Original Article

Predicting infected pancreatic necrosis based on influential factors among the most common types of acute pancreatitis: a retrospective cohort study

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Background: Biliary and hypertriglyceridemic acute pancreatitis (BAP and HTGAP) are two of the leading etiologies in China. Infected pancreatic necrosis (IPN) is a particular and noticeable condition in the late stage of these diseases; however, the influential correlated factors on IPN and how to predict IPN are unclear.

Methods: In this retrospective study, 1,116 patients whose diagnosis was BAP or HTGAP met the inclusion criteria among 1,746 enrolled cases. Clinical characteristics were carefully recorded for further investigation of the factors influencing IPN. During a 6-month follow-up, we analyzed bacterial spectra and postoperative indicators related to minimally invasive necrosectomy.

Results: Gallstones and hypertriglyceridemia were the most prevalent causes (52.6% *vs.* 11.3%). The participants with HTGAP were younger (40 *vs.* 52 years, P<0.001), had a higher rate of severe acute pancreatitis (SAP) (51.8% *vs.* 32.0%, P<0.001), and had a higher prevalence of multiple organ dysfunction syndrome (MODS) (26.4% *vs.* 19.0%, P=0.020) than BAP patients. More IPN cases were noted in the BAP group than in the HTGAP group [20.2% *vs.* 13.7%; odds ratio (OR): 1.598, 95% confidence interval (CI): 1.027 to 2.451; P=0.034]. Etiologies, C-reactive protein (CRP) levels, Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, and MODS were the factors influencing IPN. The bacterial spectra and the rates of major postoperative complications were not significantly different.

Conclusions: Patients with BAP more frequently developed IPN. Etiology was independently related to the occurrence of IPN. The APACHE II score, MODS, etiology, and CRP contributed to predicting IPN occurrence. Management of IPN substantially improved the prognosis.

Keywords: Acute pancreatitis (AP); infected pancreatic necrosis (IPN); etiology; gallstone; hyperglyceridemia

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Introduction

Acute pancreatitis (AP) is one of the common causes of acute abdominal disease and is an indication for hospitalization. Approximately 10% of all cases have persistent organ dysfunction, referred to as severe AP (SAP), which can be a life-threatening condition (1). Unlike western countries (2), hypertriglyceridemic AP (HTGAP) has become the second most common type of AP after

biliary AP (BAP) in China (3-5). A recent multicenter study in Beijing collected 2,461 cases over 5 years, and the number of inpatients was shown to increase annually. The most common etiologies by percentage were gallstones (55.75%), hypertriglyceridemia (10.36%), and alcohol (10%) (6). Same trend is reflected in many epidemiological studies (7). In addition to the different causes of BAP and HTGAP, there are significant differences in internal mechanism, population characteristics, severe cases proportion, treatment and prognosis (8).

Two peaks of mortality lie in the course of SAP. Systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS) are the major clinical manifestations in the early phase. Treatment focuses on providing intensive care, ensuring a stable internal environment, and protecting organ function. The prognosis of AP patients has dramatically improved due to active and effective etiological management (9). In the late stage, pancreatic and peripancreatic necrosis may occur in combination with infection, sepsis, and deep fungal infection. This second peak of mortality is caused by what is called infected pancreatic necrosis (IPN) (10). The cornerstone of treatment is the control of infection and surgical management of local complications (11). IPN is a serious local complication of SAP with many influencing confounding factors. It needs to be carried out in high-volume center in order to ensure sufficient sample size (12). This study focuses on the in-depth analysis of the two most common etiological types in region, including baseline characteristics, scoring indicators, laboratory examination, imaging manifestation, bacterial spectra distribution and surgical outcomes, so that the evaluation is more objective and complete. The persistent infection or fever is mainly caused by bacteria and fungus. Studying the differences of bacterial spectra is helpful to explore the influencing factors of IPN and provide references for the use of antibiotics. Throughout multivariate regression analysis, we probe into high predictive value factors of IPN to guide subsequent treatment. We present the following article in accordance with the STARD reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2933).

Methods

Patients

In this single-center retrospective study, we recruited 1,746 AP patients (≥18 years of age) admitted to Xuanwu Hospital of Capital Medical University in Beijing between 6 June 2014, and 22 September 2019. Patients with non-biliary and non-hypertriglyceridemic etiologies were excluded, including alcoholic (157 patients), traumatic (18 patients), and idiopathic (174 patients). Recurrent pancreatitis and readmission (248 patients) were also excluded. Based on the guidelines for AP (13), we established the diagnosis when 2 of the following 3 criteria were met: (I) pancreatic-type abdominal pain, (II) elevated serum amylase and/or lipase more than 3 times the upper limit of normal, and (III) imaging findings consistent with AP.

Clinical management protocol

We assigned the participants to either the BAP or HTGAP group and performed critical laboratory tests at admission and during hospitalization. The surgical approach consisted of percutaneous catheter drainage (PCD) followed, if necessary, by video-assisted retroperitoneal debridement (VARD). All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of the Xuanwu Hospital (No. [2017]036). Individual consent for this retrospective analysis was waived.

The diagnosis of BAP needed to be confirmed by documenting gallbladder stones on any cross-sectional imaging, transient fluctuations in liver chemistry values >3× the upper limit of normal, or both. Alanine transaminase (ALT) is probably the single most reliable test, with a positive predictive value of 93% for a biliary etiology when elevated threefold (14,15).

The diagnosis of HTGAP was definitive when serum triglyceride levels were >1,000 mg/dL at clinical onset. The diagnosis remained probable if the increase in serum triglyceride level was between 500 and 1,000 mg/dL, together with emulsion plasma and without any other apparent etiologies (16).

At present, the definition of IPN was taken as the presence of gas within necrotic collections on contrast-enhanced computed tomography (CT). Under the circumstances of deteriorating clinical condition, shown by fever, sepsis, leukocytosis, and persistent illness, IPN may be indicated and require appropriate treatment (17). A positive culture result by PCD or surgery was not a necessary criterion for confirmation of IPN.

Once IPN was confirmed or suspected, we conducted

image-guided PCD via the left flank to retroperitoneal peripancreatic necrosis. A step-up VARD surgery was performed if PCD alone did not resolve the IPN. Whenever possible, the intervention was postponed until 4 weeks after the onset of pancreatitis, in line with international guidelines. The tract created from the previously placed drain was used to access the retroperitoneal space, facilitating debridement with traditional laparoscopic instruments under direct visualization (18). Subsequent lavage and fistula control were made more practical by the drains left in the cavity. In general, we obtained specimens either by PCD or by surgery for bacterial sample collection. In clinical practice, the VARD procedure is especially suitable for the patients whose necrotic scope extends down to the left paracolic gutter (19).

Data collection and outcomes

The primary outcomes were the factors influencing IPN and correlations between IPN and AP etiologies. Major comorbidities were recorded in detail (e.g., cardiovascular, pulmonary, and renal complications, and diabetes). The collected data included age; gender; body mass index (BMI); CT severity index (CTSI); SIRS; Acute Physiology and Chronic Health Evaluation II (APACHE II) score; single or multiple organ failure; C-reactive protein (CRP) level; white blood cell count; nutrition; severity; local complications including acute peripancreatic fluid collection (APFC), acute necrotic collection (ANC), pancreatic pseudocyst (PP), walled-off necrosis (WON); bacterial culture results; and complications after VARD (e.g., bleeding, fistulas, ileus, portal venous thrombosis). The predefined secondary outcomes included the etiological distribution ratio, differences in the bacterial spectra, and the incidence of postoperative complications. Outpatient follow-ups took place at 3 and 6 months after discharge. Primary physicians were responsible for collecting data and completing the case-record forms.

Statistical analysis

All data were analyzed using the SAS statistical analysis package version 9.4 (SAS Inc., Cary, NC, USA). Quantitative variables with nonnormal distributions were presented as the medians [interquartile ranges (IQRs)], and those with normal distributions were presented as the mean ± standard deviation. For normally distributed data, the two groups were compared by *t*-tests, otherwise, the Mann-Whitney test was used. Categorical variables were presented as absolute numbers and percentages and analyzed using a chi-square test or Fisher's exact test. A multivariate logistic analytic model (stepwise regression) was used to identify independent risk factors of IPN with odds ratios (ORs) and 95% confidence intervals (CIs). Furthermore, receiver operating characteristic (ROC) curves were generated for each of the qualified independent risk factors to assess the predictive ability of each indicator. Significance was set at $P<0.05$.

Results

Baseline characteristics and clinical features

Between 6 June 2014 and 22 September 2019, 1,746 patients with AP were screened, of whom 1,116 were eligible. The trial profile is shown in *Figure 1*. The etiological distribution is shown in *Figure 2*. All participants were divided into two groups according to etiology: BAP (n=919) and HTGAP (n=197). The baseline characteristics of the two groups are displayed in *Table 1*. The severity categories were mild AP (MAP), moderate-severe AP (MSAP), and SAP based on the modified Atlanta criteria. The HTGAP participants were younger (40 *vs.* 52 years, P<0.001), had a higher rate of SAP (51.8% *vs.* 32.0%, P<0.01), and had a higher prevalence of MODS (26.4% *vs.* 19.0%, P=0.020) than BAP participants. Additionally, HTGAP participants had significantly higher APACHE II scores (8 *vs.* 7, P<0.001) and CRP levels (111.0 *vs.* 78.0 mg/L, P<0.001) than BAP participants. The etiological distribution was 919 patients with BAP (52.6%) and 197 with HTGAP (11.3%), those with other etiologies were excluded. Once the AP diagnosis had been confirmed, standard medical treatment was initiated, including fluid resuscitation, enteral and parental nutrition, and vital organ protection. Etiological treatments for BAP included ERCP, cholecystectomy (CCY), and bile duct exploration (462 participants), and lipid-lowering therapies for HTGAP included strict dietary restriction, fibrates, insulin, unfractionated heparin, and apheresis (17 participants).

The results revealed that IPN had occurred in 186 participants (20.2%) in the BAP group and in 27 participants (13.7%) in the HTGAP group (OR: 1.598, 95% CI: 1.027 to 2.451, P=0.034). We observed no significant differences in other local complications, including APFC (26.0% *vs.* 30.9%, P=0.155), ANC (36.1% *vs.* 42.1%, P=0.113), PP (9.4% *vs.* 8.1%, P=0.585), and WON (22.0% *vs.* 18.8%, P=0.321).

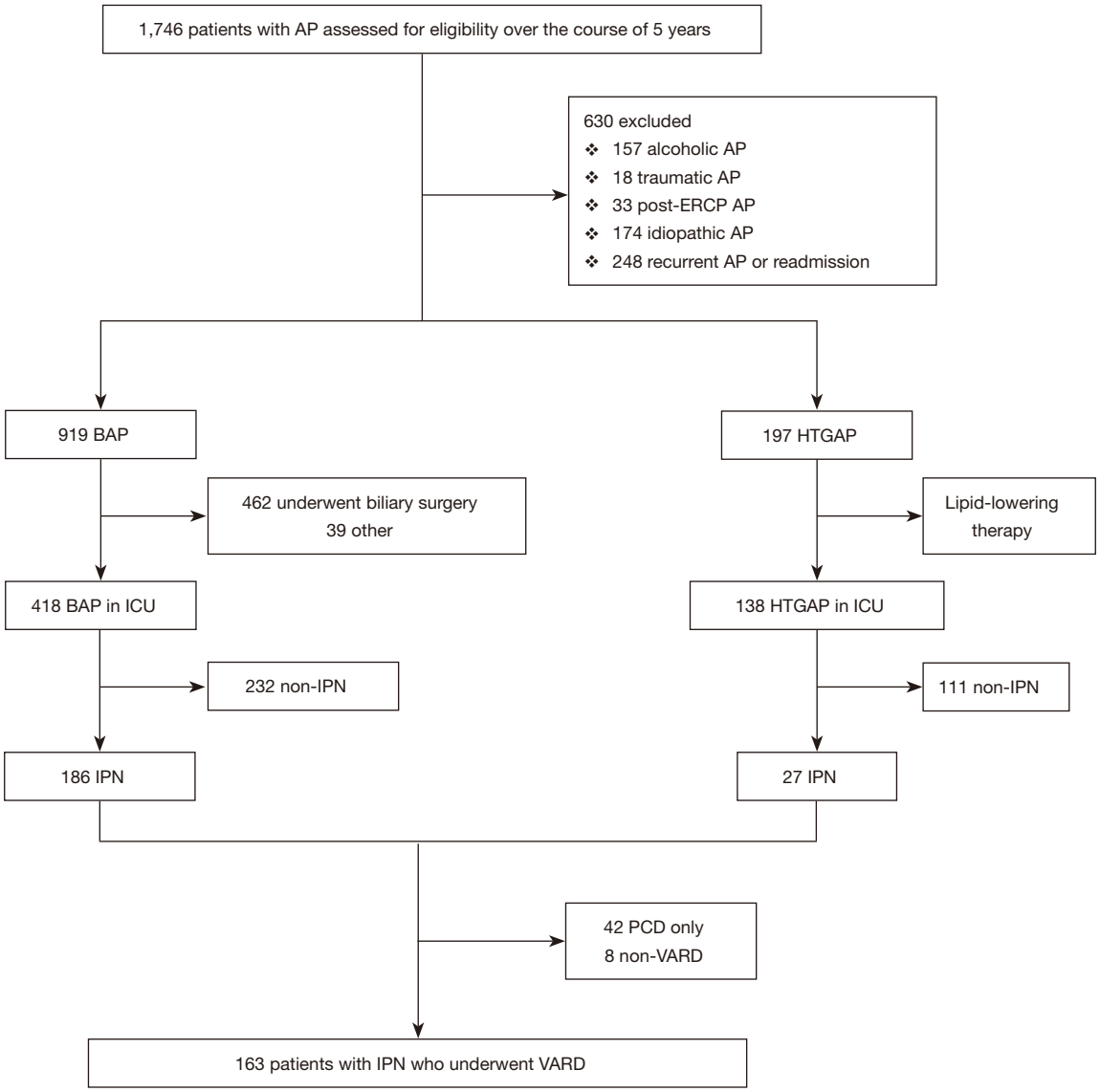

Figure 1 Trial profile. AP, acute pancreatitis; BAP, biliary acute pancreatitis; HTGAP, hypertriglyceridemic acute pancreatitis; ICU, intensive care unit; IPN, infected pancreatic necrosis; VARD, video-assisted retroperitoneal debridement; PCD, percutaneous catheter drainage.

Influential factors of IPN

We screened many variables, including gender, age, BMI, disease severity, etiologies, APACHE II scores, MODS, CRP levels, and so on. Univariate logistic regression analysis was carried out using the occurrence of IPN as the endpoint, and variables identified as meaningful were entered into multivariate regression. The primary results are shown in *Table 2*. Independent risk factors identified by the multivariate logistic analytic model (stepwise regression) included etiologies (OR: 20.358, 95% CI: 9.255 to 44.779, P<0.001), CRP levels (OR: 1.009, 95% CI: 1.001 to 1.016, P=0.025), APACHE II scores (OR: 1.837, 95% CI: 1.660 to 2.032, P<0.001), and MODS (1 *vs.* 0: OR: 31.873, 95% CI: 15.185 to 66.899, P<0.001, and MODS 2 *vs.* 0: OR: 47.982, 95% CI: 17.749 to 129.707, P<0.001). Adjusted ORs for IPN are shown in *Table 3*. We calculated the areas under the ROC curves and concluded that APACHE II scores and MODS have the highest value for predicting IPN, with areas under the curve of 0.886 and 0.787, respectively

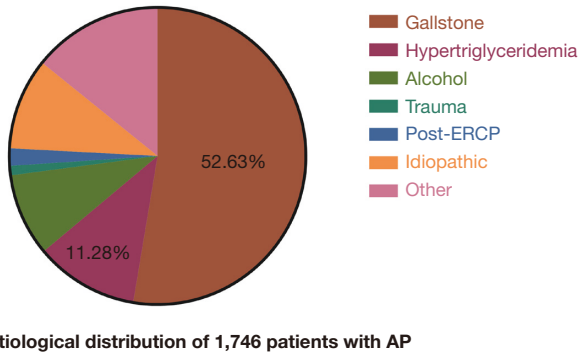

Figure 2 Etiological distribution. AP, acute pancreatitis; ERCP, endoscopic retrograde cholangiopancreatography.

(*Figure 3*). Among the 4 indicators, APACHE II scores had the highest sensitivity and specificity (*Table 4*).

Bacterial spectra

There were 158 pathogenic bacterial cultures among 213 surgeries, of which 138 (87.3%) were in the BAP group and 20 (12.7%) were in the HTGAP group. The most common bacterial strains were *Escherichia coli* (36 *vs.* 8, P=0.195), *Klebsiella pneumonia* (22 *vs.* 5, P=0.342), *Pseudomonas aeruginosa* (19 *vs.* 3, P=1.000), *Acinetobacter baumannii* (14 *vs.* 2, P=1.000), *Enterococcus* (14 *vs.* 1, P=1.000), and others (33 *vs.* 1, P=0.078). Drug resistance analysis showed that the gram-negative bacilli were susceptible to carbapenems. The resistance rates for all the antibiotic types in *K. pneumonia* exceeded 50%. The use of enzyme inhibitors significantly improved bacterial sensitivity to beta-lactams. The gram-positive bacteria were sensitive to vancomycin and tigecycline. No significant difference was shown in the bacterial spectrum between the two etiological groups, and the infections originated mostly from intestinal bacteria (*Table 5*).

Complications after surgery

The PCD was performed once IPN was confirmed or suspected. A total of 42 participants (19.7%) underwent PCD alone to alleviate their severe conditions, and VARD was not performed. Meanwhile, "one-step" VARD was performed in 13 participants who did not undergo PCD. In this study, more VARD surgeries (n=163) were carried out than endoscopic or open debridement, and the operation time was usually postponed until 4 weeks after onset (29.0 *vs.* 29.0 days, P=0.196). The most common systemic complications were bleeding (22.6% *vs.* 18.5%, P=0.634), enteral fistula (10.2% *vs.* 11.1%, P=1.000), pancreatic fistula (5.9% *vs.* 7.4%, P=1.000), ileus (4.3% *vs.* 3.7%, P=1.000), and portal venous thrombosis (1.1% *vs.* 3.7%, P=0.336). No difference was found in the median number of debridement procedures, although 6 surgeries were performed in 1 participant. Most non-surviving participants (n=5) had multiple organ failure (*Table 6*).

Discussion

With a mortality rate up to 32%, IPN develops in 33% of patients with SAP (20,21). Therefore, early, accurate prediction of IPN is crucial in determining what interventions should be taken, preventing or delaying severe complications, and reducing mortality. We identified 4 independent risk factors throughout a multivariate logistic analytic model (stepwise regression), including etiologies, CRP levels, APACHE II scores, and MODS, that were relevant to IPN. Among these factors, APACHE II scores and MODS had the highest predictive value (ROC area 0.8860 and 0.7873, respectively).

The APACHE II scores consist of acute physiology, age index, and chronic health evaluation. This scoring system is the gold standard for risk assessment of critically ill patients. A multivariate logistic regression analysis indicated that APACHE II within 24 h of admission was an independent risk factor for predicting IPN (OR: 4.77, P<0.001), which failed to clarify the predictive value and evaluation accuracy (22). In another study, the area under the curve (AUC) was 0.809 for predicting IPN and the cutoff value was 10.5, sensitivity was 90.9%, and specificity was 48.3% (23). Our study showed that according to the ROC curve analysis, the sensitivity was 99.1%, and the specificity was 66.0%. The Youden index was 0.651. Scoring can be accomplished after admission, unaffected by therapeutic factors, assessing the dynamic changes, and guiding better treatment. It was shown that MODS and IPN are the leading causes of death, and both are closely related. Multivariate analysis showed that early or preoperative MODS was relevant with postoperative IPN (24). Further study revealed that AP patients with persistent organ failure (>48 h) were more susceptible to develop IPN than those with transient organ failure (<48 h) (25,26). Our study found that HTGAP caused more damage than BAP to the circulatory, respiratory, and urinary systems (OR: 1.562, 95% CI: 0.642 to 3.631, P<0.001). The MODS was shown

Table 1 Baseline characteristics

Characteristics	BAP (n=919)	HTGAP (n=197)	P value
Age (year), median [IQR]	52.0 [39.0, 64.0]	40.0 [33.0, 52.0]	<0.001
Male gender, n (%)	518 (56.4)	154 (78.2)	<0.001
BMI (kg/m^2), mean ± SD	25.3±2.6	27.7±2.3	<0.001
Comorbidities, n (%)			
Cardiovascular disease	257 (28.0)	53 (26.9)	0.763
Pulmonary disease	74 (8.1)	16 (8.1)	0.974
Chronic renal insufficiency	37 (4.0)	6 (3.0)	0.516
Diabetes	101 (11.0)	24 (12.2)	0.630
CT severity index, median [IQR]	5 [4, 6]	6 [5, 7]	<0.001
Extent of pancreatic necrosis >50%, n (%)	239 (26.0)	57 (28.9)	0.398
Disease severity, n (%)			
SIRS	836 (91.0)	175 (88.8)	0.351
Admitted to the ICU	418 (45.5)	138 (70.1)	<0.001
Single-organ failure	294 (32.0)	65 (33.0)	0.784
Multiple-organ failure	175 (19.0)	52 (26.4)	0.020
Positive blood culture	248 (27.0)	67 (34.0)	0.047
APACHE II score, median [IQR]	7.00 [4.0, 9.0]	8.0 [6.0, 10.0]	<0.001
C-reactive protein (mg/L), median [IQR]	78.0 [59.0, 87.0]	111.0 [103.0, 130.0]	<0.001
White blood cell count (×10^9/L), mean ± SD	12.7±3.3	13.1±3.2	0.156
Time since onset of symptoms (days), mean ± SD	11.7±3.9	12.2±5.1	0.124
Antibiotics treatment, n (%)	634 (69.0)	128 (65.0)	0.272
Nutrition support, n (%)			
Enteral feeding only	349 (38.0)	79 (40.1)	0.578
Parental feeding only	83 (9.0)	18 (9.1)	0.963
Enteral and parental feeding	202 (22.0)	47 (23.9)	0.566
Oral diet	165 (18.0)	32 (16.2)	0.568
Severity (mild/moderate/severe), n (%)	469 (51.0)/156 (17.0)/294 (32.0)	55 (27.9)/40 (20.3)/102 (51.8)	<0.001
Local complications, n (%)			
APFC	239 (26.0)	61 (30.9)	0.155
ANC	332 (36.1)	83 (42.1)	0.113
PP	86 (9.4)	16 (8.1)	0.585
WON	202 (22.0)	37 (18.8)	0.321
IPN	186 (20.2)	27 (13.7)	0.034
Confirmed infected necrotic tissue, n (%)	165 (18.0)	20 (10.2)	<0.008

CT severity index scores range from 0 to 10, with higher scores indicating more extensive pancreatic necrosis and extrapancreatic collections. SIRS was defined according to the consensus-conference criteria of the American College of Chest Physicians and the Society of Critical Care Medicine. APACHE II scores range from 2 to 17, with higher scores indicating more severe disease. Organ failure was defined as a modified Marshall score ≥2 for the renal, respiratory, or cardiovascular system. ANC, acute necrotic collection; AP, acute pancreatitis; APACHE, Acute Physiology and Chronic Health Evaluation; APFC, acute peripancreatic fluid collection; BAP, biliary acute pancreatitis; BMI, body mass index; CT, computed tomography; HTGAP, hypertriglyceridemic acute pancreatitis; ICU, intensive care unit; IPN, infected pancreatic necrosis; IQR, interquartile range; PCD, percutaneous catheter drainage; PP, pancreatic pseudocyst; SD, standard deviation; SIRS, systemic inflammatory response syndrome; VARD, video-assisted retroperitoneal debridement; WON, walled-off necrosis.

Table 2 Influential factors of IPN

Variables	Univariate analysis		Multivariate analysis	
	OR (95 % CI)	P value	OR (95% CI)	P value
APACHE II	1.794 (1.652–1.949)	<0.001	1.837 (1.660–2.032)	<0.001
Etiology (Ref. = HTGAP)	1.598 (1.032–2.473)	0.036	20.358 (9.255–44.779)	<0.001
MODS				
1 *vs.* 0	21.604 (11.547–40.421)	0.227	31.873 (15.185–66.899)	<0.001
2 *vs.* 0	54.467 (26.190–113.274)	0.168	47.982 (17.749–129.707)	<0.001
CRP	1.007 (1.002–1.011)	0.002	1.009 (1.001–1.016)	0.025

1: single-organ failure; 2: multiple-organ failure. APACHE, Acute Physiology and Chronic Health Evaluation; CI, confidence interval; CRP, C-reactive protein; HTGAP, hypertriglyceridemic acute pancreatitis; IPN, infected pancreatic necrosis; MODS, multiple organ dysfunction syndrome; OR, odds ratio.

Table 3 Adjusted OR of IPN

Variables	OR	95% CI	P value
APACHE II	1.837	1.660–2.032	<0.001
MODS 0 *vs.* 1	31.873	15.185–66.899	<0.001
MODS 0 *vs.* 2	47.982	17.749–129.707	<0.001
Etiology 2 *vs.* 1	20.358	9.255–44.779	<0.001
CRP	1.009	1.001–1.016	0.025

APACHE, Acute Physiology and Chronic Health Evaluation; CI, confidence interval; CRP, C-reactive protein; IPN, infected pancreatic necrosis; MODS, multiple organ dysfunction syndrome; OR, odds ratio.

to have a higher predictive value, but the relationship between the types and duration of organ failure and IPN requires further investigation.

For BAP patients, the purported mechanisms underlying the relatively more common IPN occurrence (OR: 1.598, 95% CI: 1.027 to 2.451, P=0.034) were transient or sustained occlusion of the pancreatic duct leading to an increase in intraductal pressure and bile reflux into the pancreatic duct (27). Decreased mucosal integrity increases gut permeability, reduces gut motility, and increases the risk of bacterial translocation. The CRP level is a strong indicator of the degree of inflammation in SIRS patients (28), which may relate to the higher CRP levels in HTGAP than in BAP patients. According to the report, the AUC of CRP for predicting IPN was 0.68, cutoff value ≥430 mg/L, sensitivity was 40%, and specificity was 100% (29). Our study showed that the AUC was 0.5968 with relatively low specificity. The CRP is a non-specific acute phase protein, and other acute inflammatory diseases can also elevate it. Therefore, patients with high APACHE II scores and severe organ failure were the most dangerous. If it is a BAP and CRP continues to increase, the probability of IPN was higher. A combination of APACHE II scores, MODS, etiologies, and CRP can significantly improve predictive accuracy.

As for clinical characteristics of patients, our study showed that HTGAP accounted for 11.3% of all cases of AP, and the proportion of SAP was higher in the HTGAP group than in the BAP group (52% *vs.* 32%), indicating that HTGAP may lead to relatively more pancreatic microcirculation disorders. According to the demographic analysis, BAP is relatively more common in women (58%), which is related to the lower obesity rate among females compared with males. With regard to the age distribution, HTGAP was more common in the younger population (under 40 years of age) than in the elderly (71% *vs.* 29%). This result may reflect that hypertriglyceridemia is more common in young adults. Although the precise mechanism underlying HTGAP is not fully understood, an excess of free fatty acids (FFAs) and elevated chylomicron levels are

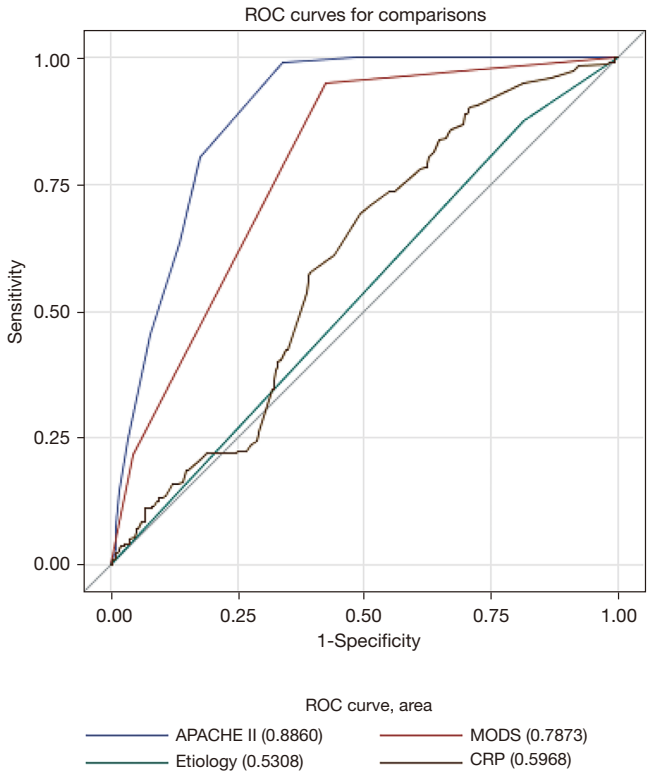

Figure 3 ROC curves of influential factors. ROC, receiver operating characteristic; APACHE, Acute Physiology and Chronic Health Evaluation; MODS, multiple organ dysfunction syndrome.

thought to increase the plasma viscosity, which may cause ischemia in the pancreas and trigger inflammation (30).

Most patients with IPN are in hypermetabolic state and extremely weak. The mucosal integrity of the gastrointestinal tract decreases, leading to an increase in gut permeability and subsequent bacterial overgrowth (31). The combined factors increase the possibility of bacterial translocation and infected necrosis. The dominant source of infection was intestinal bacteria, which confirmed this theory. When a culture-proven infection is verified, or the infection is strongly suspected, antibiotics should be used. Under this circumstance, the primary clinical manifestations are the gas collection, bacteremia, sepsis, or worsening of illness. Broad-spectrum antibiotics should be prioritized for penetrating necrosis, including carbapenems, quinolones, and metronidazole (32).

For patients with IPN, PCD undoubtedly provides a direct and effective means for controlling the infection source. The "PANTER" trial showed that 35% of patients did not need further intervention following such treatment (33). In two randomized controlled trials (RCTs) comparing various drainage approaches, it was demonstrated that PCD alone was successful in 35% and 51% of patients. In our study, 19.7% of the participants (9 in the BAP group and 4 in the HTGAP group) underwent

Table 4 ROC curves for IPN

Variables	AUC area	95% CI		P value	Cutpoint, IPN ("1")	Youden index
APACHE II	0.886	0.867	0.905	<0.001	8 (0.157)	0.651
MODS	0.787	0.762	0.812	<0.001	1 (0.256)	0.525
Etiology	0.531	0.505	0.557	0.036	1 (0.182)	0.197
CRP	0.597	0.559	0.635	<0.001	80 (0.182)	0.197

1: IPN occur. APACHE, Acute Physiology and Chronic Health Evaluation; AUC, area under the curve; CRP, C-reactive protein; IPN, infected pancreatic necrosis; MODS, multiple organ dysfunction syndrome; ROC, receiver operating characteristic.

Table 5 Bacterial spectra

Bacterial spectra	BAP (n=138), n (%)	HGAP (n=20), n (%)	P value
Escherichia coli	36 (26.1)	8 (40.0)	0.195
Klebsiella pneumonia	22 (15.9)	5 (25.0)	0.342
Pseudomonas aeruginosa	19 (13.8)	3 (15.0)	1.000
Acinetobacter baumannii	14 (10.1)	2 (10.0)	1.000
Enterococcus	14 (10.1)	1 (5.0)	1.000
Others	33 (23.9)	1 (5.0)	0.078

BAP, biliary acute pancreatitis; HTGAP, hypertriglyceridemic acute pancreatitis.

Table 6 Postoperative complications

Operative outcomes (n=213)	BAP (n=186)	HTGAP (n=27)	P value
Surgery, n (%)			
PCD	186 (100.0)	25 (92.6)	0.016
VARD	143 (76.9)	20 (74.1)	0.748
Debridements	1 [1.3,1.5]	1 [1.0,1.7]	0.448
Complications after surgery, n (%)			
Bleeding	42 (22.6)	5 (18.5)	0.634
Enteral fistula	19 (10.2)	3 (11.1)	1.000
Pancreatic fistula	11 (5.9)	2 (7.4)	1.000
Intestinal obstruction	8 (4.3)	1 (3.7)	1.000
Portal venous thrombosis	2 (1.1)	1 (3.7)	0.336
Operation time since onset (days), median [IQR]	29.0 [27.9, 29.4]	29.0 [27.8, 30.5]	0.196
Mortality, n (%)	5 (2.7)	2 (7.4)	0.487

BAP, biliary acute pancreatitis; HTGAP, hypertriglyceridemic acute pancreatitis; IQR, interquartile range; PCD, percutaneous catheter drainage; VARD, video-assisted retroperitoneal debridement.

the "one-step" method without PCD (34). Another evident advantage of the use of PCD is that other minimally invasive debridement methods can utilize the catheter tract as an entry portal.

Extensive studies have confirmed that early debridement (first 2 weeks) is associated with higher morbidity and mortality. Delayed procedure (after 4 weeks) should be the best strategy when the peripancreatic collection is well walled-off and has an evident indication (35). Minimally invasive surgical techniques, including VARD, laparoscopic transgastric debridement, and open transgastric debridement, are feasible and practical. The features of the disease and multidisciplinary discussion determine the choice of approach. Laparoscopic-guided VARD is most commonly performed in our center due to its evident advantages (e.g., widened field of vision, easy bleeding control, available equipment). The "TENSION" trial proved that the endoscopic step-up approach was not superior to the surgical step-up method in decreasing major complications and death. In the endoscopic group, the rate of pancreatic fistulas and length of hospitalization were relatively lower (36). Either endoscopic or surgical intervention should be selected according to individual clinical characteristics. Minimally invasive interventions were not shown to aggravate the severity of trauma in patients who were already in a fragile condition. Trauma control can maximize the improvement in prognosis.

Several limitations existed in this study. As a single-center retrospective study, these results represent regional clinical characteristics. Prediction for IPN is a challenging task involving clinical, laboratory, imaging indicators, and a scoring system. After admission, patients with SAP should be diagnosed under multidisciplinary team (MDT) discussion as soon as possible. In the early stage, doctors should focus on controlling the systemic inflammatory response and organ function protection. Once IPN occurs, PCD and minimally invasive surgery should be arranged after 4 weeks. Laparoscopy or endoscopy can be the first choice for debridement, but it should be carefully selected according to the location of necrosis and surgical conditions. The best effect can be achieved only by individualized treatment on the basis of principles.

Conclusions

In our study, BAP developed into IPN more frequently than did HTGAP. Etiologies, APACHE II scores, MODS, and CRP levels contributed to predicting IPN. The APACHE II scores had the highest sensitivity and specificity. Our study presents a new method of predicting IPN in the late stage. Laparoscopic-guided VARD had advantages in specific cases. The implementation of reasonable management leads

to improved prognosis.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of the Xuanwu Hospital (No. [2017]036). Individual consent for this retrospective analysis was waived.

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