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A risk nomogram for 30-day mortality in Chinese patients with acute pancreatitis using LASSO-logistic regression

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This study proposed to explore the 30-day mortality risk factors in patients with acute pancreatitis (AP) and construct a prognosis nomogram based on the Least absolute shrinkage and selection operator (LASSO) logistic regression. A retrospective study on 965 adult AP patients started from January 2017 and December 2019 was conducted. Feature selection is carried out by using LASSO regression, and the model was established through logistic regression ($P < 0.05$). The area under the receiver operating characteristic curve (AUC), calibration curves, bootstrap and decision curve analysis (DCA) were utilized for evaluating the performance of the nomogram. A sum of 965 eligible patients were participated, of whom 922 were assigned into a survival group and 43 in a non-survival group. Six independent predictors were identified as the most valuable characteristics in AP patients, including age, activated partial thromboplastin time (APTT), direct bilirubin (DBIL), lactate dehydrogenase (LDH), total protein (TP) and blood urea nitrogen (UREA). The AUC of the nomogram was 0.862 (0.806–0.918). The DCA curve indicates that this nomogram possesses good clinical application value. The nomogram we constructed demonstrates a strong capability in predicting the 30-day mortality of AP patients.

Keywords Acute pancreatitis, LASSO regression, Nomogram, 30-day mortality

Acute pancreatitis (AP) is a prevalent digestive disorder characterized by the premature activation of pancreatic enzymes within the pancreas due to various etiological factors, leading to local tissue damage and multi-organ dysfunction syndrome[1].The prevalence of AP spans from 5 to 30 cases per 100,000 individuals, with an overall case mortality rate of about 5%[2].The primary etiological factors contributing to AP contain biliary tract disorders, excessive drinking, and hypertriglyceridemia[3]. Currently, the prevalence of the disease is rising annually, posing significant challenges regarding patients' economic burden and societal healthcare pressures. The clinical course of the disease is diverse, ranging from mild to moderate and severe acute pancreatitis (SAP), with mortality rates as high as 36–50% in SAP[4]. Consequently, timely and precise evaluation of the patient's condition is essential for enhancing the patient's prognosis and mitigating their economic burden.

The nomogram serves as a sophisticated mathematical instrument for predicting disease progression or mortality based on critical parameters, and for calculating the likelihood of clinical events by integrating multiple prognostic weights derived from patient outcome analyses, ultimately benefiting both patients and healthcare professionals[5].Our research intends to acquire a nomogram for predicting the 30-day mortality risk in AP patients with laboratory factors derived from patient medical record, thereby enhancing prognosis through the early identification of clinically relevant indicators for timely intervention.

Materials and methods

Research design and participants

In the retrospective cohort study, we gathered information on AP patients aged over 18 years old, hospitalized at the First Affiliated Hospital of Nanjing Medical University between January 2017 and December 2019, were suitable for study population.

In the retrospective cohort study, we gathered information on patients aged 18 years or older diagnosed with AP who were admitted to the First Affiliated Hospital of Nanjing Medical University from January 2017

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to December 2019 and met the inclusion criteria for our study population. The AP diagnosis necessitates the presence of at least two of the following three criteria: (1) upper abdominal discomfort; (2) serum lipase or amylase levels exceeding threefold the upper limit of normal; (3) imaging findings agreed with AP on abdominal imaging[6].The exclusion criteria are delineated as follows:①Age < 18years; ② Chronic pancreatitis or pancreas carcinoma; ③Severe dysfunction of the heart, lungs, liver, kidneys, and other organs; ④ Pregnancy/lactation; ⑤ Malignant tumors, hematological disorders, and severe infections in other regions; ⑥Recent history of blood transfusion; ⑦ Coexisting mental illness; ⑧ Immune deficiency. Ultimately, our study comprised a sample of 965 patients. The research protocol has been approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (Nanjing, China). The study adheres to the principles outlined in the Declaration of Helsinki (2023-SR-043). The Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University waived the need for informed consent to use anonymized and retrospectively analyzed data.

Data acquisition and feature selection

This study encompassed admission parameters, integrating a total of 78 indexes into the study. The data encompass two primary classifications: (1) fundamental characteristics, which include demographic data (gender, age) and clinical features (24 indexes) including height, weight, etiology of pancreatitis, past medical history, body temperature, heart rate (HR), respiratory rate (RR), systolic blood pressure (SBP), diastolic blood pressure (DBP), 24 h urine excretion volume, length of hospital stay, pancreatic necrosis, pleural effusion, supplemental oxygen. (2) Admission laboratory indexes, comprising blood routine parameters [e.g., C-reactive protein (CRP), white blood cell (WBC), lymphocyte (LY) count, monocyte (Mo) count, neutrophil (NE) count, LY percentage, Mo percentage, NE percentage, red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelets (PLT), thrombocytocrit (PCT), mean platelet volume (MPV), platelet distribution width (PDW)], coagulation markers [e.g., prothrombin time (PT), international normalized ratio (PT-INR), activated partial thromboplastin time (APTT), fibrinogen (FIB), thrombin time (TT), D-dimer], biochemical results and tumor biomarkers such as alpha-fetoprotein (AFP), carbohydrate antigen 199 (CA-199), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyl transpeptidase (GGT), creatine kinase (CK), lactate dehydrogenase (LDH), along with various liver function tests and renal function metrics including urea nitrogen (UREA), creatinine (CREA) and uric acid (UA). Additionally, electrolyte levels such as potassium (K), sodium (Na), chloride (Cl), calcium (Ca) are included. Lipid profiles consist of total cholesterol (TC), triglycerides (TG), total bilirubin (TBIL) alongside direct and indirect bilirubin measurements (DBIL and IBIL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), lipoprotein (a) [Lp(a)], protein assessments including total protein (TP), albumin (ALB), globulin (GLB), glucose (GLU), serum amylase (AMY), and urine amylase (uAMY). The aforementioned data represent the initial blood test results obtained at the time of the patient's diagnosis, prior to the commencement of any treatment. Concurrently, we also collected the necessary parameters to compute the subsequent scores: Acute Physiology and Chronic Health Evaluation (APACHE II), RANSON, and the Modified Marshall scoring systems.

Follow-up

The primary endpoint was predefined as all-cause mortality within 30 days following AP diagnosis. Mortality data were collected from medical records or via telephone interviews.

Statistical method

The statistics were conducted utilizing SPSS version 26.0 statistical software (IBM Corp., Armonk, NY). The Kolmogorov-Smirnov test was used for assessing normality. Quantitative variables are expressed as medians with interquartile ranges (IQRs) / mean ± standard deviation (SD) and were assessed by the Mann-Whitney U test, the Kruskal–Wallis H test or the Student's t-test. The Chi-square test was employed to analyze categorical variables. The Least absolute shrinkage and selection operator (LASSO) has been widely utilized in the fields of model selection and predictive analysis, serving as a tool for identifying potential risk factors. Utilizing the parameters identified through LASSO regression, a predictive nomogram was constructed through the use of multivariate logistic regression. The model's discriminative performance was estimated through the area under the Receiver operating characteristic (ROC) curve (AUC), sensitivity and specificity. In addition, internally validation using a bootstrapping technique (1000 bootstrap resamples). For variables with a missing rate of less than 5%, we employed the random forest method for imputation; whereas, for variables with a missing rate of 5% or higher, we excluded them from the final analysis to ensure the reliability and rigor of the research findings. The criterion for statistical significance was established at a threshold of 0.05.

Results

Baseline characteristics and clinical profiles

A sum of 965 patients were included. Patients were categorized into a survival group ($n = 922$) and a nonsurvivor group ($n = 43$) based upon their survival status within 30 days. The specifics of our survey design are illustrated in Fig. 1. The mortality rate was 4.46%. The age of the nonsurvivors was elder than that in the survivors (67 (52–80) vs. 49 (39–63), $p < 0.001$). The clinical characteristics of two groups were compared, revealing statistically significant differences in chronic renal failure, body temperature, HR, RR, SBP, DBP, 24 h urine excretion volume, pancreatic necrosis, pleural effusion, supplemental oxygen, APACHE II, Marshall and Ranson (all $p < 0.05$). No substantial differences were found in gender, height, weight, etiology of pancreatitis, alcohol history, hypertriglyceridemia, coronary heart disease, diabetes history and length of hospital stay (all $p > 0.05$). Detailed baseline characteristics were displayed in Table 1.

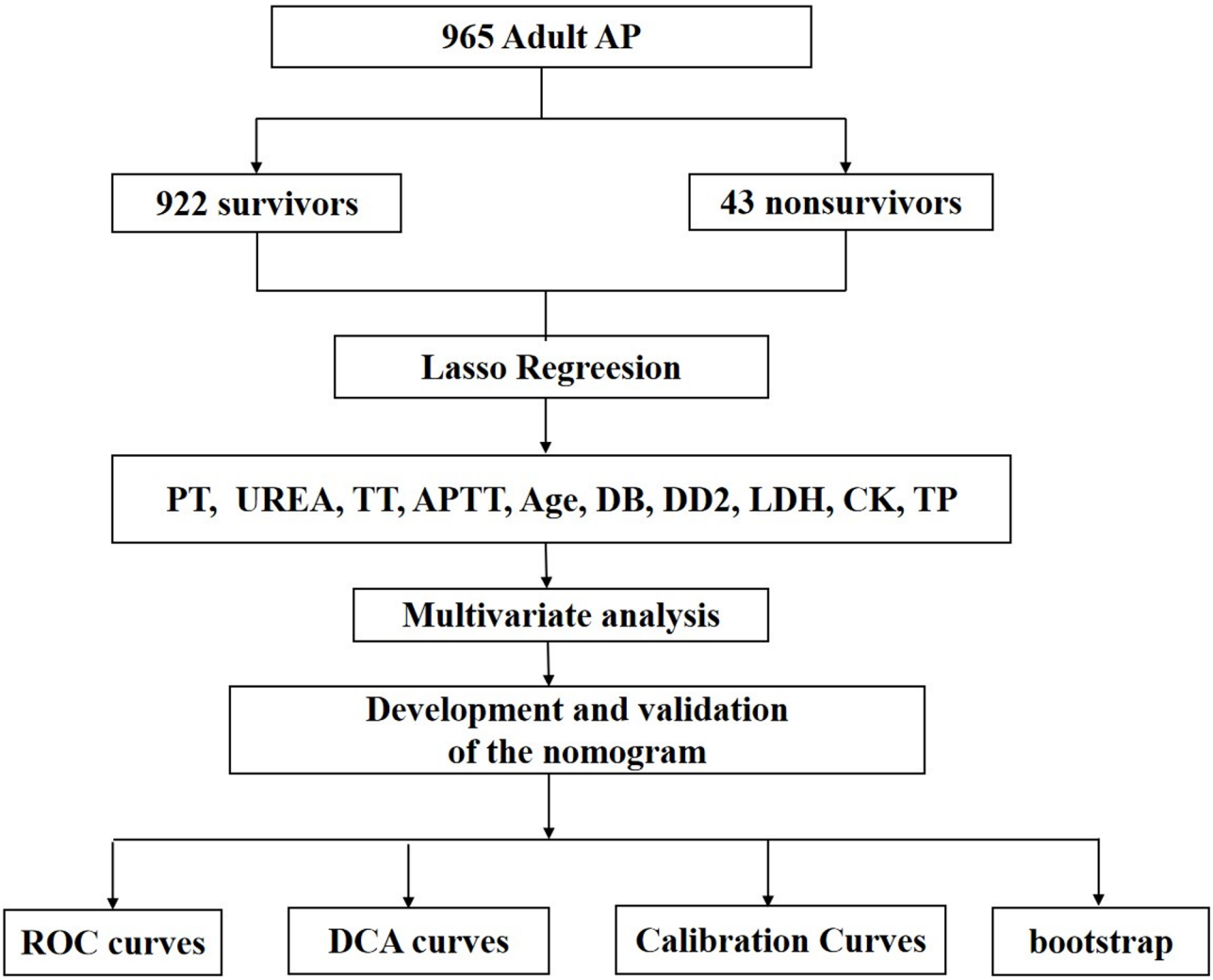

Fig. 1. Flow chart of the survey design.

Laboratory parameters in the survivor group and nonsurvivor group

We also analyzed laboratory indexes for all patients between the two groups. Results showed that CRP, WBC, NE count, NE percentage, RDW, MPV, PT, PT-INR, APTT, TT, D-dimer, CA199, AST, ALP, LDH, CK, DBIL, UREA, CREA, Na, Cl and uAMY in the non-survival group exhibited a markedly higher value compared to the survival group ($p < 0.05$). And LY count, LY percentage, RBC, HGB, HCT, PLT, PCT, FIB, TC, TP, ALB, GLB and Ca were all higher ($p < 0.05$) in the survivor group, while the remaining covariates shown no significantly difference in the two groups ($p > 0.05$). See Table 2 for details.

Prediction of risk factors based on LASSO regression

All laboratory variables were incorporated into the LASSO regression analysis, utilizing the LASSO regression for risk factor screening. Consequently, we identified a total of 10 indicators (PT, UREA, TT, APTT, age, DBIL, DD2, LDH, CK, TP), which were subsequently utilized for multivariate logistic regression (Fig. 2). Multivariate analysis demonstrated that age: hazard ratio (HR) = 1.043, 95% confidence interval (CI) 1.021–1.066, $p < 0.001$; APTT: HR = 1.044, 95% CI 1.016–1.073, $p = 0.002$; LDH: HR = 1.001, 95% CI 1.001–1.002, $p < 0.001$; DBIL: HR = 1.013, 95% CI 1.005–1.021, $p = 0.001$; TP: HR = 0.935, 95% CI 0.894–0.978, $p = 0.004$; UREA: HR = 1.038, 95% CI 1.001–1.076, $p = 0.043$ were independently associated with the 30-day mortality of AP (Table 3).

Development and validation of the nomogram

Based on the multivariate logistic regression analysis, a nomogram was developed (Fig. 3A). Receiver operating characteristic (ROC) analysis was recommended to evaluate the AUC for the nomogram. The nomogram demonstrated excellent discrimination, with an AUC of 0.862 (0.806–0.918), along with good sensitivity (77.4%) and specificity (87.1%) (Fig. 3B). Internal validation suggested that the nomogram had good predictive performance (C-index: 0.848 (0.824–0.870)) (Supplementary Fig. 1). The calibration curve revealed that the predicted probabilities of AP 30-day mortality were in excellent agreement with the actual outcomes (Fig. 3C).

Characteristic	Survivor($N=922$)	Nonsurvivor($N=43$)	p-value
Gender(male), n (%)	553 (60.0)	28 (65.1)	0.501
Age, y, M (Q1, Q3)	49 (39, 63)	67 (52, 80)	< 0.001
Height, cm, M (Q1, Q3)	168.0 (163.0, 170.8)	167.4 (163.8, 169.0)	0.281
Weight, kg, M (Q1, Q3)	70 (64, 78)	72 (66, 75)	0.435
Etiology of pancreatitis, n (%)			
Overeating, n (%)	117 (12.7)	3 (7.0)	0.268
Others (hyperlipidemia, DM, surgery), n (%)	51 (5.5)	2 (4.7)	0.805
Gallstone, n (%)	311 (33.7)	14 (32.6)	0.874
Cholecystitis/cholangitis, n (%)	234 (25.4)	9 (20.9)	0.512
Alcoholic, n (%)	103 (11.2)	3 (7.0)	0.390
Unknown aetiology, n (%)	321 (34.8)	18 (41.9)	0.345
Past medical history			
Alcohol history, n (%)	206 (22.3)	8 (18.6)	0.564
Smoking history, n (%)	175 (19.0)	7 (16.3)	0.658
Hypertriglyceridemia, n (%)	278 (30.2)	18 (41.9)	0.104
Coronary heart disease, n (%)	27 (2.9)	3 (7.0)	0.145
Chronic renal failure, n (%)	25 (2.7)	8 (18.6)	< 0.001
Diabetes, n (%)	162 (17.6)	7 (16.3)	0.828
Vital signs			
Body temperature (°C), M (Q1, Q3)	36.90 (36.60, 37.30)	37.10 (36.80, 37.70)	0.016
Heart rate (times/min), M (Q1, Q3)	81 (77, 98)	100 (84, 118)	< 0.001
Respiratory rate (times/min), M (Q1, Q3)	18.0 (17.0, 19.0)	18.0 (18.0, 21.5)	0.005
Systolic blood pressure (mmHg), M (Q1, Q3)	128 (117, 139)	120 (109, 133)	0.017
Diastolic blood pressure (mmHg), M (Q1, Q3)	79 (72, 86)	75 (70, 84)	0.037
24 h urine excretion volume (mL), M (Q1, Q3)	1,837 (1,716, 1,954)	1,539 (945, 1,982)	< 0.001
Pancreatic necrosis, n (%)	173 (18.8)	22 (51.2)	< 0.001
Pleural effusion, n (%)	474 (51.4)	36 (83.7)	< 0.001
Supplemental oxygen, n (%)	266 (28.9)	36 (83.7)	< 0.001
Length of hospital stay, d, M (Q1, Q3)	9 (7, 14)	13 (6, 19)	0.301
APACHE II, M (Q1, Q3)	5.0 (3.0, 8.0)	11.0 (7.5, 14.0)	< 0.001
Marshall, M (Q1, Q3)	2.00 (1.00, 3.00)	4.00 (2.00, 6.00)	< 0.001
Ranson, M (Q1, Q3)	1.00 (0.00, 2.00)	2.00 (1.00, 3.00)	< 0.001

Table 1. Patient demographics and baseline characteristics. M: Median, n: number, Q1: 1st Quartile, Q3: 3st Quartile.

Furthermore, the decision curve analysis (DCA) suggested that the net benefit per patient increased as the model's curve extended, thereby validating the potential clinical utility of the nomogram (Fig. 3D).

In addition, Kaplan-Meier (K-M) survival curve analysis indicated that AP patients with the value > 0.0679 were positive associated with significantly higher 30-day mortality ($p < 0.001$) (Figure. 4). We also observed that the model exhibits a positive correlation with APACHE II ($r = 0.493$, $p < 0.001$), RANSON ($r = 0.392$, $p < 0.001$), and the Modified Marshall scores ($r = 0.435$, $p < 0.001$).

Thus, clinicians can utilize the model we have established to identify high-risk populations: patients with a value > 0.0679 exhibit a significantly higher 30-day mortality rate compared to those with a value ≤ 0.0679.

Discussion

In this retrospective study, LASSO regression and multivariate logistic regression was employed to systematically identify the risk factors associated with early mortality in AP patients. The findings indicated that age, APTT, LDH, DBIL, TP, and UREA were identified as independent risk factors for 30-day death in AP patients. Furthermore, the developed nomogram showed robust predictive capability, excellent calibration performance, and significant clinical application value. In recent years, significant efforts have been dedicated to the exploration and development of systemic inflammatory biomarkers for prognostic prediction in patients with AP. These investigations have focused on a diverse range of potential biomarkers, including RDW[7], neutrophil to lymphocyte ratio (NLR)[8], CRP/Alb ratio[9], creatinine to albumin ratio (CAR)[10]. Studies have also affirmed that models or nomograms, developed through logistic methods, can notably enhance predictive performance[11,15]. Nevertheless, these studies predominantly concentrate on a single index, or ratio, or small sample sizes with limited indicators, which are insufficient to effectively adjust the confounding factors.

Previous research[12] has demonstrated that the severity of AP escalates with advancing age, accompanied by an increased mortality rate in older patients. Hong et al.[13] suggested that age could be beneficial for predicting the occurrence of persistent organ failure in AP patients. Mandalia[14] et al. reported individuals aged 70 years and

Characteristic	Survivor($N=922$)	Nonsurvivor ($N=43$)	p-value
CRP (mg/L), M (Q1, Q3)	67 (37, 90)	77 (65, 90)	0.016
WBC ($\times10^9$/L), M (Q1, Q3)	10.4 (7.1, 13.7)	13.5 (10.4, 15.8)	0.001
LY count ($\times10^9$/L), M (Q1, Q3)	1.11 (0.79, 1.50)	0.87 (0.61, 1.27)	0.017
Mo count ($\times10^9$/L), M (Q1, Q3)	0.57 (0.39, 0.80)	0.62 (0.41, 0.94)	0.341
NE count ($\times10^9$/L), M (Q1, Q3)	8.5 (5.3, 11.7)	11.6 (8.6, 13.9)	< 0.001
LY percentage (%), M (Q1, Q3)	11 (7, 17)	7 (4, 11)	< 0.001
Mo percentage (%), M (Q1, Q3)	5.90 (4.50, 7.60)	5.20 (4.16, 6.70)	0.079
NE percentage (%), M (Q1, Q3)	82 (74, 87)	88 (82, 91)	< 0.001
RBC ($\times10^{12}$/L), M (Q1, Q3)	4.29 (3.84, 4.74)	4.06 (3.28, 4.54)	0.010
HGB (g/L)	130 ± 22	119 ± 26	0.007
HCT (%), M (Q1, Q3)	39 (35, 43)	37 (29, 41)	0.015
MCV (fl.), M (Q1, Q3)	90.1 (87.2, 92.9)	90.1 (87.9, 94.5)	0.265
MCH (pg), M (Q1, Q3)	30.30 (29.40, 31.40)	30.20 (29.35, 31.40)	0.993
MCHC (g/L), M (Q1, Q3)	336 (330, 344)	332 (327, 340)	0.057
RDW (%), M (Q1, Q3)	13.30 (12.70, 14.10)	13.96 (13.25, 15.60)	< 0.001
PLT ($\times10^9$/L), M (Q1, Q3)	187 (146, 236)	151 (101, 173)	< 0.001
PCT (%), M (Q1, Q3)	0.20 (0.16, 0.25)	0.16 (0.13, 0.20)	< 0.001
MPV (fl.), M (Q1, Q3)	11.00 (10.10, 11.90)	11.40 (10.80, 12.40)	0.005
PDW (%), M (Q1, Q3)	14.30 (12.20, 16.70)	14.50 (12.75, 16.85)	0.570
PT (s), M (Q1, Q3)	13.10 (12.50, 14.00)	14.90 (13.30, 16.90)	< 0.001
PT-INR, M (Q1, Q3)	1.14 (1.09, 1.22)	1.30 (1.16, 1.50)	< 0.001
APTT (s), M (Q1, Q3)	28.6 (26.4, 31.3)	33.4 (28.9, 39.4)	< 0.001
FIB (g/L), M (Q1, Q3)	4.47 (3.22, 6.37)	4.03 (2.17, 5.27)	0.010
TT (s), M (Q1, Q3)	17.00 (16.10, 18.10)	17.70 (17.10, 20.25)	< 0.001
D-dimer (mg/L), M (Q1, Q3)	2.19 (1.01, 4.25)	4.45 (2.70, 8.07)	< 0.001
AFP (ng/mL), M (Q1, Q3)	2.26 (1.61, 3.17)	2.51 (1.84, 4.69)	0.148
CA199 (U/mL), M (Q1, Q3)	22 (12, 38)	50 (23, 81)	< 0.001
ALT (U/L), M (Q1, Q3)	32 (16, 84)	42 (21, 76)	0.240
AST (U/L), M (Q1, Q3)	30 (20, 54)	46 (34, 108)	< 0.001
ALP (U/L), M (Q1, Q3)	101 (78, 149)	119 (87, 227)	0.049
GGT (U/L), M (Q1, Q3)	93 (38, 219)	119 (40, 212)	0.576
LDH (U/L), M (Q1, Q3)	270 (209, 386)	502 (301, 667)	< 0.001
CK (U/L), M (Q1, Q3)	50 (32, 87)	137 (58, 435)	< 0.001
TBIL (μmol/L), M (Q1, Q3)	16 (11, 25)	17 (11, 48)	0.129
DBIL (μmol/L), M (Q1, Q3)	6 (4, 11)	9 (5, 34)	0.006
IBIL (μmol/L), M (Q1, Q3))	9 (6, 13)	8 (5, 17)	0.852
TC (mmol/L), M (Q1, Q3)	4.25 (3.34, 5.54)	3.32 (2.34, 3.83)	< 0.001
TG (mmol/L), M (Q1, Q3)	1.59 (0.99, 2.99)	1.73 (1.16, 2.83)	0.527
TP (g/L), M (Q1, Q3)	61 (57, 67)	54 (52, 61)	< 0.001
ALB (g/L), mean ± SD	35.2 ± 5.0	31.5 ± 5.2	< 0.001
GLB (g/L), M (Q1, Q3)	25.9 (22.6, 28.9)	22.9 (19.4, 26.9)	< 0.001
A/G	1.35 (1.20, 1.60)	1.34 (1.10, 1.60)	0.805
UREA (mmol/L), M (Q1, Q3)	5.9 (4.3, 7.9)	11.0 (7.2, 17.1)	< 0.001
Cr (μmol/L), M (Q1, Q3)	61 (50, 75)	87 (61, 163)	< 0.001
Ca (mmol/L), M (Q1, Q3)	2.12 (2.00, 2.23)	2.03 (1.78, 2.13)	< 0.001
K (mmol/L), M (Q1, Q3)	3.94 (3.65, 4.22)	3.86 (3.68, 4.29)	0.990
Na (mmol/L), M (Q1, Q3)	138.3 (136.0, 140.4)	140.9 (136.7, 145.1)	0.004
Continued			

Characteristic	Survivor($N=922$)	Nonsurvivor ($N=43$)	p-value
Cl (mmol/L), M (Q1, Q3)	103.0 (100.3, 105.6)	104.8 (101.3, 108.0)	0.026
GLU (mmol/L), M (Q1, Q3)	6.9 (5.3, 9.2)	8.0 (5.3, 9.5)	0.186
UA (μmol/L), M (Q1, Q3)	263 (189, 348)	259 (197, 329)	0.847
AMY (U/L), M (Q1, Q3)	309 (97, 866)	679 (122, 1,475)	0.053
uAMY (U/L), M (Q1, Q3)	2,299 (658, 5,431)	4,459 (1,425, 6,323)	0.042

Table 2. Laboratory parameter. M: Median, n: number, Q1: 1st Quartile, Q3: 3st Quartile, SD: Standard deviation; AFP: alpha fetoprotein; ALB: albumin; ALP: alkaline phosphatase; ALT: alanine aminotransferase; AMY: serum amylase; APACHE: acute Physiology and Chronic Health Evaluation; AST: aspartate aminotransferase; APTT: activated partial thromboplastin time; Ca: calcium; CA199: carbohydrate antigen199; CK: creatine kinase; Cl: Chlorine; CREA: creatinine; CRP: c-reactive protein; DBIL: direct bilirubin; FIB: fibrinogen; GGT: γ-glutamyl transpeptidase; GLB: globularproteins; GLU: glucose; HGB: hemoglobin; HCT: hematocrit; IBIL: indirect bilirubin; K: potassium; LDH: lactate dehydrogenase; LY: lymphocytes; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin contentration; MCV: mean corpuscular volume; MPV: mean platelet volume; Mo: monocytes; Na: Natrium; NE: neutrophils; PCT: thrombocytocrit; PDW: platelet distribution width; PLT: platelets; PT: Prothrombin time; PT-INR: international Normalized Ratio; RBC: red blood cell; RDW: red cell distribution width; TB: total bilirubin; TC: total cholesterol; TG: triglycerides; TP: total protein; TT: thrombin time; UA: uric acid; uAMY: urinary amylase; UREA: urea nitrogen; WBC: leukocyte.

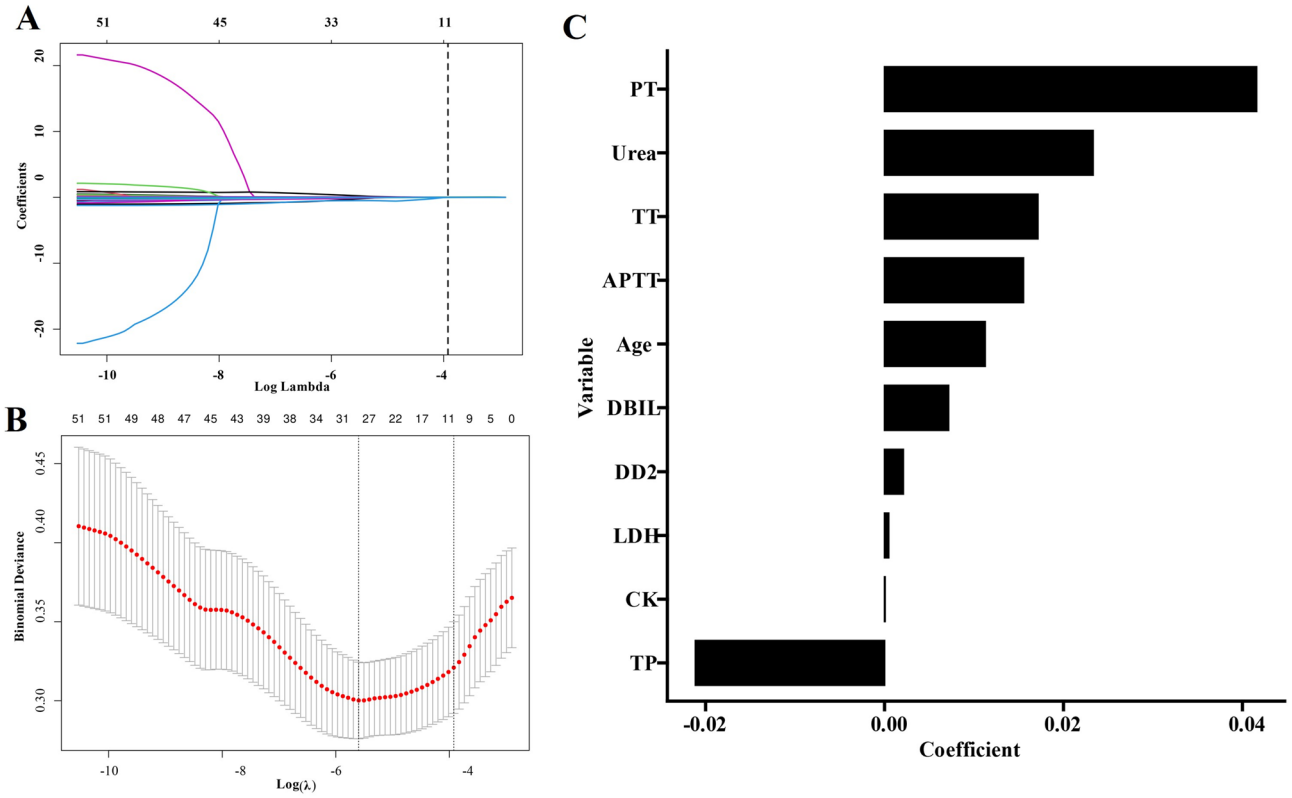

Fig. 2. Screening of variables based on LASSO regression. A The variability of coefficients with variable parameters; B LASSO regression cross-validation curve. C Potential predictors in AP.

above can be served as an independent risk factor for heightened mortality among AP patients. Our findings as well align with previous research, reinforcing the notion that age is one of the independent risk factors for 30-day mortality patient.

Alterations in coagulation function during AP may influence the clinical presentation and prognosis of patients. APTT is the most common test used to screen for endogenous coagulation disorders. APTT is prolonged when coagulation factors are deficient or coagulation dysfunction occurs. The inflammatory factors and endotoxins produced during the occurrence of AP lead to the massive release and overexpression of tissue factors, resulting in significantly prolonged PT and APTT, systemic DIC, and accelerating the progression of

Variables	Multivariate analysis		
	HR	95% CI	*p* -value
Age (year)	1.043	1.021–1.066	< 0.001
APTT (s)	1.044	1.016–1.073	0.002
LDH (U/L)	1.001	1.001–1.002	< 0.001
DBIL (μmol/L)	1.013	1.005–1.021	0.001
TP (g/L)	0.935	0.894–0.978	0.004
Urea (mmol/L)	1.038	1.001–1.076	0.043
AUC	0.862		

Table 3. Multivariate analyses in the study cohort. APTT: activated partial thromboplastin time; AUC: area under the curve; DBIL: direct bilirubin; LDH: lactate dehydrogenase; TP: total protein; UREA: urea nitrogen.

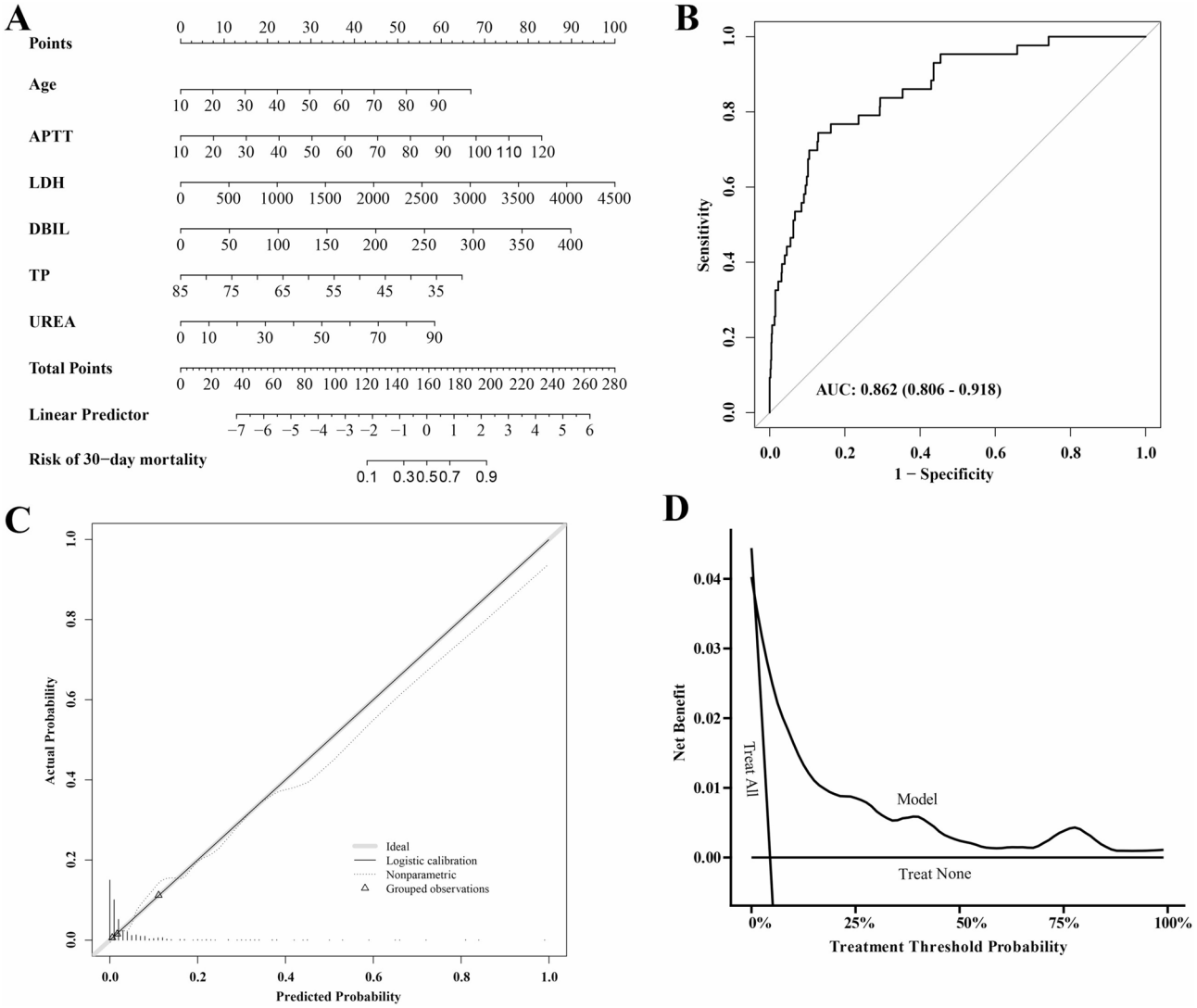

Fig. 3. Nomogram, ROC curves, calibration curves and DCA. (A) Nomogram for predicting the risk of 30-day morality in AP; (B) ROC curves for 30-day mortality; (C) Calibration curve plot for the nomogram; (D) Decision curve analysis (DCA) for the prediction model.

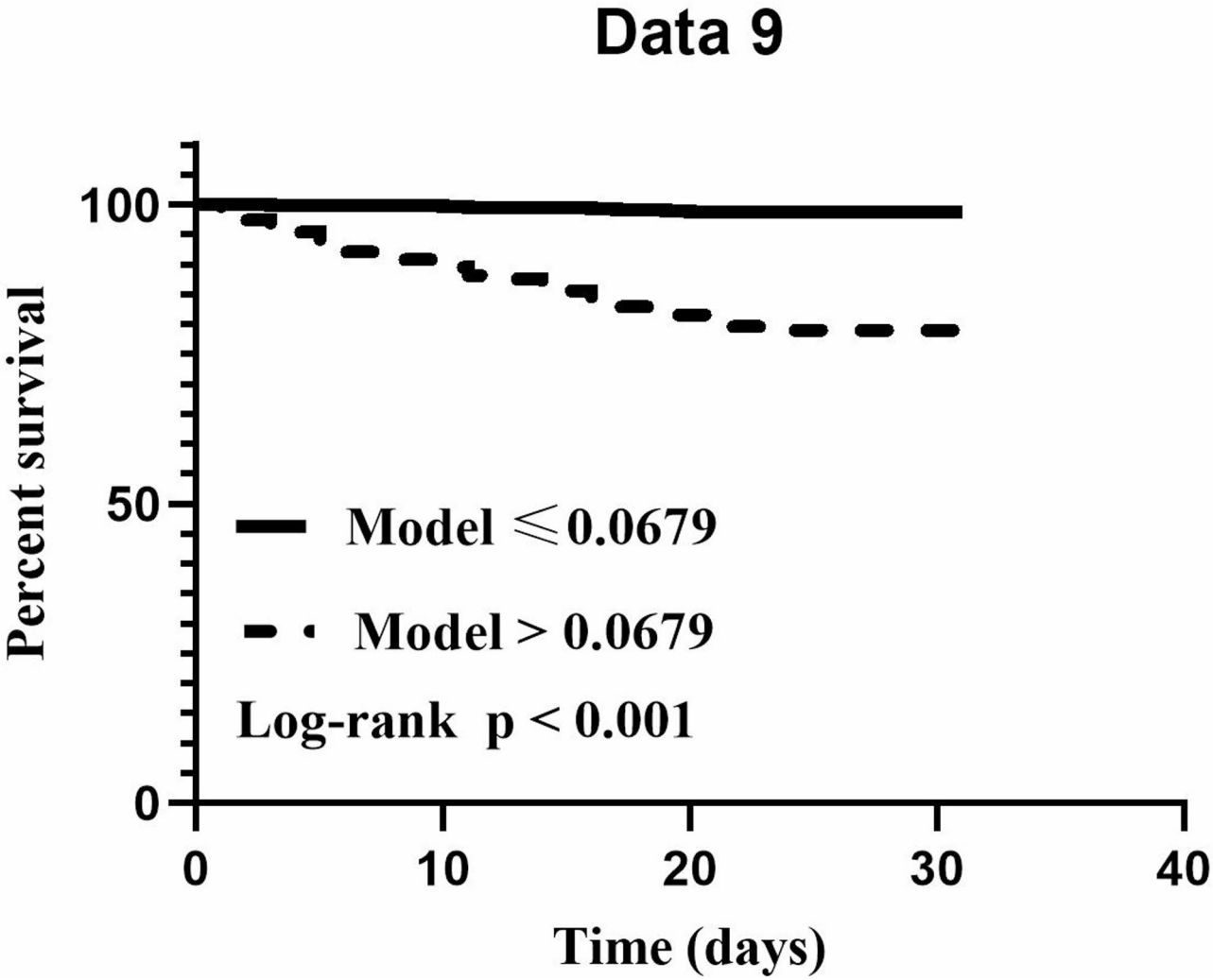

Fig. 4. Kaplan-Meier curves for 30 – day mortality.

AP[15]. Yang et al. reported that prolonged APTT increases the risk of short-term death in patients with AP[16]. Our study further corroborated that APTT was associated with the prognosis of acute pancreatitis, and APTT was significantly higher in the death group than in the survival group.

LDH is extensively distributed across human tissues and primarily serves as a biomarker for apoptosis, particularly in assessing myocardial damage and hepatic cellular injure. LDH is the earliest abnormal indicator of injury and dysfunction in the body, elevated LDH levels are frequently indicative of organ damage[17]. Consequently, it is hypothesized that LDH may play as a predictive role for adverse outcomes. During the development of acute pancreatitis, an increase in LDH may be related to ischemic necrosis of pancreatic acinic cells and organ failure associated with acute pancreatitis, including acute liver and kidney injury. In recent years, numerous studies have demonstrated that LDH is an independent risk factor for the prognosis of AP[18,19], which is in line with our study.

Serum direct bilirubin (DBIL) is a routine test item that reflects liver and bile disorders. In clinical practice, an elevated serum DBIL level is regarded as one of the indicators of cholestasis. In China, the predominant cause of AP remains cholelithiasis, particularly among elderly patients. Bile reflux into the common bile duct and obstruction of ampullar ascites by sludge or stones in the biliary tract is thought to be the cause of biliary pancreatitis[20]. As with obstructive jaundice, bilirubin levels (especially direct bilirubin) have been shown to be the most important indicator of biliary pancreatitis[21].

The TP value refers to the overall quantity of all proteins present in the serum. TP, as a marker of nutritional status, plays an important role in health evaluation. AP induces a hypermetabolic state characterized by increased lipolysis, enhanced protein catabolism, insulin resistance, and significant weight loss. These manifestations are notably more severe in advanced stages of the disease and can be exacerbated by malnutrition and infection. Our study also demonstrated that total protein levels at admission were significantly lower in the death group than in the survival group, and decreased total protein levels were an independent risk factor for acute pancreatitis mortality.

UREA is produced by the enzymes of the urea cycle, which are mainly located in the liver but are also expressed at low levels ubiquitously in other tissues. As far as we know, UREA is a firmly established marker for mortality in AP[22]. UREA upon admission/hospitalization can reflect the patient's underlying physiological condition, encompassing fluid volume deficiency and prerenal azotemia[23]. Thus, UREA might play a significant role in the early assessment of AP. Several prognostic scoring systems, such as the Ranson score, incorporate blood urea nitrogen to predict the severity and mortality of AP[24]. In this study, our data revealed that serum UREA was significantly higher in the non-survivor group than in the survivor group. Moreover, we verified that UREA is an independent risk factor for acute pancreatitis, which is consistent with previous studies.

Therefore, clinicians can leverage the predictive model to identify high-risk patients (with a value > 0.0679), enabling timely and targeted interventions that may enhance clinical outcomes.

We acknowledge that differences in patient management and clinical protocols across centers may limit the generalizability of our nomogram. To address this, we are collaborating with multiple institutions to validate our findings across diverse populations and settings. Future research will evaluate the nomogram's applicability in various geographic and demographic contexts, ensuring its robustness and broader clinical utility.

Nonetheless, certain inevitable limitations still remain. Firstly, this study was a single-center retrospective analysis characterized by selection bias and a limited sample size. The limited sample size could lead to model overfitting. In future research, we plan to validate the model in external cohorts and employ advanced variable selection methods, such as SHAP (SHapley Additive exPlanations) from machine learning algorithms. Although we have made every effort to minimize the impact of missing data on study outcomes, some degree of data incompleteness remains, which may potentially influence the research conclusions. Consequently, the efficacy and precision of the current predictive model require further validation through large-scale studies encompassing a greater number of samples. Secondly, we exclusively gathered laboratory data from the patient's initial admission rather than dynamic monitoring, as certain laboratory parameters may fluctuate during treatment such as UREA and LDH. Third, despite our efforts to include a wide range of variables, the retrospective design of this study limited the inclusion of certain indicators, such as patient comorbidities and treatment modalities, due to missing data or incomplete records. This may have restricted the model's predictive performance. Thus, the next step will involve a multi-center collaboration to select more precise features for developing the in-depth model. By this means, clinicians and patients can benefit more significantly.

Conclusions

In summary, our research has established a practical predictive nomogram that integrates common, cheap and practical parameters including age, APTT, LDH, DBIL, TP, and UREA to assess the 30-day mortality risk in AP patients. The primary advantage of this model lies in its capacity to accurately forecast the 30-day mortality risk for AP based on routine blood test. This approach obviates the necessity for further patient evaluations, rendering it both cost-effective and user-friendly.

Data availability

The data and materials can be found from the corresponding author.

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Conceptualization, Jun Zhou; Formal analysis, Jingping Liu, Min Wang, Qiuxia Ge and Jun Zhou; Investigation, Ying Chen, Jingping Liu, Min Wang and Qiuxia Ge; Methodology, Jun Zhou and Jingping Liu; Writing – original draft, Ying Chen; Writing – review & editing, Jingping Liu, Min Wang, Qiuxia Ge and Jun Zhou. All the authors have read manuscript and approved the final manuscript.

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Declarations

Approval
The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (2023-SR-043). This study protocol complied with the Declaration of Helsinki.

Informed consent
The Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University waived the need for informed consent to use anonymized and retrospectively analyzed data.

Competing interests
The authors declare no competing interests.

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