Prediction and evaluation of a nomogram model for recurrent acute pancreatitis

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Objective The purpose of this study was to investigate the influencing factors for recurrent acute pancreatitis and construct the nomogram model to predict the risk of recurrent acute pancreatitis.

Methods Patients diagnosed with acute pancreatitis in the Affiliated Hospital of Southwest Medical University were enrolled. We collected these patients' basic information, laboratory data, imaging information. Using Logistic regression and least absolute shrinkage and selection operator regression to select risk factor for Cross-Validation Criterion. To create nomogram and validated by receiver operator characteristic curve, calibration curves and decision curve analysis.

Results A total of 533 patients with acute pancreatitis were included, including 99 recurrent acute pancreatitis patients. The average age of recurrent acute pancreatitis patients was 49.69 years old, and 67.7% of them were male. At the same time, in all recurrent acute pancreatitis patients, hypertriglyceridemic pancreatitis is the most important reason (54.5%). Regression analysis and least absolute shrinkage and selection operator regression showed that smoking history, acute necrotic collection, triglyceride, and alcohol etiology for acute pancreatitis were identified and entered into the nomogram. The area under the receiver operator characteristic curve of the training set was 0.747. The calibration curve showed the consistency between the nomogram model and the actual probability.

Conclusion In conclusion, some high-risk factors like smoking history, acute necrotic collection, triglyceride, and alcohol etiology for acute pancreatitis may predict recurrent pancreatitis and their incorporation into a nomogram has high accuracy in predicting recurrence. Eur J Gastroenterol Hepatol 36: 554–562

Introduction

With current changes in diet and lifestyle, recurrent acute pancreatitis (RAP), a global clinical problem cannot be ignored [1]. Based on in-depth epidemiological studies, the current mainstream view defines RAP as multiple episodes of acute pancreatitis (AP) (≥2 times), ≥3-month interval between two episodes, and complete relief of symptoms and signs after the initial treatment [1]. The clinical etiology of RAP has been gradually clarified, including choledocholithiasis or sludge and cholestasis, Oddi sphincter dysfunction, obstruction of the main pancreatic duct or bile duct junction, anatomic ductal variation interfering with pancreatic fluid outflow, genetic mutations, and excessive alcohol consumption [2]. The damage of RAP is more significant than the first attacks, such that 50% of patients require readmission and 32% require admission to the ICU, eventually causing irreversible damage to the pancreas, mental and physical pain to the patient, affects the patient's quality of life, and consumes large amounts of medical and health resources [3].

Many experts and scholars have constructed a variety of clinical prediction models based on the etiology and severity of AP, such as line graph models, logistic regression models, and artificial intelligence models. However, there are few studies on RAP; therefore, this study aimed to construct a nomogram model of RAP based on relevant clinical indicators to provide a reference for the prevention of RAP.

Methods

Patients selection

We retrospectively analyzed patients diagnosed with AP at the Affiliated Hospital of Southwest Medical University. Patients who met the following criteria were excluded: (1) not meeting "the 2012 revision of the Atlanta Acute Pancreatitis Diagnostic and Classification Criteria; (2) incomplete clinical data; (3) chronic pancreatitis; (4) severe hepatic and renal insufficiency; and (5) history of pancreatic surgery. Finally, 533 patients were enrolled for this study. Based on the current mainstream

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view of the definition of RAP [1], we reviewed the medical records of all patients with AP and then the patients with AP were divided into RAP group and non-RAP group.

Data collection

Clinical data were collected from the electronic medical database of the Affiliated Hospital of Southwest Medical University, including age, gender, diabetes, hypertension, drinking history, smoking history, the severity of illness, complications, organ failure, BMI and laboratory test data.

Data Availability Statement: The data underlying this article are available in the article and in its online supplementary material, supplemental digital content 1, *http://links.lww.com/EJGH/A993*.

Relevant definitions

AP was diagnosed based on the Atlanta classification criteria revised in 2012. The diagnosis of AP conformed to two of the following three criteria: (1) typical abdominal pain associated with AP, (2) an increase in serum amylase and/or lipase levels to >3 times the upper normal limit, and (3) computed tomography (CT) or abdominal ultrasonography findings consistent with AP [1].

Based on in-depth epidemiological studies, the current mainstream view defines RAP as multiple episodes of AP (≥2 times), ≥3-month interval between two episodes, and complete relief of symptoms and signs after the initial treatment [1].

Biliary etiology for AP was defined as one or more gallstones or bile duct dilation and laboratory results indicative of obstructive jaundice [4]. Alcohol etiology for AP was diagnosed as regular, excessive alcohol consumption usually with a clinical history of>5 years and>50–100 g/day [5]. Triglyceride level >1000 mg/dl (11.3 mmol/L) were considered necessary to ascribe causation for hypertriglyceridemic pancreatitis (HTGP) [6]. Other less frequent causes of AP were defined as other types of AP, including endoscopic retrograde cholangiopancreatography, hypercalcaemia, pancreas divisum, tumors, genetic polymorphisms and drugs [7].

Statistical analysis

SPSS 26.0 and R 4.2 software were used for statistical analysis. All datasets were randomly divided into training and validation sets at a ratio of 7:3. The training set was used to build the nomogram model, and the test set was used to analyze the prediction performance of the model. Data are expressed as mean ± SD for normally distributed continuous variables, and comparisons between the two groups were performed using two independent sample t-tests. Enumeration data are expressed as N (%), and comparisons between the two groups were performed using the chi-square test. The rank-sum test was used for quantitative data that were not normally distributed and are expressed as medians(quartiles). The area under the receiver operating characteristic curve (AUC) was used to evaluate the discrimination ability of the model. A calibration curve was used to evaluate calibration capability, and decision curve analysis (DCA) was used to evaluate clinical effectiveness. Statistical significance was set at $P < 0.05$.

Results

Characteristics of RAP patients

A total of 533 patients with AP were enrolled, including 99 patients with RAP. The average age of the RAP patients was 49.69 years, 67.7% were male, and 56.6% had a smoking history. In all patients with RAP, hypertriglyceridemic pancreatitis was the most important cause, accounting for 54.5%, followed by patients with acute biliary pancreatitis, about 39.4%. The mean serum calcium level was 2.25 mmol/L, and triglyceride level was 6.33 mmol/L. Regarding complications, priority was given to acute necrotic collection (ANC); 39.4% of patients with a history of ANC had AP recurrence, and 20.2% of patients with acute peripancreatic fluid collection had a recurrence. Recurrence was rare in patients with pancreatic pseudocyst (PPC) and walled-off necrosis. In terms of laboratory index, the patients with recurrent pancreatitis had higher triglycerides, cholesterol, and lower high density lipoprotein and apolipoprotein A compared to the non-recurrent group ($P < 0.05$). The results are presented in Table 1.

Characteristics on the training and validation sets

The characteristics analysis and comparison results of training set and verification set were shown in Table 2.

Construction of nomogram model for risk factors of RAP

Data from the training set were used for model training, with recurrence as the dependent variable (assignment: did not occur = 0, occurred = 1). Univariate logistic regression analysis showed that ANC ($P < 0.001$), cholesterol ($P = 0.001$), triglycerides ($P < 0.001$), smoking history ($P = 0.005$), drinking history ($P = 0.008$), disease severity ($P = 0.027$), ABP ($P = 0.025$), and HTGP ($P = 0.001$) were significantly associated with the occurrence of RAP (Table 3). Multivariate logistic regression was used to screen for independent risk factors. The results showed that ANC (OR: 5.197; 95% CI: 2.340–12.051; $P < 0.001$), triglyceride (OR: 1.065; 95% CI: 1.006–1.129; $P = 0.030$) were independently associated with RAP (Table 4). The least absolute shrinkage and selection operator (LASSO) regression screened ANC, triglyceride, smoking history, alcohol etiology for AP were risk factors for RAP (Fig. 1). The variables screened by the two methods were combined, and the AUC of each combination was compared (Fig. 2). We found that ANC, triglyceride, smoking history, alcohol etiology for AP were the best predictive variables. The nomogram was shown in Fig. 3. Each variable was scored on the nomogram, and the total score was obtained by adding the scores of all variables. The estimated probability of RAP was obtained by drawing a vertical line downward from the total score. The receiver operating characteristic (ROC) curve was used to evaluate the predictive performance of the model. The area under the ROC curve of the training set was 0.747 and that of the validation set was 0.823, which showed a good

Table 1. Characteristics of recurrence of acute pancreatitis

Variable	All patients with pancreatitis (N = 533)	RAP (N = 99)	NRAP (N = 434)	*P*-value
Baseline				
Age (years)	51.53 ± 14.74	49.69 ± 13.97	51.95 ± 14.89	0.244
Gender [male; n (%)]	310 (58.2%)	66 (66.7%)	244 (56.2%)	0.060
BMI (kg/m^2)	25.55 ± 6.84	24.50 ± 2.94	25.79 ± 23.01	0.947
Diabetes, n (%)	81 (15.2%)	20 (20.2%)	61 (14.1%)	0.111
Hypertension, n (%)	126 (23.6%)	24 (24.2%)	102 (23.5%)	0.846
Smoking history, n (%)	184 (34.5%)	56 (56.6%)	128 (29.5%)	<0.001
Drinking history, n (%)	177 (33.2%)	49 (49.5%)	128 (29.5%)	<0.001
ABP, n (%)	272 (51.0%)	39 (39.4%)	233 (53.7%)	0.001
HTGP, n (%)	169 (31.7%)	54 (54.5%)	115 (26.5%)	<0.001
Alcoholic AP, n (%)	36 (6.8%)	11 (11.1%)	25 (5.8%)	0.056
MSAP + SAP, n (%)	227 (42.6%)	57 (57.6%)	170 (39.2%)	0.001
Complication				
APFC, n (%)	97 (18.2%)	20 (20.2%)	77 (17.7%)	0.574
ANC, n (%)	88 (16.5%)	39 (39.4%)	49 (11.3%)	<0.001
PPC, n (%)	12 (2.3%)	5 (5.1%)	7 (1.6%)	0.038
WON, n (%)	6 (1.1%)	3 (3.0%)	3 (0.7%)	0.081
SIRS, n (%)	129 (24.2%)	29 (29.3%)	100 (23.0%)	0.194
Respiratory failure, n (%)	32 (6.0%)	9 (9.1%)	23 (5.3%)	0.154
Renal failure, n (%)	13 (2.4%)	3 (3.0%)	10 (2.3%)	0.447
Circulatory failure, n (%)	5 (0.9%)	0 (0%)	5 (1.2%)	0.356
Septicopyemia, n (%)	2 (0.4%)	0 (0%)	2 (0.5%)	0.662
IAH, n (%)	5 (0.9%)	2 (2.0%)	3 (0.7%)	0.234
Laboratory Index				
WBC (10^9/L)	13.29 ± 5.14	13.46 ± 5.70	13.26 ± 5.01	0.930
NC (10^9/L)	10.81 (7.79–14.29)	11.13 (7.61–14.71)	10.79 (7.81–14.12)	0.968
HCT (%)	0.42 ± 0.15	0.43 ± 0.06	0.42 ± 0.56	0.227
RDW-SD(fL)	45.88 ± 17.91	44.96 ± 5.30	46.19 ± 19.68	0.978
LC (10^9/L)	1.18 ± 0.88	1.19 ± 0.70	1.17 ± 0.91	0.837
PLT (10^9/L)	208.63 ± 72.89	198.65 ± 74.70	210.91 ± 72.36	0.070
RDWCV (%)	13.10 (12.70–13.60)	13.10 (12.60–13.60)	13.10 (2.70–13.60)	0.789
CRP (mg/L)	80.67 ± 60.91	84.77 ± 65.23	79.74 ± 61.16	0.663
PCT (μg/ml)	0.52 (0.10–1.84)	0.52 (0.08–1.82)	0.53 (0.38–1.84)	0.360
ALT (U/L)	35.20 (19.54– 99.88)	31.78 (17.40–88.80)	35.80 (20.18–100.36)	0.113
AST (U/L)	30.90 (27.77–91.40)	29.10 (18.60–68.30)	31.70 (20.90–101.03)	0.232
Serum creatinine (μmol/L)	64.07 ± 32.74	61.43 ± 29.12	64.67 ± 33.52	0.190
Urea (mmol/L)	5.30 ± 2.86	5.32 ± 2.36	5.29 ± 2.96	0.621
Blood calcium (mmol/L)	2.16 (2.12–2.36)	2.25 (2.10–2.35)	2.26 (2.13–2.36)	0.438
Blood glucose (mmol/L)	7.83 (6.17–10.14)	7.97 (6.23–10.67)	7.79 (6.13–10.12)	0.422
Triglyceride (mmol/L)	2.69 (1.21–6.35)	6.33 (1.49–14.28)	2.41 (1.17–5.65)	<0.001
Cholesterol (mmol/L)	5.18 (4.12–6.21)	5.95 (4.49–9.12)	5.08 (4.11–5.95)	<0.001
HDL (mmol/L)	1.08 (0.83–1.28)	0.92 (0.73–1.14)	1.08 (0.86–1.32)	<0.001
LDL (mmol/L)	2.74 (2.04–3.27)	2.74 (1.82–3.54)	2.74 (2.10–3.22)	0.655
APOA (mmol/L)	1.1 (0.99–1.40)	0.92 (0.73–1.14)	1.19 (1.01–1.40)	0.040
APOB (mmol/L)	0.80 (0.62–1.00)	0.80 (0.38–0.97)	0.80 (0.65–1.00)	0.111

ABP, acute biliary pancreatitis; ALT, alanine aminotransferase; ANC, acute necrotic collection; APFC, acute peripancreatic fluid collection; APOA, apolipoprotein A; APOB, apolipoprotein B; AST, aspartate aminotransferase; CRP, C reactive protein; HCT, hematocrit; HDL, high-density lipoprotein; HTGP, hyper triglyceridemic pancreatitis; IAH, intra-abdominal hypertension; LC, lymphocyte count; LDL, low-density lipoprotein; MSAP, moderately severe acute pancreatitis; NC, neutrophil count; PCT, procalcitonin; PLT, platelet; PPC, pancreatic pseudocyst; RDW-CV, red blood cell distribution width-coefficient variable; RDW-SD, red blood cell distribution width-SD; SAP, severe acute pancreatitis; SIRS, systemic inflammatory response syndrome; WON, walled-off necrosis.

prediction efficiency as shown in Fig. 4. The calibration curve revealed that the actual results agreed well with the predicted results (Fig. 5). The DCA curve indicated that the prediction model had good clinical applicability, as shown in Fig. 6.

Discussion

There is no unified conclusion on the risk factors for RAP, and there is also a lack of reliable and rapid clinical tools to predict it. Presently, the Ranson, APACHE II, and CTSI scoring systems are commonly used. However, these tools are generally used to assess the severity of AP and have a poor predictive ability on the risk of RAP [8–13]. In addition, these scoring systems are complex. The Ranson scoring system includes multiple laboratory examination indicators and must be completed within 48 h of admission. The APACHE II score also requires blood gas analysis results, which are of low applicability for some primary hospitals. The CTSI scoring system involves the evaluation of pancreatic necrosis; however, the imaging manifestations of pancreatic necrosis in the early stage of admission are not obvious, and the clinical experience and professional knowledge of doctors who diagnose pancreatic necrosis are highly required. The use of the above scoring tools is relatively complicated, cannot reflect the disease situation in a more timely and intuitive way, and cannot predict the probability of RAP.

Therefore, a nomogram model was constructed to predict the risk factors for RAP, which included five predictor variables: smoking history, ANC, triglyceride, ABP, and serum calcium. We evaluated the predictive efficacy, predictive accuracy, and clinical efficacy of the model; the area under the ROC curve of the test and training sets were 73.1% and 82.8%, respectively, showing good predictive performance. Simultaneously, the actual calibration

Table 2. Characteristics about training set and validation set

Variable	Training set (N = 374)	Validation set (N = 159)	t/χ^2/Z值	*P*-value
Baseline				
Age(years)	51.18 ± 14.70	52.35 ± 14.84	–0.626	0.531
Gender [male, n (%)]	218 (58.3%)	92 (57.9%)	0.040	0.833
BMI (kg/m^2)	24.67 ± 4.24	27.62 ± 3.61	–0.986	0.326
Diabetes, n (%)	57 (15.2%)	24 (15.1%)	0.020	0.540
Hypertension, n (%)	86 (23.0%)	40 (25.2%)	0.289	0.333
Smoking history, n (%)	130 (34.8%)	54 (34.0%)	0.031	0.471
Drinking history, n (%)	123 (32.9%)	54 (34.0%)	0.058	0.442
ABP, n (%)	191 (51.2%)	81 (50.9%)	1.046	0.177
HTGP, n (%)	133 (35.6%)	36 (22.6%)	0.010	0.497
Alcoholic AP, n (%)	24 (6.4%)	11 (6.9%)	3.122	0.052
MSAP + SAP, n (%)	158 (42.2%)	69 (43.4%)	0.060	0.440
Complication				
APFC, n (%)	59 (15.8%)	38 (23.9)	4.946	0.219
ANC, n (%)	60 (16.0%)	28 (17.6%)	0.199	0.371
PPC, n (%)	11 (2.9%)	1 (0.6%)	2.710	0.084
WON, n (%)	6 (1.6%)	0 (0%)	2.580	0.118
SIRS, n (%)	94 (25.1%)	35 (22.0%)	0.592	0.256
Respiratory failure, n (%)	20 (5.3%)	12 (7.5%)	0.957	0.215
Renal failure, n (%)	11 (2.9%)	2 (1.3%)	1.329	0.203
Circulatory failure, n (%)	3 (0.8%)	2 (1.3%)	0.249	0.469
Septicopyemia, n (%)	2 (0.5%)	0 (0%)	0.853	0.492
IAH, n (%)	3 (0.8%)	2 (1.3%)	0.249	0.469
Laboratory Index				
WBC (10^9/L)	13.34 ± 5.2	13.18 ± 4.99	0.294	0.769
NC (10^9/L)	11.93 ± 11.56	11.34 ± 4.91	0.315	0.553
HCT (%)	0.42 ± 0.06	0.41 ± 0.04	0.427	0.670
RDW-SD (fL)	46.22 ± 21.16	45.08 ± 4.64	0.6733	0.501
LC (10^9/L)	1.2 ± 0.96	1.14 ± 0.63	0.715	0.472
PLT (10^9/L)	210.73 ± 73.88	203.7 ± 70.49	0.899	0.369
RDWCV (%)	13.10 (12.70–13.60)	13.00 (12.70–13.10)	–0.965	0.334
CRP (mg/L)	80.59 ± 62.61	80.86 ± 60.41	–0.047	0.963
PCT (μg/ml)	0.48 (0.10–1.84)	0.58 (0.14–1.82)	0.981	0.327
ALT (U/L)	33.75 (19.00– 99.88)	35.80 (20.50–99.88)	0.891	0.373
AST (U/L)	30.25 (20.48–101.03)	31.80 (21.07–74.70)	0.555	0.579
Serum creatinine (μmol/L)	64.87 ± 35.34	62.20 ± 25.62	0.783	0.434
Urea (mmol/L)	5.27 ± 3.08	5.34 ± 2.26	–0.313	0.755
Blood calcium (mmol/L)	2.26 (2.13–2.36)	2.25 (2.12–2.38)	0.322	0.747
Blood glucose (mmol/L)	7.98 (6.13–10.20)	7.60 (6.20–9.84)	–0.318	0.750
Triglyceride (mmol/L)	3.00 (1.21–6.90)	2.47 (1.18–5.67)	–0.693	0.488
Cholesterol (mmol/L)	5.22 (4.13–6.33)	5.16 (4.08–5.95)	–0.864	0.387
HDL (mmol/L)	1.06 (0.83–1.25)	1.08 (0.82–1.35)	1.197	0.231
LDL (mmol/L)	2.74 (1.97–3.27)	2.76 (2.14–3.29)	0.551	0.582
APOA (mmol/L)	1.19 (0.99–1.38)	1.19 (0.96–1.43)	0.985	0.325
APOB (mmol/L)	0.80 (0.61–0.98)	0.82 (0.62–1.03)	1.217	0.224

ABP, acute biliary pancreatitis; ALT, alanine aminotransferase; ANC, acute necrotic collection; APFC, acute peripancreatic fluid collection; APOA, apolipoprotein A; APOB, apolipoprotein B; AST, aspartate aminotransferase; CRP, C reactive protein; HCT, hematocrit; HDL, high-density lipoprotein; HTGP, hyper triglyceridemic pancreatitis; IAH, intra-abdominal hypertension; LC, lymphocyte count; LDL, low-density lipoprotein; MSAP, moderately severe acute pancreatitis; NC, neutrophil count; PCT, procalcitonin; PLT, platelet; PPC, pancreatic pseudocyst; RDW-CV, red blood cell distribution width-coefficient variable; RDW-SD, red blood cell distribution width-SD; SAP, severe acute pancreatitis; SIRS, systemic inflammatory response syndrome; WON, walled-off necrosis.

and standard calibration curves had a high degree of fit, and clinical applicability was strong. Our model can assess the risk of pancreatitis recurrence early, more rapidly, and in an intuitive manner and conduct an early clinical intervention.

Smoking is a traditional risk factor for pancreatitis onset and has been demonstrated in several studies [14–16]. The 2020 International Consensus Guideline: Risk factors for chronic pancreatitis indicate an independent, dose-dependent relationship between smoking and increased risk of pancreatitis [17]. In addition, some studies have found that smoking is an independent risk factor for the recurrence of HTGP [18]. Our study found that the smoking rate of patients with RAP reached 57.6%, and multivariate analysis also confirmed that smoking was an independent risk factor for RAP. Our results were consistent with these results. However, the pathogenic mechanisms of smoking in pancreatic injury remain unclear. Studies have found that long-term cigarette smoke inhalation leads to a higher expression of the inflammatory marker IL-6 in acinar, islet, and ductal cells, which contributes to the damage of pancreatic cells through oxidative stress [19]. Therefore, patients with a long-term smoking history and a history of pancreatitis should receive life education and regular physical examinations to reduce the probability of recurrence of pancreatitis.

ANC is a common complication of AP. It has been reported that ANC and its complications account for 70–86% of mortality of patients with pancreatitis, and the prognosis is very poor [20]. Some studies have reported that ANC can cause severe inflammatory reactions around the pancreas, resulting in morphological and functional damage to the pancreas, decreased levels of secreted pancreatic enzymes, and poor digestion of lipids, which may be one of the reasons for RAP [21]. In addition, the long-term inflammatory reaction can cause pancreatic necrosis, which is not accurately identified by CT in the early stage, resulting in rapid recurrence after

conservative treatment [22,23]. Ahmed Ali found that ANC was independently associated with the recurrence of pancreatitis. Our data showed that approximately 40% of patients with previous ANC had recurrence [24]. However, there are few large-scale studies on ANC in RAP, and there is no unified conclusion on the mechanism by which ANC causes RAP. Therefore, patients with initial AP complicated with ANC should regularly undergo abdominal color Doppler ultrasound after discharge to evaluate the recovery of peripancreatic necrosis and minimize the mortality rate.

Triglycerides can be hydrolyzed into a large number of free fatty acids, which can enhance the toxic effects of cellular inflammatory factors and cause cellular necrosis and damage. In addition, the blood remains in a viscous state for a long time, and the aggregation and embolism of serum lipid particles affect the pancreatic microcirculation, resulting in long-term ischemia and hypoxia of the pancreas, which is very susceptible to AP [25]. Many studies have shown that high triglyceride levels are associated with the recurrence of pancreatitis. In a study by Zafrir, multivariate Cox analysis found that peak triglyceride levels >3000 mg/dl and recent triglyceride levels >500 mg/dl were independent risk factors for the recurrence of pancreatitis [26]. In our cohort, the average triglyceride level of patients with RAP was 6.33 mmol/L, which was significantly higher than the normal level. Undoubtedly, high triglyceride levels are an absolute risk factor for RAP, and early lipid-lowering therapy is necessary for patients with hyperlipidemia, particularly those with a history of pancreatitis.

Alcohol-induced AP is by far the most common form of AP [27]. A 10-year retrospective study from China found that the estimate number of death caused by alcohol-induced AP was 3327.29 in 2019. Meanwhile, the disease burden caused by alcohol use was most serious among young and middle-aged male, reaching the highest value in the age group of 35 to 54 [28]. In our study, the average age in RAP group was 49.69 years, which was consistent with the above results. The most common reason for alcohol-induced AP was alcoholism. In Russia, 63% of all male pancreatitis deaths could be attributed to alcohol consumption. The vast majority of patients did not abstain from alcohol after recovery from primary pancreatic acinar cells, which greatly increased the probability of recurrence of pancreatitis [29]. A study revealed that in-hospital patients' education markedly reduces alcohol consumption after alcohol-induced AP [30]. Therefore, we should strengthen patient' education, which could low the occurrence of AP caused by alcohol.

This study has some limitations. First, it was a single-center retrospective study, which may have selection bias.

Table 3. Univariate logistic analysis of risk factors for recurrence of acute pancreatitis

Predictor variable	OR	95% CI	*P*-value
Age (year)	0.988	(0.970–1.007)	0.210
Gender, n (%)	1.124	(0.653–1.934)	0.674
BMI (kg/m^2)	1.001	(0.941–1.066)	0.966
Diabetes, n (%)	1.659	(0.847–3.250)	0.140
Hypertension, n (%)	1.088	(0.584–2.028)	0.791
Smoking history, n (%)	2.175	(1.269–3.729)	0.005
Drink history, n (%)	2.080	(1.210–3.574)	0.008
ABP, n (%)	0.525	(0.298–0.922)	0.025
HTGP, n (%)	2.567	(1.486–4.436)	0.001
Alcoholic AP, n (%)	2.031	(0.806–5.515)	0.133
MSAP + SAP	1.830	(1.071–3.126)	0.027
APFC, n (%)	1.227	(0.571–2.639)	0.600
ANC, n (%)	4.317	(2.345–7.948)	<0.001
PPC, n (%)	0.360	(0.102–1.269)	0.112
WON, n (%)	0.207	(0.041–1.047)	0.057
SIRS, n (%)	0.707	(0.405–1.307)	0.287
Respiratory failure, n (%)	0.849	(0.275–2.628)	0.777
Renal failure, n (%)	2.181	(0.274–7.339)	0.461
Circulatory failure, n (%)	0.425	(0.038–4.755)	0.487
Septicopyemia, n (%)	0.782	(0.342–0.976)	0.863
WBC (10^9/L)	1.01	(0.960–1.062)	0.709
NR (10^9/L)	0.995	(0.966–1.026)	0.762
HCT, n (%)	5.452	(0.050–590.424)	0.478
RDWSD (fL)	0.976	(0.908–1.038)	0.447
LC (10^9/L)	1.02	(0.785–1325)	0.884
PLT (10^9/L)	0.997	(0.993–1.001)	0.153
RDWCV (%)	0.946	(0.779–1.150)	0.578
CRP (mg/ml)	1.000	(0.996–1.004)	0.979
PCT (μg/ml)	0.897	(0.748–1.075)	0.238
ALT (U/L)	0.998	(0.996–1.001)	0.126
AST (U/L)	0.999	(0.998–1.001)	0.331
Serum creatinine (μmol/L)	0.992	(0.980–1.003)	0.161
Urea (mmol/L)	0.982	(0.893–1.081)	0.713
Blood calcium (mmol/L)	1.06	(0.357–3.148)	0.917
Blood glucose (mmol/L)	0.99	(0.926–1.058)	0.763
Triglyceride (mmol/L)	1.076	(1.040–1.114)	<0.001
Cholesterol (mmol/L)	1.121	(1.045–1.202)	0.001
HDL (mmol/L)	0.653	(0.319–1.339)	0.245
LDL (mmol/L)	1.123	(0.895–1.409)	0.316
APOA (mmol/L)	0.758	(0.335–1718)	0.507
APOB (mmol/L)	0.565	(0.286–1.118)	0.101

ABP, acute biliary pancreatitis; ALT, alanine aminotransferase; ANC, acute necrotic collection; APFC, acute peripancreatic fluid collection; APOA, apolipoprotein A; APOB, apolipoprotein B; AST, aspartate aminotransferase; CRP, C reactive protein; HCT, hematocrit; HDL, high-density lipoprotein; HTGP, hyper triglyceridemic pancreatitis; IAH, intra-abdominal hypertension; LC, lymphocyte count; LDL, low-density lipoprotein; MSAP, moderately severe acute pancreatitis; NC, neutrophil count; PCT, procalcitonin; PLT, platelet; PPC, pancreatic pseudocyst; RDW-CV, red blood cell distribution width-coefficient variable; RDW-SD, red blood cell distribution width-SD; SAP, severe acute pancreatitis; SIRS, systemic inflammatory response syndrome; WON, walled-off necrosis.

Table 4. Multivariable logistic analysis of risk factors for recurrence of acute pancreatitis

Predictor variable	β	SE	*P*-value	OR	95% CI
ANC	1.648	0.416	<0.001	5.197	(2.340–12.051)
Triglyceride	0.063	0.029	0.030	1.065	(1.006–1.129)
Cholesterol	0.003	0.055	0.952	1.003	(0.901–1.111)
Smoking history	0.517	0.368	0.160	1.676	(0.812–3.449)
HTGP	0.297	0.418	0.477	1.346	(0.594–3.087)
ABP	0.212	0.404	0.601	1.236	(0.567–2.790)
Drinking history	0.159	0.384	0.678	1.173	(0.550–2.486)
MSAP + SAP	−0.386	0.378	0.308	0.680	(0.314–1.396)

ABP, acute biliary pancreatitis; ANC, acute necrotic collection; HTGP, hyper triglyceridemic pancreatitis; MSAP, moderately severe acute pancreatitis; SAP, severe acute pancreatitis.

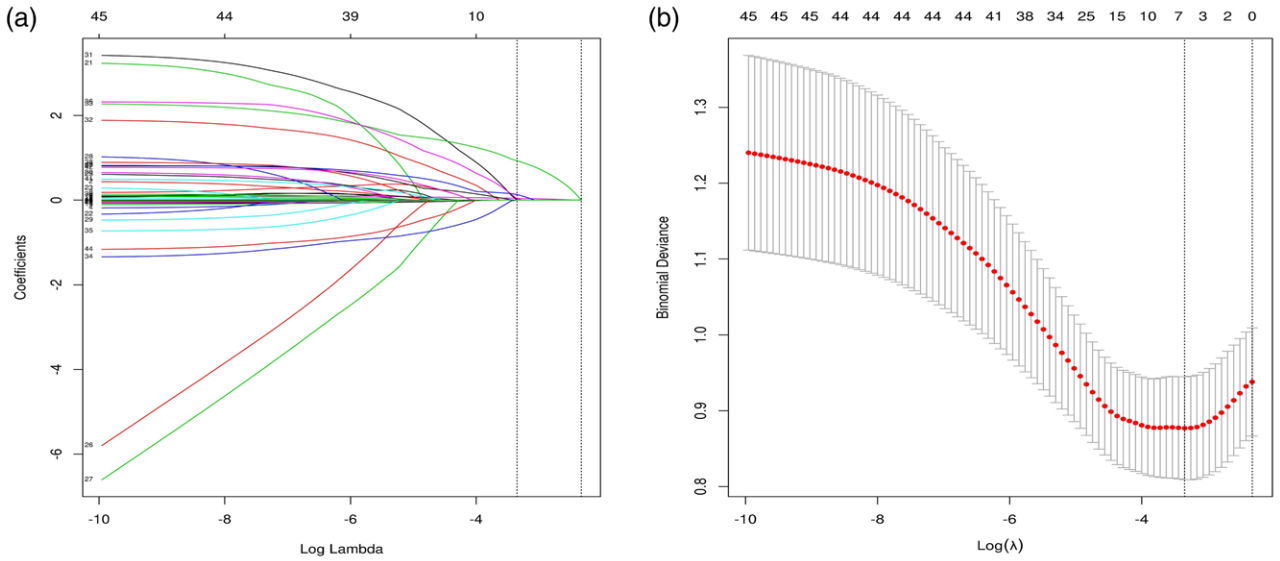

Fig. 1 . LASSO regression model. LASSO regression model to select candidate variables associated with CVC. (a) Tuning parameter (lambda:λ) selection in the LASSO model used 10-fold cross-validation via minimum criteria. (b) LASSO coefficient profiles of the features against the log(λ).

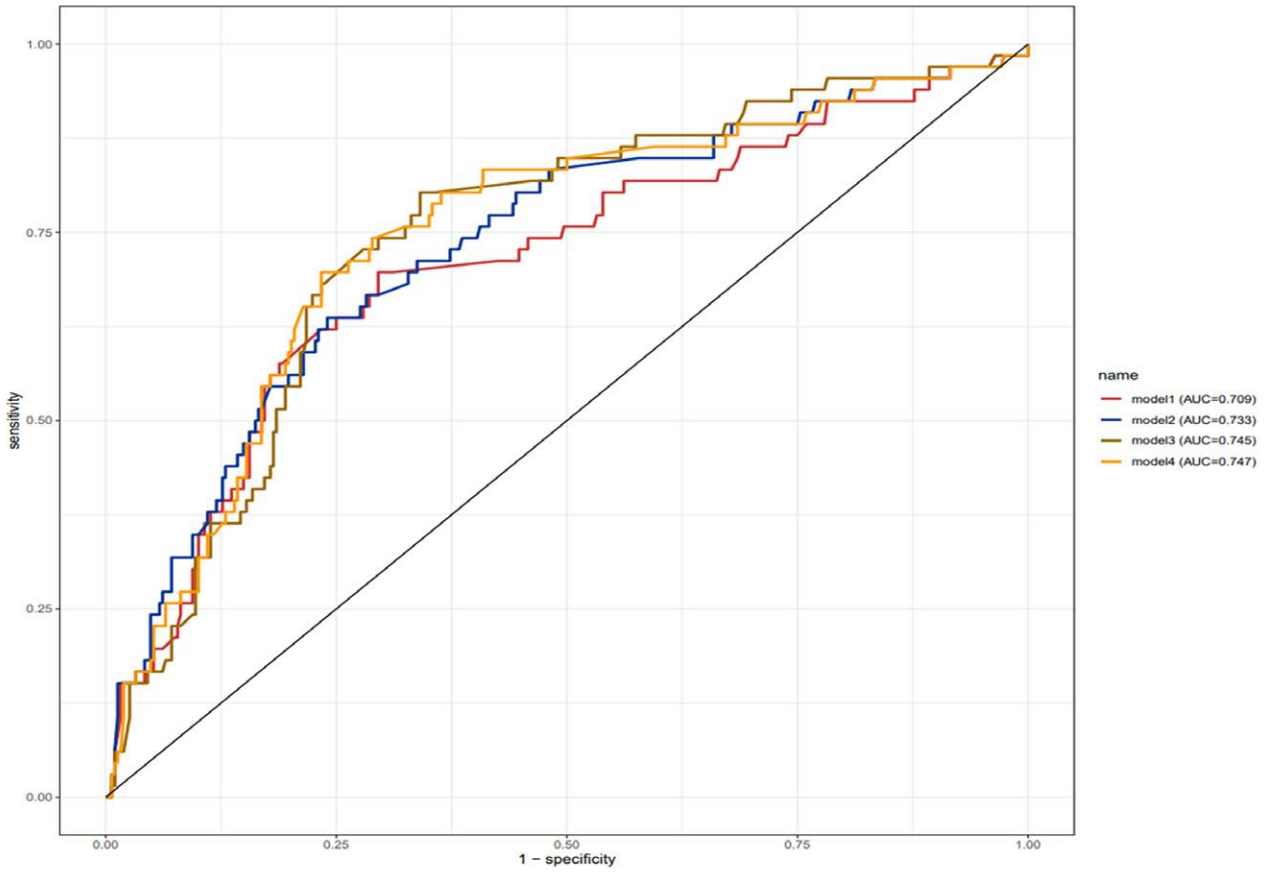

Fig. 2 . Receiver operator characteristic curve for model selection. Model 1: ANC and triglyceride; model 2: ANC, triglyceride, and smoking history; model 3: triglyceride, smoking, and alcohol-induced AP; model 4: ANC, triglyceride, smoking history, and alcohol-induced AP.

Second, it included laboratory test results at the time of the initial admission and failed to observe dynamic changes in some indicators. Third, the smoking age and time from initial onset to relapse of smoking patients were not stratified in detail, which may have had an impact on the study results.

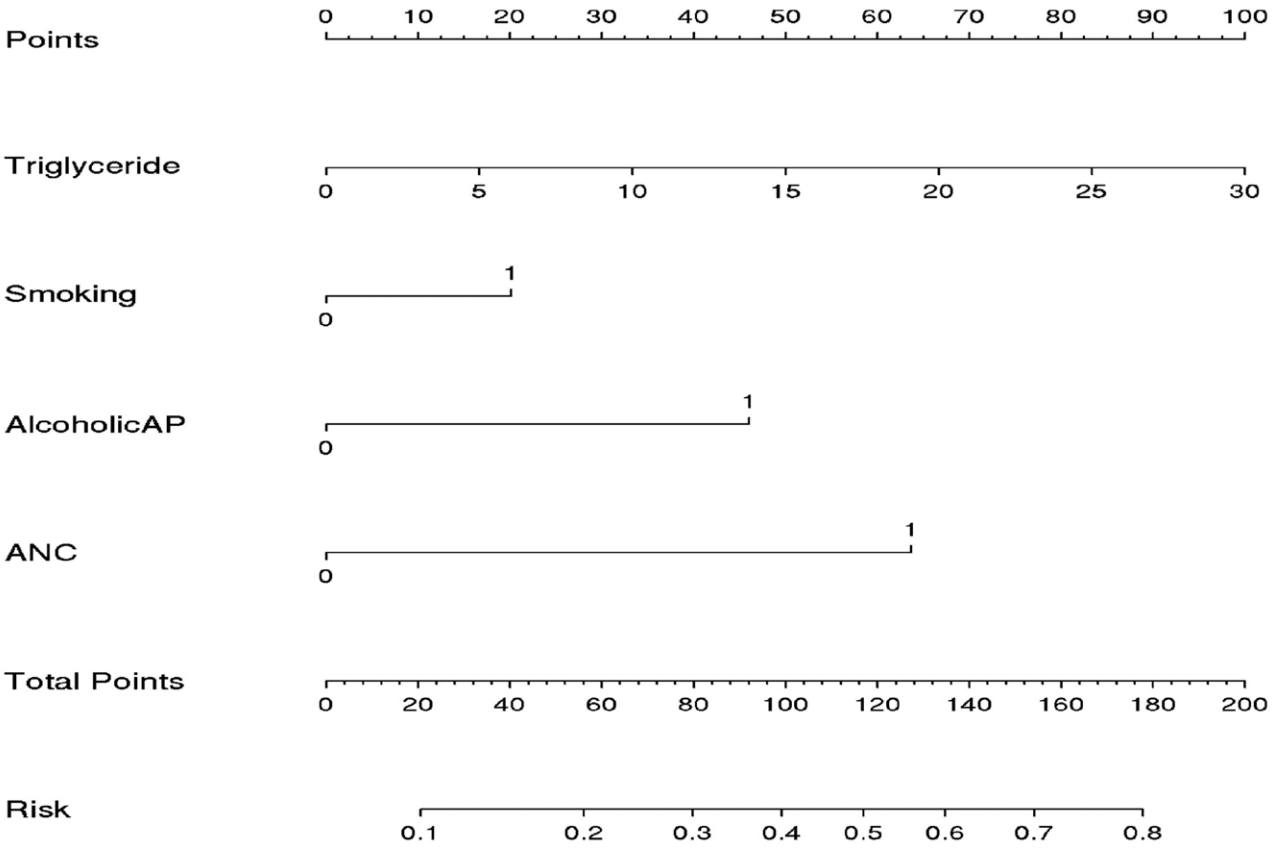

Fig. 3 . Nomogram to predict RAP. All points are summed to generate a total points. A vertical line is drawn at the 'total points' axis to the 'linear predictor' axis for risk evaluation. RAP, recurrent acute pancreatitis

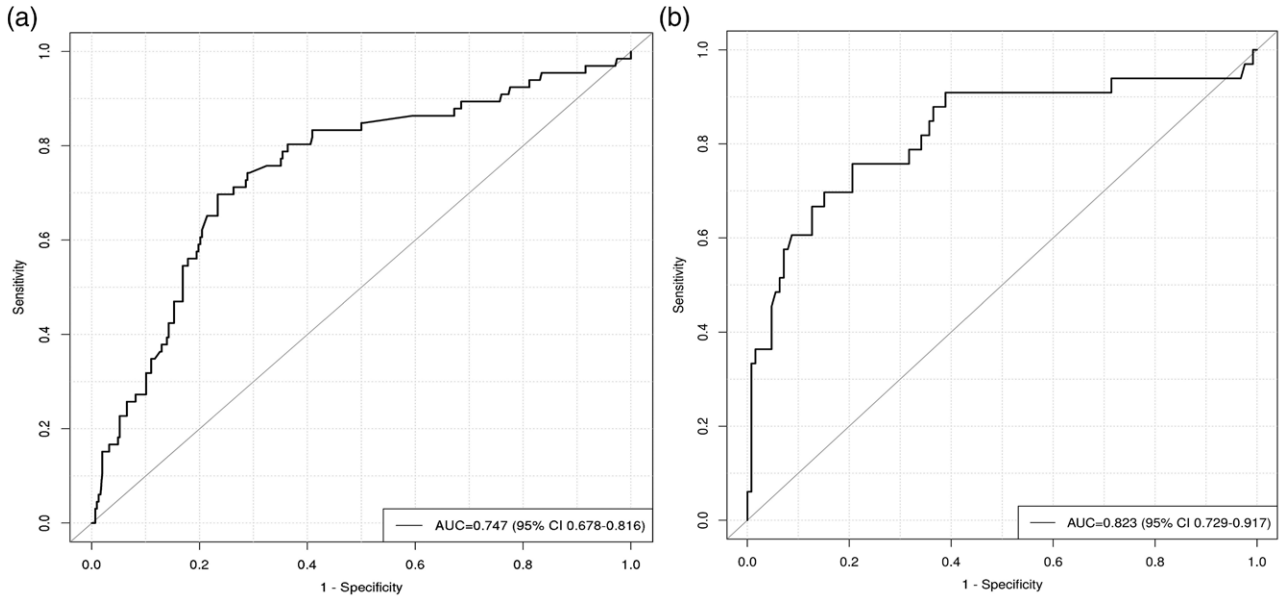

Fig. 4 . The receiver operator characteristic curves of nomogram. (a) is training set and (b) is validation set.

Conclusion

In conclusion, some high-risk factors like smoking history, ANC, triglyceride, alcohol etiology for AP may predict recurrent pancreatitis and their incorporation into a nomogram has high accuracy in predicting recurrence. To a certain extent, it can be used to predict a high-risk population for recurrent pancreatitis and reduce the recurrence probability of pancreatitis.

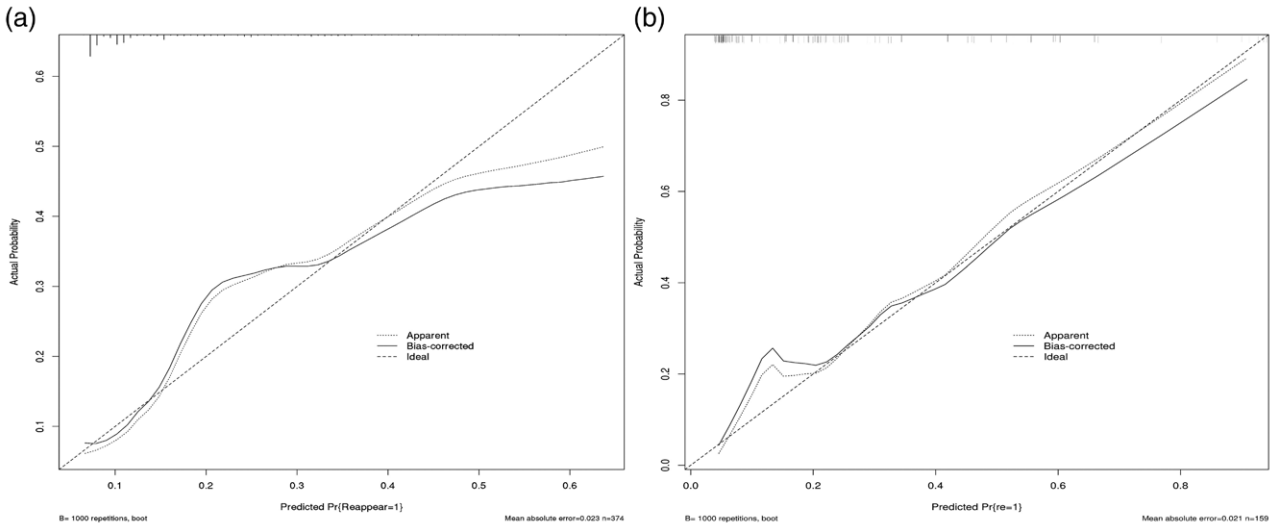

Fig. 5 . The calibration curve of nomogram. (a) is training set and (b) is validation set.

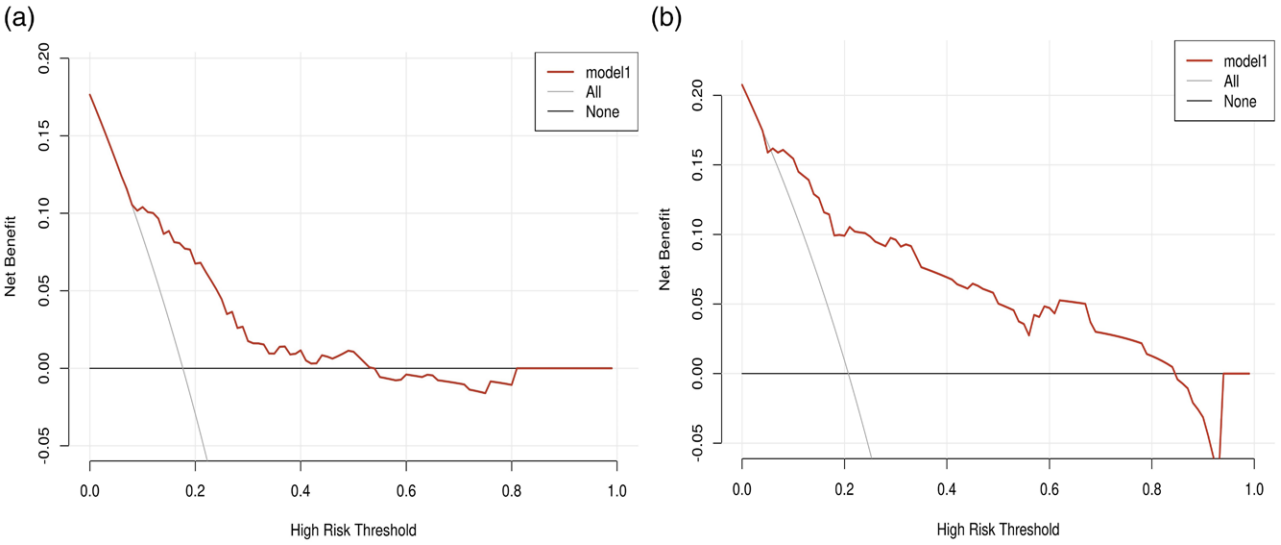

Fig. 6 . The decision curve analysis of the nomogram. (a) is training set and (b) is validation set.

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Conflicts of interest

There are no conflicts of interest.

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