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ARTICLE

A Prediction Model for the Diagnosis of Sepsis Based on the Classification of Acute Gastrointestinal Injury

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Abstract

Aims/Background The existing screening approaches for sepsis demonstrate lower sensitivity, potentially resulting in misdiagnosis of septic conditions. The gastrointestinal tract is the primary and most susceptible organ during sepsis. Therefore, this study aims to establish and evaluate a predictive model for sepsis based on the classification of acute gastrointestinal injury (AGI), to improve diagnostic sensitivity.

Methods This retrospective study included patients with confirmed infections or suspected infections who were admitted to the general ward of Changshu Hospital Affiliated to Soochow University (Changshu First People's Hospital, China) between April 2023 and December 2023. Patients were randomly divided into a developing cohort (n = 1667) and a validation cohort (n = 712) in a 7:3 ratio. Furthermore, data were collected for various variables, including general variables, inflammatory factors, hemodynamic variables, organ dysfunction variables, and tissue perfusion variables. Univariate analysis was used to screen the risk factors associated with sepsis, and logistic regression analysis was employed to identify the independent predictive factors. The nomogram of the model was constructed based on these independent predictive factors. Additionally, the prediction significance of the model was evaluated using receiver operating characteristic (ROC) curves, calibration curves, and decision curve analysis (DCA) across both the developing and validation cohorts.

Results Out of the total of 2379 patients in the study, the sepsis rate was 12.5%. The incidence of AGI in septic patients was 96.0%, with 23.2% in grade I, 52.3% in grade II, 16.1% in grade III, and 4.4% in grade IV. Factors like age (Odds Ratio (OR) = 1.029, 95% Confidence Interval (CI) 1.015–1.043, $p < 0.01$), hypotension (OR = 3.863, 95% CI 2.372–6.290, $p < 0.01$), oxygen saturation (SpO_2) (OR = 0.795, 95% CI 0.751–0.840, $p < 0.01$), thrombocytopenia (OR = 5.657, 95% CI 2.835–11.289, $p < 0.01$) and AGI grade (OR = 7.151, 95% CI 5.040–10.144, $p < 0.01$) were observed as independent predictors for sepsis. Based on these five variables, a predictive model nomogram (model B) was developed. Model B achieved area under the curve (AUC) of 0.947 (95% CI 0.932–0.963) and 0.962 (95% CI 0.945–0.978) for the developing and validation cohorts, respectively, which were significantly higher than the AUC value of quick Sequential Organ Failure Assessment (qSOFA) (model A). Furthermore, the calibration curves for both the developing and validation datasets were close to the ideal model. Decision curve analysis revealed that model B exhibited a better net clinical benefit than model A.

Conclusion This study developed and validated a novel model based on AGI that could predict sepsis patients with infections in general wards, significantly helping in clinical decision-making.

Key words: gastrointestinal; organ dysfunction scores; sepsis; general wards; diagnosis

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Introduction

Sepsis is a common and severe condition with a mortality rate of about 30% (Prest et al, 2021; Im et al, 2022). It is characterized by a systemic inflammatory response triggered by infection, which can lead to multiple organ failure and shock. Early identification and the prompt implementation of goal-directed therapy are essential to reduce mortality and improve outcomes (De Backer et al, 2024). The Sequential Organ Failure Assessment (SOFA) score, despite its long-standing use in clinical practice, is not utilized outside the Intensive Care Unit (ICU). The third international consensus on sepsis and septic shock proposed the quick Sequential Organ Failure Assessment (qSOFA) scoring system as a screening tool for patients with infection or suspected infection to identify sepsis (Seymour et al, 2016). qSOFA consists of three indicators, including the respiratory rate of $\geq$22 beats per minute, altered consciousness, and systolic blood pressure of $\leq$100 mmHg. This scoring system is designed to help clinicians identify sepsis or those at risk of developing sepsis in general wards. However, qSOFA relies primarily on three simple clinical parameters that may not fully capture the condition of all sepsis cases and has relatively limited sensitivity, potentially missing some cases of sepsis (Wang et al, 2022). Hence, there is an urgent need for more comprehensive tools to effectively identify the occurrence of sepsis.

Gastrointestinal tract is often the primary organ affected during the onset of sepsis (Castro et al, 2023). A study revealed that among septic patients admitted to the ICU, 69% were categorized as acute gastrointestinal injury (AGI) I at the time of admission, while 31% were classified as AGI II. Over the ensuing days, the proportion of patients progressing to AGI III escalated to 2%, 29%, 47%, and 50% on days 3, 5, 7, and 10, respectively (Tyszko et al, 2023). In another multicenter study, the median AGI grading score among sepsis patients was found to be 1.5 $\pm$ 0.9 (Jiang et al, 2020). Sepsis can impair gastrointestinal function directly or indirectly through various mechanisms, such as systemic inflammatory response and vascular endothelial injury, and results in vasodilation and microcirculatory disturbances, reducing gastrointestinal blood flow. Damage to intestinal mucosal epithelial cells and disruption of connexins increases intestinal permeability. Furthermore, dysregulation of inflammatory mediators and the neuroendocrine system disrupts gastrointestinal motility, gastric acid secretion, and digestive enzyme production. Additionally, ischemia, hypoxia, and oxidative stress caused by inflammatory mediators and reactive oxygen species further contribute to mucosal injury (Yao et al, 2024). Moreover, acute gastrointestinal injury (AGI) can facilitate the penetration of bacteria and toxins from the gut into the bloodstream, exacerbating systemic inflammation and significantly elevating the risk of sepsis (Klingensmith and Coopersmith, 2023; Patil et al, 2023; Tyszko et al, 2023). In patients with sepsis, maintaining normal gastrointestinal function is crucial to ensure adequate nutritional support due to their elevated metabolic rate (Collins and Huen, 2023).

Consequently, monitoring gastrointestinal function is crucial in assessing the severity of illness and predicting prognosis in patients afflicted with infections (Gai et al, 2022). However, the current screening criteria for sepsis don't include gas-

trointestinal function. Therefore, this study aims to develop and validate predictive models for sepsis diagnosis by integrating AGI grading with relevant clinical indicators. Our goal is to enhance the sensitivity of early sepsis identification in general wards, facilitating timely intervention to improve patient prognosis. We hope that our findings will support clinicians in making more informed decisions.

Methods

Recruitment of Study Participants and Their Data Collection

This study included patients with infections or suspected infections admitted to the general ward of Changshu Hospital Affiliated to Soochow University (Changshu First People's Hospital, China) between April 2023 and December 2023. The clinical data and relevant information of each patient were obtained from the hospital's electronic medical record system. The retrospective observational study design was approved by the Ethics Review Committee of Changshu First People's Hospital (Approval No.: L2024049) and adhered to the ethical standards outlined in the Declaration of Helsinki. As this is a retrospective study, some patients could not be contacted or had died, the study solely analyzes existing data without any intervention. Throughout the study, we protected patients' privacy and ensured that their personal information remained undisclosed. Moreover, the Ethics Review Committee of Changshu First People's Hospital granted a waiver of informed consent.

Only patients with complete data were included in this study. Inclusion criteria included the use of antibiotics during hospitalization and the collection of microorganism cultures within a specific time period. If antibiotics are used first, the culture must be retained within 24 hours. In contrast, if the culture was collected first, antibiotics must be administered within 72 hours. The infection time point was defined as the earliest occurrence of either of these two events (Singer et al, 2016). However, patients under 18 years, those who were pregnant, those who died within 3 days after admission, and those who abandoned treatment were excluded from the study cohort.

The designated personnel was responsible for collecting and inputting relevant information and data. The data extracted from electronic medical records included common variables, circulatory variables, inflammation variables, organ dysfunction variables, and tissue perfusion variables (following the Sepsis 2.0 guidelines by Levy et al, 2003). AGI classification (Hai et al, 2024), based on the AGI criteria of the European Society of Critical Care Medicine in 2012, as well as qSOFA, and SOFA scores, were evaluated within the 24 hours before or after infection diagnosis. The worst value documented during this period was utilized for the relevant data and score calculation. Furthermore, the length of hospital stays, ICU admission, and survival rates were also recorded.

Finally, 2379 patients were included in the study, with 298 (12.5%) septic cases. The patients were randomly divided into a developing cohort (n = 1667) and a validation cohort (n = 712) using a 7:3 ratio, as determined by R programming language.

Patient Outcome in the Two Experimental Groups

The primary outcome for both the developing and validation cohorts was the occurrence of sepsis within 48 hours of infection. The diagnostic criteria for sepsis were set as follows: in patients with infection or suspected infection, the SOFA score increased by $\geq$2 points, suggesting organ dysfunction (Rhodes et al, 2017).

Predictors and Baseline Characteristics of the Patients

The predictors were defined based on the diagnostic indexes of qSOFA, Sepsis 2.0, and AGI grading. Data included patient demographics (age, gender, and source of infection), general parameters (temperature, heart rate, respiratory rate, changes in mental status, significant edema, and hyperglycemia without diabetes), inflammatory parameters (white blood cell (WBC) count, plasma C-reactive protein (CRP), and plasma procalcitonin (PCT)), hemodynamic variables (systolic blood pressure), organ dysfunction variables (oxygen saturation (SpO_2), creatinine, platelet (PLT) count, international normalized ratio (INR), activated partial thromboplastin time (APTT), and tissue perfusion variables (mottling)). Certain indicators, such as central venous oxygen saturation, cardiac index, and lactic acid, were not included because of the unavailability of relevant data in most medical records.

Missing Data and Possible Biases Handling

Since the proportion of missing values in our dataset is relatively low, comprising approximately 5% of the total, and preliminary analyses indicate the missing data are entirely random, we conducted the analysis using complete cases, excluding any records with missing data. To minimize selection bias, participants were recruited from various departments, infection sources, and age groups across the entire hospital. Data were collected via case report forms by designated and trained researchers to reduce information bias. Additionally, multiple regression analyses were used to control for several potential confounding factors, thereby minimizing bias in our study.

Statistical Analysis

Predictors' Processing

Age and SpO_2 were used as continuous variables, while other continuous variables, including temperature, heart rate, and respiratory rate, were classified based on the optimal cut-off value derived from the Sepsis 2.0 version. Sex and source of infection were included as categorical variables.

Logistic Regression Analysis

The Kolmogorov-Smirnov test was used to assess the normality of continuous variables. Data with skewed distribution were expressed as median (interquartile range) and compared using the Mann-Whitney U rank test. However, rates were compared employing χ^2 test. Within contingency tables, if any cell had a theoretical frequency of less than one, Fisher's exact test was applied. In univariate analysis, variables with a p-value of <0.05 were selected, and multicollinearity between the variables was examined. Furthermore, the highly correlated variables

were excluded, and the remaining variables were introduced into logistic regression analysis utilizing the enter method. A p-value of <0.05 was considered statistically significant.

Model Development and Validation

Model A was established based on the qSOFA criteria, while model B was constructed utilizing the results of the logistic regression analysis. A nomogram for model B was developed using R software (version 4.4.1, R Core Team, Boston, MA, USA).

The diagnostic value of the predictive models was evaluated using receiver operating characteristic (ROC) analysis. Furthermore, its consistency was evaluated by plotting a calibration curve, and the net benefit was determined using decision curve analysis (DCA) in both the developing and internal validation cohorts. All statistical analyses were performed using SPSS 27.0 (IBM, Armonk, NY, USA) and R 4.4.1 (R Core Team, Boston, MA, USA).

Results

Comparison of Baseline Characteristics Between the Two Study Cohorts

This study recruited 2655 patients with infection and suspected infection. After excluding 48 patients under 18 years of age, 23 pregnant patients, 16 patients who died within 3 days after admission, and 189 patients who either withdrew from the treatment or had missing data, 2379 patients remained in the study. Of these, 1667 patients were included in the developing cohort and 712 in the validation cohort. Furthermore, 298 patients (12.5%) had sepsis, 109 (4.6%) were admitted to the ICU, and 42 (1.8%) died (Fig. 1). The overall incidence of AGI was 50.9%, with 33.6% in grade I, 14.7% in grade II, 2.1% in grade III, and 0.5% in grade IV. The incidence of AGI in sepsis patients was 96.0%, with 23.2% in grade I, 52.3% in grade II, 16.1% in grade III, and 4.4% in grade IV. The description of baseline characteristics in both the developing and validation cohorts is detailed in Table 1, indicating no statistically significant differences between the two cohorts.

Model Development

Univariate Analysis of the Risk Factors Associated With Sepsis

Univariate analysis showed that age, temperature, heart rate, tachypnea, altered consciousness, severe edema, hyperglycemia, WBC count, CRP, PCT, hypotension, SpO_2, elevated creatinine level, coagulation dysfunction, thrombocytopenia, mottle, AGI grade, and qSOFA scores were significantly associated with the occurrence of sepsis (p-value < 0.05, Table 2).

Multivariate Regression Analysis of the Risk of Sepsis

Multivariate regression analysis was performed for the factors with $p < 0.05$ in univariate analysis. The Variance Inflation Factor (VIF) values for each factor were as follows: age 1.068, body temperature 1.295, heart rate 1.268, tachypnea 9.737, altered consciousness 2.994, severe edema 1.185, hyperglycemia 1.044, WBC count 1.112, CRP greater than the reference limit 1.182, PCT greater than

the reference limit 1.401, elevated creatinine greater than the reference limit 1.036, SpO_2 1.247, hypotension 14.907, coagulation dysfunction 1.254, thrombocytopenia 1.149, mottle 1.144, AGI grade 1.327, and qSOFA 33.926. qSOFA was excluded from the model due to multicollinearity between qSOFA, tachypnea, and hypotension. However, the new VIF values for each factor were as follows: age 1.067, body temperature 1.294, heart rate 1.267, tachypnea 1.371, altered consciousness 1.145, severe edema 1.179, hyperglycemia 1.039, WBC count 1.111, CRP greater than the reference limit 1.182, PCT greater than the reference limit 1.400, elevated creatinine greater than the reference limit 1.035, SpO_2 1.247, hypotension 1.129, coagulation dysfunction 1.223, thrombocytopenia 1.149, mottle 1.142, and AGI grade 1.326.

Furthermore, advanced age ($\beta = 0.029$, Odds Ratio (OR) = 1.029), hypotension ($\beta = 1.351$, OR = 3.863), thrombocytopenia ($\beta = 1.733$, OR = 5.657), and higher AGI grade ($\beta = 1.967$, OR = 7.151) were found as significant risk factors associated with sepsis. Conversely, the lowest risk of sepsis was observed in patients with higher SpO_2 levels ($\beta = -0.230$, OR = 0.795) (Table 3). Additionally, model A was developed for identifying sepsis using the qSOFA scores, while model B was created by integrating the AGI grading along with clinical parameters, those with $p < 0.05$ in the multifactorial analysis.

Nomogram Construction

Based on the results of logistic regression analysis, the nomogram of model B was developed to predict sepsis in patients with infections in general wards (Fig. 2).

For each infected patient, we collected several parameters and assigned a score to each parameter based the Table 3. The scores for all parameters were summed to obtain a total score. This score is located on the 'total points' axis, and the corresponding value on the probability axis indicates the likelihood of developing sepsis.

Model Validation

Separate ROC curves were developed for each model (Table 4). In the developing cohort, the area under the ROC curves of model B was 0.947 (95% Confidence Interval (CI) 0.932–0.963), and for model A was 0.758 (95% CI 0.723–0.792). The sensitivities were 89.3% and 68.8% for model B and model A, respectively, with specificities of 86.8% for model B and 81.4% for model A ($p < 0.01$, Fig. 3A). However, in the validation cohort, the area under the ROC curves for models B and A were 0.962 (95% CI 0.945–0.978) and 0.761(95% CI 0.709–0.814), respectively. The sensitivities were 95.7% for model B and 66.7% for model A, with specificities of 83.0% and 82.7%, respectively ($p < 0.01$, Fig. 3B). Furthermore, calibration plots demonstrated that predicted probabilities for both models were consistent with the actual incidence in both cohorts (Fig. 4A–D). Decision curve analysis (DCA) indicated that model B offered greater net benefits in both the developing and validation cohorts and was clinically more beneficial and effective than model A (Fig. 5).

Table 1. Comparison of basic information between the developing and validation cohorts.

Variables	Developing cohort (n = 1667)	Validation cohort (n = 712)	Test value (Z/χ^2)	*p*-value
Age [year-old, M (Q1–Q3)]	62 (47–74)	63 (48–75)	–1.282	0.200
Gender (male) [n (%)]	905 (54.3)	391 (54.9)	0.079	0.779
Source of infection (n, %)			6.691	0.082
Lung	809 (48.5)	317 (44.5)		
Digestive system	549 (32.9)	255 (35.8)		
Urinary system	223 (13.4)	89 (12.5)		
Blood flow and others	86 (5.1)	51 (7.2)		
Body temperature (n, %)			5.274	0.072
>38 °C	490 (29.4)	183 (25.7)		
36–38 °C	1171 (70.2)	523 (73.5)		
<36 °C	6 (0.4)	6 (0.8)		
Heart rate (n, %)			-	0.572
>100 bpm	473 (28.4)	191 (26.8)		
60–100 bpm	1192 (71.5)	521 (73.2)		
<60 bpm	2 (0.1)	0 (0)		
Tachypnea (≥22 bpm) (n, %)	177 (10.6)	66 (9.3)	0.989	0.320
Altered consciousness (GCS score ≤13) (n, %)	43 (2.6)	13 (1.8)	1.233	0.267
Severe edema (n, %)	9 (0.5)	2 (0.3)	0.273	0.601
Hyperglycemia (>10 mmol/L) (n, %)	318 (19.1)	138 (19.4)	0.030	0.862
WBC count (n, %)			2.236	0.327
$>12 \times 10^9$/L	258 (15.5)	118 (16.6)		
4–12×10^9/L	1282 (76.9)	529 (74.3)		
$<4 \times 10^9$/L	127 (7.6)	65 (9.1)		
CRP greater than the reference limit (n, %)	1090 (65.4)	465 (65.3)	0.001	0.971
PCT greater than the reference limit (n, %)	175 (10.5)	73 (10.3)	0.032	0.858
Hypotension (SBP ≤100 mmHg) (n, %)	324 (19.4)	133 (18.7)	0.184	0.668

Table 1. Continued.

Variables	Developing cohort (n = 1667)	Validation cohort (n = 712)	Test value (Z/χ^2)	p-value
SpO_2 without oxygen [%, M (Q1–Q3)]	96 (94–98)	96 (93–98)	–1.121	0.262
Elevated creatinine greater than the reference limit (n, %)	207 (12.4)	79 (11.1)	0.824	0.364
Coagulation dysfunction (n, %) (INR >1.5, APTT >60 s)	22 (1.3)	4 (0.6)	2.651	0.103
PLT $<100 \times 10^9$/L	112 (6.7)	43 (6.0)	0.378	0.539
Mottle (n, %)	2 (0.1)	1 (0.1)	-	1.000
AGI grade [grade, M (Q1–Q3)]	1 (0–1)	0 (0–1)	–0.111	0.912
qSOFA score [score, M (Q1–Q3)]	0 (0–0)	0 (0–0)	–0.696	0.486
SOFA score [score, M (Q1–Q3)]	0 (0–1)	0 (0–1)	–1.357	0.175
Sepsis (n, %)	205 (12.3)	93 (13.1)	0.266	0.606
Admission to ICU (n, %)	72 (4.3)	37 (5.2)	0.879	0.349
Mortality (n, %)	32 (1.9)	10 (1.4)	0.763	0.382
Length of hospital stay [day, M (Q1–Q3)]	8 (6–12)	9 (6–12)	–1.477	0.140

WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; SBP, systolic blood pressure; SpO_2, oxygen saturation; INR, international normalized ratio; APTT, activated partial thromboplastin time; PLT, platelet; AGI, acute gastrointestinal injury; qSOFA, quick Sequential Organ Failure Assessment; SOFA, Sequential Organ Failure Assessment; ICU, Intensive Care Unit; GCS, Glasgow Coma Scale.

Table 2. Univariate analysis of factors predictive of sepsis.

Variables	Sepsis group (n = 205)	Non-sepsis group (n = 1462)	Test value (Z/χ^2)	*p*-value
Age [year-old, M (Q1–Q3)]	74 (62–83)	60 (45–71)	–8.980	<0.01
Gender (male) [n (%)]	121 (59.0)	784 (53.6)	2.112	0.146
Source of infection (n, %)			4.157	0.245
Lung	95 (46.3)	714 (48.8)		
Digestive system	75 (36.6)	474 (32.4)		
Urinary system	21 (10.3)	202 (13.8)		
Blood flow and others	14 (6.8)	72 (5.0)		
Body temperature (n, %)			-	<0.01
>38 °C	108 (52.7)	382 (26.1)		
36–38 °C	92 (44.9)	1079 (73.8)		
<36 °C	5 (2.4)	1 (0.1)		
Heart rate (n, %)			-	<0.01
>100 bpm	111 (54.1)	362 (24.8)		
60–100 bpm	92 (44.9)	1100 (75.2)		
<60 bpm	2 (1.0)	0 (0)		
Tachypnea (≥22 bpm) (n, %)	78 (38.0)	99 (6.8)	185.325	<0.01
Altered consciousness (GCS score ≤13) (n, %)	25 (12.2)	18 (1.2)	86.003	<0.01
Severe edema (n, %)	9 (4.4)	0 (0)	56.617	<0.01
Hyperglycemia (>10 mmol/L) (n, %)	73 (35.6)	245 (16.8)	41.391	<0.01
WBC count (n, %)			130.700	<0.01
$>12 \times 10^9$/L	85 (41.5)	173 (11.8)		
$4–12 \times 10^9$/L	98 (47.8)	1184 (81.0)		
$<4 \times 10^9$/L	22 (10.7)	105 (7.2)		
CRP greater than the reference limit (n, %)	180 (87.8)	910 (62.2)	51.904	<0.01
PCT greater than the reference limit (n, %)	89 (43.4)	86 (5.9)	269.550	<0.01
Hypotension (SBP ≤100 mmHg) (n, %)	100 (48.8)	224 (15.3)	128.541	<0.01

Table 2. Continued.

Variables	Sepsis group (n = 205)	Non-sepsis group (n = 1462)	Test value (Z/χ^2)	*p*-value
SpO_2 without oxygen [%, M (Q1–Q3)]	89 (86–97)	97 (95–98)	–10.617	<0.01
Elevated creatinine greater than the reference limit (n, %)	46 (22.4)	161 (11.0)	21.585	<0.01
Coagulation dysfunction (n, %) (INR >1.5, APTT >60 s)	14 (6.8)	8 (0.5)	49.765	<0.01
PLT $<100 \times 10^9$/L	55 (26.8)	57 (3.9)	150.840	<0.01
Mottle (n, %)	2 (1.0)	0 (0)	-	0.015
AGI grade [grade, M (Q1–Q3)]	2 (1–2)	0 (0–1)	–18.267	<0.01
qSOFA score [score, M (Q1–Q3)]	1 (0–1)	0 (0–0)	–15.867	<0.01
SOFA score [score, M (Q1–Q3)]	2 (2–3)	0 (0–1)	–27.114	<0.01
Admission to ICU (n, %)	71 (34.6)	1 (0.1)	519.799	<0.01
Mortality (n, %)	31 (15.1)	1 (0.1)	208.473	<0.01
Length of hospital stay [day, M (Q1–Q3)]	11 (8–17.5)	8 (6–11)	–8.633	<0.01

WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; SBP, systolic blood pressure; SpO_2, oxygen saturation; INR, international normalized ratio; APTT, activated partial thromboplastin time; PLT, platelet; AGI, acute gastrointestinal injury; qSOFA, quick Sequential Organ Failure Assessment; SOFA, Sequential Organ Failure Assessment.

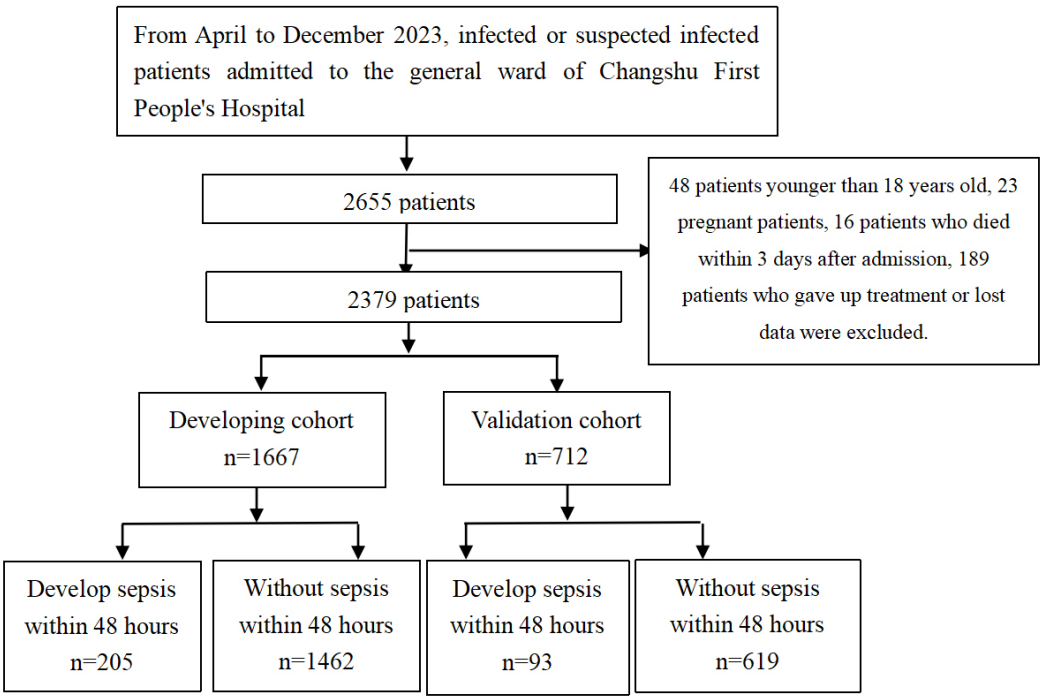

Fig. 1. A flowchart of the study design and patient selection. The figure was created using the WPS office (version 12.1.0.20288, Kingsoft Corporation Limited, Beijing, China).

Discussion

Sepsis remains a public health concern worldwide due to its high incidence and mortality rates (Wang and Zhong, 2024). Therefore, there is a need for reliable screening tools for quickly and accurately assessing the disease condition, enabling early treatment, and improving patient prognosis. Initially, Sepsis 1.0 was originally diagnosed using the Systemic Inflammatory Response Syndrome (SIRS) score (Dellinger et al, 2013), but its oversensitivity and lack of specificity alleviated its efficacy. To address these challenges, Sepsis 2.0 introduced more stringent screening criteria (Rhodes et al, 2017), though the complexity of this tool hindered its clinical utility. In 2016, Sepsis 3.0 was developed, focusing on organ dysfunction caused by infection, and recommending qSOFA as a screening indicator for systemic infection in non-ICU settings (Yao et al, 2024). However, studies reported that while qSOFA has high specificity, its sensitivity for identifying sepsis ranges from 28.5–53%, and its sensitivity for predicting mortality at 7 days and 28 days in infected patients is 34.4% and 26.9%, respectively, resulting in risk of missed diagnosis and delayed treatment (Rahmatinejad et al, 2023; Schertz et al, 2023; Tiwari et al, 2023). In our study, qSOFA indicated a sensitivity of 68.8% in the developing cohort and 66.7% in the validation cohort.

Table 3. Multivariate regression analysis of predictive factors of sepsis.

Variables	β	Standard error (S.E.)	Wald	p-value	OR	95% CI
Age	0.029	0.007	16.896	<0.01	1.029	1.015–1.043
Body temperature	0.314	0.258	1.478	0.224	1.358	0.825–2.269
Heart rate	0.449	0.264	2.880	0.090	1.566	0.933–2.630
Tachypnea	0.632	0.324	3.806	0.051	1.882	0.997–3.553
Altered consciousness	0.157	0.595	0.070	0.792	1.170	0.364–3.757
Severe edema	19.710	1.085×10^4	0.000	0.999	3.631×10^8	0.000
Hyperglycemia	0.339	0.267	1.609	0.205	1.403	0.831–2.369
WBC count	0.229	0.165	1.910	0.167	1.257	0.909–1.738
CRP greater than the reference limit	0.173	0.335	0.267	0.606	1.189	0.616–2.293
PCT greater than the reference limit	0.554	0.309	3.205	0.073	1.740	0.949–3.191
Hypotension	1.351	0.249	29.516	<0.01	3.863	2.372–6.290
SpO_2 without oxygen	–0.230	0.029	64.418	<0.01	0.795	0.751–0.840
Elevated creatinine greater than the reference	0.560	0.302	3.441	0.064	1.751	0.969–3.166
Coagulation dysfunction	–0.355	0.793	0.200	0.655	0.701	0.148–3.320
PLT $<100 \times 10^9$/L	1.733	0.353	24.165	<0.01	5.657	2.835–11.289
Mottle	15.189	2.624×10^4	0.000	1.000	3.949×10^8	0.000
AGI grade	1.967	0.178	121.559	<0.01	7.151	5.040–10.144
Constant	14.046	2.683	27.415			

WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; SpO_2, oxygen saturation; PLT, platelet; AGI, acute gastrointestinal injury; CI, Confidence Interval; OR, Odds Ratio.

Table 4. ROC curve for each predictive model.

Group	Model	AUC (95% CI)	Cut-off value	Specificity (%)	Sensitivity (%)	*p*-value (compared with model A)
Developing cohort	A	0.758 (0.723–0.792)	0.137	81.4	68.8	-
	B	0.947 (0.932–0.963)	0.105	86.8	89.3	<0.01
Validation cohort	A	0.761 (0.709–0.814)	0.137	82.7	66.7	-
	B	0.962 (0.945–0.978)	0.087	83.0	95.7	<0.01

AUC, area under the curve; ROC, receiver operating characteristic.

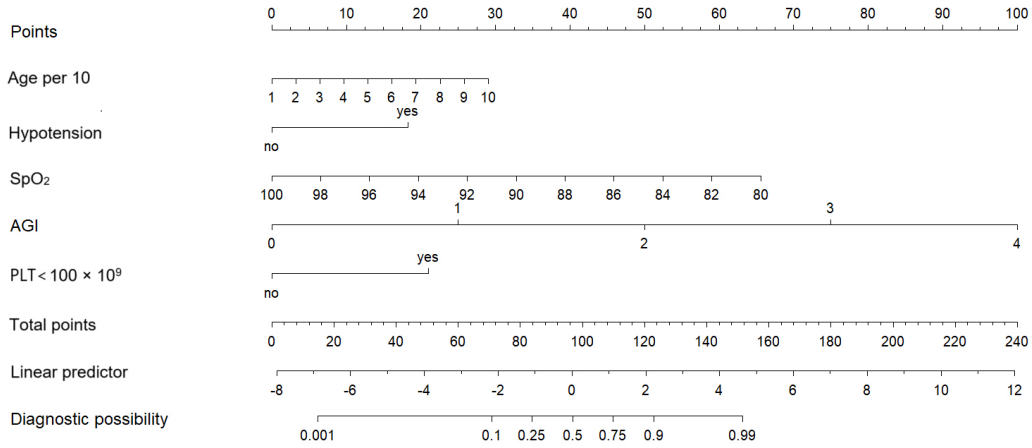

Fig. 2. The nomogram for model B. SpO_2, oxygen saturation; AGI, acute gastrointestinal injury.

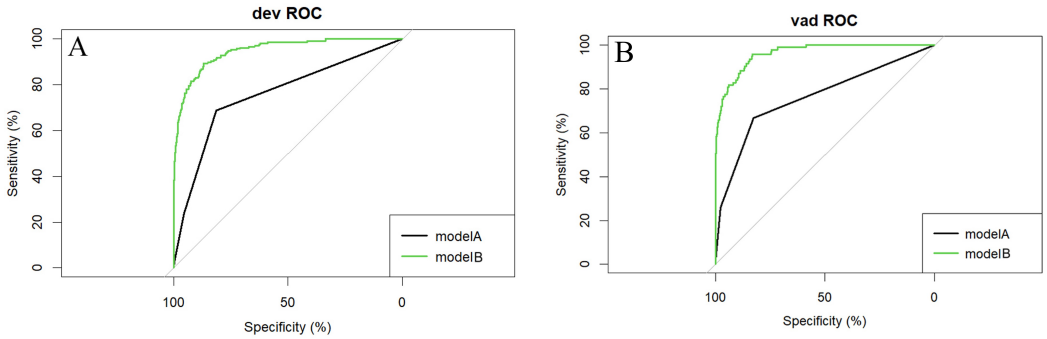

Fig. 3. ROC analysis of the sepsis models. (A) Developing cohort. (B) Validation cohort. ROC, receiver operating characteristic.

Our study included 2379 patients, with the increased number of infected patients admitted during the study attributed to several factors. As a tertiary care general hospital, Changshu Hospital Affiliated to Soochow University has high medical standards and 1265 beds, can accommodate a large number of patients. Additionally, Changshu City's dense population and robust economy contribute to a significant pool of potential infectious disease cases. Seasonal factors, such

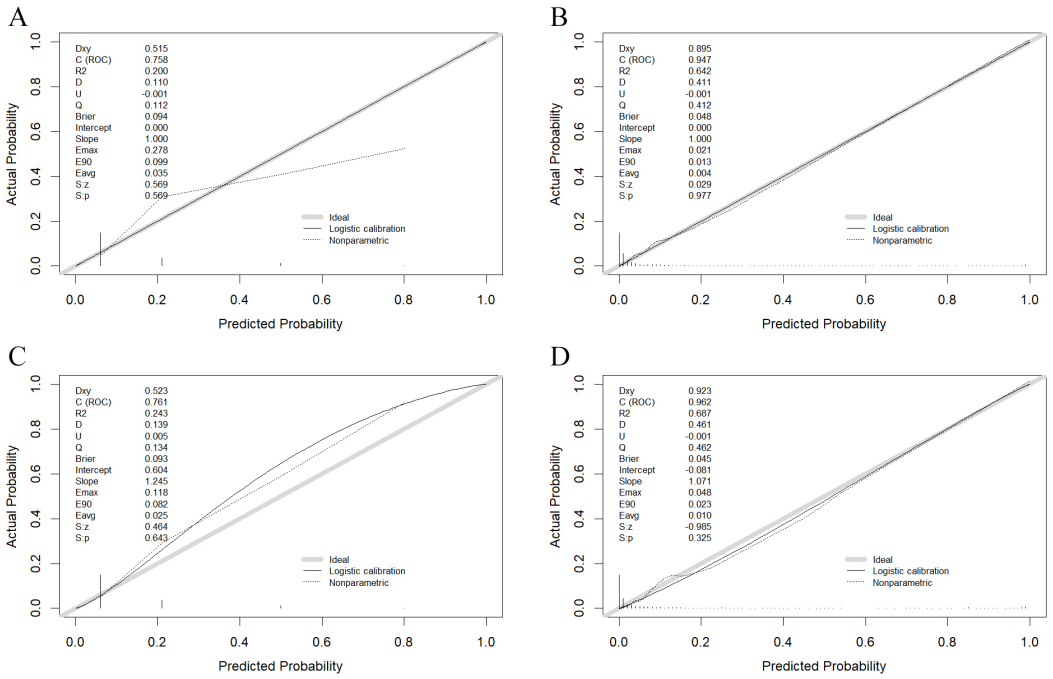

Fig. 4. Calibration plot for each model. (A) Developing cohort of model A. (B) Developing cohort of model B. (C) Validation cohort of model A. (D) Validation cohort of model B.

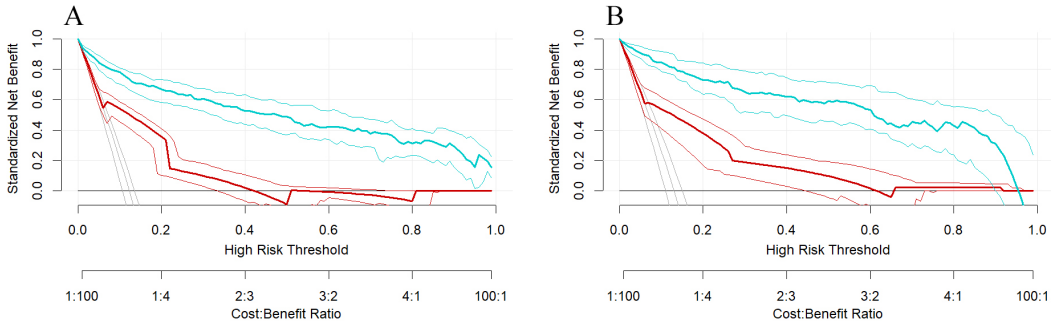

Fig. 5. Decision curve analysis (DCA) for each model. (A) Developing cohort. (B) Validation cohort. The red curve represents model A, the blue curve represents model B, the gray curve represents all of them benefited, and the black curve represents none of them benefited.

as spikes in Coronavirus Disease (COVID)-19 infections and prevalent influenza cases, further exacerbate influx of infected patients during this timeframe. We developed and validated a prediction model based on AGI grading for early and rapid screening of sepsis patients in general wards. The model contains 5 key variables, including age, hypotension, SpO_2, thrombocytopenia, and AGI grade. In the developing cohort, the model exhibited a sensitivity of 89.3% and a specificity of 86.8%. Compared to qSOFA, this model enhances sensitivity without compromising specificity, thereby reducing the incidence of missed diagnoses of sepsis. It ensures that a greater proportion of critically ill patients with infections are accurately identified, improving the precision and timeliness of treatment. Through internal validation and comparison with the qSOFA scoring system, the model demonstrated immense

potential for clinical application, facilitating the rapid diagnosis of sepsis in general wards.

Our study revealed AGI grade as an independent risk factor for sepsis. The release of inflammatory mediators, capillary leakage, fluid exudation, vasoconstriction, and diastolic disorders during sepsis disrupt the intestinal mucosal barrier and result in gastrointestinal dysfunction. This mechanism affects nutrient digestion and absorption, impairs the balance of intestinal flora and their products, and impacts gastrointestinal endocrine and immune functions. The consequent "enterogenic sepsis" followed by pathophysiological changes can lead to multi-organ failure. Therefore, the gut plays a crucial role in downstream complications (Patel et al, 2024; Shang et al, 2024), and the gastrointestinal tract is often the initiating organ of sepsis and the most susceptible organ. In 2012, the European Society of Intensive Care Medicine proposed a definition and grading criteria for AGI, integrating factors of gastrointestinal bleeding, gastrointestinal paralysis, diarrhea frequency, feeding intolerance, bowel sounds, and intra-abdominal pressure (Hai et al, 2024).

The incidence of AGI is relatively high among critically ill patients, with the mortality rate rising along with the severity of AGI (Zhong et al, 2021). Patients exhibiting septic shock with AGI grade III to IV show higher heart rates and mottle scores, lower mean arterial pressure, substantially lower urine output, and a correlation between AGI failure and ICU mortality (Klanovicz et al, 2023). Similar to previous studies, factors like age, hypotension, hypoxia, and thrombocytopenia are found to be strong independent risk factors for sepsis (Michels et al, 2022; Kausch et al, 2024; Hua et al, 2023; Giustozzi et al, 2021; Xu et al, 2024). Research indicates that sepsis-related mortality is independent of comorbidities and associated with older age, with decreased expression of genes involved in cytokine signaling, innate and adaptive immunity, and increased expression of genes correlated with hemostasis and endothelial cell activation in patients aged $\geq$70 years compared to those aged $<$50 years (Michels et al, 2022). Additionally, the risk of sepsis during ventilator use is associated with prolonged hypoxemia prior to sepsis (SpO_2 $<$80% for an average duration of 10–300 seconds) (Kausch et al, 2024). Thrombocytopenia is known as a predictor of poor prognosis in sepsis (Hua et al, 2023), potentially due to mechanisms such as disseminated intravascular coagulation, leading to platelet activation and thrombosis, as well as bone marrow suppression resulting in impaired megakaryocyte maturation. Furthermore, the body's autoimmune response can produce anti-platelet antibodies, causing increased platelet destruction; moreover, an excessive inflammatory response further elevates platelet consumption and thrombocytopenia can also be caused by medications, such as antineoplastic drugs and antibiotics (Giustozzi et al, 2021; Xu et al, 2024). Therefore, these factors should be carefully monitored while treating infected patients to ensure effective management.

Unlike the qSOFA screening criteria, the prediction model variables did not involve impairments in consciousness or respiratory rate. The assessment of consciousness is influenced by subjective factors, thereby potentially limiting its utility in the early detection of sepsis (El Chakhtoura et al, 2017). Additionally, an increased respiratory rate is not always a specific indicator of sepsis, as it can be

caused by various other factors such as cardiopulmonary diseases, anxiety, or physical activity. Moreover, some sepsis patients may not demonstrate an increased respiratory rate in the early stages, potentially resulting in missed diagnosis if this factor is relied upon solely.

Concerning the current sepsis screening criteria, the qSOFA score is widely utilized; nevertheless, its sensitivity is relatively low, which may lead to missed diagnosis of genuine sepsis cases. The qSOFA score depends on three general indicators—respiratory rate, level of consciousness, and systolic blood pressure—which can also be abnormal in non-sepsis circumstances. As a result, the qSOFA score may incorrectly diagnose non-sepsis patients as having sepsis while failing to detect milder cases of the condition. A recent study devised the Early Assessment of Sepsis Engagement (EASE) model, a clinical tool designed for the early identification of potential sepsis patients, comprising components such as alcohol consumption, pulmonary infection, temperature, respiratory rate, heart rate, serum urea nitrogen, and white blood cell count. The model exhibited an area under the curve (AUC) of up to 86.5% (95% CI, 84.2%–88.8%). However, its AUC in internal validation was significantly lower, at 72.2% (95% CI, 66.6%–77.7%), likely due to its focus on primarily inflammation-related indicators, which may not comprehensively assess overall organ function (Guo et al, 2023). Our study addresses this limitation by incorporating the AGI staging, compensating for the gap in organ function assessment and enhancing the sensitivity and specificity of sepsis prediction when combined with other clinical indicators. The variables in the new model can be quickly obtained through patient interviews, with the only test results (PLT count) available within about 10 minutes. This makes the model valuable for early screening of high-risk patients. In our study, the median score for sepsis patients was 105. According to the model's nomogram, patients reaching this score should undergo prompt clinical intervention or be transferred to the ICU for further treatment, as this score indicates a higher risk of sepsis.

However, there are still some limitations in this study: (1) the selected indicator is based on a single time point, and the best time window for observing changes remains unclear; (2) there is no distinction between chronic and acute organ dysfunction; (3) the prediction model lacks external validation, warranting further multicenter investigation for broader utility.

Conclusion

The prediction model for the diagnosis of sepsis based on the classification of acute gastrointestinal injury demonstrates higher predictive efficacy and accuracy in detecting sepsis, which is effective in guiding clinicians to make prompt decisions and take appropriate measures early, thereby holding substantial clinical significance.

Key Points

- Gastrointestinal dysfunction can manifest early in sepsis.
- Acute gastrointestinal dysfunction affects the prognosis of sepsis patients.
- The prediction model for sepsis detection, classified by acute gastrointestinal injury, improves the sensitivity and specificity of early identification.

Availability of Data and Materials

The data presented in this study are available from the corresponding author upon reasonable request.

Author Contributions

Conception and design: SY and SL; Methodology: SY, CX and SL; Software: SY, CX; Validation: CY, LY; Formal analysis, SY, CY and LP; Investigation: SY, SL, CX, SW, CY, LY and LP; Data curation: SY, SL; Writing—original draft: SY, CX, SL, SW and CY; Writing—review & editing: SY, CX, SL, SW, CY, LY and LP; Supervision: CX, SL; Project administration: SY; Funding acquisition: SY and CX. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

All procedures were performed in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Changshu First People's Hospital (Approval No.: L2024049). The Ethics Review Committee of Changshu First People's Hospital granted a waiver of informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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