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Original Article

Application of D-LA and APOB/A1 combined with SIRI score in acute pancreatitis and concurrent infectious pancreatic necrosis

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Abstract: Objective: To explore the clinical value of D-lactate (D-LA), apolipoprotein B/A1 ratio (APO B/A1) and systemic immune-inflammatory response index (SIRI) in acute pancreatitis (AP) progression and concurrent infectious pancreatic necrosis. Method: This retrospective study included 116 AP patients (Jun 2021 - Dec 2024, Chongqing University Qianjiang Hospital). Patients were assigned to the model group, categorized into bedside indices for severity in acute pancreatitis (BISAP) of mild (n=57), moderate (n=31), and severe (n=28) subgroups. D-LA, APOB/A1, SIRI, and BISAP were compared. Correlations were analyzed via Pearson. Patients were also divided into an infected group (36 cases) and a non-infected group (80 cases) to compare clinical data as well as the above indices. Multivariate logistic regression identified its influencing factors. An external cohort (54 patients) validated the model via ROC and calibration curves. Result: As the severity of AP worsens, D-LA, APO B/A1, and SIRI all increase, and D-LA, APO B/A1, and SIRI were positively correlated with BISAP scores (r=0.503, 0.563, 0.314, P<0.05). According to statistics, The infected group had older age, and higher TC, TG, serum creatinine, D-LA, APOB/A1, and SIRI than the non-infected group (all P<0.05). Multivariate logistic regression identified D-LA, APOB/A1, and SIRI as risk factors for infectious pancreatic necrosis in AP patients (all P<0.05). The combined detection of these three indicators had a higher AUC for assessing infectious pancreatic necrosis than single detection (Z=2.581, 3.669, 2.945, all P<0.05). The model group showed good predictive performance (AUC=0.859), and the external validation group confirmed consistent accuracy (AUC=0.846). Conclusion: D-LA, APO B/A1, SIRI correlate with AP severity and the combined model enables early assessment and personalized measures.

Keywords: D-Lactic acid, apolipoprotein B, apolipoprotein A1, systemic immune inflammatory response index, acute pancreatitis, infectious pancreatic necrosis

Introduction

Acute pancreatitis (AP) is a common acute abdominal disorder in clinical practice, characterized by acute onset, complex and variable conditions, with the presence of complications [1]. The pathological process of AP exhibits dynamic evolutionary features. It begins with a local inflammatory response triggered by early pancreatic autodigestion, progresses to systemic inflammatory response syndrome, and in some patients, further develops into multiple organ dysfunction syndrome and infectious pancreatic necrosis (IPN) [2]. IPN is one of the severe and life-threatening complications of AP, with an incidence of approximately 10%-30%. It significantly increases patient mortality and raises treatment costs [3, 4]. Therefore, early assessment of AP progression and the risk of developing IPN is crucial for timely adjustment of treatment strategies and improvement of patient prognosis. D-lactic acid (D-LA) is a metabolic product of intestinal bacteria. When intestinal barrier function is impaired, large amounts of D-LA are released into the bloodstream, making it a reliable indicator to reflect

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the severity of intestinal barrier damage [5]. Apolipoprotein B (APOB) and apolipoprotein A1 (APOA1) are key components of lipoproteins. The APOB/A1 ratio is closely associated with inflammatory responses and lipid metabolism disorders, and plays an important role in various inflammatory diseases [6, 7]. The Systemic Immune Inflammation Response Index (SIRI) is a novel inflammatory index calculated based on peripheral blood white blood cell count, lymphocyte count, and monocytes, which can comprehensively reflect the immune inflammatory status of the body [8, 9]. Currently, there is insufficient evidence to support the clinical application of D-LA, APOB/A1, and SIRI combined scoring in assessing AP progression and concurrent IPN. This study aims to explore the clinical value of D-LA and APOB/A1 combined with SIRI scoring in the progression of AP and the development of concurrent IPN, and the results are reported as follows.

Clinical data

Retrospective collection of clinical data from 116 AP patients admitted to Chongqing University Qianjiang Hospital from June 2021 to December 2024 was included in the model group. According to the bedside index for severity in acute pancreatitis (BISAP) [10], the patients were divided into mild (57 cases), moderate (31 cases), and severe groups (28 cases). A total of 0-2 points was classified as mild AP, 3-4 points were classified as moderate to severe, and 5 points was classified as severe. Clinical data from 54 patients was selected during the same period as the external validation cohort. This study was conducted after approval by the medical ethics committee of Chongqing University Qianjiang Hospital.

Inclusion criteria: (1) Meets the diagnostic criteria specified in the Chinese Guidelines for the Diagnosis and Treatment of Acute Pancreatitis [11], including: ① Acute onset and persistent severe abdominal pain; ② Serum amylase activity >3 times the normal upper limit; (2) Complete clinical data; (3) No recent immunosuppressants or corticosteroids; (4) Good compliance and willingness to actively cooperate with research.

Exclusion criteria: (1) Concomitant chronic pancreatitis; (2) Combined with pancreatic cancer and other malignant tumors; (3) Combined with autoimmune diseases such as systemic lupus erythematosus; (4) Combined with blood system diseases such as coagulation disorders; (5) Accompanied by organ dysfunction such as liver and kidney; (6) Combined with infectious diseases such as hepatitis B.

Methods

All patient information was collected from the hospital case system, including gender, age, body mass index, education level, place of residence, underlying medical history, smoking history, alcohol consumption history, blood pressure, fasting blood glucose, and heart rate. Blood pressure and heart rate were measured in the morning, and the average of three measurements was taken.

Blood (5 ml) from the elbow was collected from all patients on the day after admission, and 2 ml was processed using a fully automatic blood cell analyzer (Shenzhen Mindray Biomedical; model: BC-20s); Registration number: (Yue Xie Zhu Zhuzhun 20152220916). Monocyte, neutrophil count, and lymphocyte count were determined. The remaining 3 ml was centrifuged at 3,000 r/min for 15 minutes, with a radius of 10 cm, using a fully automatic biochemical analyzer (Shandong Boke Biotechnology Industry; model: BK-1200); Registration number: (LuXie Zhuzhun 20192220157). Total cholesterol (TC), triglycerides (TG), hemoglobin, and creatinine were tested. A fully automatic chemiluminescence immunoassay analyzer (Shandong Boke Diagnostic Technology; model: BKI1100); Registration number: (Luxie Zhuzhun 20202220932) was adopted to detect serum sodium, potassium, calcium, and phosphorus levels. Enzyme-linked immunosorbent assay was used to detect D-LA levels. Immunoturbidimetry was used to detect the levels of APO B and APO A1, and the APO B/A1 ratio was calculated. SIRI score was calculated based on the formula SIRI = neutrophil count × monocyte count/lymphocyte count.

According to the Chinese Guidelines for the Diagnosis and Treatment of Acute Pancreatitis [11], patients were evaluated for concurrent IPN based on the following criteria: ① Mixed pus and necrotic tissue were observed in pancreatic lesions; ② Enhanced CT scans revealed the typical “bubble sign”; ③ Pathogen infection was confirmed via pathogen detection of drain-

Table 1. Comparison of general information of the three groups of patients [($\bar{x}$±s), *n* (%)]

Variable	Mild group (*n*=57)	Intermediate group (*n*=31)	Severe group (*n*=28)	χ^2/F	P
Gender (Male/Female)	31/26	16/15	15/13	0.062	0.969
Age (years)	54.58±5.72	54.18±5.36	54.73±5.66	0.079	0.092
Body mass index (kg/m^2)	22.49±2.31	22.37±2.28	22.41±2.33	0.030	0.970
Educational attainment				0.062	0.969
High school and below	44 (72.19)	24 (77.42)	21 (75.00)		
College and above	13 (22.81)	7 (22.58)	7 (25.00)		
Current address				0.077	0.962
Cities and towns	40 (70.18)	21 (67.74)	19 (67.86)		
Countryside	17 (29.82)	10 (32.26)	9 (32.14)		
History of hypertension	31 (54.39)	17 (54.86)	19 (67.86)	1.544	0.462
History of diabetes	30 (52.63)	17 (54.84)	16 (57.14)	0.159	0.924
History of hyperlipidemia	32 (56.14)	20 (64.52)	16 (57.14)	0.614	0.736
Smoking history	29 (50.88)	15 (48.39)	15 (53.57)	0.158	0.924
Drinking history	20 (35.09)	12 (38.71)	12 (42.86)	0.492	0.782

age fluid or pancreatic necrotic tissue. The incidence of IPN among patients was calculated, and patients were divided into an infected group (IPN-positive) and a non-infected group (IPN-negative).

Statistical methods

Data were analyzed using SPSS 26.0 and R4.2.1. Count data were expressed as [n (%)] and analyzed by chi-square test. Kolmogorov-Smirnov (K-S) test were used to assess the normality of data distribution. Normally distributed continuous data were described as mean ± standard deviation (SD), with inter-group comparisons performed using the independent-samples t-test and multi-group comparisons using repeated-measures analysis of variance (ANOVA). Pearson correlation analysis was performed to examine the linear correlations between D-LA, APOB/A1, SIRI, and BISAP scores. The correlation coefficient (r) and *P* value were calculated to determine the correlation. Multiple logistic regression analysis was used to investigate the influencing factors of infectious pancreatic necrosis in AP patients. The variance inflation factor (VIF) was used to assess multicollinearity among independent variables. A forest plot was generated using Graphpad Prism 8.0 based on OR value and 95% CI.

Receiver operating characteristic (ROC) curves were constructed to calculate the area under the curve (AUC) values, aiming to compare the predictive performance of individual indicators and their combined detection, as well as to determine cut-off values and other relevant parameters. Calibration curves were plotted using the Bootstrap method; the goodness-of-fit test and mean absolute error were used to evaluate the consistency and accuracy between the predicted and actual values of the model. At the same time, validity of the model was validated using an external validation cohort. A two-tailed P<0.05 was considered statistically significant.

Results

Comparison of general information among mild, moderate, and severe groups

There was no statistically significant difference in clinical data among the mild, moderate, and severe groups of patients (*P*>0.05), as shown in **Table 1**.

Comparison of D-LA, APO B/A1, SIRI, and BISAP scores among mild, moderate, and severe groups

As AP progressed, D-LA, APO B/A1, SIRI, and BISAP scores increased, with the severe group being significantly higher than the other groups (all *P*<0.05), as shown in **Table 2**.

Correlation between D-LA, APO B/A1, SIRI scores and BISAP scores

Pearson analysis showed that D-LA, APO B/A1, SIRI were positively correlated with BISAP

Table 2. Comparison of D-LA, APO B/A1, SIRI, and BISAP scores among mild, moderate, and severe groups ($\bar{x}\pm s$)

Group	n	D-LA (mg/L)	APO B/A1	SIRI (Score)	BISAP (Score)
Mild group	57	3.67±0.43	1.57±0.36	5.19±1.26	2.92±0.25
Moderate to severe group	31	3.95±0.47*	1.93±0.44*	5.87±1.49*	3.86±0.29*
Severe group	28	4.52±0.59*,#	2.55±0.68*,#	6.35±1.73*,#	5.37±0.33*,#
F value		29.055	39.946	6.808	712.969
P value		<0.001	<0.001	0.002	<0.001

Note: D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index; Compared with the mild group, *P<0.05; Compared with the moderate to severe group, #P<0.05.

Table 3. D-LA, APO B/A1, SIRI score and BISAP score correlation

Entry	BISAP	
	r	*P*
D-LA	0.503	<0.001
APO B/A1	0.563	<0.001
SIRI	0.314	0.006

Note: D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index; SIRI: Systemic Immune Inflammatory Response Index.

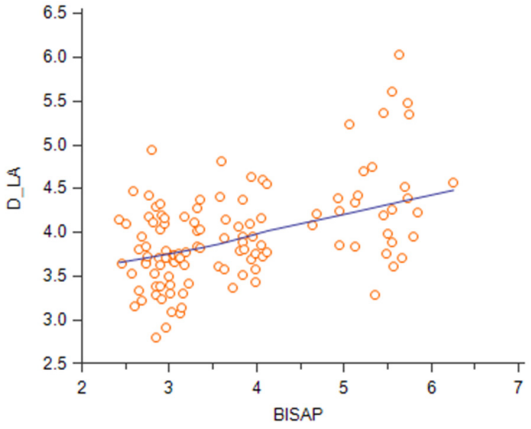

Figure 1. Correlation between D-LA and BISAP scores. Note: D-LA: D-Lactic acid. BISAP: bedside index for severity in acute pancreatitis.

(*r*=0.503, 0.563, 0.314, *P*<0.05). See **Table 3** and **Figures 1**-**3**.

Comparison of general information between infected and non-infected groups

A total of 36 patients developed IPN, with an incidence rate of 31.03%. They were divided into an infected group of 36 cases and a non-infected group of 80 cases. The infected group was older than the non-infected group, TC, TG,

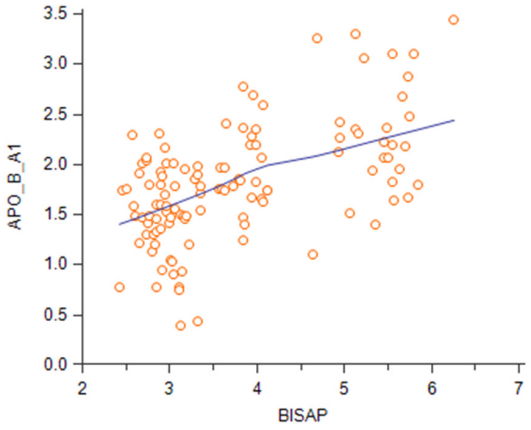

Figure 2. Correlation between APO B/A1 and BISAP scores. Note: APO B/A1: ratio of apolipoprotein B to apolipoprotein A1. BISAP: bedside index for severity in acute pancreatitis.

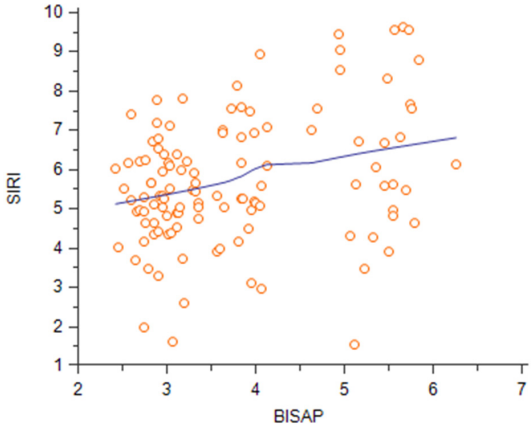

Figure 3. Correlation between SIRI and BISAP scores. Note: SIRI: Systemic Immune Inflammatory Response Index. BISAP: bedside index for severity in acute pancreatitis.

blood creatinine, D-LA, APO B/A1, and SIRI were all higher in the non-infected group (all *P*<0.05), as shown in **Table 4**.

Table 4. Comparison of general information between infected and non-infected groups [($\bar{x}$±s), *n* (%)]

Variable	Infection group (*n*=36)	Noninfectious group (*n*=80)	χ^2/t	*P*
Gender (Male/Female)	21/15	41/39	0.501	0.479
Age (years)	56.40±5.73	54.02±5.24	2.263	0.026
Body mass index (kg/m^2)	22.34±2.27	22.52±2.35	0.386	0.700
Educational attainment			0.592	0.441
High school and below	26 (72.22)	63 (78.75)		
College and above	10 (27.78)	17 (21.25)		
Current address			0.129	0.719
Cities and towns	24 (66.67)	56 (70.00)		
Countryside	12 (33.33)	24 (30.00)		
History of hypertension	19 (52.78)	48 (60.00)	0.531	0.466
History of diabetes	20 (55.56)	43 (53.75)	0.033	0.856
History of hyperlipidemia	23 (63.89)	45 (56.25)	0.597	0.440
Smoking history	18 (50.00)	41 (51.25)	0.016	0.901
Drinking history	15 (41.67)	29 (36.25)	0.309	0.578
Systolic blood Pressure (mmHg)	133.48±10.56	133.67±10.43	0.090	0.928
Diastolic pressure (mmHg)	87.62±7.63	86.59±7.47	0.682	0.496
Heart rate (Times/min)	75.29±8.45	75.36±8.29	0.042	0.967
TC (mmol/L)	4.58±0.46	4.32±0.42	2.994	0.003
TG (mmol/L)	1.27±0.22	1.20±0.18	2.322	0.022
Hemoglobin (g/L)	121.57±9.72	120.26±9.44	0.685	0.495
Serum creatinine (μmmo/L)	199.44±20.13	192.42±18.45	2.893	0.004
Serum potassium (mmol/L)	3.35±0.68	3.36±0.66	0.075	0.941
Blood sodium (mmol/L)	135.43±5.52	136.48±5.57	0.942	0.348
Serum calcium (mmol/L)	2.55±0.18	2.51±0.17	0.577	0.566
Serum phosphorus (mmol/L)	1.36±0.15	1.35±0.14	0.348	0.728
D-LA (mg/L)	4.37±0.52	3.93±0.48	4.450	<0.001
APO B/A1	2.37±0.56	1.92±0.44	4.671	<0.001
SIRI (Score)	6.17±1.52	5.02±1.26	4.260	<0.001

Note: TC: Total Cholesterol; TG: Triglyceride; D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index.

Table 5. Independent variable assignment

Independent variable	Assignment
Age	original value
TC	original value
TG	original value
Serum creatinine	original value
D-LA	original value
APO B/A1	original value
SIRI	original value

Note: TC: Total Cholesterol; TG: Triglyceride; D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index.

Influencing factors of IPN in AP patients

Concurrent IPN was considered as the dependent variable, age, TC, TG, Blood creatinine, D-LA, APO B/A1, and SIRI were independent variables, and their assigned values were shown in **Table 5**. Univariate logistic regression analysis showed that age, TC, TG, blood creatinine, D-LA, APO B/A1, and SIRI were influencing factors for AP patients with concurrent IPN (all P<0.05). Logistic multiple regression analysis found that D-LA, APO B/A1, and SIRI were risk factors for concurrent IPN in AP patients (all P<0.05), as shown in **Table 6**. According to the VIF test, there was no collinearity among the three indicators (VIF=1.058, 1.050, 1.012). After univariate logistic regression analysis, significant variables were arranged in a forest plot based on OR values, as shown in **Figure 4**. Logistic multiple regression, significant variables were arranged in a forest plot based on OR values, as shown in **Figure 5**. The circle represented the variable OR value, where OR<1

Table 6. The influencing factors of infectious pancreatic necrosis in AP patients

Factor	Univariate logistic regression analysis			Logistic regressions		
	P	*OR*	*95% CI*	*P*	*OR*	*95% CI*
Age	0.021	1.092	1.013-1.176	0.073	1.091	0.992-1.200
TC	0.009	3.458	1.372-8.717	0.274	2.079	0.561-7.709
TG	0.016	12.694	1.612-99.942	0.706	1.789	0.087-36.879
Serum creatinine	0.010	1.038	1.009-1.068	0.111	1.031	0.993-1.071
D-LA	0.001	15.486	4.367-54.913	<0.001	12.478	3.317-46.944
APO B/A1	0.014	3.028	1.251-7.330	0.026	3.676	1.167-11.583
SIRI	<0.001	1.821	1.343-2.470	0.003	1.871	1.237-2.830

Note: TC: Total Cholesterol; TG: Triglyceride; D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index.

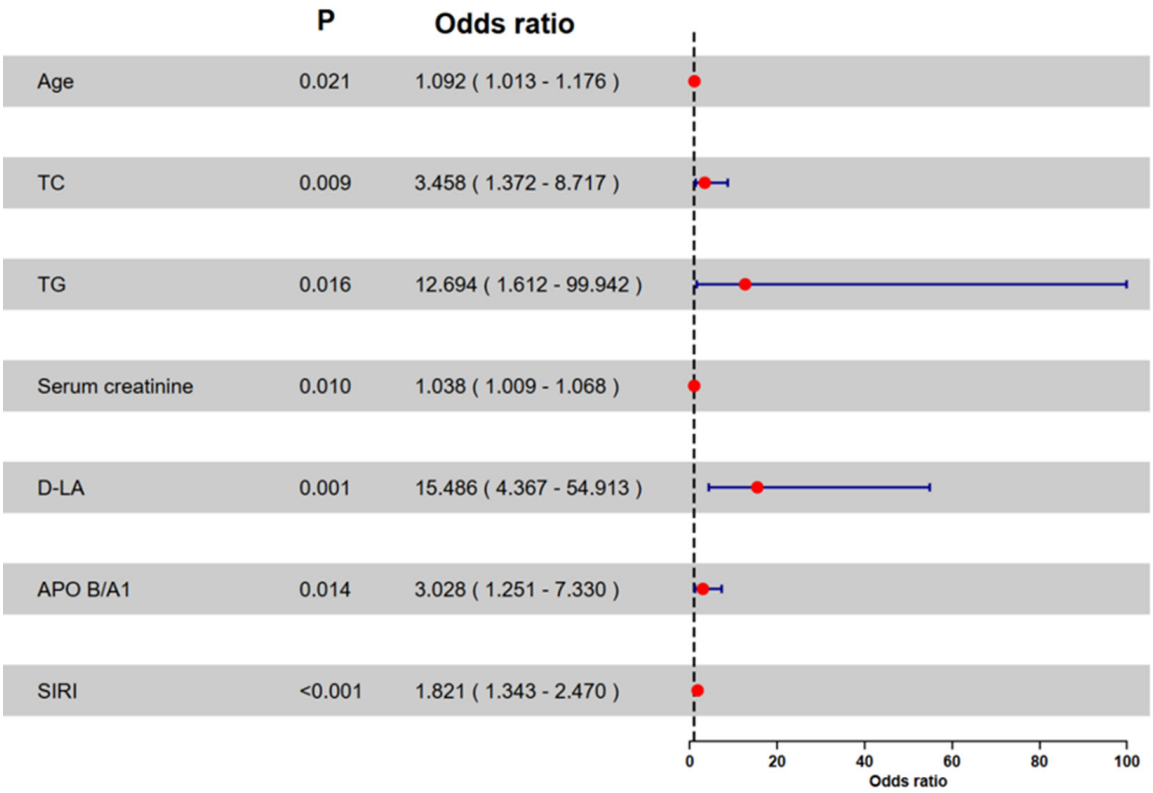

Figure 4. Forest plot of significant variables in univariate logistic regression analysis. Note: TC: Total Cholesterol; TG: Triglyceride; D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index.

indicated a negative correlation between the factor and the risk of IPN.

Value of combined detection of D-LA, APO B/A1, and SIRI in evaluating IPN in AP patients

ROC curve analysis showed that the AUC values of D-LA, APO B/A1, and SIRI combined detection for assessing IPN in AP patients were higher than those of single detection (Z=2.581, 3.669, 2.945, all P<0.05), as shown in **Table 7**, and the ROC curve was shown in **Figure 6**.

Comparison of clinical data between model group and external validation group

There was no statistically significant difference in general data between the model group and

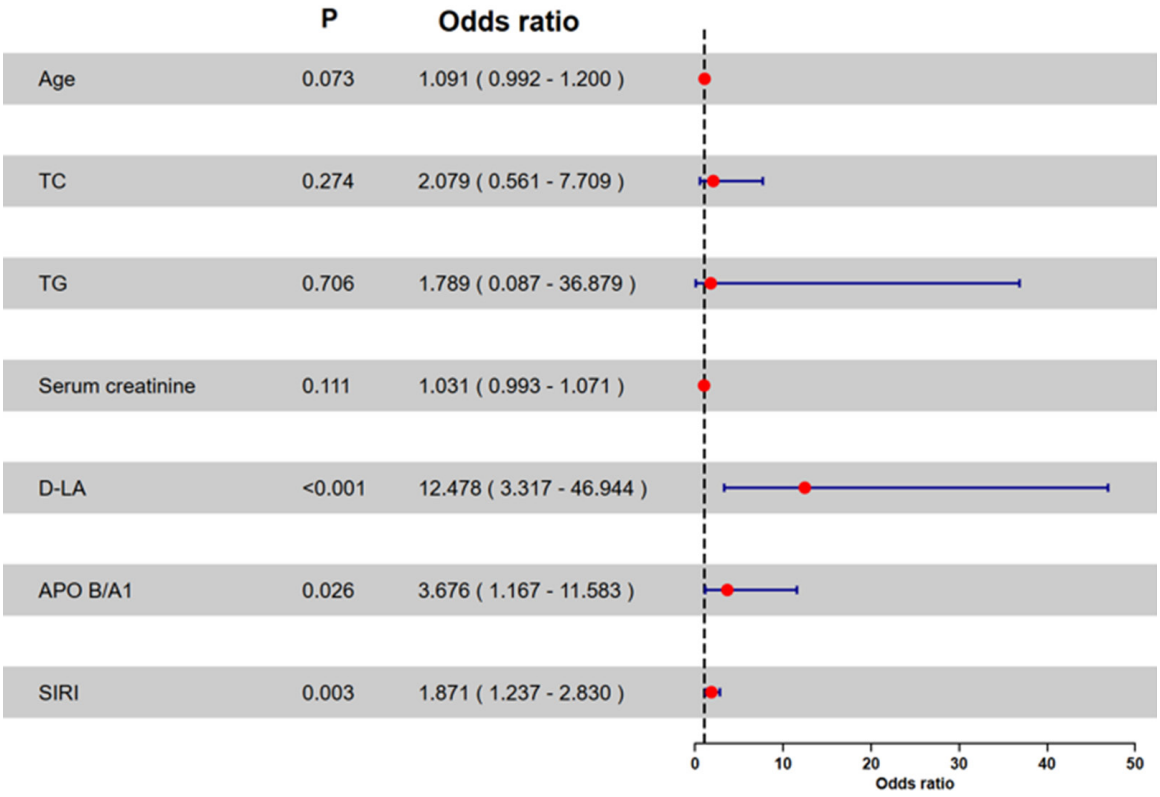

Figure 5. Forest plot of significant variables in *Logistic* multiple regression. Note: TC: Total Cholesterol; TG: Triglyceride; D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index.

Table 7. Value of combined detection of D-LA, APO B/A1, and SIRI scores in evaluating infectious pancreatic necrosis in AP patients

Index	AUC	Standard Error	95% *CI*	*P*	Cut-off	Youden index	Sensitivity (%)	Specificity (%)
D-LA	0.776*	0.046	0.690-0.849	<0.001	>4.251 mmol/L	0.442	66.67	77.50
APO B/A1	0.632*	0.058	0.537-0.720	<0.001	>2.280	0.253	52.78	72.50
SIRI	0.722*	0.051	0.631-0.801	<0.001	>4.661 score	0.376	88.89	48.75
Combined detection	0.859	0.038	0.782-0.917	<0.001		0.633	83.33	80.00

Note: D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index; Compared with combined detection, *P<0.05.

the external validation group (all P>0.05), indicating good consistency between the groups, as shown in **Table 8**.

Line chart for predicting the risk of concurrent IPN in AP patients based on logistic regression analysis

A risk prediction column chart for AP patients with concurrent IPN was established based on logistic regression analysis. The column chart included three variables, namely D-LA, APO B/A1, and SIRI. Among them, D-LA had a higher weight in the column chart, indicating its important role in risk prediction, as shown in **Figure 7**.

ROC and calibration curves were used to evaluate the predicted values and accuracy of the model group, with an AUC value of 0.859, indicating that the column chart had a high value in predicting the risk of concurrent IPN in AP patients, as shown in **Figure 8**. The calibration curve showed that the model exhibited good calibration ability, and the predicted values

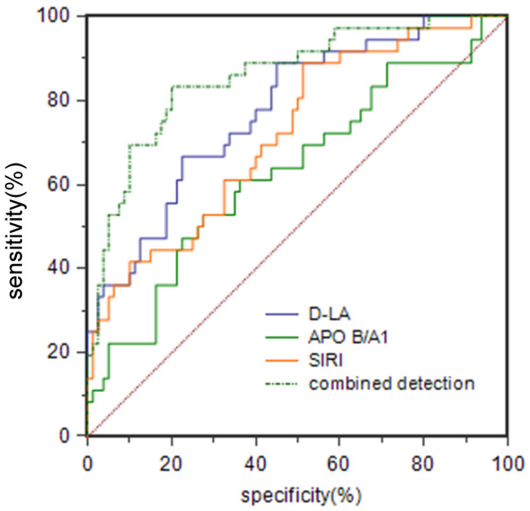

Figure 6. D-ROC curve of combined detection of LA, APO B/A1, and SIRI for evaluating the value of AP patients with concurrent infectious pancreatic necrosis. Note: D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index.

were consistent with the actual results, as shown in **Figure 9**. The goodness of fit test demonstrated a *P*-value of 0.348, indicating good fit. Calibration analysis revealed an average absolute error of 0.039, indicating good accuracy.

The ROC curve of the external validation group showed an AUC value of 0.846, indicating that the model had a good evaluation performance, consistent with the results of the model group, as shown in **Figure 10**. The calibration curve showed that the model exhibited good calibration ability, and the predicted values were consistent with the actual results, as shown in **Figure 11**. The goodness of fit test showed a *P*-value of 0.576, indicating good fit. Calibration analysis showed an average absolute error of 0.087, further verifying the model's good accuracy.

Discussion

It is reported that IPN increases patients' risk of death by 3 to 7 times, with a mortality rate as high as 30%-70% [12]. The pathogenesis of IPN is complex. It typically develops when acute pancreatitis leads to pancreatic ischemic necrosis, which impairs the pancreatic barrier. This impairment facilitates the translocation of intestinal microbiota or hematogenous spread to the necrotic area. Since necrotic tissue lacks blood supply, immune cell infiltration, and antibiotic penetration, bacteria proliferate uncontrollably, and the immune response becomes dysregulated, ultimately forming a vicious cycle of inflammation and infection [13, 14]. The traditional system for assessing AP primarily relies on serological indicators and imaging studies. Serum amylase and lipase, as classic diagnostic markers, exhibit high sensitivity for diagnosing AP, but their ability to evaluate disease severity is limited [15]. Enhanced CT is the gold standard for assessing IPN; however, its use in early dynamic disease monitoring is restricted by several factors, including radiation exposure risk, high economic cost, and atypical imaging features of early necrotic tissue [16].

D-LA is a specific marker for intestinal epithelial cell damage. When intestinal epithelial cells are impaired due to ischemia, inflammation, infection, or other factors, D-LA is released into the circulatory system [17]. APOB is primarily involved in the assembly and transport of low-density lipoproteins, and elevated levels of APOB are closely associated with atherosclerosis and thrombosis [18]. As the main component of high-density lipoproteins, APOA1 exhibits anti-inflammatory, antioxidant, and lipid metabolism-regulating properties [19]. The SIRI reflects the body's immune-inflammatory status by quantifying the interactions between neutrophils, lymphocytes, and monocytes, and it can be detected simply and rapidly [20]. The results of this study showed that as AP progressed, the levels of D-LA, APOB/A1 ratio, SIRI, and BISAP score all rose. Specifically, D-LA, APOB/A1 ratio, and SIRI were positively correlated with the BISAP score. This suggests that D-LA, APOB/A1 ratio, and SIRI are associated with AP severity and can serve as effective indicators for evaluating AP severity, providing important references for clinical disease assessment and treatment decision making. When AP occurs, large amounts of inflammatory mediators are released, causing intestinal ischemia and hypoxia. This damages intestinal mucosal epithelial cells and impairs intestinal barrier function, allowing D-LA (which is naturally present in the intestine) to enter the bloodstream through the damaged barrier, resulting in increased blood D-LA levels. The more severe the disease, the greater the intestinal barrier damage, and the more significant the increase in D-LA [21]. Additionally, the inflammatory

Table 8. Comparison of clinical data between model and external validation groups [($\bar{x}$±s), *n* (%)]

Variable	Model Group (*n*=116)	validation group (*n*=54)	χ^2/t	*P*
Gender (Male/Female)	62/54	31/23	0.233	0.629
Age (years)	55.36±5.48	55.17±5.26	0.213	0.831
body mass index (kg/m^2)	22.45±2.31	22.36±2.27	0.238	0.812
Educational attainment			0.179	0.672
High school and below	89 (76.72)	43 (79.63)		
College and above	27 (23.28)	11 (20.37)		
Current address			0.034	0.853
Cities and towns	80 (68.96)	38 (70.37)		
Countryside	36 (31.04)	16 (29.63)		
History of hypertension	67 (57.76)	33 (61.11)	0.171	0.679
History of diabetes	63 (54.31)	27 (50.00)	0.274	0.600
History of hyperlipidemia	68 (58.62)	32 (59.26)	0.006	0.937
Smoking history	59 (50.86)	26 (48.15)	0.109	0.742
Drinking history	44 (37.93)	23 (42.59)	0.335	0.563
Systolic blood Pressure (mmHg)	133.57±10.53	133.42±10.48	0.087	0.931
Diastolic pressure (mmHg)	87.68±7.52	86.64±7.26	0.849	0.397
Heart rate (Times/min)	75.29±8.32	75.47±8.55	0.130	0.897
TC (mmol/L)	4.46±0.45	4.42±0.43	0.547	0.585
TG (mmol/L)	1.25±0.21	1.22±0.19	0.893	0.373
Hemoglobin (g/L)	121.18±9.36	121.67±9.55	0.316	0.752
Serum creatinine (μmmo/L)	194.57±19.46	195.02±19.92	0.139	0.889
Serum potassium (mmol/L)	3.35±0.67	3.33±0.58	0.189	0.851
Blood sodium (mmol/L)	135.92±5.64	135.73±5.33	0.208	0.835
Serum calcium (mmol/L)	2.53±0.17	2.52±0.16	0.364	0.717
Serum phosphorus (mmol/L)	1.35±0.15	1.34±0.13	0.422	0.674
D-LA (mg/L)	4.04±0.51	4.06±0.53	0.235	0.814
APO B/A1	2.09±0.48	2.05±0.45	0.516	0.606
SIRI (Score)	5.35±1.56	5.27±1.44	0.318	0.750

Note: TC: Total Cholesterol; TG: Triglyceride; D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index.

response disrupts lipid metabolism pathways. It promotes increased APOB synthesis, reduces or accelerates APOA1 synthesis, and raises the APOB/A1 ratio. This ratio reflects the exacerbation of inflammation and lipid metabolism disorders in the body, which interact with the progression of AP [22]. During AP onset, the abnormal activation of pancreatic enzymes triggers an inflammatory cascade, releasing large quantities of inflammatory factors. Under inflammatory stimulation, the immune system becomes overactivated, leading to the massive proliferation of white blood cells and platelets, a relative decrease in lymphocytes, and a subsequent increase in the SIRI score [23]. Li [24] also found that the SIRI score can be an effective indicator for assessing AP severity, which is consistent with the results of this study.

The results of this study showed that patients in the infected group were older than those in the non-infected group, and the levels of TC, TG, serum creatinine, D-LA, APOB/A1, and SIRI were significantly higher in the infected group than in the non-infected group. These findings indicate that advanced age, abnormal lipid metabolism, renal dysfunction, intestinal barrier impairment, lipid metabolism disorders, and immune-inflammatory imbalance are closely associated with the development of IPN in AP patients. The underlying mechanisms may be as follows. With increasing age, the body's immune function gradually declines, characterized by reduced activity of immune cells, impaired tissue repair capacity, and weakened defense against pathogens, all of which increase the risk of concurrent infections [25].

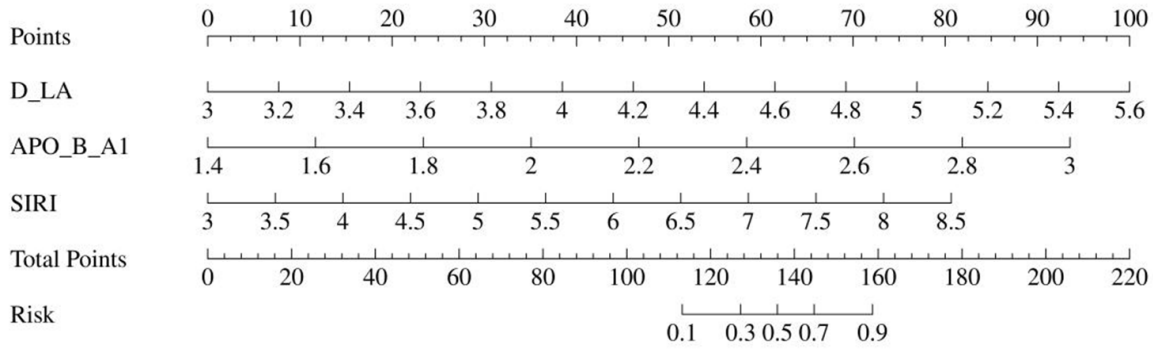

Figure 7. Line chart for predicting the risk of concurrent infectious pancreatic necrosis in AP patients based on logistic regression analysis. Note: D-LA: D-Lactic acid; APO B/A1: ratio of apolipoprotein B to apolipoprotein A1; SIRI: Systemic Immune Inflammatory Response Index.

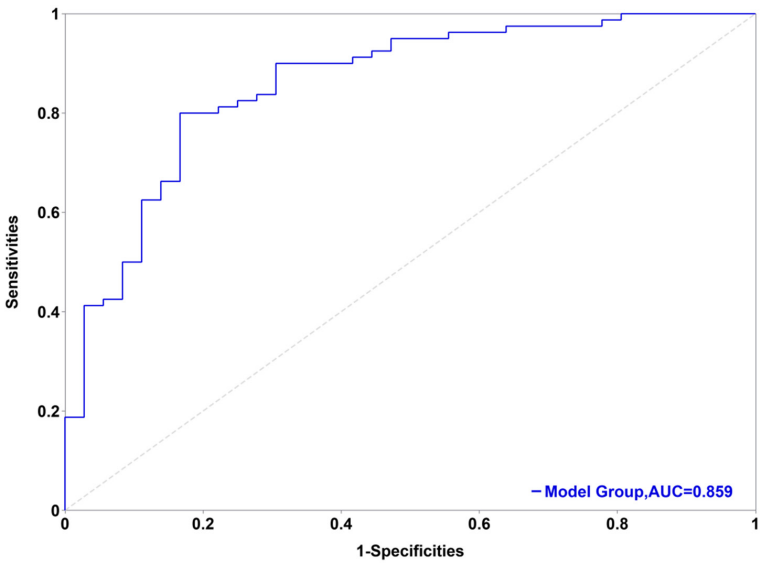

Figure 8. ROC curve of the model group.

Infection can exacerbate the "inflammatory storm", triggering the release of large quantities of inflammatory factors. These factors promote adipocyte breakdown, activate hepatic fatty acid synthase, and ultimately increase the synthesis of TC and TG [26]. Inflammatory responses can also cause renal hypoperfusion, leading to renal vasoconstriction, endothelial cell damage, decreased glomerular filtration rate, and impaired renal tubular reabsorption function. These changes disrupt serum creatinine excretion, resulting in its accumulation and elevated levels [27]. After infection of pancreatic necrotic tissue, inflammation spreads to the intestine, causing intestinal mucosal ischemia, hypoxia, and cell apoptosis. This increases intestinal barrier permeability, allowing D-LA to enter the bloodstream through the damaged barrier [28]. Additionally, inflammation interferes with hepatic apolipoprotein synthesis and metabolism. It upregulates APOB synthesis, accelerates APOA1 degradation, exacerbates lipid metabolism imbalance, and increases the APOB/A1 ratio, all of which reflects the body's lipid metabolism disorders and worsen inflammation [29]. Under infection stimulation, the immune system enhances the differentiation of bone marrow hematopoietic stem cells into granulocytes and megakaryocytes, leading to massive production of white blood cells and platelets. Meanwhile, lymphocytes decrease due to immune suppression and increased apoptosis, resulting in a corresponding rise in SIRI scores [30]. This study also found that D-LA, APOB/A1, and SIRI are independent risk factors for IPN in AP patients. Furthermore, the AUC for the combined detection of these three indicators was higher than that for single-indicator detection. This suggests that the combined detection of D-LA, APOB/A1, and SIRI has greater value in evaluating the risk of IPN in AP patients.

Elevated D-LA levels stem from intestinal barrier dysfunction. As the body's largest bacterial reservoir, the intestine allows translocation of gram-negative bacteria and their endotoxins into the circulatory system once its barrier is

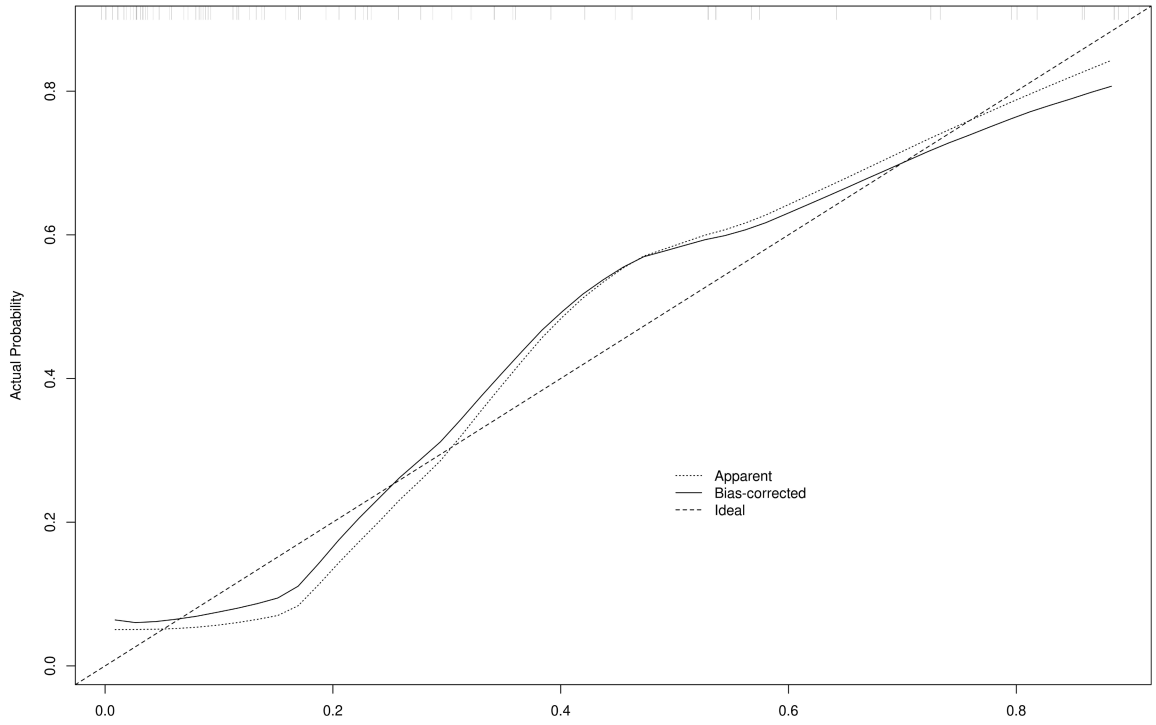

Figure 9. Calibration curve of the model group.

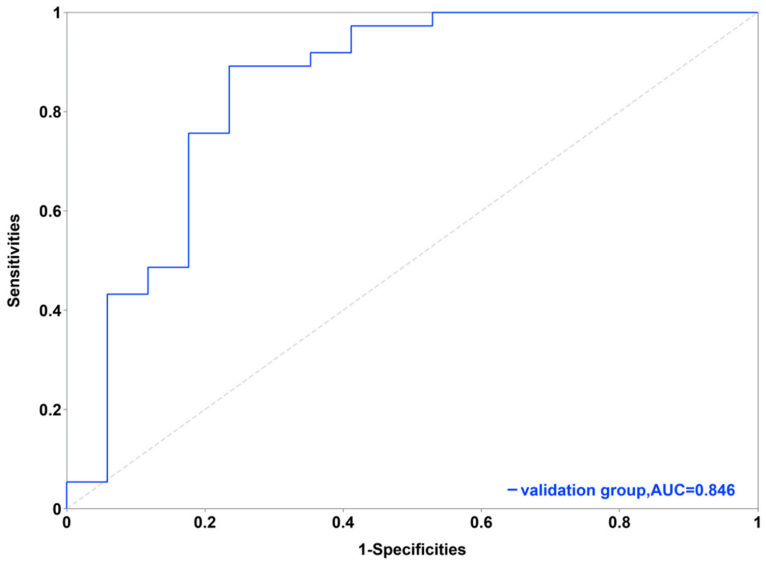

Figure 10. ROC curve of the external validation group.

disrupted, this provides a pathogenic basis for secondary infection of necrotic tissue [31]. An imbalanced APOB/A1 ratio reflects systemic lipid metabolism disorders. Specifically, high-density lipoprotein-mediated reverse cholesterol transport is impaired, which reduces cholesterol efflux from mononuclear macrophages. This impairment weakens the phagocytic and bactericidal functions of these cells, preventing them from effectively clearing pathogens in necrotic tissue [32]. Abnormal SIRI indicates a systemic imbalance in immune inflammation. Overactivated neutrophils release large quantities of inflammatory mediators, exacerbating tissue damage, while immunosuppression of lymphocytes weakens the body's defense against infection [33]. These three factors act synergistically to promote the formation of necrotic tissue, impair the body's anti-infection defense mechanisms, and increase the risk of IPN. Compared with single-indicator detection, combined detection of these three markers can better capture the pathological features of AP complicated with IPN, thereby improving evaluation efficacy. In this study, a nomogram for

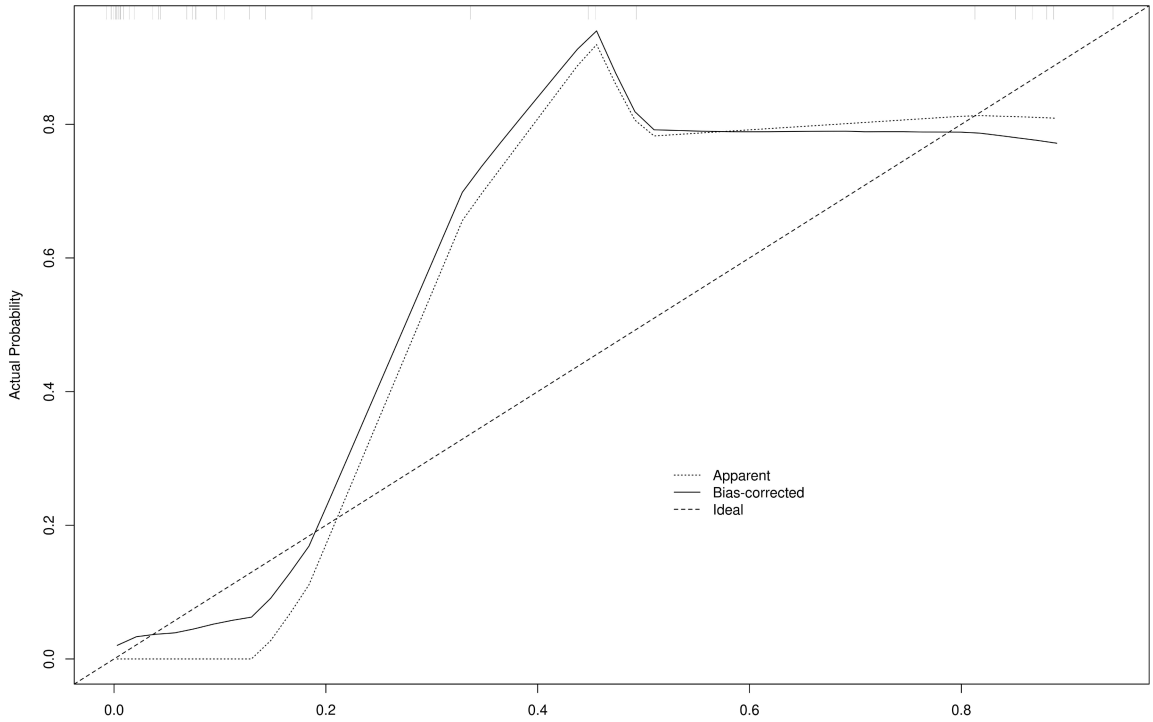

Figure 11. Calibration curve of the external verification group.

predicting the risk of IPN in AP patients was constructed based on age, D-LA, APOB/A1, and SIRI scores. The predictive performance of this nomogram was evaluated using a ROC curve, which yielded an AUC of 0.859, indicating good predictive ability. An external validation cohort further confirmed the nomogram's generalizability and reliability. The consistency of predictive factors between the external validation cohort and the model development cohort suggests that this nomogram can be applied to different patient populations, providing robust support for its clinical use. In clinical practice, this nomogram can be used to quantitatively assess the risk of early IPN in AP patients and assist in formulating personalized diagnosis and treatment plans. For high-risk patients, early interventions (such as enhanced infection monitoring and optimized antibiotic use) should be implemented, while dynamic tracking of indicator changes can help improve treatment efficiency and patient prognosis.

In summary, D-LA, APO B/A1, SIRI are correlated with AP severity and can serve as biomarkers for assessing the risk of concurrent IPN in AP patients. The jointly constructed model can be used for early assessment and personalized measures. There are several limitations to this study, such as a relatively small sample size and retrospective single center research. In multivariate regression models, it is generally recommended that each outcome event corresponds to at least 10-15 independent variables. However, the sample size and number of events included in this study's multivariate regression with three independent variables are still relatively limited, which may lead to the model's overfitting to existing data, reduced applicability to external populations, and overestimation or underestimation of risk factor effect values. To reduce the risk of overfitting, subsequent research should increase data diversity and further analyze and explore by expanding the sample size and conducting prospective multicenter studies.

Disclosure of conflict of interest

None.

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