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Pancreaticobiliary

Early prediction of organ failure under the revised Atlanta classification

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ABSTRACT

Background/Aims: This study aimed to compare the ability of conventional laboratory markers and scoring systems to early predict organ failure (OF) and to differentiate between transient and persistent OF in patients with acute pancreatitis (AP) using the revised Atlanta classification.

Materials and Methods: We retrospectively analyzed the medical records of 214 patients with AP between January 2014 and July 2015. The predictive values of laboratory markers were analyzed. The predictive accuracy of individual markers, extrapancreatic inflammation on computed tomography (EPIC), acute physiology and chronic health evaluation II (APACHE II), and bedside index for severity in acute pancreatitis (BISAP) scores were measured using the area under the receiver operating characteristic curve (AUROC).

Results: OF was diagnosed in 32 (15%) patients and persistent OF in 14 (6.5%). There were statistically significant differences between patients with and without OF with respect to white blood cell count, creatinine, blood urea nitrogen, lactate dehydrogenase, C-reactive protein, calcium (Ca), arterial partial pressure of oxygen (PaO_2), base excess (BE), APACHE II, BISAP scores, and EPIC scores. Logistic regression analysis identified Ca, PaO_2, and BE as independent predictors of OF. Using AUROC, the EPIC score had the highest accuracy for the early prediction of OF, which was 0.82. No significant differences were detected between patients with transient and persistent OF.

Conclusion: Several laboratory markers and score systems were useful for the early prediction of OF in patients with AP, of which Ca, PaO_2, and BE had highest predicting value, and EPIC score had the highest accuracy. We could not predict the duration of OF using laboratory markers.

Keywords: Acute pancreatitis, organ failure, revised Atlanta classification, extrapancreatic inflammation on computed tomography, persistent organ failure

INTRODUCTION

Acute pancreatitis (AP) is a common and potentially fatal inflammatory process. Hospital admissions for AP have been increasing in China, America, and Japan (1-3), and most patients die because of organ failure (OF) in the early phase or of infected (peri) pancreatic necrosis in the late phase. The mortality of patients with OF at admission or within 7 days after admission is >20%, and >30% of patients have persistent OF (4).

Advances in the last two decades have led to the revision of the Atlanta classification (AC) in 2012 (5). Under the revised AC (RAC), OF is defined according to a modified Marshall scoring system only (6). The presence or absence and duration of OF determine the degree of AP severity. RAC performed better than AC in predicting clinical outcomes (7,8). Most OF occurs in the first week after admission; therefore, the early prediction of OF enables the early identification of patients who need to be transferred to an intensive care unit. Few studies aimed to predict the occurrence of OF or persistent OF. The predictors included laboratory markers, imaging examination, and scoring systems. However, the majority of studies adopted the definition of OF as proposed in AC (9). In addition, the time from onset to hospital admission was not clearly defined (10-13), and the predictors were often assessed at >3 days after admission (14,15).

This study aimed to assess and compare the ability of laboratory markers and scoring systems to early predict OF and to differentiate between patients with transient and persistent OF using RAC.

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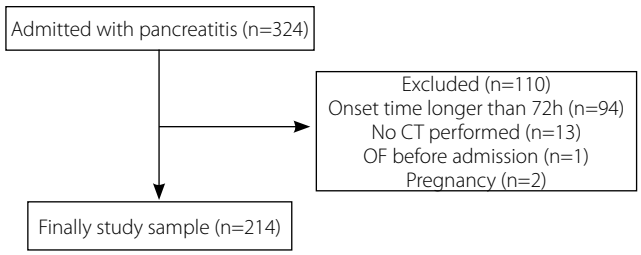

Figure 1. Patient selection and exclusion
CT: computed tomography; OF: organ failure

MATERIALS AND METHODS

Patients

This retrospective study included patients with a primary diagnosis of AP who were admitted to Xuanwu hospital between January 2014 and July 2015. After searching the hospital database, all medical records were studied. The diagnosis of AP was established on the basis of the presence of two of the following three criteria: 1) abdominal pain consistent with the disease, 2) serum amylase and/or lipase >3 times the upper limit of normal, and 3) characteristic findings from abdominal imaging (8).

Exclusion criteria were as follows: 1) time from onset to hospital admission was >72 h, 2) unacceptable abdominal computed tomography (CT) immediately before admission or within 72 h after admission, 3) patients diagnosed with OF or those who underwent invasive treatment before admission, and 4) patients who were pregnant or aged <18 years. Relapse patients were not excluded. The study design was approved by the ethics committee of our institution.

Data Collection

Data regarding parameters used in this study were easy to obtain in clinical practice, such as baseline and clinical characteristics, laboratory markers, and scoring systems. Baseline and clinical data comprised sex, age, body mass index (BMI), diabetes history, etiology of AP, time from onset to hospital admission, number of AP episodes, characteristics of OF (including type, occurrence time, and duration time of OF), and mortality. All laboratory tests were conducted in the emergency room prior to admission or within 24 h after admission and included white blood cell (WBC) count, serum creatinine (Cr), blood urea nitrogen (BUN), glucose, calcium (Ca), lactate dehydrogenase (LDH), arterial partial pressure of oxygen (PaO_2), base excess (BE), and C-reactive protein (CRP). Pleural effusion and ascites were investigated using ultrasound or radiography. Only the first CT immediately before admission or during the hospital stay was assessed to determine the side of prerenal fascial thickening and the inflammation of the retroperitoneum and mesentery. Scoring of extrapancreatic inflammation on CT (EPIC) was performed by a radiologist who was not aware of the clinical details. The acute physiology and chronic health evaluation II (APACHE II) and bedside index for severity in acute pancreatitis (BISAP) scores were calculated using data obtained within the first 24 h.

The modified Marshall system evaluates the three organ systems most commonly affected by severe AP: respiratory, cardiovascular, and renal (6). OF is defined as a score of 2 or more in any one organ system. Transient OF lasts for no more than 48 h, whereas persistent OF lasts for more than 48 h (6). Multiple OF involves more than one organ system (6).

Table 1. Demographic characteristics

Variables		Value
Sex	Male	138 (64.5%)
Age (year)		52.3
BMI (kg/m^2)		26.6
Onset to hospital Admission (hours)		30.3 (15.8-46.3)
Etiology		
	Biliary disease	96 (44.9%)
	Alcohol consumption	18 (8.4%)
	Hypertriglyceridemia	74 (34.6%)
	Other causes	6 (2.8%)
	Idiopathic causes	20 (9.3%)
OF		
	No	182 (85.0%)
	Yes	32 (15%)
Single OF		26 (12.1%)
	Respiratory	23 (10.7%)
	Renal	3 (1.4%)
	Cardiovascular	0
Multiple OF		6 (2.9%)
	Pulmonary+renal	4 (1.9%)
	Renal+circulation	1 (0.5%)
	Pulmonary+renal+circulation	1 (0.5%)
Occurrence of OF		
	First week	31 (14.5%)
	Second week	1 (0.5%)
	third week	0
Duration of OF		
	Transient	14 (6.5%)
	Persistent	18 (8.4%)

BMI: body mass index; OF: organ failure

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 21 (SPSS Inc, Chicago, IL, USA). A two-tailed P value of <0.05 was considered statistically significant. Categorical variables were described as absolute numbers and proportions, and Pearson's χ^2 test or Fisher's exact test was used to compare proportions of patients with or without OF and those with transient or persistent OF. Student's *t*-test was used to analyze continuous variables that complied with a normal distribution. Normally distributed data were expressed as mean plus standard deviation, and an independent sample t-test was used to compare patients with or without OF and those with

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Table 2. Comparison of demographic characteristics in patients with and without OF and those with transient and persistent OF

	OF	No OF	p	Transient OF	Persistent OF	p
Sex (male)	22 (68.8%)	116 (63.7%)	0.59	7 (50.0%)	15 (83.3%)	0.062
Age (years)	53.1±18.6	52.1±18.5	0.78	47.5 (31.8-64)	54.5 (40.4-75)	0.215
BMI (kg/m^2)	27.7±7.0	26.4±4.4	0.21	27.6 (24.7-29.1)	27.7 (20.7-30.5)	0.765
History of diabetes	29.6±19.95		0.30			0.365
	Yes	6 (18.8%)	50 (27.5%)		4 (28.6%)	2 (11.1%)
	No	26 (81.3%)	132 (72.5%)		10 (71.4%)	16 (88.9%)
Onset to hospital admission (h)	26.5 (19.5-48)	24 (14.8-45.3)	0.28	33 (18-54)	26.5 (18.8-47.3)	0.639
Etiology			0.78			>0.05
	Biliary disease	14 (43.8%)	82 (45.1%)		5 (35.7%)	9 (50.0%)
	Alcohol consumption	3 (9.4%)	15 (8.2%)		2 (14.3%)	1 (5.6%)
	Hypertriglyceridemia	11 (34.4%)	63 (34.6%)		7 (50%)	4 (22.2%)
	Other causes	2 (6.3%)	4 (2.2%)		0	2 (11.1%)
	Idiopathic causes	2 (6.3%)	18 (9.9%)		0	2 (11.1%)
Number of AP episodes			0.96			0.712
	Primary	22 (68.8%)	126 (69.2%)		9 (64.3%)	13 (72.2%)
	Relapse	10 (31.3%)	56 (30.8%)		5 (35.7%)	5 (27.8%)

BMI: body mass index; OF: organ failure; AP: acute pancreatitis

transient or persistent OF. Abnormally distributed variables were expressed as median (quartile range), and the Mann-Whitney U test and the Kruskal-Wallis test were used for the analysis.

Logistic regression analysis was performed to determine independent predictors in OF. Patients with missing values were excluded from the regression analysis. Receiver operating characteristic (ROC) analysis was used to describe cutoff values for independent predictors and scoring systems. Youden's index was used to obtain an optimal cutoff value. The optimal cutoff value was expressed as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The predictive accuracy was measured by examining the area under the receiver operating characteristic curve (AUROC) with 95% confidence intervals.

RESULTS

A total of 214 patients with AP were included (Figure 1). Baseline and clinical characteristics are given in Table 1. Of the 214 patients, the mean age was 52.3 years in 64.5% of males, the mean BMI was 26.6 kg/m^2, and the mean time from onset to hospital admission was 30 h. The etiologies of AP included biliary disease (44.9%), alcohol consumption (8.4%), hypertriglyceridemia (34.6%), idiopathic causes (9.3%), and other causes (including post-ERCP, tumor, and trauma; 2.8%). OF was diagnosed in 32 (15%) patients, and 14 (6.5%) patients had persistent OF. There were 26 (12.1%) patients with single OF, and 31 (14.5%) OF events occurred in the first week after admission or at admission. Respiratory failure was the predominant type of OF, followed by renal failure. No patient died during the hospital stay. CT was performed in 32 patients with OF before or on the same day of OF diagnosis, except in one patient.

The characteristics of patients with or without OF are listed in Tables 2 and 3. No significant differences in demographics were found between patients with or without OF, including BMI, history of diabetes, time from onset to admission, etiology, and number of episodes (Table 2). WBC count and Cr, BUN, LDH, and CRP levels were significantly higher in patients with OF than in those without OF ($p<0.05$; Table 3). Ca level, PaO_2, and BE were significantly lower in patients with OF than in those without OF ($p<0.05$). The side of prerenal fascial thickening was correlated with the occurrence of OF (Table 3), and patients with bilateral prerenal fascial thickening developed OF more often than those with no or unilateral thickening ($p<0.05$). There were statistically significant trends for OF patients with increasing EPIC, APACHE II, and BISAP scores. No significant differences were detected between patients with transient and persistent OF, including all laboratory markers and scoring systems.

Logistic regression analysis of the laboratory markers identified Ca, PaO_2, and BE as independent predictors of OF, and the odds ratios are listed in Table 4. The ROC curves for each independent predictor and scoring system for the early prediction of OF are shown in Figure 2. The EPIC score had the highest accuracy for predicting OF according to AUROC, followed by PaO_2.

The optimal cutoff values for Ca, PaO_2, BE, and EPIC score were determined on the basis of the highest Youden's index generated from the ROC curves. The cut-off values of APACHE II and BISAP scores were established before data collection and were 8 and 3, respectively. The sensitivity, specificity, PPV, and NPV are presented in Table 5. The EPIC score had the highest sensitivity, whereas the APACHE II score (≥8) had the highest specificity.

DISCUSSION

In this retrospective study, we defined OF according to RAC and evaluated the usefulness of conventional predictors for the early

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Table 3. Comparison of laboratory markers and multifactorial scorings in patients with and without OF and those with transient and persistent OF

	OF	No OF	p	Transient OF	Persistent OF	p
WBC (×10^9/L)	14.8±6.5	11.5±4.0	0.008	14.4 (11.9-18.2)	13.2 (11.4-15.4)	0.291
Cr (μmol/L)	74.5 (66-117)	63 (52-75)	<0.001	74 (51.8-126.5)	75 (68.2-120.5)	0.561
BUN (mmol/L)	8.0±6.0	5.2±2.3	0.012	5.5 (4.8-8.0)	7.2 (4.6-10.8)	0.533
Glu (mmol/L)	8.13 (6.34-9.99)	7.8 (6.5-11.0)	0.963	8.1 (6.5-10.4)	8.1 (6.3-10.4)	0.866
Ca (mmol/L)	1.92 (1.71-2.15)	2.13 (2-2.25)	<0.001	1.9 (1.7-2.1)	1.9 (1.7-2.2)	0.997
LDH (U/L)	344 (219-541)	220 (171-321)	0.02	331 (222-510)	385 (215-835)	0.880
PaO_2 (mmHg)	67.3 (51.7-79.15)	78.9 (71.4-87.4)	0.001	65.8 (49.1-74.3)	67.7 (51.7-92.6)	0.697
BE	-3.3 (-5.3 to -1.25)	-1.1 (-2.5 to -1)	0.001	-3.1 (-5.6 to -1.3)	-3.3 (-6.9 to -1)	1
CRP (mg/L)	160 (61-288)	54.1 (16.35-121)	0.002	165.5 (85.0-246)	115 (30.2-345)	0.916
Side of prerenal fascial thickening	0.001			>0.05		
No	2 (6.3%)	53 (29.1%)		2 (14.3%)	0	
Unilateral	9 (28.1%)	69 (37.9%)		4 (28.6%)	5 (27.8%)	
Bilateral	21 (65.6%)	60 (33.0%)		8 (57.1%)	13 (72.2%)	
EPIC	3 (2-4)	1 (0-2)	<0.001	2.5 (1.8-3.3)	4 (2-4.3)	0.771
APACHE II		<0.001			0.113	
<8	28 (87.5%)	181 (99.5%)		14 (100%)	14 (77.8%)	
≥8	4 (12.5%)	1 (0.5%)		0	4 (22.2%)	
BISAP			<0.001			0.061
<3	21 (65.6%)	178 (97.8%)		12 (85.7%)	9 (50%)	
≥3	11 (34.4%)	4 (2.2%)		2 (14.3%)	9 (50%)	

OF: organ failure; WBC: white blood cell; Cr: creatinine; BUN: blood urea nitrogen; Glu: glucose; Ca: calcium; LDH: lactate dehydrogenase; PaO_2: arterial partial pressure of oxygen; BE: base excess; CRP: C-reactive protein; EPIC: extrapancreatic inflammation on computed tomography; APACHE II: acute physiology and chronic health evaluation II; BISAP: bedside index for severity in acute pancreatitis

Table 4. Independent predictors identified by stepwise forward logistic regression analysis of laboratory markers

	OR (95% CI)	p
Ca	0.051 (0.004–0.642)	0.021
PaO_2	0.914 (0.870–0.961)	<0.001
BE	0.784 (0.666–0.922)	0.003

OR: odds ratio; CI: confidence interval; Ca: calcium; PaO_2: arterial partial pressure of oxygen; BE: base excess

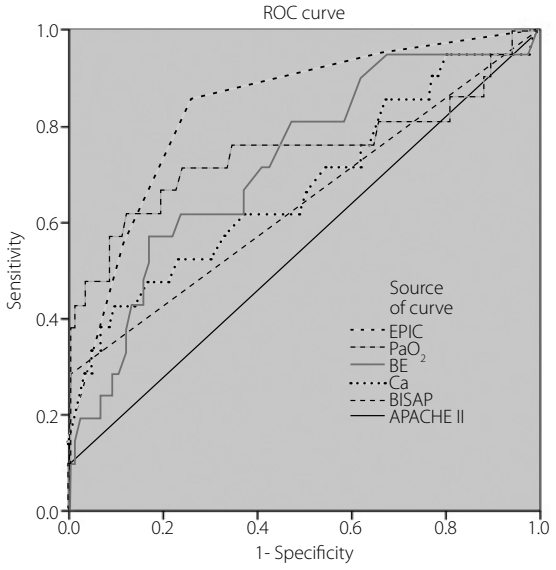

Figure 2. Receiver operating characteristic curves of independent predictors and scoring systems in predicting organ failure
EPIC: extrapancreatic inflammation on computed tomography; PaO_2: arterial partial pressure of oxygen; BE: base excess; Ca: calcium; BISAP: bedside index for severity in acute pancreatitis; APACHE II: acute physiology and chronic health evaluation II

prediction and duration of OF. The predictors in this study have been used as predictors for mortality or severity of AP. We found that several individual markers and scoring systems could predict the occurrence of OF, albeit with low to moderate accuracy, and no marker could predict the duration of OF.

In this series, gallstones were the predominant etiological factor of AP, which was consistent with the results of our previous studies (1). There were 32 patients (15%) with OF, of which 14 patients (6.5%) had severe AP according to RAC. The mortality rate in our study was 0, which was lower than that in a previous report (16). This might be attributed to patient selection and the advances in organ-supporting technology.

With the increasing prevalence of obesity, some studies have focused on the association between obesity and AP. BMI was reported to be a predictor of mortality and severity in patients with AP, whereas it was not an independent prognostic factor for OF in those with AP (17). In our study, BMI was not associated with the presence of OF in a population with relatively low BMI, and the result was similar to that of a study from Korea (14). A study from Taiwan demonstrated that patients with diabetes had a higher risk for severe attack and local complications than those without diabetes, but the risk for OF was similar between patients with and without

Table 5. The AUROC of independent laboratory markers and multifactorial scorings for the early prediction of OF

	AUROC (95% CI)	Cutoff value	Sensitivity	Specificity	PPV	NPV
Ca (mmol/L)	0.69 (0.56–0.83)	1.95	56.3%	85.2%	40%	91.7%
PaO_2 (mmHg)	0.74 (0.59–0.88)	68.6	61.9%	85.2%	22.2%	92.3%
BE	0.70 (0.59–0.81)	–3.15	57.1%	83%	38.7%	83.6%
EPIC	0.82 (0.72–0.92)	1.5	84.4%	73.6%	36%	96.4%
APACHE II	0.56 (0.44–0.68)	≥7	12.5%	99.5%	80%	86.7%
BISAP	0.66 (0.54–0.78)	≥3	34.4%	97.8%	73.3%	89.4%

AUROC: area under the receiver operating characteristic curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; Ca: calcium; PaO_2: arterial partial pressure of oxygen; BE: base excess; EPIC: extrapancreatic inflammation on computed tomography; APACHE II: acute physiology and chronic health evaluation II; BISAP: bedside index for severity in acute pancreatitis

diabetes (18). Glucose level was reported to be an independent predictor of OF (19); however, the definition of OF and the degree of AP severity were based on AC in this study. Both diabetes history and glucose levels had no correlation with the presence of OF.

Ca is not a routine predictor of inflammation but is an independent predictor of OF (20). In a previous study, the diagnostic odds ratio was 0.6, and AUROC was 0.82 (0.72-0.92) after 24 h of symptom onset (19). Our study obtained similar results. Patients with OF had lower Ca levels. Ca plays a protective role and was determined to be an independent predictor of early OF after logistic regression analysis. In our study, the odds ratio was 0.051, and AUROC was 0.71 (0.6-0.86), with an optimal cutoff value of 1.95 mmol/L. Hypocalcemia in patients with AP may result from widespread fatty necrosis (21) or the leakage of circulating Ca^{2+} into the extracellular space, which was secondary to the increased microvascular permeability that resulted from inflammation (19). Massive vascular leakage is one of the main pathophysiological events that occurs before OF (22).

C-reactive protein is a well-known marker for predicting severity, complication, and mortality of AP (10,23). Moreover, its testing is inexpensive and easily available, and it has a relatively high sensitivity and specificity within 48 h of symptom onset (10). The AUROC of the CRP level in predicting OF was 0.65 (0.42-0.80), which was higher than that of the IL-6 level and APACHE II score (10). In another report, the AUROC of CRP levels obtained within 24 h after admission in predicting OF was 0.8 (0.69-0.92), which was lower than that of the BISAP score (0.93; 0.88-0.97) (14). The two abovementioned studies did not perform logistic regression analysis. Moreover, the definition of OF and degree of severity were based on AC. In our study, CRP was correlated with the early occurrence of OF; however, logistic regression analysis revealed that CRP was not an independent predictor.

The accuracy of BUN and BISAP scoring system in predicting the severity of AP has been validated (11,24). According to previous studies, the AUROC of BUN in predicting OF was 0.81 (19) and in predicting persistent OF was 0.73 (12), suggesting that the predictive ability of BUN was low to moderate. In this study, the serum BUN level was higher in patients with OF than in those without OF; however, BUN was not considered to be an independent predictor. This was similar to previous studies (12,19).

BISAP is composed of five components, including BUN level of >25 mg/dL. Few studies have compared the relationship between the BISAP score and presence of OF. Higher BISAP scores are significantly related to the development of OF (12,14,25). Nevertheless, there are different results when considering predictive ability. The optimal cutoff values and AUROC (0.42-0.93) vary depending on the population studied (10,12,14). The predictive value of the BISAP score is better than that of the CTSI and Ranson score (14) and is comparable with that of APACHE II and Ranson scores (10,12). In this study, we again confirm that there is a significant association between the BISAP score and presence of OF; however, the AUROC of the BISAP score for the early prediction of OF is only 0.66 (0.54-0.78), indicating low accuracy.

Cr was correlated with the early occurrence of OF in this study; however, it was not an independent factor. Other studies have generated different results. One study reported that Cr was an independent factor using a logistic regression model and that it was significantly associated with an approximately 7-fold OF upon a 1-unit increase (20). However, we found that the definition of OF in that study was based on AC and that at least 41.6% patients were diagnosed with OF because of a metabolic reason. Therefore, we do not believe that the study offers convincing evidence. Nevertheless, it is reported that the serum Cr level is higher in patients with OF, despite its low to moderate accuracy in predicting OF (12). The increase in Cr level may be secondary to the occurrence of renal dysfunction, hypovolemia, dehydration, tissue hypoxia, and circulatory failure, which may emerge in patients with OF (20).

The term 'PaO_2<60 mmHg' has been described in various editions of respiratory failure. Therefore, it is easy to understand that PaO_2 can be an independent factor for the early prediction of OF, particularly when respiratory failure accounts for 70% of all types of OFs in this study. The AUROC of PaO_2 for the early prediction of OF is 0.74 (0.59-0.88), which is the highest of the independent predictors. BE is superior to pH in evaluating the clearance of metabolic acidosis (26), which is why we selected BE for our evaluation. BE has been shown to accurately reflect the changes in oxygen delivery and oxygen consumption during compensated shock (27) and is one of the most commonly used endpoints of therapy or resuscitation (28). A large cohort study demonstrated that patients with metabolic acidosis and BE lower than -2 had higher mortality rates than those without them (29). We found

that BE lower than -3.15 may be an independent factor for the early prediction of OF, and the odds ratio was determined to be 0.78 using logistic regression analysis.

The APACHE II score is widely used in predicting the mortality and severity of AP and usually has a high accuracy (10). However, its ability to predict OF is debated, despite the possibility that its accuracy is higher than most scores and individual markers (12) or lower than Ca, LDH, glucose (19), CRP, procalcitonin, and the Ranson score (10). To ensure that the data of prognostic markers were collected before diagnosis of OF, patients with an onset to admission time of >72 h were excluded. However, the limitation was that patients with longer onset times and more severe disease might have been excluded, and the proportion of patients with higher APACHE II scores was lower. Furthermore, we selected 8 as the cutoff value while collecting data. This may have been why the AUROC of the APACHE II score was relatively small. The optimal cutoff value for the early prediction of OF may be <8, and further research may be necessary.

The Balthazar score and CT Severity Index (CTSI) are used to evaluate inflammation of the pancreas and peripancreas, and CTSI incorporates the presence of pancreatic necrosis. The EPIC score indicates only extra-pancreatic inflammation. The three scores have proven useful in predicting the severity of AP (13,30). Radiological scores are rarely used to predict the possibility of OF in patients with AP. The Balthazar score has been shown to be correlated with OF in patients with AP, and it was recognized as an independent factor of in-hospital OF (20). The odds ratio in the multivariate analysis was 1.17; however, the time of CT examination was unclear (20). CTSI was also useful in predicting OF within 7 days after admission, but its predicting ability was lower than the Ranson, APACHE II, and BISAP scores (13). In another study, the EPIC score was a slightly better predictor of outcomes, such as persistent OF, intervention, and mortality, than CTSI and Balthazar scores (15). However, the time of CT examination was 3-10 days after the onset of symptoms (15).

In this study, CT examinations were performed 0.5-6 days after the onset of symptoms. We selected an EPIC score for evaluation because it can be easily obtained by clinicians and there is no need to inject contrast medium. Moreover, the EPIC score was superior to the Balthazar score and CTSI in estimating severity and mortality at this stage (13).

Pancreatic necrosis is very unlikely to occur during the very early stages of AP, limiting the diagnostic and predictive value of CTSI (13). The EPIC scores were significantly correlated with the presence of OF in this study. The AUROC of the EPIC score for the early prediction of OF was 0.82 (0.72-0.92), which was the highest of all the laboratory markers and scoring systems. The optimal cutoff value in predicting OF was 1.5. Not all patients with AP underwent CT; however, the EPIC score should be highlighted for the early prediction OF in patients with AP.

Patients with transient OF have lower mortality and morbidity than those with persistent OF (4); therefore, transient and persistent OF are classified as moderate to severe AP and severe AP, respectively, according to RAC (6). The early prediction of the duration of OF is necessary; however, studies regarding the same are few. In a retrospective cohort study, 46 consecutive patients with transient OF and 81 with persistent OF were recruited (31). There was no difference in serum LDH, CRP, and Ca levels and systemic inflammatory response syndrome scores between the two groups. Although differences were found in serum amylase levels and APACHE II and BISAP scores, to our surprise, amylase had the maximum AUROC (31). In our study, no difference was found in any of the parameters between patients with transient OF and those with persistent OF. Patient selection may be responsible for different results between the two studies. Our study only included 32 patients with OF, and we confirmed the time from onset to hospital admission to be <72 h, which was 1 week in the previous study. Similar to our description in the above paragraph regarding APACHE II scores, patients with more severe disease might be excluded. This might have explained the different predictive ability of APACHE II and BISAP scores in the two studies. A multicenter prospective study in Europe showed that CRP levels could identify patients with persistent OF having infected pancreatic and/or peri-pancreatic necrosis, but the data were collected from day 5 to 21 (32). Current laboratory markers and scoring systems were not sufficiently accurate for the early differentiation between patients with transient and persistent OF.

Of course, there are several limitations in this study. First, it is a retrospective study, and some data are missing, which may affect the predictive accuracy of our logistic regression analysis. Second, for the early prediction of OF, we limited the time from onset to admission to 72 h, and all CT examinations were performed immediately before admission or within 72 h after admission. Therefore, the results may only be applicable to specific patients. Third, the cutoff values of APACHE II and BISAP scores were established before data collection, and this may have decreased their predictive accuracy; the optimal cutoff values for the early prediction of OF may be small.

We conclude that evaluating several laboratory markers and score systems in the emergency room prior to admission or within 24 h after admission is useful for the early prediction of OF in patients with AP. In contrast, no laboratory marker or scoring system was likely to be effective in distinguishing between transient and persistent OF. Ca, PaO_2, and BE were identified as independent predictors of laboratory markers for the early prediction of OF. The EPIC score had the highest early prediction accuracy of the scoring systems. However, the predictive ability of the existing parameters was limited. For further improvement in predictive accuracy, developing new approaches or designing new perspective studies is necessary.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Xuanwu Hospital, Capital Medical University.

Informed Consent: Written informed consent was obtained from patients/patients' clients who participated in this study.

Peer-review: Externally peer-reviewed.

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