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ARTICLE

Prolonged activated partial thromboplastin time predicts poor short-term prognosis in patients with acute pancreatitis: A retrospective cohort study

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Abstract

It is unclear whether activated partial thromboplastin time (APTT) is predictive of survival in patients with acute pancreatitis (AP). Our study aimed to investigate the relationship between APTT and short-term prognosis in AP. From the Medical Information Mart for Intensive Care (MIMIC)-IV database, a total of 844 patients with AP were randomly divided into the training cohort ($n = 591$) and the validation cohort ($n = 253$) at a ratio of 7:3. Based on their APTT values, the patients were divided into the normal and high groups. The primary outcome of this study was 30- and 60-day survival. Kaplan–Meier survival analysis and Cox regression models were used to analyze associations between groups and outcomes. The training and validation cohort matched well on all parameters ($p > 0.05$). In terms of 30- and 60-day survival, Kaplan–Meier survival curves from both training and validation cohorts demonstrated a lower survival probability for patients in the high APTT group than the normal group (log-rank $p < 0.05$). In the training cohort, patients in the high APTT group had a statistically significantly higher risk of death than those in the normal group after controlling for possible confounders in Cox regression ($p < 0.05$). For the high APTT group, the hazard ratios (95% confidence interval [CI]) were 1.63 (95% CI 1.10, 2.61, $p = 0.035$) and 1.49 (95% CI 1.01, 2.38, $p = 0.041$), respectively. APTT performed as well as BISAP, Ranson, and APACHE II models in predicting 30- and 60-day survival in patients with AP. The results above have been verified in the validation cohort. Prolonged APTT in patients with AP may increase the risk of short-term death.

Study Highlights

WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?

The lack of biomarkers for predicting the short-term prognosis of acute pancreatitis (AP) is a significant problem. Patients with AP are often suffering from coagulation disorders. Activated partial thromboplastin time (APTT) is a biomarker that represents the endogenous coagulation pathway. This study was designed

Yuping Yang and Shenshen Du contributed equally to the work.

to investigate the short-term prognostic value of APTT in patients with AP in intensive care units.

WHAT QUESTION DID THIS STUDY ADDRESS?

Activated partial thromboplastin time is a biomarker of short-term prognosis in patients with AP. Patients with prolonged APTT have a poor 30- and 60-day survival.

WHAT DOES THIS STUDY ADD TO OUR KNOWLEDGE?

This study demonstrates the short-term prognostic value of APTT in patients with AP. APTT performed as well as BISAP, Ranson, and APACHE II models in predicting 30- and 60-day survival rates in patients with AP. However, it is simpler and more convenient than those models. Clinicians should pay attention to coagulation in patients if their APTT is prolonged. Correcting endogenous coagulation disorders may improve the prognosis of such patients.

HOW MIGHT THIS CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?

Activated partial thromboplastin time serves as a prognostic biomarker in patients with AP, providing a means for risk stratification. If the patient's APTT appears to be prolonged, it suggests that clinicians should take appropriate measures to prevent the patient's condition from deteriorating.

INTRODUCTION

Acute pancreatitis (AP) is among the most common gastroenterological conditions that result in hospitalization in the intensive care unit (ICU).[1] AP is a complicated disease with varying severity and course. It remains a significant cause of death.[2] In patients with biliary AP, hepcidin and systemic inflammatory response syndrome may predict patient prognosis.[3] Using serum hydroxybutyrate dehydrogenase early in the course of AP may help predict its severity.[4] Increased arterial blood lactic acid concentration is associated with increased 28-day mortality in patients with severe AP.[5] Proper management depends on prompt diagnosis and severity classification. Scoring systems are useful adjuncts but should not replace clinical judgment. Thus, early diagnosis and management of death-related risk factors may improve outcomes in patients with AP.

Despite some limitations, the bedside index for severity in acute pancreatitis (BISAP), Acute Physiology and Chronic Health Examination (APACHE)-II, computed tomography severity index (CTSI), and Ranson criteria are most commonly used to determine the prognosis of AP.[6–8] The BISAP score is an effective tool for risk stratification in patients with AP. It contains clinically relevant and easily accessible components. BISAP scores are comparable in prognostic accuracy to the results of other scoring systems, even better than Ranson criteria and CTSI.[6,9] Activated partial thromboplastin time (APTT), BISAP, Ranson, and APACHE II were compared in this study for their potential ability to predict short-term prognosis of patients with AP.

Activated partial thromboplastin time is the most common test to screen endogenous coagulation disorders. When there is a deficiency in coagulation factors or coagulation dysfunction, APTT is prolonged.[10] In patients with sepsis, mortality increases in patients with prolonged APTT.[11] Prolonged APTT also results in more severe organ failure in patients with sepsis.[12] Furthermore, prolonged APTT is associated with a higher risk of mortality in patients admitted to the ICU.[13] However, it remains unclear whether prolonged APTT is related to short-term prognosis in patients with AP.

MATERIALS AND METHODS

Data source

The data for this retrospective cohort study were obtained from the Medical Information Mart for Intensive Care (MIMIC)-IV database between 2008 and 2019.[14]

All personal information about the patients was recoded following the Health Insurance Portability and Accountability Act, and all identifiable information was omitted. Thus, informed consent is not needed from the patients. The MIMIC-IV project was approved by the ethics committees of the Massachusetts Institute of Technology (United States) and Beth Israel Deaconess Medical Center (United States), and the first author and corresponding author have been approved as authorized users for access to the MIMIC-IV database (first author

ID: 46483333; corresponding author ID: 40297010). The study was performed to comply with the Declaration of Helsinki principles.

Participants

From the MIMIC IV database, 1033 patients admitted to the ICU for an AP exacerbation were extracted. Among these patients are those who suffer from alcoholic AP, biliary AP, drug-induced AP, and unspecified AP. The exclusion criteria were as follows: patients who died within 24 h in the ICU, patients younger than 18 years old, patients with more than one ICU admission, patient with hemophilia, patients without APTT records, patients with APTT records 23. In the end, a total of 844 patients with AP were selected for the study. Moreover, they were randomly divided into the training cohort ($n = 591$) and the validation cohort ($n = 253$) at a ratio of 7:3 (Figure 1). Because the normal ranges for APTT values are 23–37, patients with an APTT value of 23–37 were selected in the normal APTT group, and those with a value >37 were chosen in the high APTT group.

Data extraction

For this retrospective cohort study, the extracted variables included sex, age, medical history, the condition assessment record form, routine blood tests, routine biochemical tests, use of vasopressors, duration of ICU stay and hospital stay, and vital status at discharge. The patient's blood and biochemical tests were performed on the patient's first day in the ICU. When there were multiple test values for a variable, the average of these values was used for analysis.

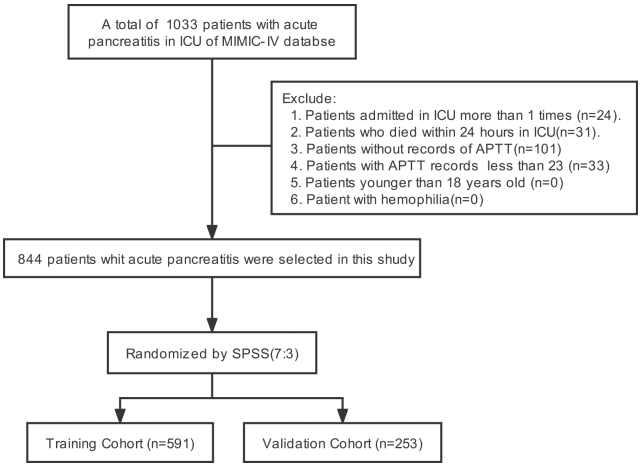

FIGURE 1 Flow diagram of patient selection. APTT, activated partial thromboplastin time; ICU, intensive care unit; MIMIC-IV, Medical Information Mart for Intensive Care IV database.

Primary and secondary outcomes

The primary outcome was 30- and 60-day survival in two groups: the normal APTT group and the high APTT group.

Statistical analysis

Categorical variables are expressed as a number (percentage) and continuous variables as a mean (SD). To compare the two groups, we used *t*-tests, Chi-square (χ^2) tests, or Wilcoxon rank-sum tests. The survival analysis was conducted using Kaplan–Meier (KM) and Cox proportional hazard regression models. SPSS version 26 (IBM SPSS) was used for the statistical analysis. Any $p < 0.05$ was defined as statistically significant.

RESULTS

Baseline characteristics between training cohort and validation cohort

A total of 844 patients with AP were enrolled and randomly divided into the training cohort ($n = 591$) and the validation cohort ($n = 253$) at a ratio of 7:3. There were no significant differences between the two cohorts in gender, age, APTT values, mortality, ICU admission time, Sequential Organ Failure Assessment (SOFA) score, BISAP score, Ranson score, APACHE II score, medical histories (including diabetes, coronary heart disease, hypertension, chronic kidney disease, chronic obstructive pulmonary disease, cirrhosis, and gallstones), complications (including acute kidney injury, hepatic encephalopathy, sepsis, pleural effusion, ascites, and ventilator use), and laboratory test results ($p > 0.05$; Table 1). In summary, the training cohort and validation cohort were well matched in all parameters.

Baseline characteristics of training cohort population

A total of 591 patients with AP were enrolled in the training cohort. There were no significant differences in age, gender, etiologies, heart failure, pleural effusion, BISAP scores, Ranson score, or APACHE II score between patients in the high and normal APTT groups ($p > 0.05$; Table 2). Patients in the high APTT group had a higher incidence of acute kidney injury, sepsis, ascites, and disseminated intravascular coagulation (DIC; $p < 0.001$; Table 2). In the high APTT group, vasopressors were used more frequently and ICU stays were longer than the

TABLE 1 Characteristics of training and validation cohorts

Factors	Training ($n = 591$)	Validation ($n = 253$)	p Value
Male	344 (58.2%)	146 (57.7%)	0.893
Age (year)	60.2 ± 17.3	60.0 ± 17.8	0.863
APTT (>37 s)	144 (24.4%)	66 (26.1%)	0.596
Death	81 (13.7%)	34 (13.4%)	0.918
ICU admission time (day)	6.2 ± 9.0	6.6 ± 11.2	0.567
Hospital admission time (day)	16.8 ± 16.5	16.9 ± 19.4	0.924
SOFA score	5.9 ± 4.1	6.1 ± 4.1	0.309
BISAP score	2.0 ± 0.9	1.9 ± 0.9	0.838
Rason score	4.1 ± 1.6	4.2 ± 1.6	0.902
APACHE II	26.9 ± 5.5	27.3 ± 5.4	0.649
Medical histories			
Diabetes	161 (27.2%)	66 (26.1%)	0.729
Coronary heart disease	41 (6.90%)	17 (6.70%)	0.909
Hypertension	99 (16.8%)	55 (21.7%)	0.086
Chronic kidney disease	98 (16.6%)	53 (20.9%)	0.126
COPD	19 (3.2%)	10 (4.0%)	0.590
Cirrhosis	60 (10.2%)	30 (11.9%)	0.462
Gallstones	6 (1.2%)	1 (0.4%)	0.268
Complications			
Acute kidney injury	292 (49.4%)	120 (47.4%)	0.599
Hepatic encephalopathy	14 (2.4%)	9 (3.6%)	0.331
Sepsis	173 (29.3%)	71 (28.1%)	0.723
Pleural effusion	86 (14.6%)	26 (10.2%)	0.083
Ascites	93 (15.7%)	37 (14.6%)	0.682
Ventilator use	72 (12.2%)	41 (16.2%)	0.116
Laboratory tests			
White blood cells ($\times 10^9$/L)	14.0 ± 8.1	14.0 ± 7.9	0.952
Platelets ($\times 10^9$/L)	225.5 ± 139.9	227.7 ± 138.1	0.836
Hemoglobin (g/dL)	11.2 ± 2.6	11.5 ± 2.7	0.153
Lymphocytes ($\times 10^9$/L)	10.2 ± 8.3	10.7 ± 10.4	0.521
Monocytes ($\times 10^9$/L)	4.8 ± 3.0	5.0 ± 3.4	0.457
Neutrophils ($\times 10^9$/L)	79.9 ± 12.7	80.0 ± 13.8	0.863
Hematocrit (%)	34.1 ± 7.5	34.9 ± 7.7	0.109
Albumin (g/L)	3.1 ± 0.7	3.1 ± 0.7	0.854
Anion gap (mmol/L)	17.2 ± 6.7	17.4 ± 5.7	0.667
Bicarbonate (mmol/L)	21.2 ± 5.9	20.5 ± 5.2	0.087
Sodium (mmol/L)	138.3 ± 5.8	137.1 ± 6.1	0.632
Potassium (mmol/L)	4.2 ± 0.9	4.2 ± 0.9	1.000
Calcium (mg/dl)	8.0 ± 1.2	7.9 ± 1.1	0.272
Bun (mmol/L)	29.8 ± 27.2	30.0 ± 26.9	0.938
Creatinine (mg/dl)	1.8 ± 2.0	1.9 ± 1.9	0.398
Glucose (mg/dl)	163.8 ± 134.4	160.1 ± 123.6	0.722
ALT (U/L)	252.5 ± 936.7	191.0 ± 671.4	0.369
AST (U/L)	433.0 ± 1666.4	365.1 ± 1586.8	0.595
Total bilirubin (μmol/L)	2.7 ± 4.7	3.4 ± 6.3	0.107
ALP (U/L)	159.3 ± 155.1	169.7 ± 200.3	0.476
CK-MB (ng/ml)	12.9 ± 37.0	18.8 ± 37.9	0.278
INR	1.6 ± 1.2	1.5 ± 1.0	0.244
Prothrombin time (s)	17.6 ± 11.9	16.6 ± 10.8	0.232

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; APACHE, Acute Physiology and Chronic Health Examination; APTT, activated partial thromboplastin time; AST, aspartate transaminase; BISAP, bedside index for severity in acute pancreatitis; CK-MB, creatine kinase-MB; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; INR, International Normalized Ratio; SOFA, Sequential Organ Failure Assessment.

normal group ($p < 0.001$; Table 2). In terms of patients in the high APTT group, SOFA scores were higher than those in the normal group (8.3 ± 4.4 vs. 5.1 ± 3.6, $p < 0.001$; Table 2). More importantly, the mortality rates of the patients in the high APTT group were higher than those in the normal group at 30- and 60-day follow-up ($p < 0.001$; Table 2). Based upon these results, it indicates that patients in the high APTT group were sicker.

Patients in the high APTT group have a poor short-term prognosis

The 30-day mortality is 12.9% in the training cohort, and 60-day mortality is 13.7%. The KM survival curves from both the training and validation cohorts showed that patients in the high APTT group had a lower survival probability in 30- and 60-day survival than patients in the normal group ($p < 0.05$; Figure 2).

In Cox regression model analysis, patients in the high APTT group continued to have higher 30- and 60-day mortality, ICU mortality, and hospital mortality than those in the normal group despite controlling for potential confounders (including age, gender, heparin, DIC, and medical history of diabetes, coronary heart disease, hypertension, chronic obstructive pulmonary disease, chronic kidney disease, and cirrhosis, $p < 0.05$; Table 3). The hazard ratios (HRs; 95% confidence interval [CI]) of 30- and 60-day mortality were 1.63 (1.10, 2.61, $p = 0.035$) and 1.49 (1.01, 2.38, $p = 0.041$), respectively. In line with the training cohort, the results of the validation cohort also demonstrated the above results ($p < 0.001$; Table 3).

After analyzing whether the DIC or sepsis affect the short-term prognosis of patients with AP by a multivariate proportional hazards model, we found that prolonged APTT was a prognostic factor for the short-term prognosis of patients

TABLE 2 Baseline characteristics of the patients with AP in the training cohort

Factors	Normal APTT group	High APTT group	*p* Value
Age (year)	59.9 ± 17.4	61.7 ± 16.9	0.256
Gender			
Male	259 (57.9%)	85 (59.0%)	0.818
Female	188 (42.1%)	59 (41.0%)	
Etiologies of AP			
Unspecified	376 (84.3%)	125 (86.8%)	0.506
Biliary	35 (7.8%)	8 (5.6%)	
Alcohol	33 (7.4%)	9 (6.3%)	
Drug	2 (0.4%)	2 (1.4%)	
Acute kidney injury			
No	246 (55.0%)	53 (36.8%)	**<0.001**
Yes	201 (45.0%)	91 (63.2%)	
Heart failure			
No	365 (81.8%)	111 (77.1%)	0.209
Yes	82 (18.2%)	33 (22.9%)	
Sepsis			
No	338 (75.6%)	64 (44.4%)	**<0.001**
Yes	109 (24.4%)	80 (55.6%)	
Ventilator			
No	404 (90.4%)	115 (79.9%)	**0.001**
Yes	43 (9.6%)	29 (20.1%)	
Pleural effusion			
No	384 (89.9%)	121 (84.0%)	0.055
Yes	63 (10.1%)	23 (16.0%)	
Ascites			
No	388 (86.8%)	110 (76.4%)	**0.003**
Yes	59 (13.2%)	34 (23.6%)	
Vasopressors			
No	322 (72.0%)	58 (40.3%)	**<0.001**
Yes	125 (28.0%)	86 (59.7%)	
DIC			
No	446 (99.8%)	141 (99.3%)	**0.018**
Yes	1 (0.2%)	3 (0.7%)	
Length of stay (day)			
ICU	5.3 ± 7.7	9.0 ± 11.7	**<0.001**
Hospital	15.9 ± 16.2	19.5 ± 17.2	**0.021**
BISAP score	1.9 ± 0.9	2.1 ± 1.0	0.150
SOFA score	5.1 ± 3.6	8.3 ± 4.4	**<0.001**
Rason score	4.1 ± 1.5	4.4 ± 1.6	0.139
APACHE II	26.5 ± 5.7	27.7 ± 5.1	0.179
30-day mortality			
No	409 (91.5%)	106 (74.3%)	**<0.001**
Yes	38 (8.5%)	38 (25.7%)	
60-day mortality			
No	406 (90.8%)	104 (72.2%)	**<0.001**
Yes	41 (9.2%)	40 (27.8%)	

Note: The complications listed in the table are those that occurred during the admission of the patients with acute pancreatitis. The bolded numbers indicate significance at the *p* value <0.05 level.

Abbreviations: AP, acute pancreatitis; APACHE, Acute Physiology and Chronic Health Examination; APTT, activated partial thromboplastin time; BISAP, the bedside index for severity in acute pancreatitis; DIC, disseminated intravascular coagulation; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment.

with AP independent of comorbid DIC or sepsis. The HR (95% CI) of 30- and 60-day mortality were 1.68 (1.06, 2.67) ($p = 0.026$) and 1.56 (1.04, 2.44) ($p = 0.041$), respectively.

Results of subgroup analysis

Despite the difference in the HRs (95% CI) and the corresponding *p* value in different groups, the *p* values of the interaction test results for age, gender, diabetes, coronary heart disease, heart failure, chronic obstructive pulmonary disease, chronic kidney disease, and cirrhosis are all >0.05, indicating that these factors have no significant influence on the mortality of APTT. However, cirrhosis is a risk factor for death in patients with AP (Interaction *p* value < 0.001; Table 4). Consistent with the training cohort, the results of the validation cohort also identified the above results (Table 4).

Prolonged APTT predicts short-term mortality performed as well as BISAP, Ranson, and APACHE II scores in patients with AP

In order to test the ability of prolonged APTT in predicting 30- and 60-day mortality in patients, we uniformly defined normal APTT as 0 and prolonged APTT as 1. After that, a receiver operating characteristic curve (ROC) analysis was carried out to compare its predictive ability with BISAP, Ranson, and APACHE II in predicting the short-term prognosis of patients with AP. In the training cohort, the extended APTT performed as well as the BISAP, Ranson, and APACHE II models in predicting the 30-day survival (area under the receiver operating characteristic curve [AUROC]: 0.661 vs. 0.633, 0.689, 0.666, respectively) and 60-day survival (AUROC: 0.658 vs. 0.634, 0.672, 0.680, respectively) in patients with AP (Figure 3a,b). Consistent with the training cohort, the results of validation cohort

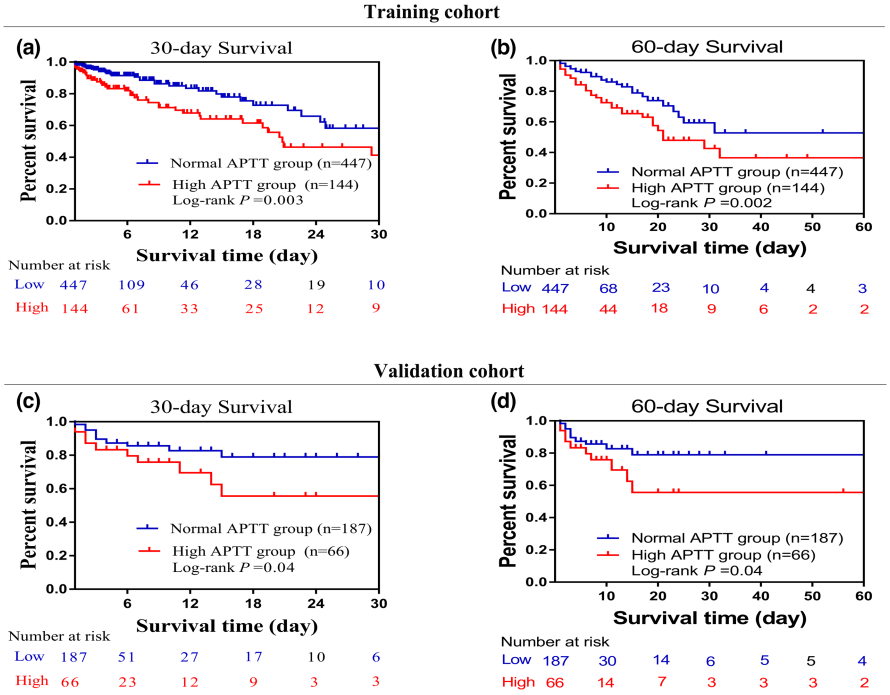

FIGURE 2 Patients with acute pancreatitis in the high APTT group had a higher short-term mortality risk. (a,b) Kaplan–Meier estimates 30- and 60-day survival in normal and high groups of training cohort; (c,d) Kaplan–Meier estimates 30- and 60-day survival in normal and high groups of validation cohort. APTT, activated partial thromboplastin time.

TABLE 3 HRs (95% CIs) for all-cause mortality across groups

	Training cohort		Validation cohort	
	High vs. normal		High vs. normal	
Factors	**HR (95% CI)**	***p* Value**	**HR (95% CI)**	***p* Value**
30-day mortality				
Unadjusted	1.98 (1.26, 3.12)	0.034	3.02 (1.53, 5.95)	0.001
Adjusted	1.63 (1.10, 2.61)	0.035	3.90 (1.83, 8.35)	<0.001
60-day mortality				
Unadjusted	1.82 (1.17, 2.84)	0.008	3.02 (1.53, 5.95)	0.001
Adjusted	1.49 (1.01, 2.38)	0.041	3.90 (1.83, 8.35)	<0.001
ICU mortality				
Unadjusted	1.82 (1.17, 2.84)	0.008	3.02 (1.53, 5.95)	0.001
Adjusted	1.59 (1.01, 2.38)	0.041	3.90 (1.83, 8.35)	<0.001
Hospital mortality				
Unadjusted	2.37 (1.52, 3.70)	<0.001	3.41 (1.72, 6.76)	<0.001
Adjusted	1.98 (1.24, 3.14)	0.004	4.61 (2.06, 10.33)	<0.001

Note: Cox proportional hazards regression models were used to calculate HRs with 95% CIs. Model 1 was unadjusted. Model 2 was adjusted for age, gender, use of heparin, disseminated intravascular coagulation, and patient's past medical history of diabetes, coronary heart disease, hypertension, chronic obstructive pulmonary disease, chronic kidney disease, and cirrhosis.

Abbreviations: CIs, confidence intervals; HRs, hazard ratios; ICU, intensive care unit.

also indicated that prolonged APTT performed as well as the BISAP, Ranson, and APACHE II models in predicting the 30-day survival (AUROC: 0.672 vs. 0.532, 0.648, 0.669, respectively) and 60-day survival (AUROC: 0.672 vs. 0.532, 0.648, 0.669, respectively) in patients with AP (Figure 3c,d). Based on the above results, APTT prolongation may have predictive value for predicting the short-term prognosis of patients with AP.

DISCUSSION

Considering APTT levels are closely associated with AP, 844 patients from an extensive critical care medical database were selected for this study. After adjusting for age, gender, use of heparin, DIC, and pre-existing medical conditions, including diabetes, coronary heart disease, hypertension, chronic kidney disease, chronic obstructive

TABLE 4 Subgroup analysis of the associations between all-cause mortality

	Training cohort			Validation cohort		
	High vs. normal			High vs. normal		
Factors	HR (95% CI)	*p* Value	*p*-Interaction	HR (95% CI)	*p* Value	*p*-Interaction
Age (year)						
<60	3.75 (1.57, 8.97)	0.003	0.070	11.46 (1.40, 93.58)	0.023	0.10
≥60	0.75 (0.44, 1.29)	0.287		2.34 (0.92, 5.94)	0.073	
Gender						
Male	3.24 (1.71, 6.12)	<0.001	0.09	3.02 (1.53, 5.95)	0.001	0.067
Female	0.97 (0.48, 1.95)	0.927		3.10 (1.62, 6.01)	0.001	
Diabetes						
No	2.29 (1.33, 3.95)	0.003	0.249	3.10 (1.44, 6.67)	0.004	0.332
Yes	1.23 (0.54, 2.80)	0.623		2.78 (0.61, 12.55)	0.185	
CHD						
No	1.90 (1.19, 3.04)	0.007	0.087	3.61 (1.75, 7.44)	0.001	0.701
Yes	1.58 (0.35, 7.14)	0.553		0.038 (0.00, 3.53)	0.656	
Heart failure						
No	2.21 (1.29, 3.78)	0.004	0.285	3.43 (1.50, 7.84)	0.003	
Yes	1.14 (0.49, 2.66)	0.767		1.55 (0.47, 5.09)	0.474	
COPD						
No	1.84 (1.16, 2.92)	0.010	0.055	2.65 (1.33, 5.26)	0.006	0.061
Yes	1.33 (0.27, 6.68)	0.729		2.3 (0.00, 3.56)	0.616	
CKD						
No	2.21 (1.32, 3.71)	0.003	0.285	3.84 (1.61, 9.18)	0.002	0.160
Yes	1.20 (0.48, 3.02)	0.695		2.44 (0.74, 8.06)	0.142	
Cirrhosis						
No	1.51 (0.91, 2.51)	0.110	<0.001	1.79 (0.77, 4.15)	0.173	<0.001
Yes	3.51 (1.98, 12.58)	0.044		9.9 (1.26, 77.99)	0.029	

Note: High vs. normal means high APTT group vs. normal APTT group.

Abbreviations: APTT, activated partial thromboplastin time; CHD, coronary heart disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; HR, hazard ratio.

pulmonary disease, and cirrhosis, we found that patients in the prolonged APTT group had significantly higher mortality at 30 and 60 days than those in the normal group. In patients with AP, APTT prolongation was positively associated with acute kidney injury, sepsis, ventilator use, and ascites. These conditions indicate critical illness. Patients who suffer from one or more of these complications often has a poor prognosis. The results of the ROC test showed that APTT was comparable to BISAP, Ranson, and APACHE II in predicting short-term mortality in patients with AP. However, it was more straightforward and more convenient than BISAP, Ranson, and APACHE II. Although the results of the interaction test indicated that cirrhosis was a risk factor for patients with prolonged APTT, there was no statistical difference in the baseline information on cirrhosis between the normal and prolonged APTT groups. Additionally, APTT was a prognostic biomarker for the short-term prognosis of patients with AP independent of comorbid DIC or sepsis. So prolonged APTT is reliable and convincing in determining the short-term prognosis of patients with AP.

The APTT is a functional measure of the intrinsic and common pathways of the coagulation cascade.[15] In most cases, a prolonged APTT indicates a deficiency of coagulation factors in the body or reduced activity of coagulation factors or antibodies to coagulation factors.[10] A patient with protracted APTT is at higher risk for bleeding, particularly internal bleeding. Severe cases can lead to shock or even patient death.[16,17] In addition, we found that patients with AP who had prolonged APTT had a higher incidence of DIC than those with normal APTT. Therefore, clinicians should make aware of the possibility of bleeding in patients with a prolonged APTT. In patients with coronavirus pneumonia with diabetes

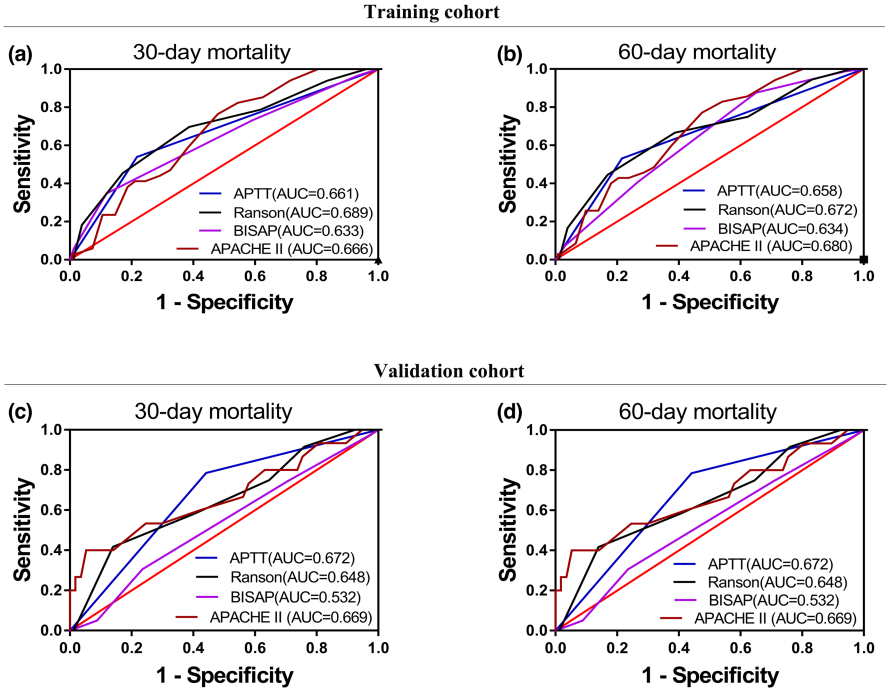

FIGURE 3 APTT performed as well as BISAP, Ranson, APACHE II models in predicting 30- and 60-day survival in patients with acute pancreatitis. (a,b) Receiver operating curves (ROC) for the abilities of risk models to predict 30- and 60-day survival of acute pancreatitis patients in training cohort; (c,d) ROC for the abilities of risk models to predict 30- and 60-day survival of acute pancreatitis patients in the validation cohort. APACHE, Acute Physiology and Chronic Health Examination; APTT, activated partial thromboplastin time; AUC, area under the curve; BISAP, bedside index for severity in acute pancreatitis.

mellitus, patients with elevated APTT have an increased risk of in-hospital death.[18] APTT was an independent predictor of 30-day mortality in patients with septic shock caused by intra-abdominal infection admitted to the ICU.[19] In sepsis, prolonged APTT significantly impacted its severity and outcome.[12] Several studies have shown that prolonged APTT increases the risk of death in patients in the ICU with sepsis.[11–13,20] Sepsis is associated with increased APTT, and a prolonged APTT in patients with AP indicates the possibility of sepsis, and awareness should be raised to prevent and control infection in patients. Moreover, infection, sepsis, and infectious shock are common complications of AP.[21,22] Our study also found that extended APTT increases the risk of short-term death in patients with AP.

Activated partial thromboplastin time performed as well as BISAP, Ranson, and APACHE II models in predicting 30- and 60-day survival rates in patients with AP. Prolonged APTT in patients with AP may increase the risk of short-term death.

AUTHOR CONTRIBUTIONS

Y.Y., S.D., and B.N. wrote the manuscript and designed the research. Y.Y., S.D., W.Y., and Y.K. performed the research and analyzed the data.

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CONFLICT OF INTEREST

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