameters showed progressive deterioration, including heart rate, respiratory rate, and lactate levels (1.46, 2.85, 6.07 mmol/L), with similar trends in anion gap and SOFA scores (6, 8, 12 points). Laboratory markers revealed progressive organ dysfunction across tertiles, as evidenced by increasing INR (1.2, 1.4, 1.8), creatinine (82.1, 95.3, 123.7 μmol/L), and decreasing albumin (35.2, 32.1, 29.8 g/L) (all p-values were less than 0.001). Comorbidities including sepsis (23.0%, 43.7%, 51.8%), AKI (50.8%, 70.1%, 81.6%), and cirrhosis (27.0%, 39.2%, 46.8%) demonstrated tertile-dependent increases using the χ^2 test ($p < 0.001$). Mortality outcomes showed pronounced gradients: hospital mortality increased from 25.6% in Q1 to 60.3% in Q3, and 365-day mortality increased from 23.2 to 57.4% (both $p < 0.001$). No significant differences were observed for gender distribution, diabetes prevalence, or history of a myocardial infarction across tertiles.

Association between LAR and all-cause mortality

28-day mortality

In the Cox regression analysis of 28-day mortality, LAR was divided into tertiles (Q1-Q3), using Q1 as the reference group. Compared to Q1, Q2 showed a significantly higher mortality risk across all models (Model 1: HR = 2.08, 95% CI 1.58–2.73, $p < 0.001$; Model 2: HR = 2.12, 95% CI 1.61–2.79, $p < 0.001$; Model 3: HR = 1.48, 95% CI 1.10–1.97, $p = 0.009$). The association was more pronounced for Q3 (Model 1: HR = 4.94, 95% CI 3.67–6.65; Model 2: HR = 5.22, 95% CI 3.86–7.04; Model 3: HR = 3.02, 95% CI 2.14–4.24; all $p < 0.001$). A significant dose-response relationship was observed across all models (p for trend < 0.001).

90-day mortality

For 90-day mortality, Cox regression analyses revealed a significant link between higher LAR tertiles (Q1-Q3) and increased mortality risk. Compared to Q1 (reference), Q2 had a HR of 1.95 (95% CI 1.54–2.47, $p < 0.001$) in the unadjusted Model 1 and 1.97 (95% CI 1.56–2.50, $p < 0.001$) in Model 2 after adjusting for age and sex. Further adjustment for clinical and laboratory variables in Model 3 weakened the association (HR = 1.32, 95% CI 1.03–1.69, $p = 0.029$). The highest tertile (Q3) showed a stronger association, with HRs of 3.95 (95% CI 3.01–5.19, $p < 0.001$) in Model 1, 4.12 (95% CI 3.13–5.43, $p < 0.001$) in Model 2, and 2.29 (95% CI 1.68–3.11, $p < 0.001$) in Model 3. A significant dose-response association was found in all models (p for trend < 0.001).

365-day mortality

For 365-day mortality, Cox regression models also demonstrated a significant association between higher LAR tertiles (Q1-Q3) and increased mortality risk. Compared to Q1, Q2 exhibited an HR of 1.86 (95% CI 1.48–2.33, $p < 0.001$) in the unadjusted Model 1 and 1.88 (95% CI 1.50–2.36, $p < 0.001$) in Model 2 after age and sex adjustment. Further adjustment for clinical and laboratory covariates in Model 3 reduced the association but it remained significant (HR = 1.28, 95% CI 1.00–1.62, $p = 0.047$). For Q3, the association was stronger, with HRs of 3.68 (95% CI 2.82–4.81, $p < 0.001$) in Model 1, 3.83 (95% CI 2.93–5.01, $p < 0.001$) in Model 2, and 2.16 (95% CI 1.60–2.92, $p < 0.001$) in Model 3. A clear dose-response relationship was observed in all models (p for trend < 0.001). Further details are provided in Table 2.

Analysis of Kaplan-Meier and ROC curves

K-M analysis

K-M analysis showed that the Q3 group had significantly higher mortality rates than the Q2 and Q1 groups at all assessed time points. Specifically, the 28-day mortality rates were 52.5% in Q3 vs. 28.2% in Q2 vs. 14.8% in Q1 ($P < 0.001$). The 90-day mortality rates were 56.0% in Q3 vs. 36.3% in Q2 vs. 20.9% in Q1 ($P < 0.001$). Similarly, the 365-day mortality rates were 56.0% in Q3 vs. 36.3% in Q2 vs. 20.9% in Q1 ($P < 0.001$). All these differences were statistically significant (Fig. 2).

ROC curve analysis

Receiver operating characteristic (ROC) curve analysis was performed to evaluate seven prognostic indicators: LAR, lactate, ALB, SOFA score, AIMS65, and the combined models SOFA + LAR and AIMS65 + LAR. LAR alone demonstrated moderate discriminative ability for predicting all-cause mortality, yielding AUCs of 0.681, 0.664, and 0.653 for 28-day, 90-day, and 365-day mortality, respectively. These values were higher than those of

Table 1 Patient demographics and baseline characteristics

Variables	Total (*n*=1210)	Q1 (*n*=224) LAR < 0.8	Q2(*n*=355) 0.8 ≤ LAR < 1.64	Q3(*n*=141)LAR ≥ 1.64	*p*-value
Demographic					
Age(year)	66 (55, 77)	67 (57, 78)	65 (55, 76)	61 (49, 72)	≤ 0.001
Gender, *n*(%)					0.241
Male	752 (62.1%)	284 (39.8%)	123 (34.6%)	51 (36.2%)	
Female	458 (37.9%)	430 (60.2%)	232 (65.4%)	90 (63.8%)	
Race, *n*(%)					0.002
White	778 (64.3%)	476 (66.7%)	230 (64.8%)	72 (51.1%)	
Other	432 (35.7%)	238 (33.3%)	125 (35.2%)	69 (48.9%)	
Vital Signs					
HR(beats/min)	94 (80, 109)	92 (76, 106)	98 (85, 112)	103 (87, 117)	< 0.001
SBP (mmHg)	116 (100, 133)	119 (101, 136)	113 (100, 129)	110 (96, 125)	< 0.001
DBP (mmHg)	65 (55, 77)	66 (55, 78)	65 (56, 78)	62 (52, 72)	0.025
MAP (mmHg)	78 (67, 91)	78 (68, 92)	77 (67, 91)	75 (64, 86)	0.024
RR (beats/min)	20 (16, 24)	19 (16, 23)	20 (17, 24)	21 (17, 26)	0.004
Temperature(℃)	98.10 (97.60, 98.60)	98.20 (97.70, 98.70)	98.10 (97.50, 98.60)	97.90 (97.30, 98.50)	< 0.001
Comorbidity					
Sepsis, *n*(%)	392 (32.4%)	164 (23.0%)	155 (43.7%)	73 (51.8%)	< 0.001
AKI, *n*(%)	727 (60.1%)	363 (50.8%)	249 (70.1%)	115 (81.6%)	< 0.001
Cirrhosis, *n*(%)	398 (32.9%)	193 (27.0%)	139 (39.2%)	66 (46.8%)	< 0.001
Diabetes, *n*(%)	352 (29.1%)	212 (29.7%)	101 (28.5%)	39 (27.7%)	0.846
HF, *n*(%)	376 (31.1%)	248 (34.7%)	94 (26.5%)	34 (24.1%)	0.004
MI, *n*(%)	113 (9.3%)	64 (9.0%)	38 (10.7%)	11 (7.8%)	0.524
IHD, *n*(%)	387 (32.0%)	246 (34.5%)	109 (30.7%)	32 (22.7%)	0.020
Laboratory Indicators					
Hemoglobin(10^9/l)	9.18 (8.08, 10.53)	9.15 (8.05, 10.43)	9.15 (8.08, 10.60)	9.37 (8.30, 10.70)	0.4132
Platelet(10^9/L)	141 (85, 223)	158 (97, 234)	137 (87, 213)	93 (67, 161)	< 0.001
RDW(%)	16.26 (14.81, 18.33)	16.00 (14.67, 17.95)	16.62 (14.96, 18.80)	16.73 (15.24, 19.37)	< 0.001
RBC(10^9/L)	3.03 (2.63, 3.52)	3.02 (2.65, 3.51)	3.05 (2.60, 3.59)	3.02 (2.63, 3.52)	0.851
WBC(10^9/L)	12 (8, 17)	11 (8, 15)	13 (9, 19)	15 (9, 19)	< 0.001
ALB(g/dl)	2.90 (2.48, 3.30)	3.00 (2.60, 3.40)	2.70 (2.30, 3.17)	2.43 (2.00, 2.90)	< 0.001
Lactate(mmol/L)	1.95 (1.40, 2.91)	1.46 (1.10, 1.80)	2.85 (2.40, 3.48)	6.07 (4.77, 8.24)	< 0.001
AG (m Eq/l)	14.5 (12.0, 18.0)	13.7 (11.3, 16.8)	15.0 (12.2, 18.2)	19.0 (15.7, 25.0)	< 0.001
TCa(mg/dl)	8.06 (7.60, 8.55)	8.11 (7.70, 8.60)	7.97 (7.50, 8.47)	7.87 (7.30, 8.47)	< 0.001
Chloride(m Eq/l)	104 (100, 109)	105 (100, 109)	104 (99, 109)	102 (98, 107)	< 0.001
Glucose(mg/dL)	134 (109, 172)	129 (107, 161)	142 (115, 185)	148 (113, 204)	< 0.001
Potassium(m Eq/l)	4.22 (3.83, 4.70)	4.13 (3.80, 4.60)	4.30 (3.87, 4.85)	4.35 (4.00, 5.08)	< 0.001
Sodium(m Eq/l)	138.5 (134.8, 141.5)	139.0 (135.5, 141.8)	137.6 (133.8, 141.5)	137.4 (133.2, 141.0)	< 0.001
INR	1.50 (1.25, 1.85)	1.40 (1.20, 1.67)	1.62 (1.35, 1.98)	1.97 (1.58, 2.42)	< 0.001
PT(s)	16 (14, 20)	15 (13, 18)	18 (15, 21)	21 (17, 26)	< 0.001
APTT(s)	35 (29, 45)	32 (27, 41)	36 (30, 48)	44 (37, 54)	< 0.001
ALT(IU/L)	31 (17, 71)	26 (15, 52)	37 (19, 108)	64 (27, 425)	< 0.001
AST(IU/L)	54 (26, 152)	39 (22, 91)	70 (41, 214)	163 (56, 910)	< 0.001
TBIL(mg/dl)	1.2 (0.6, 3.5)	0.9 (0.5, 2.3)	1.6 (0.7, 4.9)	3.3 (1.2, 8.4)	< 0.001
Creatinine (mg/dl)	1.35 (0.87, 2.43)	1.20 (0.80, 2.30)	1.37 (0.90, 2.37)	1.90 (1.14, 2.83)	< 0.001
BUN (mg/dl)	33 (20, 55)	32 (19, 56)	35 (22, 55)	32 (25, 48)	0.248
SOFA	7.0 (4.0, 11.0)	6.0 (3.0, 9.0)	8.0 (5.0, 11.0)	12.0 (8.0, 15.0)	< 0.001
SIRS	3.00 (2.00, 3.00)	3.00 (2.00, 3.00)	3.00 (2.00, 4.00)	3.00 (3.00, 4.00)	< 0.001
Treatment					
CRRT, *n*(%)	176 (14.5%)	640 (89.6%)	303 (85.4%)	91 (64.5%)	< 0.001
MV, *n*(%)	1,014 (83.8%)	586 (82.1%)	305 (85.9%)	123 (87.2%)	0.138
Clinical outcome					
Hospital stay	12 (6, 23)	11 (6, 21)	15 (7, 26)	12 (5, 23)	0.003

Table 1 (continued)

Variables	Total (*n*=1210)	Q1 (*n*=224) LAR < 0.8	Q2(*n*=355) 0.8 ≤ LAR < 1.64	Q3(*n*=141)LAR ≥ 1.64	*p*-value
ICU stay	4 (2, 7)	3 (2, 6)	4 (2, 9)	4 (2, 10)	< 0.001
Hospital mortality	481 (29.6%)	183 (25.6%)	145 (40.8%)	85 (60.3%)	< 0.001
ICU mortality	353 (21.7%)	124 (17.4%)	110 (31.0%)	73 (51.8%)	< 0.001
28 d mortality	302 (18.6%)	106 (14.8%)	100 (28.2%)	74 (52.5%)	< 0.001
90 d mortality	396 (24.4%)	149 (20.9%)	129 (36.3%)	79 (56.0%)	< 0.001
365 d mortality	434 (26.7%)	166 (23.2%)	136 (38.3%)	81 (57.4%)	< 0.001

SBP systolic blood pressure, *DBP* diastolic blood pressure, *MAP* mean arterial pressure, *HR* Heart rate, *RR* Respiratory rate, *AKI* acute kidney injury, *HF* Heart Failure, *MI* Myocardial Infarction, I*HD* Ischemic Heart Disease, *RDW* erythrocyte distribution width, *RBC* red blood cell continuous renal replacement therapy, *WBC* white blood cell, *ALB* Albumin, *AG* Anion Gap, *TCa* total calcium, *INR* international normalized ratio, *PT* prothrombin time, *APTT* Activated Partial Thromboplastin Time, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *TBIL* Total Bilirubin, *BUN* Blood Urea Nitrogen, *SOFA* Sepsis-Related Organ Failure Assessment Score, *SIRS* Systemic Inflammatory Response Syndrome, *LAR* lactate-to-albumin ratio, *MV* mechanical ventilation, *CRRT* Continuous Renal Replacement Therapy

Table 2 Association between LAR and mortality in Gastrointestinal bleeding

Variable	Model 1		Model 2		Model 3	
	HR(95%CI)	*P*-value	HR(95%CI)	*P*-value	HR(95%CI)	*P*-value
28-day mortality						
LAR(continuous)	1.60(1.50, 1.71)	< 0.001	1.60(1.50, 1.71)	< 0.001	1.45(1.33, 1.58)	< 0.001
LAR(quartiles)						
Q1	1		1		1	
Q2	2.08(1.58,2.73)	< 0.001	2.12(1.61, 2.79)	< 0.001	1.48(1.10,1.97)	< 0.001
Q3	4.94(3.67,6.65)	< 0.001	5.22(3.86,7.04)	< 0.001	3.02(2.14, 4.24)	< 0.001
P for trend		< 0.001		< 0.001		< 0.001
90-day mortality						
LAR(continuous)	1.58(1.47, 1.68)	< 0.001	1.58(1.48, 1.69)	< 0.001	1.42(1.31, 1.54)	< 0.001
LAR(quartiles)						
Q1	1		1		1	
Q2	1.95(1.54, 2.47)	< 0.001	1.97(1.56, 2.50)	< 0.001	1.32(1.03, 1.69)	0.029
Q3	3.95(3.01, 5.19)	< 0.001	4.12(3.13, 5.43)	< 0.001	2.29(1.68, 3.11)	< 0.001
P for trend		< 0.001		< 0.001		< 0.001
365-day mortality						
LAR(continuous)	1.56(1.46, 1.67)	< 0.001	1.57(1.47, 1.67)	< 0.001	1.29(1.29, 1.53)	< 0.001
LAR(quartiles)						
Q1	1		1		1	
Q2	1.86(1.48, 2.33)	< 0.001	1.88(1.50, 2.36)	< 0.001	1.28(1.00, 1.62)	0.047
Q3	3.68(2.82, 4.81)	< 0.001	3.83(2.93, 5.01)	< 0.001	2.16(1.60, 2.92)	< 0.001
P for trend		< 0.001		< 0.001		< 0.001

Model 1 : no covariates were adjusted

Model 2 : adjusted for Age and Gender

Model 3 : adjusted for Age, Gender, RACE, Temperature, Platelet, INR, BUN, SIRS, Sepsis, AKI, Cirrhosis, CRRT, MV

lactate, ALB, and the conventional AIMS65 score (AUCs of 0.644, 0.637, and 0.630, respectively), indicating the superior standalone prognostic value of LAR.

Furthermore, integrating LAR with existing scoring systems enhanced predictive performance. The addition of LAR to the AIMS65 model increased the AUCs to 0.710 (28-day), 0.694 (90-day), and 0.684 (365-day), suggesting that LAR provides incremental prognostic value beyond traditional scores. Similarly, combining LAR with the SOFA score further improved predictive accuracy, with the SOFA + LAR model achieving AUCs of 0.741, 0.723, and 0.719 for 28-day, 90-day, and 365-day mortality, respectively (Table 3; Fig. 3).

Decision curve analysis

Supplementary Fig. 1 presents the DCA comparing SOFA alone with SOFA + LAR across three follow-up periods (28-day, 90-day, and 365-day). At all time points, the SOFA + LAR model showed a superior net benefit compared to the SOFA score alone. These findings suggest that incorporating LAR into the SOFA scoring system improves mortality risk stratification and enhances clinical utility.

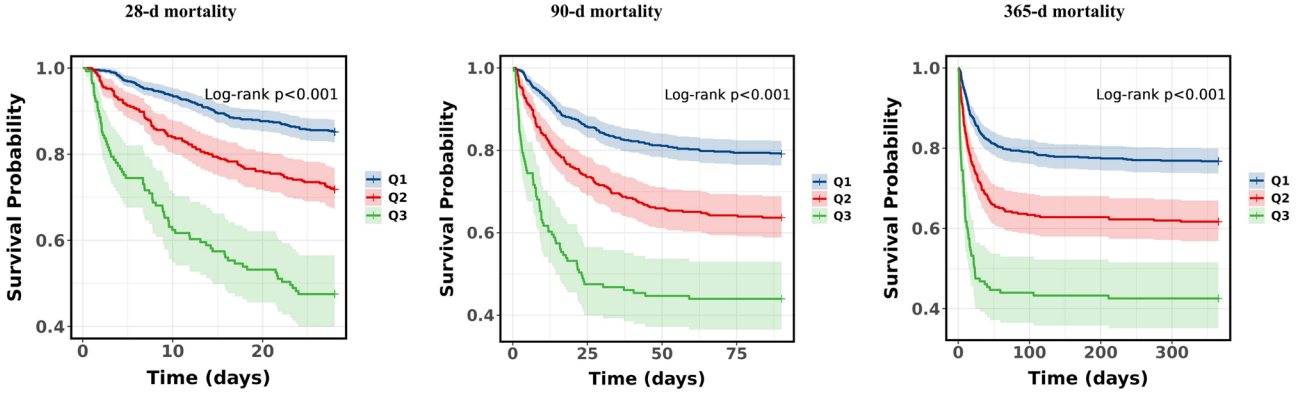

Fig. 2 K-M survival analysis curves for all-cause mortality in patients with GIB at 28-day (**A**), 90-day (**B**), and 365-day (**C**) of hospital admission

Association between LAR and GIB prognosis: a restricted cubic spline analysis

To explore potential nonlinear relationships, RCS regression analysis was conducted. Results showed a significant linear correlation between LAR and adverse GIB prognosis (P -nonlinear > 0.05 at all time points, P -overall < 0.001). This correlation persisted across follow - up intervals at 28, 90, and 365 days. As LAR levels increased, clinical outcomes worsened. Figure 4 presents the RCS curves illustrating this relationship.

Subgroup analyses of LAR on clinical outcomes in GIB patients

Stratified subgroup analyses were performed across prespecified variables, including age, sex, race, sepsis, diabetes, cirrhosis, CRRT, and mechanical ventilation, to assess potential interaction effects. Results indicated that LAR showed consistent predictive performance across all subgroups (P for interaction > 0.006), highlighting its robustness as a reliable prognostic biomarker. Detailed comparisons of subgroup analyses are presented in Fig. 5.

Predictor screening and nomogram model construction

To create a clinically useful predictive model, the Boruta machine - learning algorithm was employed to identify 5 key prognostic factors: SOFA score, LAR, APTT, sepsis status, and blood urea nitrogen (Supplementary Fig. 2). Incorporating these factors into a nomogram enabled the prediction of individual survival rates at 28, 90, and 365 days (Fig. 6). The reliability of the model was confirmed by ROC analysis, which yielded AUC values of 0.780 (95% CI: 0.750–0.811), 0.777 (95% CI: 0.749–0.805), and 0.773 (95% CI: 0.745–0.800) for mortality at those time points, respectively, indicating high predictive accuracy. The nomogram's ROC curve is presented in Supplementary Fig. 3.

To further assess the model's internal validity and discriminative consistency, non-parametric bootstrap resampling with 1,000 iterations was performed. The bias-corrected Harrell's concordance indices (C-indices) were 0.776, 0.772, and 0.768 for 28-day, 90-day, and 365-day mortality, respectively, indicating stable and reliable performance across all evaluated time points.

Calibration of the nomogram was assessed using calibration plots, which are presented in the revised Supplementary Fig. 4. These plots revealed close concordance between predicted and observed outcomes, confirming the accuracy and reliability of the model's calibration.

Discussion

Our results identify the LAR as a standalone predictor for both short-term and long-term all-cause mortality in critically ill patients with GIB. Kaplan–Meier survival analysis demonstrated significantly poorer outcomes among patients with elevated LAR (P < 0.001), while restricted cubic spline modeling confirmed a linear relationship between LAR and mortality risk. Subgroup analyses revealed no significant interaction effects, indicating consistent prognostic performance across diverse clinical strata. LAR alone exhibited moderate discriminative ability, with AUC values exceeding those of lactate or albumin individually and closely approximating the predictive performance of the AIMS65 score. Importantly, when LAR was integrated with AIMS65, the combined model yielded superior prognostic accuracy compared to AIMS65 or SOFA score alone. These findings support the utility of LAR as a clinically accessible and physiologically meaningful biomarker that enhances risk stratification in critically ill GIB populations.

In recent years, several prognostic indicators have been proposed for critically ill GIB patients, including red blood cell distribution width (RDW) [17], serum anion gap [18], and the hemoglobin-to-RDW ratio [19]. Although these markers show promise, their routine use in clinical prognostication remains limited. There is therefore an ongoing need for simpler, more accessible, and clinically actionable biomarkers to facilitate early risk stratification and guide timely interventions.

Table 3 Information of ROC curves in Fig. 3

Variable	AUC(%)	95%CI(%)	Threshold	Sensitivity	Specificity
28-d					
LAR	0.681	0.645–0.717	0.801	0.621	0.660
Lactate	0.669	0.631–0.706	2.400	0.575	0.690
Albumin	0.563	0.523–0.603	2.550	0.411	0.729
SOFA	0.730	0.696–0.763	10.000	0.582	0.754
SOFA + LAR	0.741	0.708–0.775		0.221	0.966
AIMS65	0.644	0.610–0.679	3.000	0.418	0.783
AIMS65 + LAR	0.709	0.675–0.744		0.975	0.135
90-d					
LAR	0.664	0.631–0.698	0.801	0.583	0.669
Lactate	0.649	0.614–0.683	2.380	0.541	0.696
Albumin	0.569	0.532–0.605	2.550	0.392	0.734
SOFA	0.712	0.680–0.743	8.000	0.695	0.613
SOFA + LAR	0.723	0.692–0.754		0.246	0.927
AIMS65	0.637	0.605–0.669	3.000	0.398	0.792
AIMS65 + LAR	0.694	0.661–0.726		0.946	0.137
365-d					
LAR	0.653	0.619–0.686	0.801	0.567	0.670
Lactate	0.635	0.602–0.669	2.38	0.517	0.693
Albumin	0.572	0.536–0.607	2.550	0.397	0.740
SOFA	0.710	0.679–0.741	8.000	0.684	0.618
SOFA + LAR	0.719	0.688–0.749		0.274	0.920
AIMS65	0.630	0.598–0.662	3.000	0.386	0.793
AIMS65 + LAR	0.684	0.652–0.716		0.935	0.154

ROC receiver operating characteristic, *AUC* area under the curve, *CI* confidence interval, *LAR* Lactate-to-albumin ratio, *SOFA* Sepsis-related Organ Failure Assessment score, *AIMS65* Albumin, INR, Mental status, Systolic blood pressure, and Age ≥ 65 years

The prognostic value of LAR has been validated across diverse conditions. In sepsis, LAR outperformed lactate and albumin alone in predicting ICU mortality (AUC: 0.869 vs. 0.816 and 0.812) [20]. In acute myocardial infarction, each one-unit increase in LAR was associated with a 2.15-fold rise in 28-day mortality (HR = 2.15; 95% CI: 1.64–2.83) [21]. In GIB specifically, a retrospective study demonstrated that LAR surpassed both the BUN-to-albumin ratio and AIMS65 in predicting ICU admission and in-hospital mortality [22].

The pathophysiological rationale linking elevated LAR to poor outcomes in GIB involves hypovolemia-induced hypoperfusion, anaerobic lactate production [23–25], and impaired lactate clearance due to hepatic dysfunction [26, 27]. Elevated lactate levels have consistently been associated with adverse outcomes in GIB [28, 29], and their clearance reflects resuscitation efficacy [30]. Meanwhile, inflammation-induced vascular leakage and hypoalbuminemia—exacerbated by hepatic dysfunction, malnutrition, and catabolism [31–34]—contribute to systemic decompensation.

Thus, LAR serves not only as a static marker of illness severity but also as a dynamic indicator of perfusion status and physiological reserve. Its clinical utility extends to triage, prognosis, and potentially guiding fluid and albumin therapy in GIB patients.

Although this study employed a prognostic modeling framework, we acknowledge that certain modifiable factors, such as lactate levels and albumin concentration, may be influenced by therapeutic interventions. The emerging method of Target Trial Emulation (TTE) [35, 36] provides a promising approach for simulating randomized controlled trials using observational data. This is particularly relevant in critically ill populations, where conducting randomized trials presents substantial logistical and ethical challenges. By adopting the TTE approach, future studies could more accurately replicate real-world clinical decision-making, offering deeper insights into the causal effects of potential interventions in the management of GIB.

Although this study leveraged large-scale real-world data from the MIMIC-IV database, several limitations must be acknowledged. First, the absence of a standardized gastrointestinal bleeding severity grading system precluded stratified analyses across clinically distinct subgroups, potentially obscuring severity-dependent prognostic patterns. Second, key clinical variables, such as bleeding etiology (e.g., variceal vs. non-variceal), anatomical location (upper vs. lower gastrointestinal tract), endoscopic intervention details, and transfusion data, were not available in the database. This limitation restricted our ability to conduct more refined prognostic assessments focusing on etiology, treatment interventions, or resuscitation strategies. Moreover, due to the significant heterogeneity of GIB patients with respect to etiology, disease severity, and prognosis, this study did not perform analyses in more specific clinical subgroups. Existing studies [37, 38] have proposed methods for subtype identification, which could help further refine

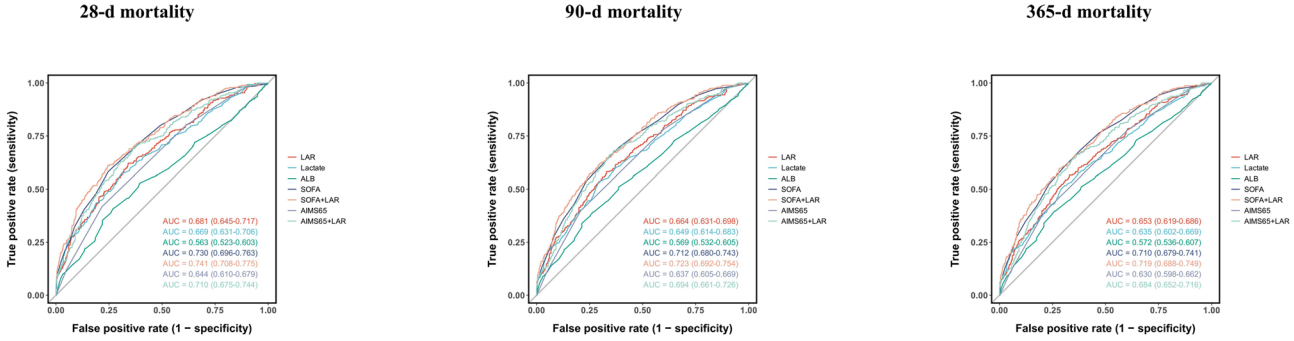

Fig. 3 ROC curves for predicting all-cause mortality in patients with GIB at 28-d (**A**), 90-d (**B**) and 365-d (**C**) of hospital admission

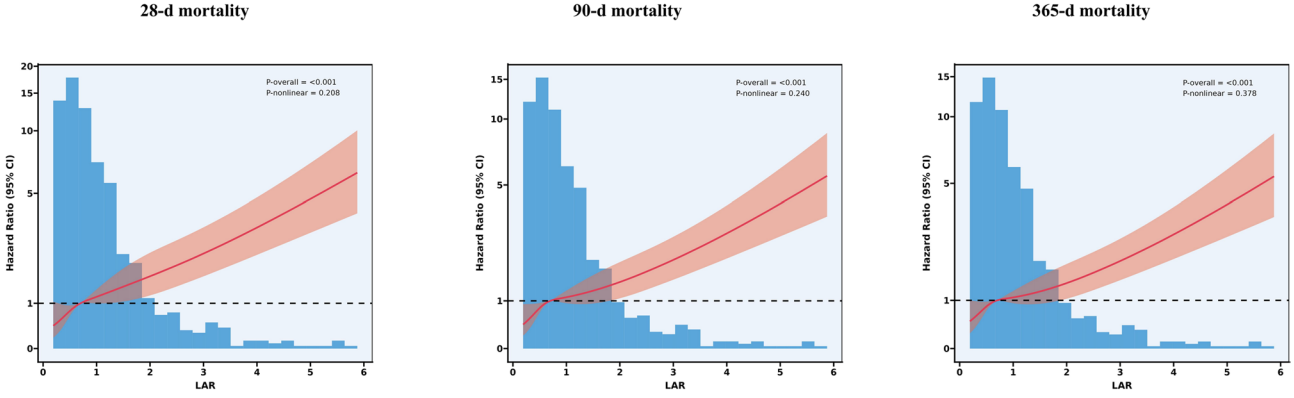

Fig. 4 Association between LAR and Survival with the RCS function at 28-d (**A**), 90-d (**B**), and 365-d (**C**) after admission

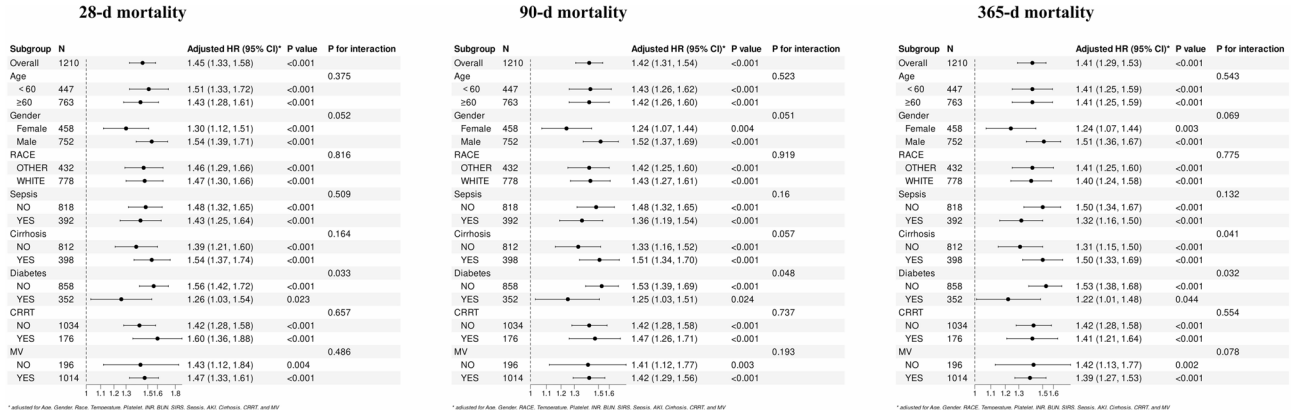

Fig. 5 Forest plots of subgroup analysis of the relationship between all-cause mortality and LAR in patients with GIB admitted 28-d (**A**), 90-d (**B**), and 365-d (**C**)

the classification of clinical subgroups, thereby improving prognostic accuracy. Future research should adopt these methods, stratifying patients based on bleeding etiology and anatomical site to more precisely assess the accuracy of prognostic models and explore the role of the LAR in different clinical subgroups. Third, the study focused on static LAR measurements, which may limit the prognostic precision. Dynamic LAR measurements, which can track changes in lactate and albumin levels over time, could provide a more comprehensive risk assessment. Future studies should consider incorporating dynamic LAR to evaluate evolving mortality risk and enhance the prognostic utility of LAR in critically ill GIB patients. Finally, the retrospective, registry-based design introduces inherent risks of selection bias and residual confounding, which may limit the generalizability of our findings despite rigorous statistical adjustments.

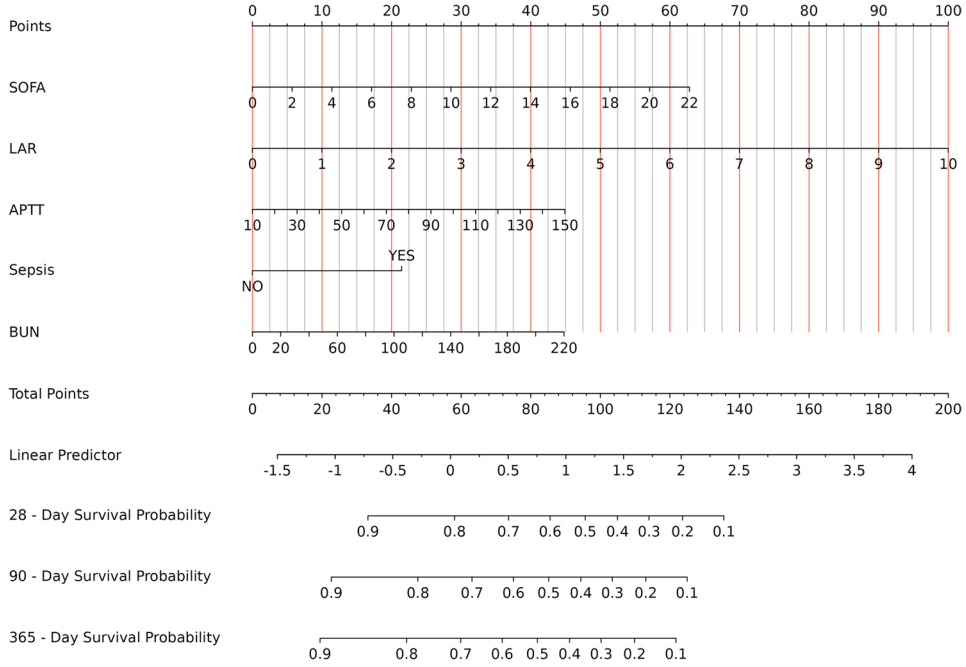

Fig. 6 Nomogram for Assessing Mortality Risk in Critical GIB

Conclusion

Our results demonstrate that the LAR exhibits significant associations with both short- and long-term mortality in critically ill patients with gastrointestinal bleeding, suggesting its potential as a prognostic biomarker for GIB. However, further large-scale, prospective multicenter studies are warranted to validate its clinical applicability.

Abbreviations

LAR	lactate-to-albumin ratio
GIB	gastrointestinal bleeding
K-M	Kaplan-Meier
ROC	receiver operating characteristic
DCA	Decision curve analysis
MODS	multi-organ dysfunction syndrome
ICU	intensive care unit
WBC	white blood cell
BUN	blood urea nitrogen
Cr	creatinine
TB	total bilirubin
ALB	albumin
AST	aspartate aminotransferase
ALT	alanine aminotransferase
APTT	activated partial thromboplastin time
INR	international normalized ratio
AG	anion gap
RDW	red cell distribution width
SOFA	Sequential Organ Failure Assessment score
AKI	acute kidney injury
HF	heart failure
MI	myocardial infarction
IHD	ischemic heart disease
CRRT	continuous renal replacement therapy
MV	mechanical ventilation
HR	hazard ratios
AUC	area under the curve

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-04244-9.

Supplementary Material 1. DCA curves for SOFA versus SOFA+LAR in patients with GIB at 28-d, 90-d, and 365-dof hospital admission.

Supplementary Material 2. The feature importance analysis based on Boruta pinpoints critical predictors for 28-day mortality in GIB patients.

Supplementary Material 3. The nomogram's ROC curve at 28-d, 90-d, and 365-dafter hospital admission for patients with GIB.

Supplementary Material 4. Calibration curves for the nomogram at 28-d, 90-d, and 365-dafter hospital admission for patients with GIB.

Supplementary Material 5.

Acknowledgements
Not applicable.

Authors' contributions
XY.Y and J.Y, LH.L wrote the main manuscript text. SS.Y and XS.Y prepared Figs. 1, 2, 3, 4, 5 and 6. JQ.Y prepared Tables 1, 2 and 3 and S1-4. All authors reviewed the manuscript.

Funding
The authors declare that they received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate
This database was approved by the Institutional Review Board of the Beth Israel Denconess Medical center (2001P-001699/14). All personal identifiers have been de-identified, with real patient data replaced by randomly assigned numbers. Consequently, the need for ethical approval and informed consent

was waived. Our research was conducted in accordance with the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 18 June 2025 / Accepted: 11 August 2025
Published online: 26 September 2025

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