

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article



Development of a nomogram to predict 30-day mortality of sepsis patients with gastrointestinal bleeding: An analysis of the MIMIC-IV database

Bing Sun ^a, Yu-lin Man ^a, Qi-yuan Zhou ^b, Jin-dong Wang ^c, Yi-min Chen ^a, Yu Fu ^a, Zhao-hong Chen ^a, ^{*}

- ^a Burn & Wound Repair Department, Fujian Burn Institute, Fujian Burn Medical Center, Fujian Provincial Key Laboratory of Burn and Trauma, Fujian Medical University Union Hospital, Fuzhou, 350001, Fujian, China
- b Emergency Department, The Second Hospital of Hebei Medical University, Shijiazhuang 050000, Hebei, China
- ^c Shengli Clinical Medical College, Fujian Medical University, Department of Thoracic Surgery, Fujian Provincial Hospital, Fuzhou 350001, Fujian, China

ARTICLE INFO

ABSTRACT

Keywords: Sepsis Gastrointestinal bleeding GIB Nomogram MIMIC-IV *Background:* We aimed to establish and validate a prognostic nomogram model for improving the prediction of 30-day mortality of gastrointestinal bleeding (GIB) in critically ill patients with severe sepsis.

Methods: In this retrospective study, the current retrospective cohort study extracted data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, then partitioned the cohort randomly into training and validation subsets. The cohort was partitioned into training and validation subsets randomly. Our primary endpoint was 30-day all-cause mortality. To reduce data dimensionality and identify predictive variables, the least absolute shrinkage and selection operator (LASSO) regression was employed. A prediction model was constructed by multivariate logistic regression. Model performance was evaluated using the concordance index (C-index), receiver operating characteristic (ROC) curve, and decision curve analysis (DCA).

Results: The analysis included 1435 total patients, comprising 1005 in the training cohort and 430 in the validation cohort. We found that age, smoking status, glucose, (BUN), lactate, Sequential Organ Failure Assessment (SOFA) score, mechanical ventilation≥48h (MV), parenteral nutrition (PN), and chronic obstructive pulmonary disease (COPD) independently influenced mortality in sepsis patients with concomitant GIB. The C-indices were 0.746 (0.700–0.792) and 0.716 (0.663–0.769) in the training and validation sets, respectively. Based on the area under the curve (AUC) and DCA, the nomogram exhibited good discrimination for 30-day all-cause mortality in sepsis with GIB.

Conclusions: For sepsis patients complicated with GIB, we created a unique nomogram model to predict the 30-day all-cause mortality. This model could be a significant therapeutic tool for clinicians in terms of personalized treatment and prognosis prediction.

^{*} Corresponding author. 29 Xinquan Road, Fuzhou City, Fujian Province, China. *E-mail address*: doctorczh@163.com (Z.-h. Chen).

1. Introduction

Severe sepsis represents more major, and an under-recognized health-care problem worldwide, with fatality rates as high as 30% reported [1,2]. According to estimates, 30 million cases of septicemia occur worldwide each year, with 6 million people passing away as a result of the condition [3,4]. As a result, sepsis has been dubbed "the defining medical condition of the twenty-first century" [5]. GIB is one of the most serious consequences of severe sepsis in patients that can be fatal. Moreover, clinically significant GIB has been linked to a 7-fold elevated risk of mortality in patients in critical condition [6]. Gastrointestinal function is essential for the emergence and progression of multiple organ dysfunctions in extreme situations including sepsis and severe trauma. Although while GIB was frequently curable, it nevertheless placed a heavy financial burden on society and had a profoundly detrimental impact on the patient, including hemodynamic instability, vomiting, and stomach pain or discomfort, all of which would impede the disease's recovery. Although the prevalence varies widely depending on geographical region, previous studies have consistently indicated that males and the elderly experience a higher occurrence. Due to mucosal ischemia, altered mucosal permeability, and increased acid generation, stress ulcers may raise the risk of GIB in the setting of bloodstream infection or sepsis. The prognosis of individuals with GIB complicated by sepsis has not been well assessed despite these results. A small number of studies suggested that regular stress ulcer prevention may not be essential for individuals with severe sepsis [7]. Several risk factors for GIB mortality have been examined over the past decade, including age and widespread infection [8]. There are presently no credible and strong prediction models available to assess the risk of death in severe sepsis aggravated by GIB.

Nomograms are extensively utilized in forecasting disease prognosis and recurrence. Their primary utility lies in condensing complex statistical prediction models into a singular numerical probability of certain events (like mortality or recurrence) tailored to the individual circumstances of patients [9]. These tools convert intricate mathematical models into straightforward graphical forms, facilitating quick and precise prognostic or treatment outcome estimations for specific ailments by medical professionals and researchers [10]. This efficiency fosters the integration of nomograms in clinical decision-making processes. Typically, nomograms are derived from clinical trial or observational study data, employing statistical techniques to draw connections between disease prognosis and a range of clinical indicators [11]. This study developed and validated a nomogram model to predict the mortality of a sepsis population paired with GIB during an ICU stay using standard lab variables from the MIMIC-IV database.

2. Methods

2.1. Data origin

A retrospective cohort study was performed utilizing the electronic medical records from version 2.0 of the MIMIC-IV database, a multifaceted critical care repository from Beth Israel Deaconess Medical Center (BIDMC). Our institution exempted the requirement for BIDMC Institutional Review Board (IRB) approval and informed consent, as investigators adhering to data usage prerequisites are sanctioned access to MIMIC-IV by the IRB (Researcher Approval Code: 48692881). This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

2.2. Study population and data exclusion

The database was screened to identify sepsis-associated ICU admissions for adults (age ≥ 18 years). For this study, only data from the first ICU admission of each episode was utilized. Furthermore, patients hospitalized for < 24 h or with preexisting cirrhosis were omitted.

This research included patients from the MIMIC-IV database who satisfied the criteria for sepsis. The Sepsis-3 criteria were used to define sepsis [4]. To identify the cohort and extract the relevant clinical information, structured query language (SQL) was employed. Specifically, the SQL queries retrieved the first available patient data documented after admission, comprising demographics, vital signs, laboratory tests, and baseline problems. ICD-9 and ICD-10 diagnosis codes were used to identify GIB and concomitant conditions.

In this investigation, only data from the patient's initial ICU hospitalization were evaluated in this study for patients who had multiple ICU hospitalizations. The baseline characteristics data were obtained as the average value within the first 24 h of admission. Variables with more than 20% missing data were eliminated from this research. For variables with <20% missing data, multiple imputation using the "MICE" package in R was performed to fill in missing values based on other predictor variables. The extracted information mostly consisted of: (1) Demographic characteristics: gender (male, female) and age. (2) Vital signs: heart rate (HR), respiratory rate (RR), temperature (T) and oxygen saturation (SpO₂). (3) Laboratory tests: creatinine, glucose, hemoglobin, platelet, lactate, international normalized ratio (INR), albumin, hematocrit (HCT), prothrombin time (PT), BUN, neutrophil (NEUT) and white blood cell (WBC). (4) Blood gas analysis: PH and partial pressure of oxygen (pO2). (5) Score system: SOFA and Simplified Acute Physiology Score II (SAPS II). (6) RBC transfusion, $MV \ge 48h$, vasoactive drugs, PN and Endoscope using. (7) Baseline complications: hypertension, diabetes, congestive heart failure (CHF), chronic liver disease (CLD), COPD, and malignancy. The included variable was the average of 24 h of ICU hospitalization. The main result of this study was 30 days of all-cause mortality.

2.3. Statistical analysis

In the model-development phase, the dataset was divided into two distinct groups: a training group (70%, n = 1005) and a

validation group (30%, n = 430). The former was utilized for developing the prognostic nomogram model, whereas the latter was utilized to assess the model's accuracy. Clinical data characteristics were assessed by the chi-square test between the training and validation groups. Descriptive statistics for patient characteristics were determined by calculating the mean (SD) for continuous variables and the count (%) for categorical variables.

The patients in training set were categorized into two groups on the basis of their survival status within 30 days, either deceased or alive. Variables were then displayed and compared across these groups. Our study identified and eliminated confounders affecting the independent risk factors, then, performed LASSO regression and multivariate logistic regression analysis to determine the impact of them on 30-days mortality. The LASSO regression analysis was used to determine the most powerful predictive characteristic from the selected training set [12]. Ultimately, a prognostic nomogram model of 30-days all-cause death was developed utilizing multivariate logistic analysis on the basis of the training set. A comparable corrected C-index (1000 bootstrap resamples) of the nomogram was additionally achieved in the training set. The clinical usefulness of the prediction model was assessed using DCA [13].

All statistical analysis were carried out using R software (version 4.2.1) and SPSS (version 25.0). A two-sided p-value less than 0.05 indicated statistical significance.

3. Results

3.1. Baseline characteristics

Initially, patients diagnosed with sepsis complicated by GIB between 2008 and 2019 were identified from the MIMIC-IV dataset. Subsequently, 33,244 patients who fulfilled the exclusion criteria were removed, and the study focused on 1435 patients for analysis (Fig. 1). This group included 433 individuals who died within 30 days after admission. Patients were then randomly assigned to either the training or validation sets (n = 1005 vs. 430), with a hypothesized ratio of 7:3. The median age for patients in the training set was 70.4 years (interquartile range, 60.5 to 83.2), and 40.7% (n = 409) were female. In contrast, the validation set comprised 183 female patients (42.7%), with a median age of 70.3 (interquartile range, 61–82 years). All-cause mortality rates within 30 days of admission were 29.8% and 31% for sepsis complicated with GIB patients without significant differences between the training and validation sets (p > 0.05), suggesting that their baseline characteristics were comparable (Table 1).

LASSO regression analysis.

In this research, we utilized a LASSO regression approach with 10-fold cross-validation to analyze 33 variables, including baseline characteristics such as age, gender, and various laboratory parameters (T, HR, RR, SpO2, glucose, hemoglobin, lactate, INR, PT, creatinine, BUN, albumin, HCT, WBC, NEUT, platelet count, PH, pO2) and treatment factors (SOFA, SAPS II, RBC transfusion, $MV \ge 48$

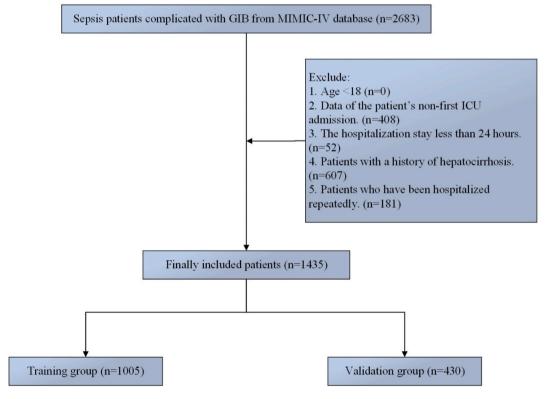


Fig. 1. Flowchart of patients included in the study.

 Table 1

 Demographic characteristics of sepsis patients complicated with GIB.

Variables	Total ($n = 1435$)	Training $(n = 1005)$	Validation ($n = 430$)	<i>p</i> -value
Death, n (%)				0.690
No	1002 (69.8)	706 (70.3)	296 (69)	
Yes	433 (30.2)	299 (29.8)	134 (31)	
Age, years	70.38 ± 15.86	70.41 ± 16.03	70.27 ± 15.5	0.642
Gender, n (%)				0.537
Female	593 (41.3)	410 (40.8)	183 (42.7)	
Male	842 (58.7)	595 (59.33)	247 (57.3)	
Smoking, n (%)	· · = (· · · ·)	010 (01100)	(5, 15)	0.718
No	1001 (69.8)	705 (70.1)	296 (69)	****
Yes	434(30.2)	300 (29.9)	134 (31)	
BMI, kg/m ²	26.97 ± 8.84	27.8 ± 7.52	27.69 ± 7.95	0.631
LOS, days	14.66 ± 14.45	14.56 ± 14.66	14.93 ± 13.98	0.662
Vital signs	14.00 ± 14.43	14.30 ± 14.00	14.55 ± 15.56	0.002
T, °C	36.80 ± 0.62	36.8 ± 0.63	36.81 ± 0.60	0.584
-	19.93 ± 3.99	19.94 ± 4.03		
RR, times/min			19.9 ± 3.9	0.885
HR, times/min	88.71 ± 16.40	88.62 ± 16.65	88.97 ± 15.87	0.398
SpO2, %	97.15 ± 2.20	97.15 ± 2.31	97.15 ± 1.92	0.500
Laboratory test				
Hemoglobin, g/dL	9.85 ± 2.00	9.89 ± 2.04	9.75 ± 1.93	0.233
HCT, %	29.90 ± 5.90	30.04 ± 6.0	29.58 ± 5.62	0.186
WBC, 10 ⁹ /L	13.21 ± 10.84	13.23 ± 11.34	13.18 ± 9.6	0.624
NEUT, 10 ⁹ /L	11.02 ± 7.99	10.97 ± 8.02	11.11 ± 7.93	0.982
Platelet, 10 ⁹ /L	213.08 ± 119.40	214.59 ± 119.19	209.17 ± 119.91	0.310
Glucose, mg/dL	145.61 ± 52.87	146.53 ± 53.54	143.57 ± 51.41	0.323
Albumin, g/L	2.96 ± 0.67	2.95 ± 0.67	2.99 ± 0.66	0.453
Creatinine, mg/dL	1.88 ± 1.73	1.88 ± 1.74	1.88 ± 1.71	0.772
BUN, mg/dL	41.11 ± 29.30	40.58 ± 29.17	42.43 ± 29.59	0.211
Lactate, mg/dL	2.53 ± 2.10	2.6 ± 2.25	2.37 ± 1.6	0.570
INR	1.57 ± 0.84	1.59 ± 0.86	1.54 ± 0.79	0.474
PT, s	17.13 ± 8.14	17.31 ± 8.39	16.72 ± 7.55	0.648
PH	7.36 ± 0.08	7.36 ± 0.09	7.36 ± 0.09	0.695
pO2, %	150.90 ± 77.99	150.88 ± 76.09	151.19 ± 82.59	0.734
Score system	130.90 ± 77.99	130.00 ± 70.07	131.17 ± 02.37	0.754
SOFA	6.07 ± 3.60	6.03 ± 3.6	6.18 ± 3.56	0.340
SAPS II	42.90 ± 14.46	42.66 ± 14.23	43.47 ± 15.01	0.283
	42.90 ± 14.40	42.00 ± 14.23	43.47 ± 13.01	
RBC transfusion, n (%)	570 (40.0)	401 (00.0)	170 (41 5)	0.625
No	579 (40.3)	401 (39.9)	178 (41.5)	
Yes	854 (59.7)	603 (60.1)	251 (58.5)	
MV, n (%)				0.950
No	709 (49.3)	496 (49.3)	213 (49.7)	
Yes	726 (50.7)	509 (50.7)	217 (50.3)	
Vasoactive agent, n (%)				0.991
No	808 (56.2)	566 (56.4)	242 (56.2)	
Yes	627 (43.8)	439 (43.6)	188 (43.8)	
PN, n (%)				0.905
No	1314 (91.6)	921 (91.7)	393 (91.4)	
Yes	121 (8.4)	84 (8.3)	37 (8.6)	
Endoscope using, n (%)				0.068
No	1072 (74.7)	736 (73.2)	336 (78.3)	
Yes	363 (25.3)	269 (26.8)	94 (21.7)	
Baseline complications, n (%)	()	()	(/	
Hypertension	984 (68.7)	695 (69.2)	289 (67.4)	0.527
Diabetes	412 (28.8)	906 (90.2)	386 (90)	0.783
			* *	
CHF	545 (38.0)	389 (38.7)	156 (36.4)	0.428
CLD	169 (11.8)	123 (12.3)	47 (11)	0.544
COPD	229 (16.0)	163 (16.2)	66 (15.4)	0.746
Malignancy	129 (9.0)	87 (8.7)	42 (9.8)	0.562

LOS, length of stay; HR, heart rate; RR, respiratory rate; MAP, mean arterial pressure; INR, international normalized ratio; PT, prothrombin time; BUN, blood urea nitrogen; WBC, white blood cell; SOFA, sequential organ failure assessment; PN, parenteral nutrition; MV, mechanical ventilation; CHF, congestive heart failure; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disorder.

h, use of vasoactive drugs, parenteral nutrition, endoscopic procedures, and comorbidities like hypertension, diabetes, CHF, CLD, COPD, malignancy). These were evaluated to identify predictors of 30-day all-cause mortality in sever sepsis patients combined with GIB. After careful consideration, the model highlighted ten variables as the most significant predictors at an optimal lambda value (λ = 0.01005025), namely age, T, HR, SpO2, creatinine, glucose, lactate, INR, BUN, albumin, WBC, NEUT, pO2, SOFA, SAPS II, MV \geq 48 h, vasoactive drug use, parenteral nutrition, endoscopic interventions, CHF, CLD, COPD, and malignancy (Fig. 2).

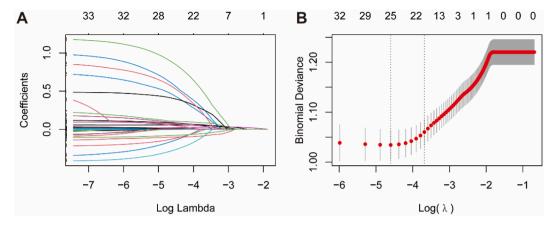


Fig. 2. LASSO's clinical feature selection. The variation features of the LASSO regression coefficient of 33 variables are shown in Panel (A), and each curve in the figure indicates the variation trace of the coefficient of each independent variable. Panel (B) depicts the process of cross-validating the best acceptable parameter value in the LASSO model.

3.2. Selection of risk factors for 30-day mortality

To identify factors independently associated with 30-day all-cause mortality rates of admission in sepsis patients combined with GIB, a multivariate logistic regression analysis was conducted on the independent variables. The LASSO-selected predictors were screened, and the analysis revealed that the following factors are significantly linked with an elevated risk of 30-day all-cause mortality, as presented in Table 2: age (OR = 1.064, 95% CI = 1.027-1.103, p < 0.001), smoking (OR = 0.265, 95% CI = 0.098-0.718, p = 0.009), glucose (OR = 0.008, 0.008), 0.0080 CI = 0.0081, actate (OR = 0.0081, 0.0082, 0.0083, 0.0083, 0.0083, 0.0084, 0.0085, 0.0085, 0.0086, 0.0087, 0.0087, 0.0087, 0.0088, 0.0089,

3.3. The development and assessment of nomogram model

To construct a prognostic nomogram for estimating the 30-day all-cause in-hospital mortality risk among sepsis patients with GIB, the nine factors chosen for the multivariate logistic regression analysis were as follows: age, smoking, glucose, BUN, lactate, SOFA, MV, PN, and COPD were used to construct the model in the training set. The resulting nomogram is presented in Fig. 3, with lactate having the highest impact on patient prognosis, followed by SOFA and age. The total number of points from the vertical axis can be used to estimate the probability of 30-day all-cause mortality. In this study, the C-indices of our nomogram were 0.746 (95%CI: 0.700–0.792) and 0.716 (95%CI: 0.663–0.769) for the training and validation sets, respectively. These results were reinforced by the ROC analysis, which supported the nomogram's discriminatory capacity (Fig. 4). Collectively, these findings signify that our nomogram model could reliably forecast 30-day mortality. DCA further exhibited that our nomogram yielded superior net benefit over a wide spectrum of threshold probabilities (Fig. 5), underlining its possible clinical utility. Moreover, calibration plots demonstrated concordance between the nomogram-predicted and actual mortality rates. This alignment verifies the predictive accuracy of the proposed nomogram (Fig. 6).

Table 2Multivariate logistic regression analyses of independent predictors for 30-day all-cause death in sepsis patients complicated with GIB.

Variables	В	Wald	OR	95%CI	p-value
Age	0.062	11.639	1.064	1.027-1.103	< 0.001
Smoking	-1.328	6.814	0.265	0.098-0.718	0.009
Glucose, mg/dL	0.008	6.046	1.008	1.002-1.015	0.014
BUN, mg/dL	0.017	3.969	1.017	1-1.035	0.046
Lactate, mg/dL	0.321	4.77	1.378	1.033-1.838	0.029
SOFA	0.122	4.245	1.130	1.006-1.268	0.039
MV	1.091	4.264	2.977	1.057-8.387	0.039
PN	1.687	5.277	5.402	1.281-22.782	0.022
COPD	1.427	5.743	4.165	1.297-13.379	0.017

SOFA, sequential organ failure assessment; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disorder.

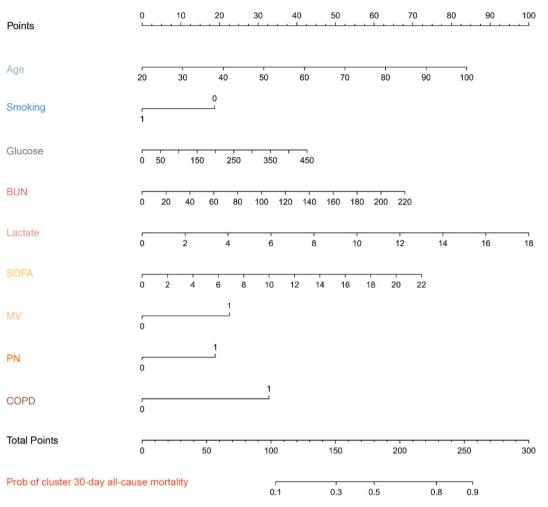


Fig. 3. Nomogram for sepsis patients with GIB complications to determine risk score and 30-day mortality. Age, smoking, glucose, BUN, lactate, SOFA, MV, PN, and COPD level were given scores by connecting the respective values to the "score" line by drawing a line upward. The total of these scores, represented on the "Total score" line, relates to estimates of 30-day mortality in GIB-complicated sepsis patients.

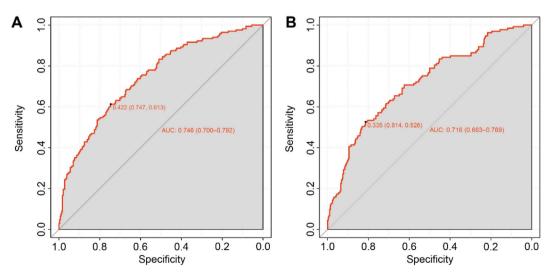


Fig. 4. Analysis of the receiver operating characteristic curves in the training (A) and validation (B) cohorts to predict 30-day all-cause mortality.

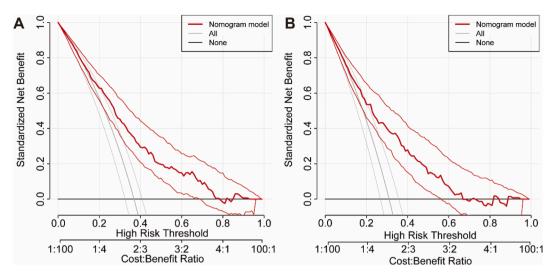


Fig. 5. Decision curve analysis for the training (A) and validation (B) cohorts, revealing the net advantage of using the nomogram.

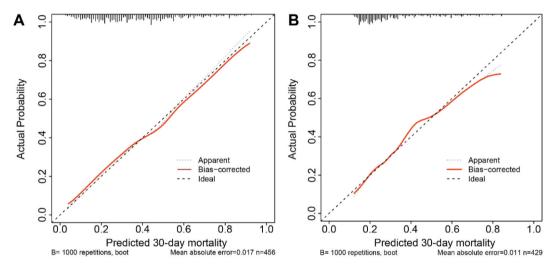


Fig. 6. Analysis of calibration curves in the training (A) and validation (B) cohorts. The horizontal axis depicts the nomogram-predicted likelihood of 30-day survival, whereas the vertical axis depicts actual 30-day mortality.

4. Discussion

In this study, we accessed clinical and survival data on 1435 septic patients complicated with GIB from the MIMIC-IV database. Nine indicators of 30-day mortality in sepsis patients with GIB including Age, smoking, glucose, BUN, lactate, SOFA, $MV \ge 48h$, PN, and COPD were identified by LASSO regression and multivariable logistic analysis and utilized to create a predictive nomogram. The nomogram's discrimination and calibration were found to be efficient. This innovative nomogram performed well in both the primary cohorts and validation cohorts, as measured by the AUC calibration curves, decision curve analyses and survival curves. As a result, this nomogram might be used rapidly and successfully in clinical practice.

Sepsis is described as a potentially fatal organ malfunction produced by an unbalanced host response to infection [7]. Sepsis, the most prevalent cause of mortality in the critical care unit, can cause acute kidney damage and numerous organ failures. A recent study demonstrated that concurrent GIB increased sepsis mortality by 9% [14]; consequently, it is critical to develop a sepsis-GIB associated prediction model that is early, rapid, and accurate. To the best of our knowledge, this is the first study to develop a prognostic model for risk factors influencing all-cause death within 30 days in sepsis patients with GIB using the MIMIC-IV database.

Individuals with sepsis exacerbated by gastrointestinal bleeding have a higher chance of organ dysfunction, indicating a poor prognosis. The SOFA score objectively grades organ failure severity in sepsis and predicts critically unwell patient outcomes. Schoe et al. [15] previously reported that the SOFA score exhibited significant discriminatory power for ICU mortality in a cohort of 36,632 patients, with an AUC of 0.865 (0.864–0.866). Here, we identified SOFA as a major risk factor affecting prognosis of septic patients

with GIB (OR = 1.130, 95% CI = 1.006-1.268, p = 0.039). This suggests that in patients with sepsis who are complicated by GIB, the SOFA score may serve as an early warning indication for 30-day all-cause death. Furthermore, age has generally been recognized as a significant risk factor in severe illnesses such as cardiovascular disease, GIB, and severe sepsis [16,17]. It should be emphasized that Age (OR = 1.064, 95% CI = 1.027-1.103, p < 0.001) was revealed to be the most significant independent risk indicators for 30-day all-cause death in septic patients complicated with GIB. This serves as a reminder to physicians to give special attention to elderly patients who have bad prognoses owing to the passage of time.

In laboratory tests, glucose has been indicated as a possible risk factor and has been connected with the severity of sepsis in combination with GIB. Fast blood glucose levels are prevalent in critically sick individuals, not only those with diabetes. The onset and progression of sepsis, along with its complications, are influenced by oxidative stress. The data from our research suggests that glucose measurements (OR = 1.008, 95%CI = 1.002–1.015, p = 0.014) in the initial 24-h period post-ICU admission are a substantial risk factor impacting the 30-day mortality rate from all causes in sepsis patients with GIB complications. Interestingly, our results also demonstrate that the severity of GIB is related to BUN levels, which is in line with previous studies [18,19]. Typically, BUN levels increase a few hours after a bleed, peak at 1–2 days, and return to normal after 3–4 days. Hematocrit and hemoglobin levels may not change significantly due to blood concentration during the early stages of bleeding. Therefore, BUN levels outperform hemoglobin levels in detecting the severity of GIB in its early stages. Additionally, Early elevation of BUN has been linked to the prognosis of individuals with acute pancreatitis and GIB. Arihan et al. observed that high BUN concentration at admission was highly related with poor outcomes in patients with serious illnesses, even after correcting for confounding variables such as renal impairment [20]. Moreover, Harazim et al. also support BUN levels as a reliable and independent predictor of 28-day mortality in critically ill patients admitted to an ICU [21]. Our study found that BUN is a statistically significant prognosticator of 30-day all-cause death. Increased BUN levels have been demonstrated to have an impact on patient outcomes, emphasizing the significance of early dynamic monitoring of renal function markers and prompt implementation of therapies as needed.

Lactic acid (lactate) is a common clinical indicator of urgent and serious disorders that has been associated to a range of different conditions, which includes heart failure, COVID-19, and acute mesenteric ischemia [22–24]. Elevated levels of lactic acid in the blood are often found in individuals suffering from severe sepsis or septic shock [25]. Initial and recurrent lactic acid measurements have been utilized to assess patients' risk and potentially guide therapeutic measures [26,27]. The precise pathogenesis continues to be disputed and may be multifactorial, relating more to obstruction of metabolic pathways and/or cytotoxicity, while tissue hypoperfusion is frequently hypothesized as an etiology of increased lactate concentrations [28,29]. According to Liu et al., elevated lactic acid levels are an independent predictor of death in sepsis patients, with a higher discriminative capacity than qSOFA [30]. Creatinine was found to be a statistically significant predictor of all-cause death within 30 days in this study. Lactate concentrations correlate with patient prognosis, underscoring the importance of physicians tracking renal function biomarkers dynamically and administering therapies accordingly.

It is worth noting that smoking (OR = 0.265, 95% CI = 0.098-0.718, p = 0.009) was found to be an independent predictor of sepsis patients with GIB in our research. Smoking may be beneficial to the prognosis of sepsis complicated with GIB. As compared to smoking individuals, nonsmokers had a poorer prognosis following GIB. Several reasons can explain this. (1) Several researchers who explored the association between smoking and stroke patient prognosis found inconsistent results, notably the smoking paradox. Several of them observed that smoking in stroke patients was independently related with a proper medical outcome following endovascular treatment (EVT) [30,31]. (2) Due to data constraints, we are unable to validate the patient's smoking period, smoking cessation, and age of smoking beginning, which may impact patient outcomes. Furthermore, we discovered that the usage of MV [32] and PN, as well as COPD, are related with worse outcomes in sepsis patients with GIB. This might be related to the patients' poor physical health as well as their disparate baseline characteristics.

There were also a few constraints to this study. (1) As a single-center retrospective study using MIMIC-IV data, our analysis has inherent selection bias that may affect result accuracy. (2) Certain variables (C-reactive protein, procalcitonin, PH value of gastric liquid, and so on) are missing due to the limits of the MIMIC-IV database. (3) The present study's results were solely checked internally. Our results require external validation through large multicenter studies to enhance generalizability.

5. Conclusions

We constructed a prognostic nomogram with comprehensive performance integrating nine predictors - age, smoking, glucose, BUN, lactate, SOFA score, MV, PN, and COPD - to forecast 30-day survival in ICU septic patients with GIB. This nomogram exhibited satisfactory performance could be instrumental in risk stratification and decision-making processes for sepsis patients complicated with GIB undergoing clinical management.

Declaration

The author(s) have reported no possible conflicts of interest in this article.

Funding statement

The National Key Clinical Specialty Discipline Construction Program of the 14th Five-Year Plan for Fujian Medical Development, China ([2021]76), and Fujian Provincial Key Laboratory of Burn and Trauma, China.

Data availability statement

The data utilized was accessed from online repositories. Specifically, the MIMIC-IV database (version 2.0) hosted at https://physionet.org/content/mimiciv/2.0/was the source, under approval code 48692881.

Ethical approval

For this research involving human subjects, local laws and institutional guidelines negated the necessity for ethical approval and review. Similarly, obtaining written informed consent from participants was not mandated by national legislation and institutional protocols.

CRediT authorship contribution statement

Bing Sun: Writing – review & editing, Writing – original draft. Yu-lin Man: Validation, Conceptualization. Qi-yuan Zhou: Methodology, Investigation. Jin-dong Wang: Software, Project administration. Yi-min Chen: Supervision. Yu Fu: Visualization. Zhao-hong Chen: Validation, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] C. Bouza, T. López-Cuadrado, Z. Saz-Parkinson, J.M. Amate-Blanco, Epidemiology and recent trends of severe sepsis in Spain: a nationwide population-based analysis (2006-2011), BMC Infect. Dis. 14 (2014) 1–13.
- [2] D.F. Gaieski, J.M. Edwards, M.J. Kallan, M.E. Mikkelsen, M. Goyal, B.G. Carr, The relationship between hospital volume and mortality in severe sepsis, Am. J. Respir. Crit. Care Med. 190 (2014) 665–674.
- [3] C. Fleischmann, A. Scherag, N.K. Adhikari, C.S. Hartog, T. Tsaganos, P. Schlattmann, D.C. Angus, K. Reinhart, Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations, Am. J. Respir. Crit. Care Med. 193 (2016) 259–272.
- [4] M. Singer, C.S. Deutschman, C.W. Seymour, M. Shankar-Hari, D. Annane, M. Bauer, R. Bellomo, G.R. Bernard, J.-D. Chiche, C.M. Coopersmith, The third international consensus definitions for sepsis and septic shock (Sepsis-3), JAMA 315 (2016) 801–810.
- [5] F. Venet, G. Monneret, Advances in the understanding and treatment of sepsis-induced immunosuppression, Nat. Rev. Nephrol. 14 (2018) 121-137.
- [6] M. Bardou, J.-P. Quenot, A. Barkun, Stress-related mucosal disease in the critically ill patient, Nat. Rev. Gastroenterol. Hepatol. 12 (2015) 98–107.
- [7] Y. Sasabuchi, H. Matsui, A.K. Lefor, K. Fushimi, H. Yasunaga, Risks and benefits of stress ulcer prophylaxis for patients with severe sepsis, Crit. Care Med. 44 (2016) e464–e469.
- [8] A.H. Huang, Y. Liu, Y.-C. Hsien, T.-C. Hsu, D. Yen, W.-T. Hsu, H.-Y. Lin, S.-C. Chen, C.-C. Lee, NTUH Health Data Science Research Group, Survival impact and clinical predictors of acute gastrointestinal bleeding in patients with bloodstream infection, J. Intensive Care Med. 36 (2021) 63–69.
- [9] V.P. Balachandran, M. Gonen, J.J. Smith, R.P. DeMatteo, Nomograms in oncology: more than meets the eye, Lancet Oncol. 16 (2015) e173-e180.
- [10] X. Wang, M. Zhao, C. Zhang, H. Chen, X. Liu, Y. An, L. Zhang, X. Guo, Establishment and clinical application of the nomogram related to risk or prognosis of hepatocellular carcinoma: a review, J. Hepatocell. Carcinoma (2023) 1389–1398.
- H. Wu, P. Ding, J. Wu, C. Sun, H. Guo, S. Chen, S. Lowe, P. Yang, Y. Tian, Y. Liu, A new online dynamic nomogram: construction and validation of a predictive model for distant metastasis risk and prognosis in patients with gastrointestinal stromal tumors, J. Gastrointest, Surg. (2023) 1–16.
 T. Xie, O. Xin, X. Zhang, Y. Tong, H. Ren, C. Liu, J. Zhang, Construction and validation of a nomogram for predicting survival in elderly patients with cardiac
- [12] T. Xie, Q. Xin, X. Zhang, Y. Tong, H. Ren, C. Liu, J. Zhang, Construction and validation of a nomogram for predicting survival in elderly patients with cardiac surgery, Front. Public Health 10 (2022) 972797.
- [13] T. Fan, H. Wang, J. Wang, W. Wang, H. Guan, C. Zhang, Nomogram to predict the risk of acute kidney injury in patients with diabetic ketoacidosis: an analysis of the MIMIC-III database, BMC Endocr. Disord. 21 (2021) 1–11.
- [14] A. Granholm, L. Zeng, J.C. Dionne, A. Perner, S. Marker, M. Krag, R. MacLaren, Z. Ye, M.H. Møller, W. Alhazzani, Predictors of gastrointestinal bleeding in adult ICU patients: a systematic review and meta-analysis, Intensive Care Med. 45 (2019) 1347–1359.
- [15] A. Schoe, F. Bakhshi-Raiez, N. de Keizer, J.T. van Dissel, E. de Jonge, Mortality prediction by SOFA score in ICU-patients after cardiac surgery; comparison with traditional prognostic-models, BMC Anesthesiol. 20 (2020) 1–8.
- [16] Q. Guo, M. Wu, H. Li, H. Ouyang, R. Sun, J. Wang, Y. Zhang, Development and validation of a prognostic nomogram for myocardial infarction patients in intensive care units: a retrospective cohort study, BMJ Open 10 (2020) e040291.
- [17] S. Fukuda, Y. Shimodaira, K. Watanabe, S. Takahashi, K. Sugawara, Y. Suzuki, N. Watanabe, S. Koizumi, T. Matsuhashi, K. Iijima, Risks for rebleeding and inhospital mortality after gastrointestinal bleeding in a tertiary referral center in Japan, Digestion 101 (2020) 31–37.
- [18] M. Tomizawa, F. Shinozaki, R. Hasegawa, Y. Shirai, Y. Motoyoshi, T. Sugiyama, S. Yamamoto, N. Ishige, Patient characteristics with high or low blood urea nitrogen in upper gastrointestinal bleeding, World J. Gastroenterol. WJG. 21 (2015) 7500.
- [19] K. Al-Naamani, N. Alzadjali, A.N. Barkun, C.A. Fallone, Does blood urea nitrogen level predict severity and high-risk endoscopic lesions in patients with nonvariceal upper gastrointestinal bleeding? Can. J. Gastroenterol. Hepatol. 22 (2008) 399–403.
- [20] O. Arihan, B. Wernly, M. Lichtenauer, M. Franz, B. Kabisch, J. Muessig, M. Masyuk, A. Lauten, P.C. Schulze, U.C. Hoppe, Blood Urea Nitrogen (BUN) is independently associated with mortality in critically ill patients admitted to ICU, PLoS One 13 (2018) e0191697.
- [21] M Harazim, K Tan, M Nalos, M Matejovic, Blood urea nitrogen independent marker of mortality in sepsis, Biomed. Pap. 167 (1) (2023) 24–29.
- [22] G. Gjesdal, O.Ö. Braun, J.G. Smith, F. Scherstén, P. Tydén, Blood lactate is a predictor of short-term mortality in patients with myocardial infarction complicated by heart failure but without cardiogenic shock, BMC Cardiovasc. Disord. 18 (2018) 1–8.
- [23] A. Alharthy, W. Aletreby, F. Faqihi, A. Balhamar, F. Alaklobi, K. Alanezi, P. Jaganathan, H. Tamim, S.A. Alqahtani, D. Karakitsos, Clinical characteristics and predictors of 28-day mortality in 352 critically ill patients with COVID-19: a retrospective study, J. Epidemiol. Glob. Health. 11 (2021) 98.
- [24] R. Sumbal, M.M.A. Baig, A. Sumbal, Predictors of mortality in acute mesenteric ischemia: a systematic review and meta-analysis, J. Surg. Res. 275 (2022) 72–86.
- [25] K. Stahl, P. Wand, B. Seeliger, P.D. Wendel-Garcia, J.J. Schmidt, B.M. Schmidt, A. Sauer, F. Lehmann, U. Budde, M. Busch, Clinical and biochemical endpoints and predictors of response to plasma exchange in septic shock: results from a randomized controlled trial, Crit. Care 26 (2022) 1–14.
- [26] S. Lokhandwala, L.W. Andersen, S. Nair, P. Patel, M.N. Cocchi, M.W. Donnino, Absolute lactate value vs relative reduction as a predictor of mortality in severe sepsis and septic shock, J. Crit. Care 37 (2017) 179–184.

[27] R. Bou Chebl, C. El Khuri, A. Shami, E. Rajha, N. Faris, R. Bachir, G. Abou Dagher, Serum lactate is an independent predictor of hospital mortality in critically ill patients in the emergency department: a retrospective study, Scand. J. Trauma Resusc. Emerg. Med. 25 (2017) 1–7.

- [28] M. Garcia-Alvarez, P. Marik, R. Bellomo, Sepsis-associated hyperlactatemia, Crit. Care 18 (2014) 1-11.
- [29] L.W. Andersen, J. Mackenhauer, J.C. Roberts, K.M. Berg, M.N. Cocchi, M.W. Donnino, Etiology and Therapeutic Approach to Elevated Lactate Levels, Elsevier, 2013, pp. 1127–1140.
- [30] Z. Liu, Z. Meng, Y. Li, J. Zhao, S. Wu, S. Gou, H. Wu, Prognostic accuracy of the serum lactate level, the SOFA score and the qSOFA score for mortality among adults with Sepsis, Scand. J. Trauma Resusc. Emerg. Med. 27 (2019) 1–10.
- [31] R. Iglesias-Rey, A. Custodia, M.L. Alonso-Alonso, I. López-Dequidt, M. Rodríguez-Yáñez, J.M. Pumar, J. Castillo, T. Sobrino, F. Campos, A. da Silva-Candal, The smoking paradox in stroke patients under reperfusion treatment is associated with endothelial dysfunction, Front. Neurol. 13 (2022) 841484.
- [32] B. Popoff, E. Besnier, B. Dureuil, B. Veber, T. Clavier, Effect of early hyperoxemia on mortality in mechanically ventilated septic shock patients according to Sepsis-3 criteria: analysis of the MIMIC-III database, Eur. J. Emerg. Med. 28 (2021) 469–475.