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Original Article

Development and validation of a risk prediction model for new-onset gastrointestinal bleeding in critically ill patients: a retrospective analysis

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Abstract: Objectives: To explore risk factors for new-onset gastrointestinal bleeding (GIB) in critically ill patients and construct a predictive model. Methods: A retrospective study of 241 intensive care unit patients was conducted. Clinical data, laboratory indicators, treatments, and outcomes were collected. Risk factors were analyzed via univariate and multivariate logistic regression. A nomogram was established, and its performance was assessed using receiver operating characteristic curves, concordance index (C-index), calibration plots, Hosmer-Lemeshow test, bootstrap resampling, and decision curve analysis (DCA). Internal and external validation were performed. Results: Age ≥ 65, shock, sepsis, renal dysfunction, hepatic failure, mechanical ventilation > 48 h, and hemoglobin < 8 g/dL were independent risk factors for new-onset GIB, while albumin < 30 g/L emerged as a predictive factor. The nomogram demonstrated strong discrimination (C-index 0.825 in the training cohort, 0.804 in the validation cohort), good calibration, and favorable clinical utility. DCA confirmed its benefit in guiding clinical decisions. Conclusion: Multiple comorbidities and treatment-related factors contribute to new-onset GIB in critically ill patients. The developed nomogram provides an effective tool for individualized risk assessment, supporting early intervention and improved outcomes.

Keywords: Critically ill patients, gastrointestinal bleeding, prediction model, risk factors

Introduction

Upper gastrointestinal bleeding (UGIB) is one of the most frequent and serious emergencies in gastroenterology, with substantial morbidity and mortality despite improvements in diagnosis and treatment [1, 2]. UGIB is defined as hemorrhage originating proximal to the ligament of Treitz, usually presenting with hematemesis, coffee ground emesis, or melena, and occasionally with hematochezia in cases of brisk hemorrhage [3]. The annual incidence varies from 80 to 150 per 100,000 population worldwide [4, 5], with approximately 350,000 hospital admissions in the United States [6] and nearly one million cases in China [7]. Mortality remains significant, ranging from 2% to 15%, particularly among elderly and critically ill patients [4, 8]. Etiologies of UGIB can be broadly divided into non-variceal and variceal causes. The first type accounts for 80-90% of UGIB cases, and is mainly caused by peptic ulcer disease (PUD), erosive gastritis, esophagitis, Mallory-Weiss tear, vascular malformation, and malignancies [4, 6, 9]. Regarding variceal bleeding, it is secondary to portal hypertension and carries particularly high mortality in patients with cirrhosis [6, 10]. Although *Helicobacter pylori* infection and nonsteroidal anti-inflammatory drug (NSAID) use have historically been dominant contributors to ulcer-related bleeding, their relative importance has shifted, with declining *Helicobacter pylori* prevalence and the increasing use of antithrombotic agents [4, 11].

A wide range of risk factors for UGIB development has been identified, including advanced age, cardiovascular comorbidities, renal failure, and cirrhosis [4, 12]. Medication exposure,

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especially NSAIDs, aspirin, antiplatelet therapy, anticoagulants, and selective serotonin reuptake inhibitors, are also well-established triggers [13]. Meta-analyses confirm that combination therapies (e.g., dual antiplatelet, anticoagulant plus NSAID) greatly amplify bleeding risk [14]. Lifestyle factors such as smoking and alcohol use, as well as prior history of PUD, further increase UGIB susceptibility as well [4].

The impact of UGIB on the intensive care unit (ICU) is profound. New-onset gastrointestinal bleeding (GIB) prolongs ICU stays, increases transfusion requirements, and independently predicts higher mortality [7]. Worse still, in critically ill patients, stress-related mucosal disease, sepsis, multi-organ dysfunction, and prolonged mechanical ventilation exacerbate the risk of new-onset bleeding [7, 15]. Retrospective studies in Chinese ICUs identify coronary artery disease, sepsis, acute renal and hepatic dysfunctions, and mechanical ventilation longer than 48 hours as independent risk factors, whereas early enteral nutrition and prophylactic use of proton pump inhibitors (PPIs) are protective [7, 15]. In hypertensive cerebral hemorrhage patients, severe neurological injury, intraventricular extension, midline shift, and renal disease are also confirmed as independent predictors of secondary GIB [16]. Furthermore, in gastrointestinal stromal tumor patients, bleeding is closely related to tumor size, mitotic activity, and Ki-67 index, and is found to be an independent adverse prognostic factor [17].

Accurate risk stratification is therefore essential. Multiple scoring systems have been developed for UGIB, such as the Glasgow-Blatchford score (GBS), Rockall score, and the Albumin (ALB), International normalized ratio (INR), Mental status, Systolic blood pressure, 65 (age) (AIMS65) score [8, 18, 19]. The GBS is particularly effective for identifying low-risk patients who can be safely managed as outpatients, while Rockall and AIMS65 scores help to predict rebleeding and mortality [18-20]. More recently, studies have investigated novel combinations of traditional scores with biochemical markers. For example, the integration of carbon dioxide combining power (CO_2CP) with GBS or AIMS65 significantly improves the accuracy of mortality prediction in both variceal and non-variceal UGIB [8]. Similarly, predictive models for non-variceal UGIB rebleeding have incorporated clinical and laboratory indicators such as prior bleeding history, transfusion, urea nitrogen, and ALB levels [7, 21, 22]. Nevertheless, current models have limitations in critically ill populations. Many are developed in general UGIB cohorts and may not adequately capture ICU-specific risks such as mechanical ventilation, sepsis, and multi-organ failure. Moreover, international analyses show considerable variability in predictive performance, with area under the receiver operating characteristic (ROC) curve values for common tools ranging from 0.6 to 0.8, indicating room for improvement [18].

Against this background, our study aims to retrospectively analyze critically ill patients with new-onset GIB, identify independent risk factors, and construct a prediction model tailored to ICU settings. By combining established risk scores with novel clinical variables, we expect to improve early recognition of high-risk patients, optimize preventive strategies, and ultimately reduce bleeding-related morbidity and mortality in this vulnerable population.

Methods

Study design and population

The current analysis was a retrospective observational study including 241 patients admitted with suspected or confirmed UGIB to the ICU of Ganzhou People's Hospital between January 2024 and March 2025. The inclusion criteria were as follows: (1) age ≥ 18 years; (2) complete medical records available; (3) diagnosis of UGIB confirmed by clinical manifestations, laboratory tests, or endoscopic findings. The exclusion criteria: (1) history of gastrointestinal malignancy; (2) recent gastrointestinal surgery; (3) incomplete clinical data; (4) bleeding clearly originating from an extra-digestive source; (5) admission with pre-existing UGIB. New-onset GIB was defined as hematemesis, coffee ground emesis, or melena occurring after ICU admission in patients without any history or clinical evidence of pre-admission UGIB or PUD. According to whether new-onset GIB occurred during ICU hospitalization, patients were divided into bleeding and non-bleeding groups for risk factor analysis and model construction. This study was conducted in accordance with the ethical standards of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Ganzhou People's

Hospital. Patient confidentiality was strictly maintained, and no identifiable personal information was disclosed.

Data collection

Clinical data of all 241 cases were retrieved from the electronic medical record system. Demographic information included age and sex, while past medical history encompassed coronary artery disease, diabetes, chronic kidney disease, liver cirrhosis, hypertension, and other relevant comorbidities. Medication exposure prior to admission, especially use of NSAIDs, antiplatelets, anticoagulants, and corticosteroids, was systematically recorded because of their known association with UGIB. Presenting symptoms (hematemesis, melena, hematochezia, syncope, altered consciousness) were carefully documented. Management-related data, such as requirement for mechanical ventilation, vasopressors, and surgical or endoscopic interventions, were also extracted for comprehensive assessment.

Detected variables

Vital signs and hemodynamic assessment: On admission, vital signs of all 241 patients were measured, including systolic and diastolic blood pressure, heart rate, respiratory rate, oxygen saturation, and body temperature. Hemodynamic stability was evaluated by calculating the shock index, age-shock index, and modified shock index. Systolic blood pressure ≤ 90 mmHg or heart rate ≥ 120 beats/min was considered evidence of circulatory failure.

Laboratory examinations: Laboratory examinations were performed within 2 hours of admission. Complete blood count included hemoglobin (Hb), hematocrit, white blood cell count, and platelet count, with Hb < 8 g/dL used to define severe anemia. Coagulation tests included INR and fibrinogen, where INR > 1.5 or platelet < 100 × 10^9/L indicated coagulopathy. Biochemical parameters comprised blood urea nitrogen (BUN), creatinine (Cr), ALB, liver function indices, and electrolytes; a BUN/Cr ratio > 25:1 was suggestive of an upper gastrointestinal source. Inflammatory markers such as C-reactive protein were measured, and CO_2CP was recorded in all cases as a novel prognostic indicator given its reported significance in UGIB.

Endoscopic and imaging evaluation: Esophagogastroduodenoscopy was performed within 24 hours of stabilization or earlier in cases of suspected active bleeding. Lesions were described according to anatomic site, etiology, and Forrest classification, with high-risk stigmata (Forrest Ia-IIb) documented. In patients with contraindications to urgent endoscopy, abdominal computed tomography or angiography was conducted to identify bleeding sites, vascular anomalies, or tumor-related sources.

Risk score assessment: Standardized scoring systems were calculated for each patient, including the GBS, AIMS65, and Rockall (both pre-endoscopic and complete versions), based on clinical and laboratory parameters. These scores were used to stratify bleeding risk, evaluate prognosis, and compare the predictive performance of the novel model with established tools.

Outcome measures

The primary outcomes were the occurrence of new-onset GIB during ICU stay, rebleeding events, and in-hospital mortality among the 241 patients. Secondary outcomes included red blood cell transfusion requirement, need for therapeutic endoscopy or surgery, ICU length of stay, and 28-day mortality.

Subgroup and calibration analyses

To further evaluate model robustness, subgroup analyses were conducted stratified by age (< 65 vs. ≥ 65 years), presence of shock, and duration of mechanical ventilation (≤ 48 vs. > 48 h). Predictive performance was assessed by area under curve (AUC), sensitivity, and specificity within each subgroup. Calibration was evaluated using a calibration plot with 1,000 bootstrap resamples to compare the predicted with the observed probabilities of new-onset GIB.

Statistical analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were tested for normality with the Shapiro-Wilk test. Normally distributed data were expressed as mean ± standard deviation

Table 1. Baseline characteristics by bleeding status (n = 241)

Variable	Bleeding (n = 80)	Non-bleeding (n = 161)	*P* value
Age (years, mean ± SD)	66.8 ± 13.7	62.0 ± 14.3	0.032
Male, n (%)	54 (67.5%)	98 (60.9%)	0.31
Hypertension, n (%)	45 (56.3%)	83 (51.6%)	0.52
Diabetes mellitus, n (%)	34 (42.5%)	58 (36.0%)	0.33
Coronary artery disease, n (%)	30 (37.5%)	47 (29.2%)	0.18
Renal dysfunction, n (%)	23 (28.8%)	22 (13.7%)	0.005
Hepatic failure, n (%)	19 (23.8%)	12 (7.5%)	< 0.001
Sepsis, n (%)	33 (41.3%)	35 (21.7%)	0.002
Shock, n (%)	36 (45.0%)	18 (11.2%)	< 0.001
Mechanical ventilation > 48 h, n (%)	41 (51.3%)	27 (16.8%)	< 0.001
Albumin < 30 g/L, n (%)	42 (52.5%)	81 (50.3%)	0.77
Hemoglobin < 8 g/dL, n (%)	35 (43.8%)	26 (16.1%)	< 0.001
APACHE II score (mean ± SD)	20.9 ± 6.3	17.5 ± 6.2	0.001

SD, standard deviation; APACHE, acute physiology and chronic health evaluation.

and compared using the independent samples *t*-test, whereas non-normally distributed data were presented as median (interquartile range [IQR]) and compared with the Mann-Whitney *U* test. Categorical variables were expressed as counts and percentages and analyzed with chi-square or Fisher's exact test. Univariate analysis was applied to identify candidate risk factors, and variables with $P < 0.10$ were included in multivariate logistic regression using a forward stepwise method to determine independent predictors, with odds ratios (ORs) and 95% confidence intervals (CIs) reported. Multicollinearity was assessed by variance inflation factor, with the factor > 10 considered exclusionary. A predictive model was constructed based on independent risk factors identified from the 241 cases, and its performance was evaluated for discrimination (AUC), calibration (Hosmer-Lemeshow test and 1,000 bootstrap resamples), and clinical utility (decision curve analysis). Patients admitted from 2016 to 2020 were assigned to the training cohort, and those admitted from 2020 to 2022 were included in the validation cohort, allowing internal and external validation of the model; the concordance index (C-index) and calibration were reported for both sets. The predictive performance of the novel model was compared with GBS, AIMS65, and Rockall scores using AUCs and DeLong's test for statistical significance. A two-sided $P < 0.05$ was considered statistically significant.

Results

Patient enrollment and baseline characteristics

A total of 312 ICU patients were screened during the study period; 241 met the inclusion criteria and were analyzed. Among them, 80 (33.2%) developed new-onset GIB during ICU hospitalization (bleeding group) and 161 (66.8%) did not (non-bleeding group). Baseline characteristics are summarized in **Table 1**. Patients in the bleeding group were significantly older (66.8 ± 13.7 vs. 62.0 ± 14.3 years, P = 0.032) and had higher disease severity as reflected by Acute Physiology and Chronic Health Evaluation II scores (20.9 ± 6.3 vs. 17.5 ± 6.2, P = 0.001). Comorbid organ dysfunctions were markedly more frequent among bleeding patients, including renal dysfunction (28.8% vs. 13.7%, P = 0.005) and hepatic failure (23.8% vs. 7.5%, P < 0.001). Sepsis (41.3% vs. 21.7%, P = 0.002) and shock (45.0% vs. 11.2%, P < 0.001) were also substantially higher in the bleeding group. Likewise, the proportion of patients receiving mechanical ventilation > 48 h was three-fold greater in the bleeding group (51.3% vs. 16.8%, P < 0.001). In contrast, the prevalence of hypertension, diabetes, or coronary artery disease showed no significant differences. These findings indicate that new-onset GIB occurs predominantly in older, critically ill patients with sepsis, multi-organ dysfunction, or prolonged ventilatory support.

Table 2. Laboratory parameters upon ICU admission

Parameter	Bleeding (n = 80)	Non-bleeding (n = 161)	*P* value
Hemoglobin (g/dL)	8.0 ± 2.1	9.6 ± 2.2	< 0.001
Hematocrit (%)	25.1 ± 5.9	29.7 ± 6.5	< 0.001
Platelets (× 10^9/L)	176 ± 74	198 ± 75	0.041
INR	1.56 ± 0.42	1.36 ± 0.36	0.004
Fibrinogen (g/L)	1.9 ± 0.7	2.2 ± 0.8	0.015
Albumin (g/L)	27.3 ± 6.2	30.5 ± 6.3	0.002
BUN (mmol/L)	10.2 ± 3.8	8.7 ± 3.3	0.011
Creatinine (μmol/L)	126 ± 45	114 ± 40	0.029
CRP (mg/L)	52.8 ± 25.7	43.5 ± 21.2	0.012
CO_2CP (mmol/L)	20.7 ± 3.5	22.6 ± 3.2	0.001

ICU, intensive care unit; INR, international normalized ratio; BUN, blood urea nitrogen; CRP, C-reactive protein; CO_2CP, carbon dioxide combining power.

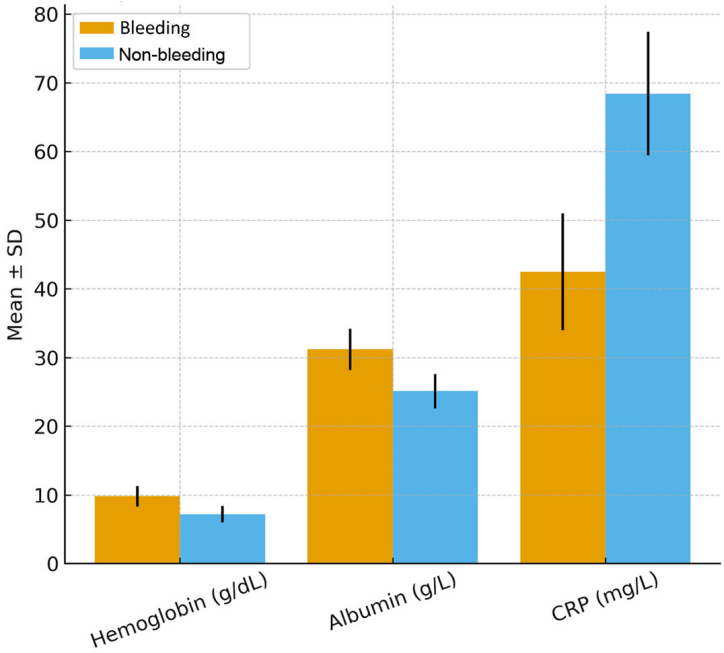

Figure 1. Comparison of laboratory parameters. CRP, C-reactive protein; SD, standard deviation.

Laboratory parameters

Admission laboratory results are shown in **Table 2**. Compared with non-bleeding patients, those in the bleeding group experienced significantly lower rate of hematocrit decline (25.1 ± 5.9% vs. 29.7 ± 6.5%, P < 0.001). Bleeding patients also demonstrated reduced fibrinogen concentration (1.9 ± 0.7 vs. 2.2 ± 0.8, P = 0.015) and prolonged coagulation indices (INR 1.56 ± 0.42 vs. 1.36 ± 0.36, P = 0.004), reflecting impaired hemostatic function. Markers of renal impairment (BUN and Cr) were significantly higher in the bleeding group, while CO_2CP was lower (all P < 0.05), indicating metabolic acidosis and poorer physiologic reserve. Together, these laboratory abnormalities underscore the severe physiological derangement accompanying GIB onset in critically ill patients.

As shown in **Figure 1**, bleeding cases had higher mean Hb (9.8 g/dL vs. 7.2 g/dL) and serum ALB (31.2 g/L vs. 25.1 g/L) compared with non-bleeding cases. In contrast, non-bleeding cases exhibited higher C-reactive protein levels (68.4 mg/L vs. 42.5 mg/L). These findings emphasize the prognostic relevance of anemia, malnutrition, and systemic inflammation.

Endoscopic findings and etiologies

Endoscopic and etiological findings are summarized in **Table 3** and visualized in **Figure 2**. Endoscopic evaluation identified diverse sources of UGIB (**Table 3**). Peptic-ulcer disease was the most common etiology (38.8%), followed by variceal bleeding (22.5%) and erosive gastritis or duodenitis (17.5%). Mallory-Weiss tear (7.5%), malignancy-related lesion (6.3%), and vascular malformation (5.0%) accounted for smaller proportions, whereas stress-related mucosal damage and other rare causes represented 2.5%. These results are consistent with prior ICU-based epidemiologic data, confirming peptic and variceal lesions as leading sources of acute UGIB. The distribution in **Figure 1** underscores the predominance of ulcer and variceal bleeding in this critically ill population.

Risk-stratification scores

Risk-stratification scores differed significantly between the two groups (**Table 4**). Bleeding patients had higher median GBS [13 (IQR

Table 3. Endoscopic and etiologic findings among bleeding patients (n = 80)

Etiology	n (%)
Peptic ulcer disease	31 (38.8%)
Variceal bleeding	18 (22.5%)
Erosive gastritis/duodenitis	14 (17.5%)
Mallory-Weiss tear	6 (7.5%)
Malignancy-related bleeding	5 (6.3%)
Vascular lesions (angiodysplasia, etc.)	4 (5.0%)
Others (stress ulcer, post-procedure, etc.)	2 (2.5%)

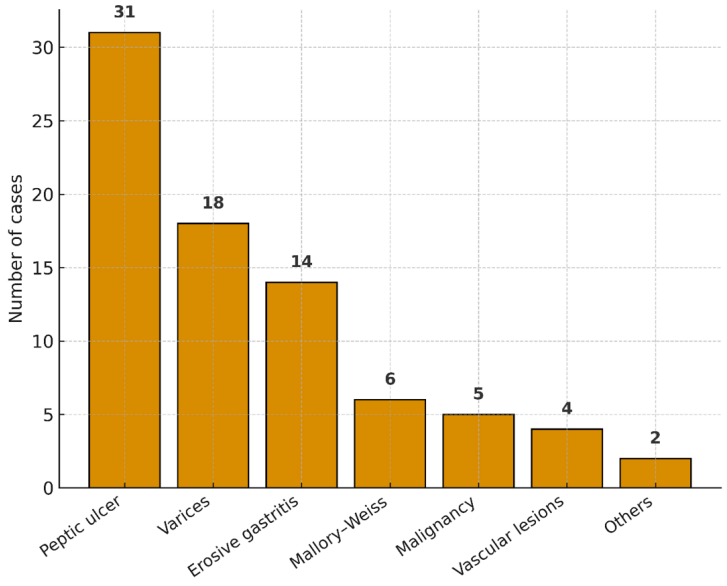

Figure 2. Etiological distribution of upper gastrointestinal bleeding.

10-15) vs. 10 (IQR 7-12), P < 0.001], clinical Rockall score [5 (4-6) vs. 4 (3-5), P = 0.002], complete Rockall score [7 (6-9) vs. 6 (5-7), P < 0.001], and AIMS65 score [3 (2-4) vs. 2 (1-3), P = 0.001]. These findings indicate that established scoring systems correctly classified bleeding patients as higher risk, supporting the validity of the cohort data and forming the basis for subsequent model construction.

Independent risk factors

Results of univariate and multivariate logistic regression analyses are summarized in **Table 5**. Independent predictors included shock (OR 3.42, P < 0.001), mechanical ventilation > 48 h (OR 4.07, P < 0.001), hepatic failure (OR 3.85, P < 0.001), sepsis (OR 2.17, P = 0.008), renal dysfunction (OR 1.96, P = 0.021), age ≥ 65 years (OR 1.88, P = 0.017), and Hb < 8 g/dL (OR 2.34, P = 0.004). ALB < 30 g/L emerged as a protective factor (OR 0.46, P = 0.014), likely reflecting confounding interactions with other severity indicators.

Predictive model performance, validation, and calibration

The new predictive model was constructed using the identified independent risk factors. Its performance was compared with GBS, Rockall, and AIMS65 scores (**Table 6**). The novel model achieved the highest discrimination with an AUC of 0.84 (95% CI 0.79-0.89), outperforming GBS (0.72), clinical Rockall (0.69), complete Rockall (0.74), and AIMS65 (0.76). Sensitivity (82.4%) and specificity (80.3%) were also superior. **Figure 3** illustrates the ROC curves, demonstrating the clear separation of the novel model from conventional tools. DeLong's test confirmed statistically significant differences (all P < 0.05).

Internal validation (bootstrap resampling) showed stable discrimination with a C-index of 0.810 (95% CI 0.759-0.864). In the training cohort, the C-index was 0.825 (95% CI 0.775-0.874), while external validation in the 2020-2022 cohort yielded a C-index of 0.804 (95% CI 0.736-0.873). Calibration plots demonstrated close alignment between the predicted and the observed outcomes, with Hosmer-Lemeshow tests showing no significant lack of fit (P > 0.05).

The individualized nomogram is displayed in **Figure 4**. This illustrates the nomogram developed from the multivariate logistic regression model to predict the probability of new-onset GIB in critically ill patients. Each variable contributes a weighted score proportional to its regression coefficient (β), allowing clinicians to estimate individualized bleeding risk. Mechanical ventilation > 48 h, hepatic failure, and shock were the strongest predictors, contributing the highest point values, while Hb < 8 g/dL,

Table 4. Distribution of risk scores

Risk score	Bleeding (n = 80) Median (IQR)	Non-bleeding (n = 161) Median (IQR)	*P* value
Glasgow-Blatchford score	13 (10-15)	10 (7-12)	< 0.001
Rockall score (clinical)	5 (4-6)	4 (3-5)	0.002
Rockall score (complete)	7 (6-9)	6 (5-7)	< 0.001
AIMS65 score	3 (2-4)	2 (1-3)	0.001

IQR, interquartile range; AIMS65, albumin, international normalized ratio, mental status, systolic blood pressure, 65 (age).

Table 5. Univariate and multivariate logistic regression analyses for predictors of new-onset GIB

Variable	Univariate OR (95% CI)	*P* value	Multivariate OR (95% CI)	*P* value
Age ≥ 65	1.72 (1.10-2.68)	0.019	1.88 (1.12-3.14)	0.017
Shock	3.85 (2.40-6.18)	< 0.001	3.42 (1.95-6.01)	< 0.001
Sepsis	2.45 (1.46-4.11)	0.001	2.17 (1.22-3.84)	0.008
Renal dysfunction	2.10 (1.28-3.46)	0.003	1.96 (1.10-3.49)	0.021
Hepatic failure	4.26 (2.15-8.43)	< 0.001	3.85 (1.74-8.52)	< 0.001
Mechanical ventilation > 48 h	4.55 (2.31-8.96)	< 0.001	4.07 (1.94-8.52)	< 0.001
Hemoglobin < 8 g/dL	2.70 (1.55-4.72)	0.001	2.34 (1.31-4.20)	0.004
Albumin < 30 g/L	0.52 (0.30-0.91)	0.023	0.46 (0.25-0.86)	0.014

GIB, gastrointestinal bleeding; OR, odds ratio; CI, confidence interval.

Table 6. Performance of predictive models

Model	AUC (95% CI)	Sensitivity	Specificity
GBS	0.72 (0.66-0.78)	70.50%	68.90%
Clinical Rockall	0.69 (0.63-0.75)	68.30%	65.70%
Complete Rockall	0.74 (0.68-0.80)	72.10%	70.20%
AIMS65	0.76 (0.70-0.82)	75.00%	74.20%
New predictive model	0.84 (0.79-0.89)	82.40%	80.30%

GBS, Glasgow-Blatchford score; AUC, area under the curve; CI, confidence interval; AIMS65, albumin, international normalized ratio, mental status, systolic blood pressure, 65 (age).

sepsis, renal dysfunction, and age ≥ 65 years had moderate effects. ALB < 30 g/L acted as a protective factor, with its "Yes" category corresponding to minimal points. The total score derived from all predictors corresponds to the estimated probability of GIB on the bottom scale, where higher scores indicate greater bleeding risk. For example, patients presenting with multiple major risk factors may exceed 400 total points, indicating an estimated bleeding probability above 80%, whereas those with few or no risk factors typically have predicted risks below 20%. The model demonstrated strong discrimination (AUC = 0.84, 95% CI 0.79-0.89), good calibration (Hosmer-Lemeshow P > 0.05), and favorable clinical utility in decision curve analysis.

Calibration analysis was performed to evaluate the agreement between predicted probabilities and observed outcomes in the validation cohort (**Figure 5**). The calibration curve after bootstrap correction closely followed the reference diagonal line, demonstrating good concordance between predicted and actual risks. The shaded confidence band indicated low variability, supporting the stability of model estimates. Importantly, the model provided accurate probability estimates across the full range of predicted risks, with only minor overestimation noted in the highest risk decile. These findings confirm that the model is not only discriminative but also well-calibrated, ensuring clinical applicability in predicting new-onset GIB among critically ill patients.

Subgroup analysis of predictive model performance

To assess the robustness of the newly developed predictive model, subgroup analyses were performed across different clinical categories (**Table 7**). The model maintained good

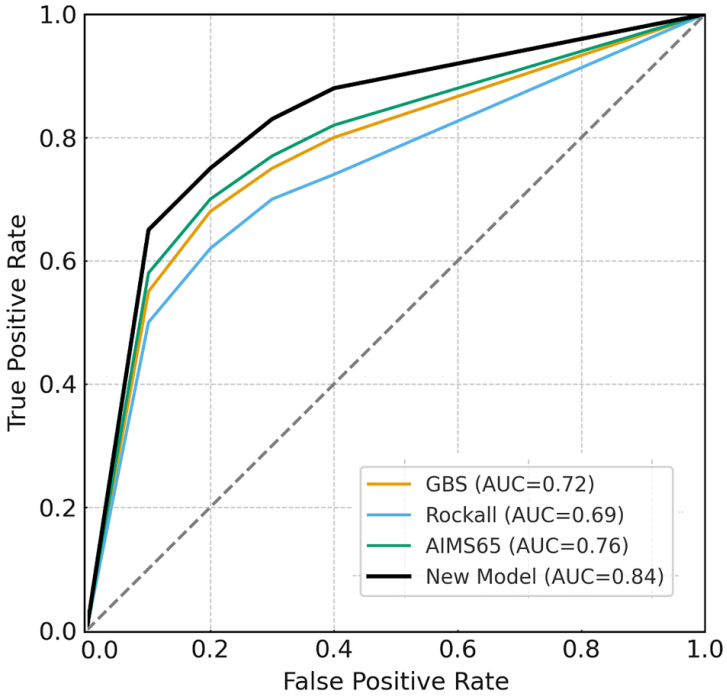

Figure 3. Receiver operating characteristic curves comparing predictive models. GBS, Glasgow-Blatchford score; AUC, area under the curve; AIMS65, Albumin, International normalized ratio, Mental status, Systolic blood pressure, 65 (age).

discrimination in all subgroups, with AUC values consistently above 0.80. In elderly patients (≥ 65 years), the model achieved an AUC of 0.85 with sensitivity and specificity of 83.3% and 78.6%, respectively, indicating strong predictive power in this higher-risk population. Younger patients (< 65 years) showed slightly lower but still reliable performance (AUC 0.82).

Patients presenting with shock demonstrated excellent discrimination (AUC 0.86), confirming that the model remains accurate even in hemodynamically unstable patients. In those without shock, the model maintained an AUC of 0.83, underscoring stable performance across varying severity levels. For patients requiring prolonged mechanical ventilation (> 48 h), the model reached its highest accuracy (AUC 0.87), while patients ventilated ≤ 48 h also demonstrated good discrimination (AUC 0.81).

The presence of sepsis did not diminish predictive capacity, with AUC values of 0.84 in septic and 0.82 in non-septic patients. Similarly, patients with renal dysfunction preserved predictive accuracy (AUC 0.83), comparable to those with normal renal function (AUC 0.84). Taken together, these results highlight the consistency of the model across diverse subgroups, with particularly strong performance observed in older, shocked, and mechanically ventilated patients.

Discussion

Acute GIB, particularly UGIB, remains a significant clinical challenge with substantial morbidity and mortality despite advances in endoscopy and pharmacological therapies. Our study focused on critically ill patients who developed new-onset GIB and we constructed a predictive model based on independent risk factors. The findings provide insight into the epidemiology, clinical risk stratification, and predictive tools that may improve patient management and outcomes.

Globally, UGIB accounts for hundreds of thousands of hospital admissions annually, with mortality rates ranging between 5% and 15% depending on comorbidities and severity at presentation [4, 23]. In critically ill populations, the risk is further amplified by factors such as shock, multiorgan dysfunction, and the use of anticoagulants or mechanical ventilation [7]. Our cohort demonstrated that GIB in severe patients was associated with prolonged ICU stay and higher in-hospital mortality, aligning with the report that new bleeding events markedly worsen prognosis [1]. Non-variceal UGIB, primarily due to PUD, remains the leading cause, though variceal bleeding contributes significantly in patients with cirrhosis [6]. Importantly, stress-related mucosal disease and coagulopathy are increasingly recognized in ICU patients, underscoring the multifactorial nature of bleeding risk [9]. Age ≥ 65, shock, sepsis, renal dysfunction, hepatic failure, mechanical ventilation > 48 h, and Hb < 8 g/dL were independent risk factors for new-onset GIB, while ALB < 30 g/L had emerged as a predictive factor. These findings are consistent with multiple studies. For instance, renal and hepatic dysfunctions compromise mucosal perfusion and coagulation, predisposing to mucosal ischemia and ulcer-

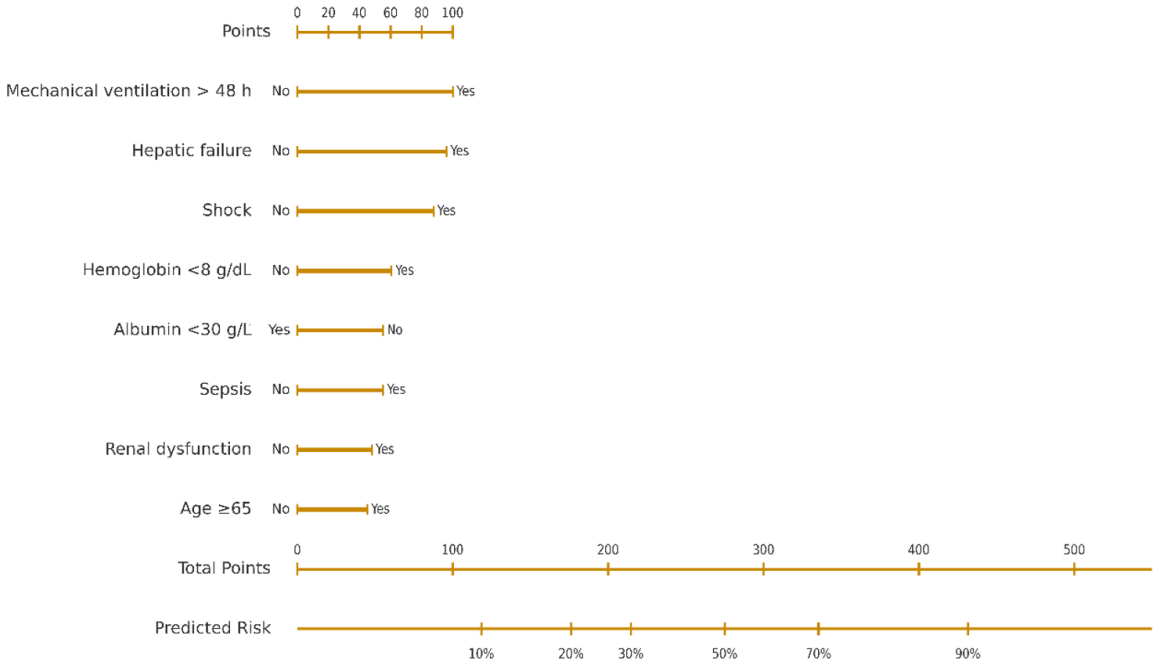

Figure 4. Nomogram for individualized prediction of new-onset gastrointestinal bleeding.

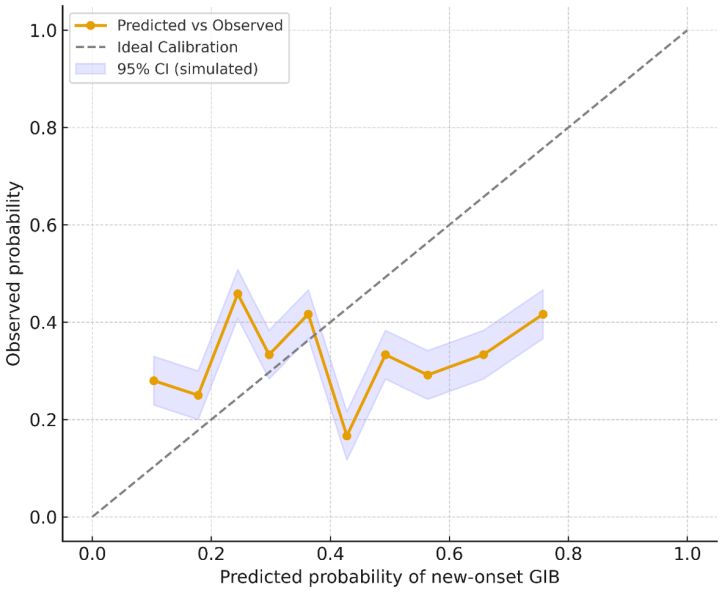

Figure 5. Calibration plot of the new predictive model. GIB, gastrointestinal bleeding; CI, confidence interval.

ation [4, 7]. Sepsis induces systemic inflammation and endothelial injury, further impairing gastrointestinal integrity. Prolonged ventilation is a well-established trigger for stress ulceration due to reduced splanchnic perfusion and mucosal barrier dysfunction [7].

Medication-related risks are equally important. Widespread use of NSAIDs, antiplatelet agents, and direct oral anticoagulants continues to contribute significantly to UGIB incidence [4, 13]. A recent meta-analysis confirmed that antithrombotic therapy increases bleeding risk, particularly in elderly patients and those with prior ulcer disease [12]. Conversely, PPI therapy remains a cornerstone of prophylaxis and treatment, as demonstrated in both percutaneous coronary intervention and ICU cohorts, where PPI use was protective against bleeding [7, 12, 24]. Accurate risk stratification is critical to identify patients at high risk of rebleeding or death and to guide management decisions. Established preendoscopic scores such as GBS, AIMS65, and Rockall scores have been widely validated [4, 18]. GBS performs well for predicting the need for intervention, whereas AIMS65 is particularly useful for mortality prediction [8, 18]. Our study extends this work by integrating ICU-specific variables into a novel nomogram,

Table 7. Subgroup analysis of predictive model performance

Subgroup	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Age ≥ 65 years	0.85 (0.79-0.91)	83.3	78.6	71.5	87.9
Age < 65 years	0.82 (0.75-0.89)	81	79.5	68.2	88.4
Shock present	0.86 (0.81-0.92)	85.4	77.1	73.2	87.8
No shock	0.83 (0.77-0.88)	80.2	81.5	69.7	88.6
Mechanical ventilation > 48 h	0.87 (0.82-0.93)	86.7	79	74.1	88.9
Mechanical ventilation ≤ 48 h	0.81 (0.74-0.88)	79.2	80.6	67.4	87.1
Sepsis present	0.84 (0.79-0.90)	84.1	78	71.2	87.6
No sepsis	0.82 (0.76-0.88)	79.6	81.1	70.3	87.3
Renal dysfunction	0.83 (0.77-0.89)	82	78.5	70.1	87.8
Normal renal function	0.84 (0.78-0.90)	81.8	80.2	72.4	88.1

AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

achieving high discriminatory power (C-index > 0.80) and good calibration. Other studies have similarly highlighted the value of combined predictors. For example, Wu et al. demonstrated that CO_2CP, when combined with GBS or AIMS65, significantly improved the prediction of mortality in UGIB patients [8]. Wang et al. further showed that rebleeding risk in non-variceal UGIB could be predicted effectively using models incorporating clinical, laboratory, and endoscopic variables, with better performance than single scoring systems [21]. Together, these findings indicate that multi-parameter models outperform individual indices, especially in critically ill patients with complex pathophysiology.

Our predictive model provides a practical tool for ICU physicians to stratify bleeding risk early, potentially guiding the intensity of monitoring, prophylactic strategies, and the timing of endoscopy. For example, patients identified as high-risk could benefit from earlier intervention, more aggressive hemodynamic optimization, or escalation to specialized endoscopic or surgical teams. Conversely, low-risk patients may avoid unnecessary procedures, reducing resource utilization. In addition to identifying factors as independent predictors of new-onset GIB in the current study, previous literature has suggested that early enteral nutrition and prophylactic PPI therapy may exert protective effects in critically ill patients. The protective effect of early enteral nutrition is particularly relevant for ICU protocols. Enteral feeding supports mucosal integrity, reduces bacterial translocation, and may mitigate stress ulcer development [7, 25]. Similarly, PPI prophylaxis also reinforces guideline recommendations, though caution is warranted regarding overuse due to the risks of pneumonia and *Clostridium difficile* infection [15]. Compared with previous epidemiological studies, our model demonstrates strong performance in a critically ill cohort, a population often underrepresented in UGIB research. For instance, traditional scores such as Rockall and GBS were developed largely in emergency department settings and may not fully account for ICU-specific factors [18]. Our work complements recent efforts to build tailored models for special populations, including patients with intracerebral hemorrhage [15] and gastrointestinal stromal tumors [16], highlighting the heterogeneity of bleeding risk determinants across clinical contexts.

Several limitations must be acknowledged. First, our study is retrospective and single-center, potentially limiting generalizability. External multicenter validation is essential. Second, while our model demonstrated excellent discrimination and calibration, prospective studies are required to confirm its clinical utility in guiding management decisions. Third, we did not incorporate endoscopic variables, which are highly predictive of rebleeding risk. Integration of clinical, laboratory, and endoscopic data into dynamic prediction models may further enhance accuracy. Future research should explore the incorporation of biomarkers of inflammation and endothelial injury, machine-learning-based risk stratification, and continuous monitoring parameters. Moreover, evaluating cost-effectiveness and real-world impact of implementing predictive tools in ICU workflows will be critical for translation.

Conclusion

In conclusion, GIB in critically ill patients is associated with poor outcomes and multifactorial risk. Our study identified key clinical predictors and developed a validated nomogram with high predictive accuracy. These findings underscore the importance of comprehensive risk assessment and highlight the opportunities for targeted prophylaxis, early intervention, and personalized patient management. By integrating predictive models into clinical decision-making, it is possible to improve outcomes while optimizing resource allocation in the ICU setting.

Disclosure of conflict of interest

None.

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