Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

A Simple Nomogram for Predicting the Development of ARDS in Postoperative Patients with Gastrointestinal Perforation: A Single-Center Retrospective Study

Ze Zhang[1], Haotian Zhao[2], Zhiyang Zhang[1], Lijing Jia[1], Ling Long[1], You Fu[1], Quansheng Du[1]

[1]Department of Intensive Care Unit, Hebei General Hospital, Shijiazhuang, Hebei, People's Republic of China; [2]Department of Ultrasound, Hebei General Hospital, Shijiazhuang, Hebei, People's Republic of China

Correspondence: Quansheng Du, Department of Intensive Care Unit, Hebei General Hospital, Shijiazhuang, 050000, Hebei, People's Republic of China, Email duquansheng@hebmu.edu.cn

Background: Acute respiratory distress syndrome (ARDS) is a severe form of organ dysfunction and a common postoperative complication. This study aims to develop a predictive model for ARDS in postoperative patients with gastrointestinal perforation to facilitate early detection and effective prevention.

Methods: In this single-center retrospective study, clinical data were collected from postoperative patients with gastrointestinal perforation admitted to the ICU in Hebei Provincial People's Hospital from October 2017 to May 2024. Univariate analysis and multifactorial logistic regression analysis were used to determine the independent risk factors for developing ARDS. Nomograms were developed to show predictive models, and the discrimination, calibration, and clinical usefulness of the models were assessed using the C-index, calibration plots, and decision curve analysis (DCA).

Results: Two hundred patients were ultimately included for analysis. In the development cohort, 38 (27.1%) of 140 patients developed ARDS, and in the internal validation cohort, 13 (21.7%) of 60 patients developed ARDS. The multivariate logistic regression analysis revealed the site of perforation (OR = 0.164, P = 0.006), the duration of surgery (OR = 0.986, P = 0.008), BMI (OR = 1.197, P = 0.015), SOFA (OR = 1.443, P = 0.001), lactate (OR = 1.500, P = 0.017), and albumin (OR = 0.889, P = 0.007) as the independent risk factors for ARDS development. The area under the curve (AUC) was 0.921 (95% CI: 0.869, 0.973) for the development cohort and 0.894 (95% CI: 0.809, 0.978) for the validation cohort. The calibration curve and decision curve analysis (DCA) demonstrate that the nomogram possesses good predictive value and clinical practicability.

Conclusion: Our research introduced a nomogram that integrates six independent risk factors, facilitating the precise prediction of ARDS risk in postoperative patients following gastrointestinal perforation.

Keywords: gastrointestinal perforation, acute respiratory distress syndrome, prediction model, nomogram

Introduction

Acute respiratory distress syndrome (ARDS) is defined by significant, widespread inflammatory damage to the lung parenchyma, which arises from various predisposing risk factors, such as pulmonary or non-pulmonary infections, trauma, aspiration, or shock.[1–3] Intra-abdominal infections (IAI) as an extrapulmonary cause of acute respiratory distress syndrome (ARDS), and an observational study showed that 16% of ARDS were caused by sepsis of extrapulmonary origin.[4] There are many causes of abdominal infections, including appendicitis, cholecystitis, and gastrointestinal perforation, among which the incidence of gastrointestinal perforation is about one-third, and the mortality rate can be up to 30% ~ 50%.[5,6] Moreover, ARDS also increases health care resource utilization, with substantial increases in lengths of stay and hospital costs, and although most ARDS survivors regain normal or near-normal lung function, many still suffer complications such as muscle weakness and psychological sequelae of severe disease.[7,8]

Received: 18 September 2024
Accepted: 29 December 2024
Published: 7 January 2025

Lung-protective ventilation, prone ventilation has been shown to be effective in the treatment of ARDS, and glucocorticoids, high PEEP, and neuromuscular blockers may be beneficial in specific patients.[9] It is due to the heterogeneity of ARDS that the American Thoracic Society released a statement in 2021 proposing that precision medicine should be combined with genomics, biology, and environmental factors to individualize the treatment of ARDS;[10] therefore, it is necessary to analyze the risk factors in the clinical work and individualize the treatment of ARDS due to different etiologies. Early diagnosis and intervention can help improve the prognosis of ARDS. Currently, the focus of both domestic and international research has shifted from the treatment of ARDS to the prevention of ARDS in order to reduce the morbidity and mortality associated with ARDS.[11] Previous studies have modeled certain scores to predict the risk of postoperative pneumonia, acute lung injury (ALI), or ARDS in patients.[12–14] However, most of these studies have based their models on the general population or on multiple types of surgeries, and many of the predictors included in the models are not applicable to patients undergoing specific types of surgery.[15,16]

In conclusion, there are few predictors or predictive models for assessing the likelihood of developing ARDS in postoperative patients with gastrointestinal perforation. Therefore, effective grading, predictors, or prediction models are valuable for early identification of the risk of developing ARDS in postoperative patients with gastrointestinal perforation. The aim of our study was to develop a comprehensive and effective personalized scoring system based on demographic and clinical characteristics for predicting the probability of secondary ARDS in patients after surgery for gastrointestinal perforation.

Method

Study Design and Populations

This retrospective, single-center observational study was conducted from October 2017 to May 2024 at Hebei Provincial People's Hospital. The study was approved by the Ethics Committee of Hebei Provincial People's Hospital (No. 2023–68). Informed consent was waived due to the retrospective and observational nature of the study. The Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) +artificial intelligence (AI) statement was used as reporting guideline.[17]

Postoperative patients with gastrointestinal perforation treated in the Department of Intensive Care Unit (ICU) of Hebei Provincial People's Hospital from October 1, 2017, to May 1, 2024, were selected as study subjects. Eligible patients were included when: 1. Age ≥18 years; 2. Length of stay in the ICU ≥ 24 hours. Exclusion criteria were: 1. Diagnosis of ARDS at the time of ICU admission; 2. Patients on palliative care; 3. Patients with underlying lung disease; 4. Patients with malignant tumors or other immunodeficiencies; 5. Pregnant or lactating women.

In the end, we included 200 postoperative patients with gastrointestinal perforation and excluded 68 patients. Then, based on a development set ratio verification set of approximatively 7: 3, 140 patients were included in the development cohort and 60 patients were included in the validation cohort (Figure 1). All patients were treated according to the hospital's medical guidelines. The outcome of our study was the incidence of ARDS in postoperative patients with gastrointestinal perforation. ARDS is diagnosed with reference to the Berlin definition.[18]

Data Collection

Demographic information and other clinical characteristics were collected prior to the admission of patients requiring surgery after the initial emergency room evaluation by reviewing the medical records of study participants. 1. Demographic information: gender, age, smoking and drinking history, body mass index (BMI); 2. Other comorbidities in patients; 3. Vital signs upon admission to the emergency room: temperature, heart rate, blood pressure, respiratory rate, and pulse oximetry; 4. Laboratory investigations upon admission to the emergency room: routine blood tests, biochemistry, blood gas analysis, procalcitonin, interleukin 6, and C-reactive protein; 5. Clinical acute physiology and chronic health evaluation II (APACHE II), sequential organ failure assessment (SOFA) after admission to the ICU, central venous pressure (CVP), and intra-abdominal pressure (IAP); 6. Clinical data should also be collected, such as onset time, the duration of surgery, the site of perforation, laparoscope or laparotomy, diameter of perforation, and amount of bleeding.

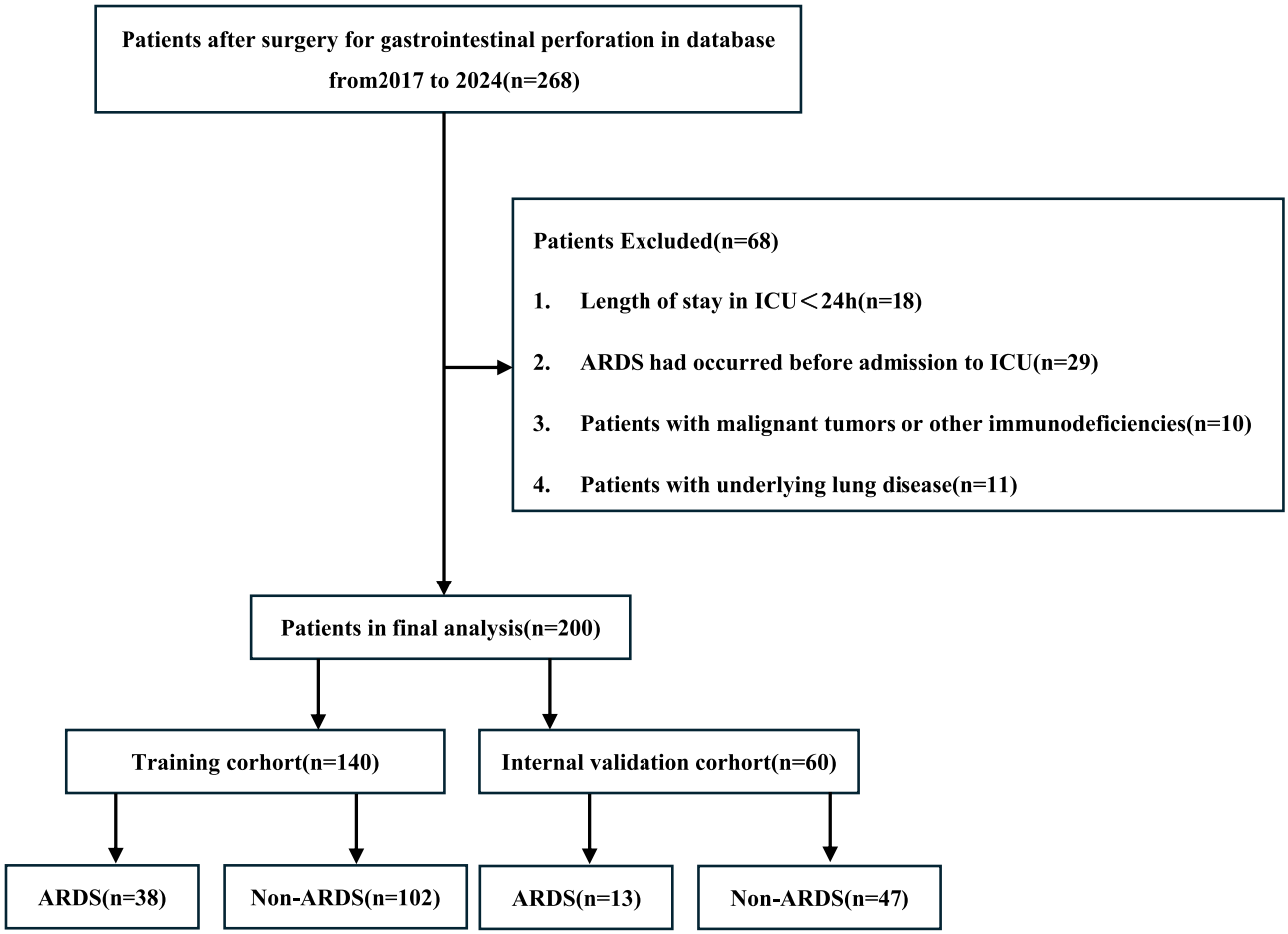

Figure 1 Flow chart for patient selection.
Abbreviation: ARDS, acute respiratory distress syndrome.

Dealing with Missing Data

To comprehensively address the issue of missing values in the dataset, we utilized the VIM and mice packages in R to visualize and process the missing data. The VIM package offers various visualization techniques, including the missing plot, marginal histogram, and correlation matrix, which enhance our understanding of the patterns of missingness in the data. IAP was not included in the univariate analysis because its missing values were greater than 50%. All other missing values were less than 20%, and these data were interpolated multiple times were handled by a multiple imputation method, as previously reported.[19] The method is based on a complete conditional specification in which separate models interpolate each incomplete variable. The multivariate imputation by chained equation algorithm can impute mixes of continuous, binary, and unordered and ordered categorical data.[20] Multiple interpolation was performed using chained equations to estimate missing data for 5 iterations. This generated 5 complete datasets for model development and the 5th dataset was finally selected for analysis.

Estimating Parameter Effects

Risk factors for the development of ARDS were screened using univariate analysis, and factors with $P < 0.1$ were included in multivariate logistic regression analysis to screen for independent predictors of the development of ARDS. Odds ratios (ORs) and their respective 95% confidence intervals (CI) were used to quantify the risk. Variables proved to be significantly associated with outcome at univariate analysis were entered in a multivariable model. A backward stepwise selection approach was used to limit the number of variables in the final multivariable model to significant

https://doi.org/10.2147/JIR.S496559

independent predictors of ARDS. A nomogram was constructed based on the results of the final multivariable model, making it possible to estimate the probability of developing ARDS.

Assessing the Model's Performance

The final model's discriminative power was assessed based on the area under the curve (AUROC) of the subject's operating characteristics. An AUROC greater than 0.7 indicates good model discrimination. We used the Hosmer-Lemeshow goodness-of-fit test and calibration curves to assess the calibration of the ARDS prediction model column-line plots. In addition, the Harrell C index was calculated to quantify the discriminatory performance of the ARDS prediction model column-line plots. Decision curve analysis (DCA) was used to determine the clinical validity of the ARDS prediction model by quantifying the net benefit of different threshold probabilities in the dataset.[21] The net benefit was calculated by subtracting the proportion of all false-positive patients from the proportion of true-positive patients and weighing the relative harms of abandoning the intervention against the negative consequences of unnecessary intervention.

Statistical Methods

Data were analyzed using R4.2.2 software. Measurement information conforming to normal distribution was expressed as mean ± standard deviation (x ± s), and comparisons between groups were made using the *t*-test for two independent samples; non-normally distributed measurements were expressed as median and interquartile spacing, and comparisons between two independent samples were made using the non-parametric test. Count data were expressed as frequencies or percentages, and comparisons between groups were made using the chi-square test. Differences in two-sided P values < 0.05 were considered statistically significant. All analyses were performed using R software v4.2.2 (R Core Team, Vienna, Austria) using the "compareGroups", "VIM", "mice", "pROC", "rms", "rmda", "ResourceSelection", "calibrationcurves", and "glmnet" packages.

Results

Clinical Characteristics

A total of 268 postoperative patients with gastrointestinal perforation admitted to the ICU and 68 were excluded based on exclusion criteria (Figure 1). The included patients were divided into the development cohort (140 patients) and the validation cohort (60 patients). We compared the baseline characteristics of the datasets before and after imputation and found no significant differences between the two groups (P > 0.05), as shown in Table 1. Further ROC analysis on the development cohorts before and after imputation, along with DeLong test results, showed no statistically significant differences (P = 0.737), as shown in Figure 2. This indicates that the datasets before and after imputation are comparable

Table 1 Baseline Characteristics of Postoperative Patients with Gastrointestinal Perforation in the Before Imputation Dataset and the Imputation Dataset

Variables	Overall	Before Imputation	Imputation	*P* value
	N=400	N=200	N=200	
BMI (kg/m^2)	22.3 (3.74)	22.3 (3.75)	22.3 (3.75)	1.000
Age (years)	72.0 [62.0;80.0]	72.0 [62.0;80.0]	72.0 [62.0;80.0]	1.000
Gender				1.000
Male	262 (65.5%)	131 (65.5%)	131 (65.5%)	
Female	138 (34.5%)	69 (34.5%)	69 (34.5%)	
Smoking	98 (24.5%)	49 (24.5%)	49 (24.5%)	1.000

(*Continued*)

Table 1 (Continued).

Variables	Overall	Before Imputation	Imputation	*P* value
	N=400	N=200	N=200	
Alcoholism	28 (7.00%)	14 (7.00%)	14 (7.00%)	1.000
Hypertension	146 (36.5%)	73 (36.5%)	73 (36.5%)	1.000
Diabetes	40 (10.0%)	20 (10.0%)	20 (10.0%)	1.000
Coronary Heart Disease	60 (15.0%)	30 (15.0%)	30 (15.0%)	1.000
Cerebrovascular Diseases	66 (16.5%)	33 (16.5%)	33 (16.5%)	1.000
Acute Kidney Injury	146 (36.5%)	73 (36.5%)	73 (36.5%)	1.000
APACHEII	13.0 [10.0;18.0]	13.0 [10.0;18.0]	13.0 [10.0;18.0]	1.000
SOFA	5.00 [3.00;7.00]	5.00 [3.00;7.00]	5.00 [3.00;7.00]	1.000
Temperature (°C)	36.9 [36.4;37.6]	36.9 [36.4;37.6]	36.9 [36.4;37.6]	1.000
Heart Rate (beat/min)	105 (21.3)	105 (21.3)	105 (21.3)	1.000
Respiratory Rate (breath/min)	22.0 [20.0;27.2]	22.0 [20.0;27.2]	22.0 [20.0;27.2]	1.000
SBP (mmHg)	130 (27.4)	130 (27.4)	130 (27.4)	1.000
DBP (mmHg)	74.7 (16.2)	74.7 (16.2)	74.7 (16.2)	1.000
MAP (mmHg)	93.2 (17.9)	93.2 (17.9)	93.2 (17.9)	1.000
SpO2 (%)	96.0 [93.0;98.0]	96.0 [93.0;98.0]	96.0 [93.0;98.0]	1.000
Onset Time (hours)	24.0 [10.0;48.0]	24.0 [10.0;48.0]	24.0 [10.0;48.0]	1.000
The Duration of Surgery (minutes)	130 [90.0;171]	130 [90.0;171]	130 [90.0;171]	1.000
Diameter of Perforation (cm)	0.80 [0.50;1.50]	0.80 [0.50;1.50]	0.80 [0.50;1.50]	0.995
The Site of Perforation				1.000
Lower GI tract	168 (42.0%)	84 (42.0%)	84 (42.0%)	
Upper GI tract	232 (58.0%)	116 (58.0%)	116 (58.0%)	
Surgical Approach				1.000
Laparoscope	194 (48.5%)	97 (48.5%)	97 (48.5%)	
Laparotomy	206 (51.5%)	103 (51.5%)	103 (51.5%)	
Seroperitoneum (mL)	400 [200;800]	400 [200;800]	400 [200;800]	0.898
Amount of Bleeding (mL)	10.0 [5.00;20.0]	10.0 [5.00;20.0]	10.0 [5.00;20.0]	0.933
Transfusion	120 (30.0%)	60 (30.0%)	60 (30.0%)	1.000
Intraoperative Fluid Balance (mL)	2505 [1945;3375]	2505 [1945;3375]	2505 [1945;3375]	1.000
Shock	256 (64.0%)	128 (64.0%)	128 (64.0%)	1.000
CVP (mmHg)	10.0 [7.00;12.0]	10.0 [7.00;12.0]	10.0 [7.00;12.0]	0.968
PCT (ng/mL)	10.3 [3.69;24.7]	10.3 [3.69;24.7]	10.4 [3.64;24.8]	0.987
CRP (mg/L)	107 [30.8;220]	109 [33.9;220]	105 [28.9;220]	0.654

(*Continued*)

https://doi.org/10.2147/JIR.S496559

Table 1 (Continued).

Variables	Overall	Before Imputation	Imputation	*P* value
	N=400	N=200	N=200	
White blood cell (×10^9 /L)	10.4 [6.26;14.5]	10.4 [6.26;14.5]	10.4 [6.26;14.5]	1.000
Hemoglobin (g/L)	124 (29.1)	124 (29.1)	124 (29.1)	1.000
Platelet (×10^9/L)	238 [179;298]	238 [179;298]	238 [179;298]	1.000
Bicarbonate (mmol/L)	21.1 [18.8;23.5]	21.1 [18.8;23.5]	21.1 [18.8;23.5]	1.000
Lactate (mmol/L)	2.20 [1.50;3.50]	2.20 [1.50;3.50]	2.20 [1.50;3.50]	1.000
Albumin (g/L)	31.6 (8.09)	31.6 (8.10)	31.6 (8.09)	0.978
Prealbumin (g/L)	9.50 [6.95;12.3]	9.50 [7.00;12.4]	9.45 [6.90;12.3]	0.834

Notes: Data are shown as median with interquartile range (IQR) for continuous variables and number with percentage for categorical variables.

Abbreviations: BMI, Body Mass Index; APACHE, Acute Physiology and Chronic Health Evaluation score; SOFA, Sequential Organ Function Assessment; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MBP, Mean Blood Pressure; SpO2, pulse oximetry-derived oxygen saturation; GI, gastrointestinal; CVP, central venous pressure; CRP, C-reactive protein.

in terms of baseline characteristics and predictive performance. The incidence of ARDS was 38 (27.1%) in the development cohort and 13 (21.7%) in the internal validation cohort. Baseline demographics and clinical characteristics are shown in Table 2. Aside from two variables, namely BMI and the perforation diameter, which exhibited significant differences, the other clinical characteristics showed no variation between the development and validation cohorts.

Model Development

Univariate analysis of the correlation between demographic and clinical variables and the development of ARDS among postoperative patients with gastrointestinal perforation in Table 3. As shown, variables significantly related to ARDS development were BMI (OR 1.232; 95% CI, 1.089–1.394; P =0.001), Smoking (OR 3.177; 95% CI, 1.409–7.166;

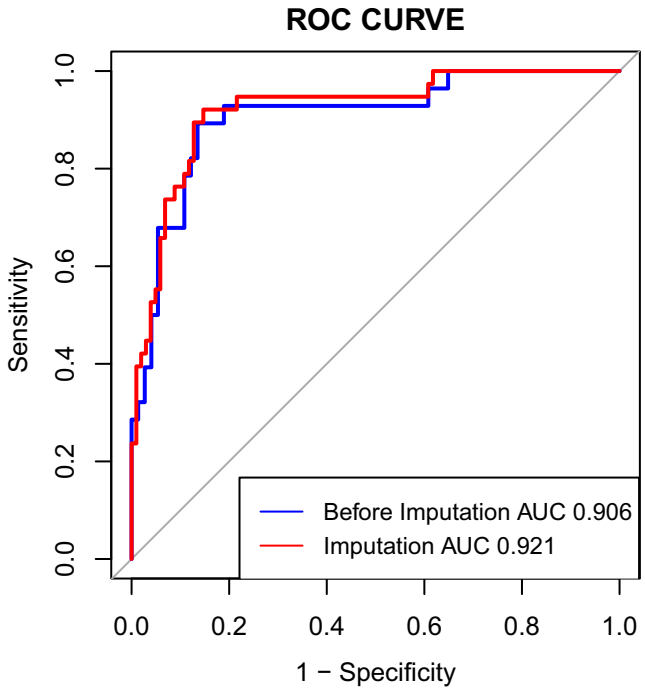

Figure 2 ROC curves of the development cohorts before and after imputation.
Abbreviation: ROC, receiver-operating characteristic.

Table 2 Baseline Characteristics of Postoperative Patients with Gastrointestinal Perforation in the Development Cohort and Validation Cohort

Variables	Overall	Development Cohort	Validation Cohort	*P* value
	N=200	N=140	N=60	
BMI (kg/m^2)	22.3 (3.75)	21.9 (3.60)	23.2 (3.94)	0.035
Age (years)	72.0 [62.0;80.0]	72.5 [63.0;80.0]	70.5 [58.0;79.0]	0.418
Gender				0.299
Male	131 (65.5%)	88 (62.9%)	43 (71.7%)	
Female	69 (34.5%)	52 (37.1%)	17 (28.3%)	
Smoking	49 (24.5%)	35 (25.0%)	14 (23.3%)	0.943
Alcoholism	14 (7.00%)	10 (7.14%)	4 (6.67%)	1
Hypertension	73 (36.5%)	49 (35.0%)	24 (40.0%)	0.608
Diabetes	20 (10.0%)	11 (7.86%)	9 (15.0%)	0.198
Coronary Heart Disease	30 (15.0%)	21 (15.0%)	9 (15.0%)	1
Cerebrovascular Diseases	33 (16.5%)	20 (14.3%)	13 (21.7%)	0.28
Acute Kidney Injury	73 (36.5%)	50 (35.7%)	23 (38.3%)	0.848
APACHEII	13.0 [10.0;18.0]	13.5 [10.0;19.0]	12.0 [9.00;16.0]	0.238
SOFA	5.00 [3.00;7.00]	5.00 [3.00;7.00]	5.50 [4.00;8.00]	0.34
Temperature (°C)	36.9 [36.4;37.6]	36.8 [36.5;37.7]	37.0 [36.4;37.5]	0.777
Heart Rate (beat/min)	105 (21.3)	105 (20.3)	107 (23.4)	0.425
Respiratory Rate (breath/min)	22.0 [20.0;27.2]	21.0 [20.0;26.0]	22.0 [20.0;28.0]	0.248
SBP (mmHg)	130 (27.4)	129 (26.8)	132 (28.9)	0.533
DBP (mmHg)	74.7 (16.2)	73.7 (16.1)	77.0 (16.4)	0.201
MAP (mmHg)	93.2 (17.9)	92.3 (17.9)	95.3 (17.9)	0.274
SpO2 (%)	96.0 [93.0;98.0]	96.0 [93.0;98.0]	95.0 [92.0;98.0]	0.158
Onset Time (hours)	24.0 [10.0;48.0]	20.0 [9.00;48.0]	24.0 [13.0;48.0]	0.084
The Duration of Surgery (minutes)	130 [90.0;171]	130 [93.8;170]	128 [90.0;175]	0.948
Diameter of Perforation (cm)	1.12 (1.03)	1.21 (1.08)	0.91 (0.87)	0.041
The Site of Perforation				0.925
Lower GI tract	84 (42.0%)	58 (41.4%)	26 (43.3%)	
Upper GI tract	116 (58.0%)	82 (58.6%)	34 (56.7%)	
Surgical Approach				0.156
Laparoscope	97 (48.5%)	73 (52.1%)	24 (40.0%)	
Laparotomy	103 (51.5%)	67 (47.9%)	36 (60.0%)	

(*Continued*)

Table 2 (Continued).

Variables	Overall	Development Cohort	Validation Cohort	*P* value
	N=200	N=140	N=60	
Seroperitoneum (mL)	400 [200;800]	325 [200;800]	500 [188;825]	0.522
Amount of Bleeding (mL)	10.0 [5.00;20.0]	10.0 [5.00;20.0]	10.0 [5.00;20.0]	0.935
Transfusion	60 (30.0%)	44 (31.4%)	16 (26.7%)	0.614
Intraoperative Fluid Balance (mL)	2505 [1945;3375]	2446 [1938;3250]	2622 [2079;3605]	0.225
Shock	128 (64.0%)	91 (65.0%)	37 (61.7%)	0.772
CVP (mmHg)	10.0 [7.00;12.0]	10.0 [7.00;12.0]	10.5 [7.00;12.2]	0.338
Procalcitonin (ng/mL)	10.4 [3.64;24.8]	10.8 [3.74;26.3]	8.19 [3.64;21.4]	0.502
CRP (mg/L)	105 [28.9;220]	96.5 [26.8;220]	119 [38.3;196]	0.399
White blood cell ($\times 10^9$ /L)	10.4 [6.26;14.5]	10.5 [6.40;14.4]	9.80 [6.08;15.4]	0.761
Hemoglobin (g/L)	124 (29.1)	123 (27.3)	125 (33.1)	0.674
Platelet ($\times 10^9$/L)	238 [179;298]	224 [174;296]	242 [184;312]	0.435
Bicarbonate (mmol/L)	21.1 [18.8;23.5]	21.1 [19.0;23.6]	21.2 [17.9;23.4]	0.475
Lactate (mmol/L)	2.20 [1.50;3.50]	2.20 [1.60;3.50]	2.18 [1.34;3.55]	0.345
Albumin (g/L)	31.6 (8.09)	31.8 (7.80)	31.3 (8.79)	0.702
Prealbumin (g/L)	9.45 [6.90;12.3]	9.55 [7.40;12.4]	8.15 [5.57;11.9]	0.085

Notes: Data are shown as median with interquartile range (IQR) for continuous variables and number with percentage for categorical variables.

Abbreviations: BMI, Body Mass Index; APACHE, Acute Physiology and Chronic Health Evaluation score; SOFA, Sequential Organ Function Assessment; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MBP, Mean Blood Pressure; SpO2, pulse oximetry-derived oxygen saturation; GI, gastrointestinal; CVP, central venous pressure; CRP, C-reactive protein.

Table 3 Univariate and Multivariate Logistic Regression Analyses of Risk Factors for ARDS in Postoperative Patients with Gastrointestinal Perforation

Variables	Univariate Analysis			Multivariate Analysis		
	OR	CI	*P*	OR	CI	*P*
BMI (kg/m^2)	1.232	1.089–1.394	0.001	1.197	1.036–1.384	0.015
Age(years)	0.980	0.953–1.007	0.136			
Gender						
Male	Ref					
Female	0.510	0.224–1.162	0.109			
Smoking	3.177	1.409–7.166	0.005	3.711	0.985–13.989	0.053
Alcoholism	1.882	0.5–7.081	0.349			
Hypertension	0.686	0.306–1.539	0.361			
Diabetes	2.424	0.694–8.465	0.165			

(*Continued*)

Table 3 (Continued).

Variables	Univariate Analysis			Multivariate Analysis		
	OR	CI	P	OR	CI	P
Coronary Heart Disease	0.400	0.111–1.444	0.162			
Cerebrovascular Diseases	0.632	0.197–2.03	0.441			
Acute Kidney Injury	4.259	1.941–9.347	<0.001			
APACHEII	1.133	1.064–1.206	<0.001			
SOFA	1.663	1.37–2.019	<0.001	1.443	1.165–1.786	0.001
Temperature (°C)	1.489	0.985–2.252	0.059			
Heart Rate (beat/min)	1.025	1.005–1.045	0.012			
Respiratory Rate (breath/min)	1.152	1.08–1.229	<0.001			
SBP (mmHg)	0.996	0.982–1.01	0.581			
DBP (mmHg)	0.975	0.95–1	0.047			
MAP (mmHg)	0.984	0.963–1.005	0.137			
SpO2 (%)	0.866	0.788–0.951	0.003			
Onset Time (hours)	1.004	0.998–1.01	0.164			
The Duration of Surgery (minutes)	1.005	0.999–1.01	0.093	0.986	0.976–0.995	0.008
Diameter of Perforation (cm)	0.912	0.636–1.309	0.620			
The Site of Perforation						
Lower GI tract	Ref					
Upper GI tract	0.249	0.113–0.547	0.001	0.164	0.045–0.603	0.006
Surgical Approach						
Laparoscopic	Ref					
Laparotomy	1.300	0.616–2.744	0.491			
Seroperitoneum (mL)	1.001	1.001–1.001	0.007			
Amount of Bleeding (mL)	1.002	0.998–1.006	0.262			
Transfusion	1.642	0.752–3.582	0.213			
Intraoperative Fluid Balance (mL)	1.001	1.001–1.001	0.001			
Shock	3.887	1.494–10.116	0.005			
CVP (mmHg)	1.160	1.047–1.284	0.005			
Procalcitonin (ng/mL)	1.011	0.997–1.025	0.151			
CRP (mg/L)	1.003	0.999–1.007	0.039			
White blood cell ($\times 10^9$ /L)	1.000	0.958–1.044	0.991			
Hemoglobin (g/L)	1.006	0.993–1.02	0.374			
Platelet ($\times 10^9$/L)	0.998	0.994–1.002	0.265			

(*Continued*)

https://doi.org/10.2147/JIR.S496559

Table 3 (Continued).

Variables	Univariate Analysis			Multivariate Analysis		
	OR	CI	P	OR	CI	P
Bicarbonate (mmol/L)	0.991	0.905–1.084	0.839			
Lactate (mmol/L)	1.447	1.187–1.763	<0.001	1.500	1.073–2.098	0.017
Albumin (g/L)	0.854	0.799–0.912	<0.001	0.889	0.816–0.969	0.007
Prealbumin (g/L)	1.037	0.95–1.133	0.418			

Notes: The data were calculated using logistic regression analysis.
Abbreviations: 95% CI: 95% confidence interval; OR, odds ratio; BMI, Body Mass Index; APACHE, Acute Physiology and Chronic Health Evaluation score; SOFA, Sequential Organ Function Assessment; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MBP, Mean Blood Pressure; SpO2, pulse oximetry-derived oxygen saturation; GI, gastrointestinal; CVP, central venous pressure; CRP, C-reactive protein.

P =0.005), Acute Kidney Injury (OR 4.259; 95% CI, 1.941–9.347; P <0.001), APACHEII (OR 1.133; 95% CI, 1.064–1.206; P <0.001), SOFA (OR 1.663; 95% CI, 1.37–2.019; P <0.001), temperature (OR 1.489; 95% CI, 0.985–2.252; P =0.059), heart rate (OR 1.025; 95% CI, 1.005–1.045; P =0.012), respiratory rate (OR 1.152; 95% CI, 1.08–1.229; P <0.001), DBP (OR 0.975; 95% CI, 0.95–1; P =0.047), SpO2 (OR 0.866; 95% CI, 0.788–0.951; P =0.003), the duration of surgery (OR 1.005; 95% CI, 0.999–1.01; P =0.093), the site of perforation Upper gastrointestinal tract perforation (OR 0.249; 95% CI, 0.113–0.547; P =0.001), seroperitoneum (OR 1.001; 95% CI, 1.001–1.001; P =0.007), intraoperative fluid balance (OR 1.001; 95% CI, 1.001–1.001; P =0.001), shock (OR 3.887; 95% CI, 1.494–10.116; P =0.005), CVP (OR 1.160; 95% CI, 1.047–1.284; P =0.005), CRP (OR 1.003; 95% CI, 0.999–1.007; P =0.039), white blood cell (OR 1.000; 95% CI, 0.958–1.044; P =0.991), lactate (OR 1.447; 95% CI, 1.187–1.763; P <0.001), albumin (OR 0.854; 95% CI, 0.799–0.912; P <0.001). All these parameters were included in the multivariate logistic regression model. Finally, the multivariate logistic regression analysis revealed the site of perforation (OR = 0.164, P = 0.006), the duration of surgery (OR = 0.986, P = 0.008), BMI (OR = 1.197, P = 0.015), SOFA (OR = 1.443, P = 0.001), lactate (OR = 1.500, P = 0.017), and albumin (OR = 0.889, P = 0.007) as the independent risk factors for ARDS development.

Model Visualization and Performance

The model that incorporated the above independent predictors was developed and is presented as a nomogram (Figure 3). We assessed the ability of our final model to distinguish between patients occurring ARDS using the c-statistic. The C index of the nomogram was 0.921 (95% CI: 0.869, 0.973) in the development cohort and 0.894 (95% CI: 0.809, 0.978) in the validation cohort (Figure 4A and B). Combined with the sensitivity, specificity, positive predictive value (PPV) of the receiver operating characteristic (ROC) in the training set and validation set in Table 4, and negative predictive value (NPV), this proves that the nomogram performs well in terms of predictive power. The calibration curves showed excellent agreement between the predictive probability and actual recurrence rate in both cohorts (Figure 5A and B). To avoid overfitting of the present model, the Hosmer-Lemeshow goodness-of-fit test was used. The test score was 0.750 in the development cohort and 0.514 in the internal validation cohort, which indicates that the model fit was acceptable Brier scores were 0.097 for the development cohort and 0.122 for the validation cohort, indicating some consistency in the calibration ability of the model across the two datasets. The decision curve analysis showed that the net benefit of using the prediction model was evident in both cohorts (Figure 6A and B). The horizontal and vertical axes illustrate the threshold probability and net benefit, respectively. The lines connecting these axes depict the advantages of various predictive variables. The development cohort decision curve analysis curves indicate that when the threshold probability ranges from 2% to 100%, the validation cohort decision curve analysis curves indicate that when the threshold probability ranges from 1% to 90%, employing this nomogram in the present study to predict the risk of ARDS could yield additional benefits.

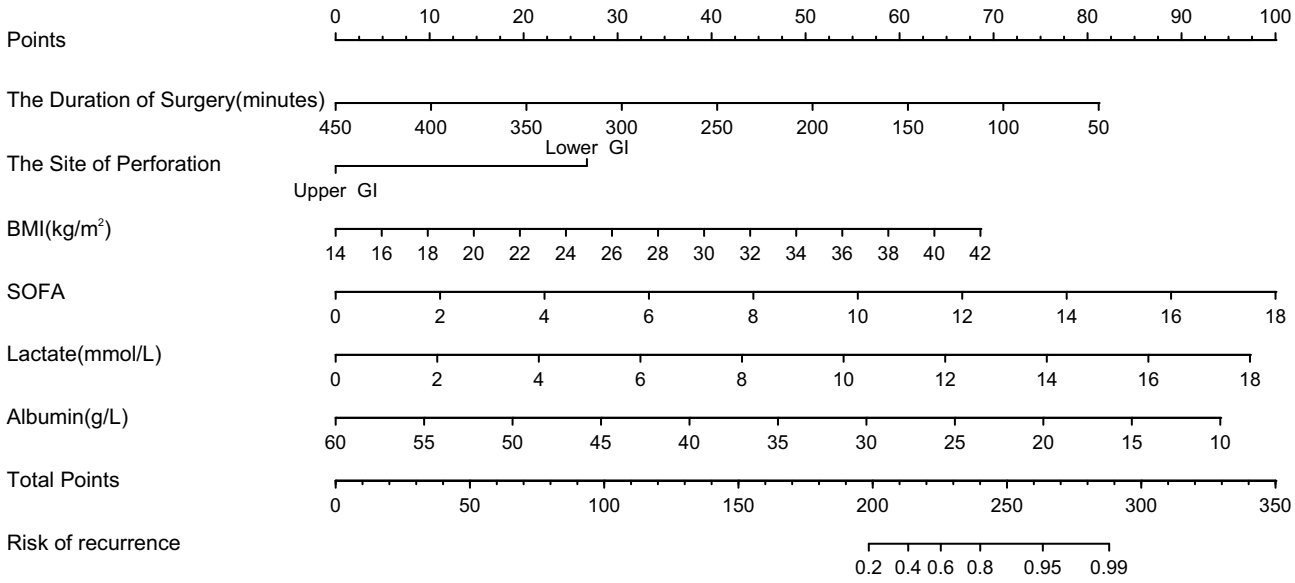

Figure 3 Nomogram for predicting the development of ARDS in postoperative patients with gastrointestinal perforation.
Abbreviation: ARDS, acute respiratory distress syndrome.

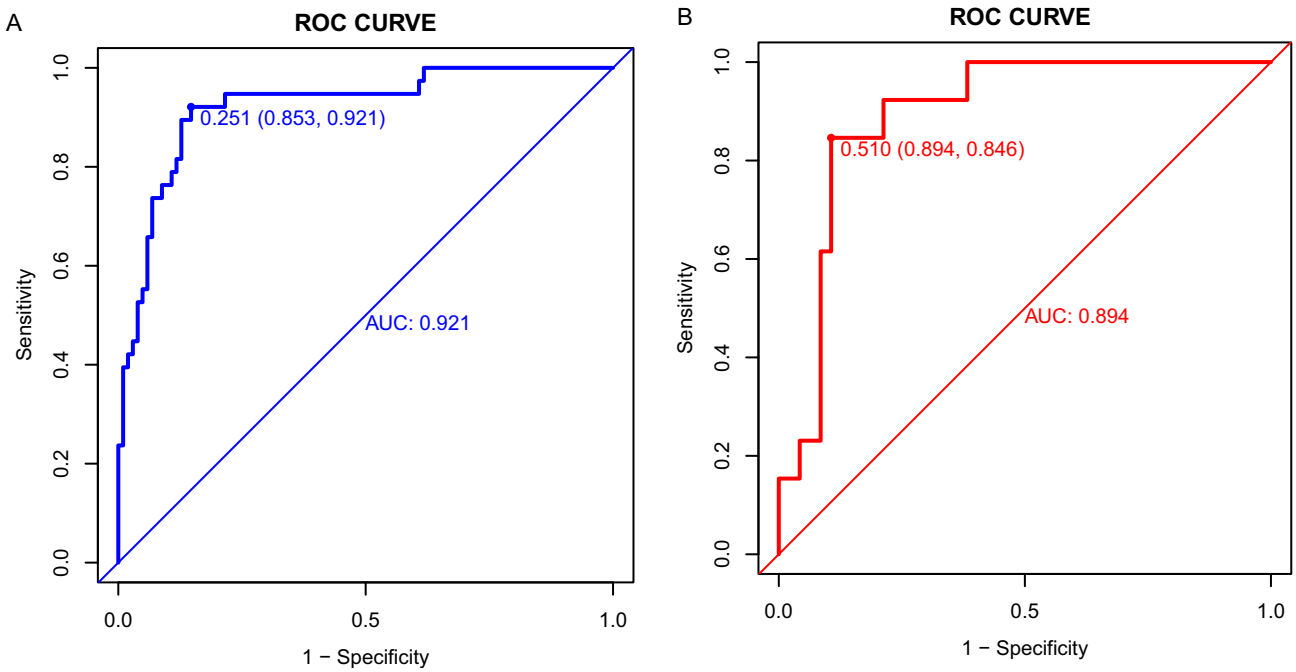

Figure 4 (**A**) The ROC curve of the nomogram for the development cohort. (**B**) The ROC curve of the nomogram for the validation cohort.
Abbreviation: ROC, receiver-operating characteristic.

Discussion

To the best of our knowledge, no predictive model has been identified for the occurrence of ARDS in postoperative patients with peritonitis secondary to gastrointestinal perforation. In this research, we developed a predictive model utilizing logistic regression, incorporating six variables: the site of perforation, the duration of surgery, BMI, SOFA, lactate, and albumin. The model's differentiation and calibration assessments demonstrated its robustness, while the decision curve analysis indicated a favorable applicability in clinical settings. Evaluating the clinical features and

https://doi.org/10.2147/JIR.S496559

Table 4 Model Performance Metrics for Development and Validation Cohorts

Cohort	Sensitivity	Specificity	PPV	NPV
Development	0.921	0.853	0.7	0.967
Validation	0.846	0.894	0.4	0.967

Notes: The data were calculated using logistic regression analysis.
Abbreviations: PPV, positive predictive value; NPV, Negative predictive value.

associated risk factors of patients who experience ARDS following gastrointestinal perforation surgery is of great value for the early detection of ARDS and the improvement of therapeutic outcomes.

Some scholars have noted that the type and severity of abdominal infection are influenced by the site, size and duration of the perforation.[5] This study identified the perforation site as an independent risk factor for ARDS, with lower

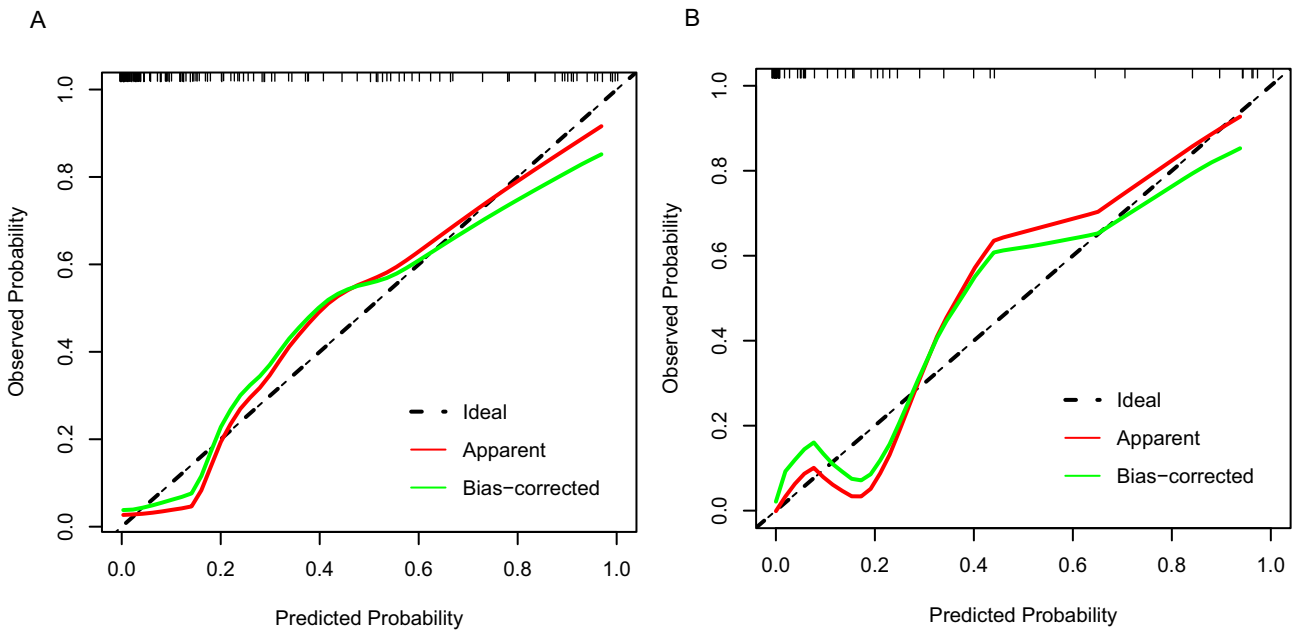

Figure 5 (**A**) Calibration curve in the development cohort. (**B**) Calibration curve in the validation cohort.

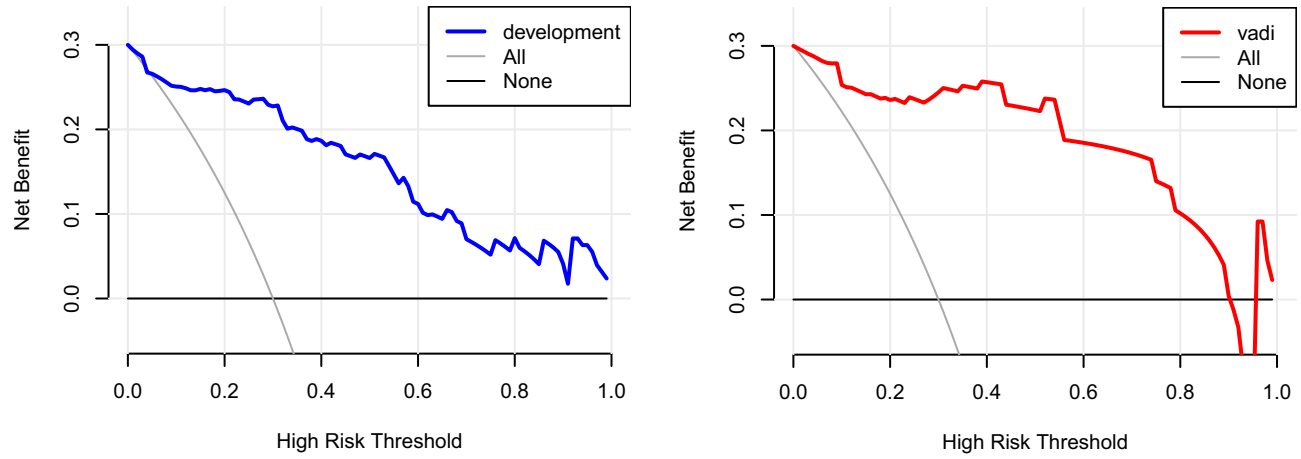

Figure 6 (**A**) The DCA of the nomogram for the development cohort. (**B**) The DCA of the nomogram for the validation cohort.
Abbreviation: DCA, decision curve analysis.

https://doi.org/10.2147/JIR.S496559

gastrointestinal tract perforations posing a higher risk. The microbial colonization varies across gastrointestinal organs, influenced by the local microenvironment. The upper gastrointestinal perforation contains acidic contents or aggressive bile and pancreatic fluid, whereas the lower gastrointestinal perforation contains a relatively neutral environment. Organ-specific fluid composition affects bacterial numbers and species composition, which may lead to different initial presenting symptoms than perforation, which may aid in diagnosis. Patients with upper gastrointestinal perforation often present with intense acute pain due to rapid chemical peritonitis, usually followed by systemic inflammatory response syndrome (SIRS), which may lead to rapid clinical deterioration, which on the other hand may lead to earlier hospitalization to avoid delays.[22–24] Lower gastrointestinal perforation may not present with immediate pain associated with the perforation and tend to have a slower clinical progression with secondary bacterial peritonitis or localized abscess formation. Peritoneal contamination from intraluminal colonic contents progressively leads to the development of purulent or faecal peritonitis or intra-abdominal abscesses. Patients with the lower gastrointestinal perforation are more likely to suffer organ damage due to the lack of initial symptoms, which often leads to late presentation. This research uniquely establishes that the location of perforation within the gastrointestinal tract serves as a significant risk factor for predicting ARDS, indicating that lower gastrointestinal tract perforations carry a higher risk than upper ones, offering essential insights for clinical practice.

It was noted in the 1980s that the duration of surgery, whether major or relatively minor, is clearly positively associated with postoperative morbidity. In addition, prolonged anesthesia may also lead to an increased incidence of postoperative atelectasis and other pulmonary complications.[25] Bianchi et al conducted a prospective study of patients undergoing scheduled pulmonary resection and found that the increase in postoperative pulmonary complications was significantly correlated with the duration of surgery.[26] A study by María Teresa Gómez-Hernández et al also confirmed that prolonged surgical time leads to an increase in postoperative pulmonary complications.[27] Huang et al performed a risk factor analysis of cardiac surgery patients with concomitant ARDS and also found prolonged surgery time to be an independent risk factor.[16] Surgical duration reflects the complexity of the procedure, with longer duration usually implying more trauma and complexity of the patient's condition, which is consistent with the results obtained in this study.

Obesity has become a global problem that jeopardizes human health. It is currently one of the biggest health issues that affects all age groups, populations and countries of all income levels. Although the impact of obesity on ICU mortality is debated, it seems to be associated with morbidity and increased resource utilization.[28,29] BMI is commonly used as a measure of obesity. Obese patients have increased oxygen consumption, production of carbon dioxide, work of breathing, and abdominal pressure, whereas compliance of the respiratory system and functional residual capacity are decreased.[30] A meta-analysis of 30,583 patients showed a higher incidence of ARDS in obese patients.[31] While previous studies have focused on the relationship between obesity and mortality, there is now a growing interest in the relationship between obesity and morbidity.[32] In a study of 2637 patients undergoing cardiac or aortic surgery, Huang et al found that a body mass index >30 kg/m^2 was an independent risk factor for the development of ARDS and Gong et al found that BMI was associated with an increased risk of ARDS and was associated with weight-dependent manner and increased length of hospitalization, but not with mortality.[16,32] This is consistent with the results of this study, which suggest that critical care clinicians should be aware of the possibility of increased risk for ARDS in their obese and severely obese patients and hold implications about how such patients should be ventilated or managed.

A predictive model for ARDS post-trauma integrates early objective clinical variables, such as massive blood transfusion, APACHE II score, and age.[12] In our study, age showed no statistical difference in single factor screening, likely due to the predominance of elderly patients with digestive tract perforation. The APACHE II score, a widely accepted tool for assessing severity and prognosis in critically ill patients, is calculated within 24 hours of admission. The higher the score, the more severe the disease and the greater the risk of mortality in the hospital.[33,34] SOFA is a scale widely used in emergency, medicine, surgery and ICU to assess the condition and prognosis of patients with multiple organ failure, which can dynamically reflect changes in organ function.[35–37] In our study, we investigated the relationship between APACHE II and SOFA scores in relation to ARDS. APACHE II demonstrated a significant difference in univariate analysis but not in multivariate analysis, while SOFA emerged as a key risk factor for predicting ARDS incidence. The underlying causes may not directly correlate with vital sign alterations during inflammatory injuries. As a holistic measure of organ failure, SOFA more accurately represents disease severity.

In this study, lactate was found to be one of the factors to predict ARDS. Lactate, a product of anaerobic oxygenation of glucose, is often considered a marker of tissue hypoxia and inadequate tissue perfusion. The role of lactate as a substrate of oxidation distribution and gluconeogenesis, although it is not the main pathway of energy generation, still has important pathophysiological significance. Elevated lactate can also occur when patients develop lung injury due to an inflammatory response, and changes in lactate levels may reflect alterations in the patient's ventilatory efficiency.[38] Patients with ARDS after digestive tract perforation are essentially the result of impaired organ function, with reduced ventilatory oxygenation, inadequate tissue oxygenation and increased blood lactate production caused by ARDS, which provided a theoretical basis for our research results.

Clinicians tend to pay more attention to conventional inflammatory markers such as CRP, leukocytes, neutrophils, and procalcitonin, while relatively ignoring patients' albumin. Albumin is the highest protein in plasma, which is mainly synthesized by the liver, accounting for about 55% of the plasma protein content, and is a multifunctional protein with both colloidal solution properties and pharmacological properties.[39] It has many physiological functions, such as regulating plasma colloid osmotic pressure, maintaining microvascular circulation integrity and capillary permeability. One of the key factors preventing capillary extravasation is the plasma colloid osmotic pressure formed by albumin.[40] Patients with digestive tract perforation often have insufficient energy intake in the early stage, and due to the presence of acute peritonitis, albumin breakdown is significantly increased, resulting in hypoproteinemia. Prior research has concentrated on the correlation between albumin levels and mortality in ARDS, while neglecting the impact on the pathogenesis of ARDS. Kumar et al conducted an analysis involving 386 trauma patients, revealing that albumin significantly influenced the onset of ARDS and the 28-day mortality rate.[41] Our research further substantiated that reduced serum albumin concentrations serve as a significant risk factor for the development of ARDS. Therefore, nutritional assessment and support are important in patients with digestive tract perforation.

In conclusion, we developed and validated a parsimonious ARDS risk prediction model for postoperative ARDS in a single-center cohort of postoperative patients with gastrointestinal tract perforation, which includes six predictors that effectively differentiate the risk of postoperative ARDS. This tool facilitates early identification of high-risk patients and prevention and treatment of ARDS by clinicians.

This research also has several limitations. First, given the retrospective design of our study, inherent bias may exist. Second, certain factors of interest, such as intra-abdominal pressure, were not included as predictors because of excessive missing values. Third, intraoperative mechanical ventilation parameters were not available, such as tidal volume, and large intraoperative fluctuations in tidal volume may also contribute to lung injury. Finally, it is important to note that this was a single-center cohort with a significantly limited sample size, and the predictive model was only internally validated; the accuracy and generalizability of our model may vary. Therefore, more clinical data from multiple centers should be analyzed to validate our findings.

Conclusions

Our study develops a predictive nomogram specifically for assessing the risk of ARDS in postoperative patients following gastrointestinal perforation. This model incorporates six readily available and clinically significant independent risk factors (the site of perforation, the duration of surgery, BMI, SOFA, lactate, and albumin), which fills a critical gap in perioperative management, providing a practical tool for early risk identification and individualized management strategies.

Ethics Approval and Consent to Participate

Ethics approval was obtained from the Ethics Committee of Hebei Provincial People's Hospital (No. 2023-68), with waiver of written informed consent due to retrospective non-interventional design. Our research was conducted in accordance with the Declaration of Helsinki.

Acknowledgments

The authors thank all the participants of this study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas. All authors drafted, revised or reviewed the article, and agreed on the journal in which the article will be submitted, gave final approval for the version to be published. All authors agree to be accountable for all aspects of the work.

Funding

This study was supported by the Medical Science Research Program of Hebei Province (20241153), Hebei Natural Science Foundation (H2020307040), the Government-funded Training Program for Excellent Talents in Clinical Medicine (ZF2020003, ZF2024008), the National Clinical Key Specialty Project Fund, and the Hebei Key Medical Discipline Fund. The study was implemented with the assistance of the Department of Critical Care Medicine, Hebei Provincial People's Hospital.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wick KD, Ware LB, Matthay MA. Acute respiratory distress syndrome. *BMJ*. 2024;387:e076612. doi:10.1136/bmj-2023-076612
2. Meyer NJ, Gattinoni L, Calfee CS. Acute respiratory distress syndrome. *Lancet*. 2021;398(10300):622–637. doi:10.1016/S0140-6736(21)00439-6
3. Grieco DL, Maggiore SM, Roca O, et al. Non-invasive ventilatory support and high-flow nasal oxygen as first-line treatment of acute hypoxemic respiratory failure and ARDS. *Intensive Care Med*. 2021;47(8):851–866. doi:10.1007/s00134-021-06459-2
4. Bellani G, Laffey JG, Pham T, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA*. 2016;315(8):788. doi:10.1001/jama.2016.0291
5. Langell JT, Mulvihill SJ. Gastrointestinal perforation and the acute abdomen. *Med Clin North Am*. 2008;92(3):599–625. doi:10.1016/j.mcna.2007.12.004
6. Sartelli M, Catena F, Ansaloni L, et al. Complicated intra-abdominal infections worldwide: the definitive data of the CIAOW Study. *World J Emerg Surg*. 2014;9:37. doi:10.1186/1749-7922-9-37
7. Cheung AM, Tansey CM, Tomlinson G, et al. Two-year outcomes, health care use, and costs of survivors of acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2006;174(5):538–544. doi:10.1164/rccm.200505-693OC
8. Herridge MS, Tansey CM, Matté A, et al. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med*. 2011;364(14):1293–1304. doi:10.1056/NEJMoa1011802
9. Qadir N, Sahetya S, Munshi L, et al. An update on management of adult patients with acute respiratory distress syndrome: an official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med*. 2024;209(1):24–36. doi:10.1164/rccm.202311-2011ST
10. Shah FA, Meyer NJ, Angus DC, et al. A research agenda for precision medicine in sepsis and acute respiratory distress syndrome: an official American Thoracic Society research statement. *Am J Respir Crit Care Med*. 2021;204(8):891–901. doi:10.1164/rccm.202108-1908ST
11. Gong MN, Thompson BT. Acute respiratory distress syndrome: shifting the emphasis from treatment to prevention. *Curr Opin Crit Care*. 2016;22(1):21–37. doi:10.1097/MCC.0000000000000275
12. Watkins TR, Nathens AB, Cooke CR, et al. Acute respiratory distress syndrome after trauma: development and validation of a predictive model*. *Crit Care Med*. 2012;40(8):2295–2303. doi:10.1097/CCM.0b013e3182544f6a
13. Gajic O, Dabbagh O, Park PK, et al. Early identification of patients at risk of acute lung injury: evaluation of lung injury prediction score in a multicenter cohort study. *Am J Respir Crit Care Med*. 2011;183(4):462–470. doi:10.1164/rccm.201004-0549OC
14. Kor DJ, Lingineni RK, Gajic O, et al. Predicting risk of postoperative lung injury in high-risk surgical patients. *Anesthesiology*. 2014;120(5):1168–1181. doi:10.1097/ALN.0000000000000216
15. Kor DJ, Warner DO, Alsara A, et al. Derivation and diagnostic accuracy of the surgical lung injury prediction model. *Anesthesiology*. 2011;115(1):117–128. doi:10.1097/ALN.0b013e31821b5839
16. Huang L, Song M, Liu Y, et al. Acute respiratory distress syndrome prediction score: derivation and validation. *Am J Crit Care*. 2021;30(1):64–71. doi:10.4037/ajcc2021753
17. Collins GS, Moons KGM, Dhiman P, et al. TRIPOD+AI statement: updated guidance for reporting clinical prediction models that use regression or machine learning methods. *BMJ*. 2024;385:e078378. doi:10.1136/bmj-2023-078378
18. ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23). doi:10.1001/jama.2012.5669
19. Zhang Z. Multiple imputation with multivariate imputation by chained equation (MICE) package. *Ann Transl Med*. 2016;4(2):30. doi:10.3978/j.issn.2305-5839.2015.12.63
20. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med*. 2011;30(4):377–399. doi:10.1002/sim.4067
21. Vickers AJ, Van Calster B, Steyerberg EW. Net benefit approaches to the evaluation of prediction models, molecular markers, and diagnostic tests. *BMJ*. 2016;352:i6. doi:10.1136/bmj.i6
22. Wittmann DH, Schein M, Condon RE. Management of secondary peritonitis. *Ann Surg*. 1996;224(1):10–18. doi:10.1097/00000658-199607000-00003
23. Lyon C, Clark DC. Diagnosis of acute abdominal pain in older patients. *Am Fam Physician*. 2006;74(9):1537–1544.

24. Nathens AB, Rotstein OD. Therapeutic options in peritonitis. *Surg Clin North Am*. 1994;74(3):677–692. doi:10.1016/S0039-6109(16)46336-X
25. Scott CF. Length of operation and morbidity: is there a relationships? *Plast Reconstr Surg*. 1982;69(6):1017–1021. doi:10.1097/00006534-198206000-00024
26. Bianchi RCG, de Souza JN, Giaciani CDA, Hoehr NF, Toro IFC. Prognostic factors for complications following pulmonary resection: pre-albumin analysis, time on mechanical ventilation, and other factors. *J Bras Pneumol*. 2006;32(6):489–494. doi:10.1590/s1806-37132006000600004
27. Gómez-Hernández MT, Forcada C, Varela G, Jiménez MF; Spanish Group of Video-assisted Thoracic Surgery (GEVATS). Operating time: an independent and modifiable risk factor for short-term complications after video-thoracoscopic pulmonary lobectomy. *Eur J Cardiothorac Surg*. 2022;62(6):ezac503. doi:10.1093/ejcts/ezac503
28. Sakr Y, Alhussami I, Nanchal R, et al. Being overweight is associated with greater survival in ICU patients: results from the intensive care over nations audit. *Crit Care Med*. 2015;43(12):2623–2632. doi:10.1097/CCM.0000000000001310
29. Rosvall BR, Forgie K, MacLeod JB, et al. Impact of obesity on intensive care unit resource utilization after cardiac operations. *Ann Thorac Surg*. 2017;104(6):2009–2015. doi:10.1016/j.athoracsur.2017.05.047
30. De Jong A, Chanques G, Jaber S. Mechanical ventilation in obese ICU patients: from intubation to extubation. *Crit Care*. 2017;21(1):63. doi:10.1186/s13054-017-1641-1
31. Zhi G, Xin W, Ying W, Guohong X, Shuying L. "Obesity paradox" in acute respiratory distress syndrome: asystematic review and meta-analysis. *PLoS One*. 2016;11(9):e0163677. doi:10.1371/journal.pone.0163677
32. Gong MN, Bajwa EK, Thompson BT, Christiani DC. Body mass index is associated with the development of acute respiratory distress syndrome. *Thorax*. 2010;65(1):44–50. doi:10.1136/thx.2009.117572
33. Zhou T, Zheng N, Li X, Zhu D, Han Y. Prognostic value of neutrophil- lymphocyte count ratio (NLCR) among adult ICU patients in comparison to APACHE II score and conventional inflammatory markers: a multi center retrospective cohort study. *BMC Emerg Med*. 2021;21(1):24. doi:10.1186/s12873-021-00418-2
34. Salluh JIF, Soares M. ICU severity of illness scores: APACHE, SAPS and MPM. *Curr Opin Crit Care*. 2014;20(5):557–565. doi:10.1097/MCC.0000000000000135
35. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. *JAMA*. 2001;286(14):1754–1758. doi:10.1001/jama.286.14.1754
36. Minne L, Abu-Hanna A, de Jonge E. Evaluation of SOFA-based models for predicting mortality in the ICU: a systematic review. *Crit Care*. 2008;12(6):R161. doi:10.1186/cc7160
37. Raith EP, Udy AA, Bailey M, et al. Prognostic accuracy of the SOFA score, SIRS criteria, and qSOFA score for in-hospital mortality among adults with suspected infection admitted to the intensive care unit. *JAMA*. 2017;317(3):290–300. doi:10.1001/jama.2016.20328
38. Vincent JL, Quintairos E, Silva A, Couto L, Taccone FS. The value of blood lactate kinetics in critically ill patients: a systematic review. *Crit Care*. 2016;20(1):257. doi:10.1186/s13054-016-1403-5
39. Garcia-Martinez R, Caraceni P, Bernardi M, Gines P, Arroyo V, Jalan R. Albumin: pathophysiologic basis of its role in the treatment of cirrhosis and its complications. *Hepatology*. 2013;58(5):1836–1846. doi:10.1002/hep.26338
40. Uhlig C, Silva PL, Deckert S, Schmitt J, de Abreu MG. Albumin versus crystalloid solutions in patients with the acute respiratory distress syndrome: a systematic review and meta-analysis. *Crit Care*. 2014;18(1):R10. doi:10.1186/cc13187
41. Kumar M, Jain K, Chauhan R, et al. Hypoalbuminemia: incidence and its impact on acute respiratory distress syndrome and 28-day outcome in trauma patients. *Eur J Trauma Emerg Surg*. 2023;49(5):2305–2314. doi:10.1007/s00068-023-02318-5