

## Retrospective Study

# Clinical impact of preoperative acute pancreatitis in patients who undergo pancreaticoduodenectomy for periampullary tumors

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## Abstract

**AIM:** To investigate the impact of preoperative acute pancreatitis (PAP) on the surgical management of periampullary tumors.

**METHODS:** Fifty-eight patients with periampullary tumors and PAP were retrospectively analyzed. Thirty-four patients who underwent pancreaticoduodenectomy (PD) and 4 patients who underwent total pancreatectomy were compared with a control group of 145 patients without PAP during the same period.

**RESULTS:** The preoperative waiting time was significantly shorter for the concomitant PAP patients who underwent a resection (22.4 d vs 54.6 d,  $P < 0.001$ ) compared to those who did not. The presence of PAP significantly increased the rate of severe complications (Clavien grade 3 or higher) (17.6% vs 4.8%,  $P = 0.019$ ) and lengthened the hospital stay (19.5 d vs 14.5 d,  $P = 0.006$ ). A multivariate logistic regression analysis revealed that PAP was an independent risk factor for postoperative pancreatic fistula (OR = 2.91; 95%CI: 1.10-7.68;  $P = 0.032$ ) and severe complications (OR = 4.70; 95%CI: 1.48-14.96;  $P = 0.009$ ) after PD. There was no perioperative mortality.

**CONCLUSION:** PAP significantly increases the incidence of severe complications and lengthens the

hospital stay following PD. PD could be safely performed in highly selective patients with PAP.

**Key words:** Pancreaticoduodenectomy; Complications; Preoperative pancreatitis; Pancreatic fistula

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**Core tip:** To date, it remains unclear how preoperative acute pancreatitis (PAP) affects the surgical management of perampullary tumors. We analyzed patients with perampullary tumors and concomitant PAP who were treated in a high-volume center. In the present study, we showed that PAP delays the resection of perampullary tumors and significantly increases the incidence of severe complications and lengthens the hospital stay following pancreaticoduodenectomy (PD). The study results suggest that PD could be safely performed in highly selective patients with PAP.

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## INTRODUCTION

There are a large number of etiological factors involved in the development of acute pancreatitis (AP). Excluding common etiologies, such as alcohol and gallstones, it is well known that AP may occur in association with a perampullary neoplasm, which is increasingly being recognized, especially in individuals with idiopathic AP<sup>[1-3]</sup>. Furthermore, post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis is the most common cause of preoperative acute pancreatitis (PAP)<sup>[4]</sup>.

Generally, perampullary tumor patients with AP should initially be managed conservatively<sup>[5]</sup>. However, surgical resection is the sole curative measure for pancreatic cancer, and conservative treatments can significantly delay the need for the cancer operation<sup>[1]</sup>. Therefore, a dilemma arises: Can an operation successfully be performed in a patient with perampullary tumors with AP?

We analyzed patients with perampullary tumors and concomitant PAP who were treated in a high-volume center and assessed the impact of PAP on the surgical management of the perampullary tumors.

## MATERIALS AND METHODS

We performed a retrospective analysis of patients from our database with perampullary tumors and concomitant PAP at the Pancreatic Surgery Center of

West China Hospital between January 1, 2009 and December 31, 2013. This study followed the ethical guidelines of the Helsinki Declaration of 1975 (revised in 1983). The data on the patient demographics, severity of the pancreatitis, tumor stage, applied treatments, and morbidity and mortality rates were analyzed retrospectively using a prospective pancreatic database. Additional information was obtained by contacting the referring physician/hospital. The data were extracted from medical records by 2 reviewers who were blinded to the case-control status. The two reviewers independently assessed these data, and disagreements were resolved by discussion with a third reviewer. The tumor staging and lymph node status evaluation were performed based on the pathological findings.

The diagnosis of AP<sup>[6,7]</sup> was made based on the clinical symptoms (new onset or increased abdominal pain that necessitated an unplanned admission of an outpatient for more than one night or prolonged hospitalization of an inpatient), biochemical analyses (3 times the upper limit of the normal value or a significant elevation of the serum amylase and/or lipase concentrations), as well as contrast-enhanced abdominal computed tomography (CT) and/or endoscopic ultrasonography (EUS)-guided fine needle aspiration (FNA) when necessary. As controls, during the same period, consecutive patients with pancreatic and perampullary disease who did not have AP but underwent PD were also included in the study. We screened patients who had no evidence of distant metastasis or local vascular involvement (which was defined as a tumor surrounding the portal or mesenteric vessels for more than 180 degrees of their circumference or an irregular vessel margin) on a CT and/or magnetic resonance imaging (MRI) scan<sup>[8]</sup>. The interval between the CT and/or MRI examination and admission was set at less than one week. Patients with a serious coexisting illness, active bleeding, ongoing cholangitis, distant metastasis, local vascular involvement or previous preoperative biliary drainage beyond 2 wk were subsequently excluded. Patients with concomitant cholangitis or a pancreatitis episode after an ERCP were included.

From this database, we identified 58 patients with perampullary tumors and concomitant PAP. During the preoperative period, all of the patients were hospitalized and received conservative medical treatment until they were deemed operable. None of the patients required percutaneous radiological or surgical drainage prior to the tumor resection. All of the patients underwent CT and/or MRI prior to the operation, and their resectability was redetermined based on these tests. All of the patients who underwent PD were divided into two groups, which consisted of a "non-AP" group (145 patients who did not have AP) and an "AP" group (34 patients with clinical PAP).

### Definition of postoperative complications

General and surgery-related complications, including postoperative pancreatic fistula (POPF), delayed gastric emptying, intra-abdominal infection, abdominal

**Table 1** Distribution of acute pancreatitis patients who had surgery for a planned laparotomy *n* (%)

Parameter	Resected ( <i>n</i> = 38)	Not resected ( <i>n</i> = 20)	<i>P</i> value
Age (yr), mean ± SD	55.92 ± 11.01	20.8 ± 12.18	0.11
Male	16 (57.1)	16 (80)	0.098
Cause of acute pancreatitis			0.049
ERCP	10 (26.3)	1 (5)	
Unknown	28 (73.7)	19 (95)	
Balthazar CT score	2.05 ± 0.70	2.9 ± 0.85	< 0.001
Grade of severity			0.283
Mild acute pancreatitis	12 (35.3)	6 (30)	
Moderately severe acute pancreatitis	19 (55.9)	9 (45)	
Severe acute pancreatitis	3 (8.8)	5 (25)	
Time to surgery (d), mean ± SD	22.3 ± 17.0	54.6 ± 26.3	< 0.001
Type of operation			
Pancreaticoduodenectomy	34 (89.5)		
Total pancreatectomy	4 (10.5)		
Bypass procedure		7 (35)	
Exploratory laparotomy		13 (65)	

ERCP: Endoscopic retrograde cholangiopancreatography; CT: Computed tomography.

abscess formation, pneumonia, postpancreatectomy hemorrhage, and anastomotic leakage, were analyzed retrospectively using a prospective pancreatic database. The complications, including POPF<sup>[9]</sup>, delayed gastric emptying<sup>[10]</sup>, and postpancreatectomy hemorrhage<sup>[11]</sup>, were defined by standards adopted by the International Study Group of Pancreatic Surgery. The postoperative complications were recorded and graded according to the Clavien classification<sup>[12]</sup>. Severe complications were defined in this study as conditions that were grade 3 or higher based on the Clavien classification<sup>[12]</sup>. The in-hospital death of a patient for any reason was recorded.

### Statistical analysis

All of the data were collected and analyzed using the SPSS statistical program for Windows, Version 13.0 (SPSS Inc., Chicago, United States). The patient demographic and clinical characteristics across the groups were compared using the  $\chi^2$  test (or Fisher's exact test) for the categorical measures and using the *t*-test for the continuous data. Factors with *P* < 0.10 were included in the multivariate analysis. A multivariable analysis of the primary outcomes was completed using logistic regression. The final multivariate model was determined using logistic regression with backward selection in order to identify independent predictors of POPF. *P*-values less than 0.05 were considered statistically significant. The logistic model results are reported as odds ratios (ORs), two-sided 95% confidence intervals (CIs), and *P*-values.

## RESULTS

### Characteristics of the patients with periampullary tumors and concomitant PAP

Fifteen-eight patients underwent surgery. Of these,

20 (34.5%) patients were considered to have either a non-resectable pancreatic lesion or metastasis, including the following: encasement of major vessels (*i.e.*, the portal vein, superior mesenteric vessels, and vena cava) in 8 (40%) patients; presence of distant metastases in 9 (45%); and presence of distant nodal metastases in 3 (15%). A gastroenteric bypass procedure was the surgical intervention in 7 patients. Thirteen-eight (65.5%) patients were found to have lesions considered to be resectable for cure during surgery. The PD procedure was performed in 34 (58.7%) patients, and a total pancreatectomy was performed in 4 (6.9%).

The patients' characteristics are summarized in Table 1. The age and gender distribution were similar for the patients who did and did not undergo resection. Moreover, the cause of the AP and the grades of severity were comparable between the two groups. There were significantly lower Balthazar CT scores in the patients who underwent resection (mean 2.05 vs 2.9, *P* < 0.001). The preoperative waiting time was significantly shorter for the patients who underwent resection (mean 22.4 d vs 54.6 d, *P* < 0.001). The presence of neoplasms and AP was confirmed pathologically in all of the cases. A frozen section analysis of the pancreatic margin was obtained in all of the patients in whom a pancreaticojejunostomy was performed. Although all of the pancreatic resection margins were devoid of tumor and necrosis, microscopic signs of acute/subacute inflammation were noted to some degree in all of the patients.

### Demographic and intraoperative PD data

The data for the patients in each study arm are presented in Table 2. The majority of the variables did not significantly differ between the AP and non-AP groups. The mean difference between the groups in the delay to surgery was 12.4 d: the delay was 6.0 d in the AP group vs 18.4 d in the non-AP group (*P* < 0.001). After the resection, the incidence of tumor-positive lymph nodes (N1) was significantly higher in the AP group (53.3% in the AP group vs 30.2% in the non-AP group, *P* = 0.017).

### Postoperative PD data

The details of the postoperative data from the PD patients are summarized in Table 3. Complications occurred in 38% of patients in the study. Among the entire patient population, the POPF rate was 15.1% (*n* = 27). The overall incidence of POPF was significantly higher in the AP group (29.4% in the AP group vs 11.7% in the non-AP group, *P* = 0.009). Moreover, a statistical comparison of the subsets showed that there were significantly more cases of grades B and C POPF (AP vs non-AP: 20.6% vs 6.2%, *P* = 0.015) in the AP group compared to the non-AP group. There were no substantial differences in the overall complications or mortality between the two groups. However, the rate of severe complications (Clavien

**Table 2** Demographic data, operation and pathologic characteristics of pancreaticoduodenectomy patients *n* (%)

Parameter	AP ( <i>n</i> = 34)	Control ( <i>n</i> = 145)	<i>P</i> value
Patient variables			
Age (yr), mean ± SD	55.9 ± 11.26	59.0 ± 10.92	0.131
Male	21 (61.8)	93 (64.1)	0.796
Weight loss	17 (50)	59 (40.7)	0.323
Comorbid disease	9 (26.5)	47 (32.4)	0.501
Preoperative jaundice	11 (32.4)	68 (43.9)	0.124
Pancreas remnant (soft)	29 (85.3)	109 (75.2)	0.206
Pancreatic duct diameter (< 3 mm)	22 (64.7)	92 (63.4)	0.891
Treatment variables			
Preoperative biliary drainage	6 (17.6)	11 (7.6)	0.099
Time to surgery (d), mean ± SD	18.4 ± 10.76	6.0 ± 2.5	< 0.001
Intraoperative blood transfusion	11 (32.4)	62 (35.9)	0.700
Vein resection	1 (2.9)	7 (4.8)	0.632
Pathological variables			
Characteristics of resectable tumors			0.062
Pancreatic carcinoma	21 (61.8)	58 (40)	
Ampullary carcinoma	4 (11.8)	19 (13.1)	
Duodenal carcinoma	2 (5.9)	35 (24.1)	
Distal bile duct carcinoma	3 (8.8)	18 (12.4)	
Other diagnosis	4 (11.8)	15 (10.3)	
Benign: malignant ratio	4/30	130/15	1.000
Tumor-positive lymph nodes (N1)	16 (53.3)	39 (30.2)	0.017
Microscopically residual disease (R1)	1 (2.9)	2 (1.4)	0.523

grades 3 to 5) was significantly higher in the AP group (17.6%) than in the non-AP group (4.8%; *P* = 0.019). The incidences of intra-abdominal abscess, postpancreatectomy hemorrhage and intestinal fistula were also significantly higher in the patients with PAP than in the patients without. There were no significant differences between the two groups in regards to the incidences of other postoperative complications, such as delayed gastric emptying, bile leakage, and pulmonary complications. The mean hospital stay for the patients with PAP was longer than for that the control group (mean 17.4 d for the AP group vs 13.7 d for the non-AP group, *P* = 0.006).

### Risk factors influencing POPF

Univariate and multivariate analyses were used to reveal the risk factors influencing POPF after PD. As shown in Table 4, four factors were extracted as being useful for discriminating between the patients with and without POPF after PD. A multivariate logistic regression analysis revealed that the most powerful predictor was the pancreatic remnant texture. Patients with soft pancreatic remnants had a much higher likelihood of developing POPF than those with firm pancreatic remnants (OR = 9.82, 95%CI: 1.22-79.31; *P* = 0.032). We observed a much higher likelihood of developing POPF in the patients who presented with AP (OR = 2.91, 95%CI: 1.10-7.68; *P* = 0.032). Finally, there was a greater risk of developing POPF in the patients with intraoperative blood transfusion and preoperative biliary drainage requirements (OR = 2.69,

**Table 3** Postoperative data of pancreaticoduodenectomy patients *n* (%)

Parameter	AP ( <i>n</i> = 34)	Control ( <i>n</i> = 145)	<i>P</i> value
Medical complications	15 (44.1)	53 (36.6)	0.413
Grade of complications			0.086
0-1	24	116	
2	5	22	
3	4	4	
4	2	3	
5 Mortality	0	0	
Severe complications (grade 3 or more)	6 (17.6)	7 (4.8)	0.019
Pancreatic fistula	10 (29.4)	17 (11.7)	0.009
Grade A	3 (8.8)	8 (5.5)	
Grade B	2 (5.9)	7 (4.8)	
Grade C	5 (14.7)	2 (1.8)	
Grade B/C	7 (20.6)	9 (6.2)	0.015
Biliary leak	1 (2.9)	1 (0.7)	0.345
Delayed gastric emptying	10 (29.4)	28 (19.3)	0.195
Intra-abdominal collection or abscess	7 (20.6)	8 (5.5)	0.010
Hemorrhage after pancreatectomy	5 (14.7)	4 (2.8)	0.013
Gastrointestinal hemorrhage	3 (8.8)	2 (1.4)	0.048
Intra-abdominal hemorrhage	1 (2.9)	2 (1.4)	0.471
Wound infection	8 (23.5)	18 (12.4)	0.098
Intestinal fistula	2 (5.9)	0	0.035
Septicemia	1 (2.9)	5 (3.4)	1.000
Pulmonary complications	5 (14.7)	16 (11)	0.557
Postoperative length of stay (d), mean ± SD	17.4 ± 9.8	13.7 ± 6.1	0.006

95%CI: 1.08-6.71, *P* = 0.034; OR = 3.40, 95%CI: 1.05-10.99; *P* = 0.041, respectively).

### Risk factors influencing severe postoperative complications

Univariate and multivariate analyses were used to reveal the risk factors influencing severe postoperative complications (grade 3 or higher) after PD (including 4 cases in TP from the AP group). Table 5 shows the results of 9 parameters that were univariately examined as potential risk factors for 15 patients with severe postoperative complications (grade 3 or higher) after PD vs 168 patients without. Three factors were extracted as being useful for discriminating between the patients with and without severe postoperative complications: preoperative AP (OR = 4.70, 95%CI: 1.48-14.96; *P* = 0.009), comorbid disease (OR = 3.72, 95%CI: 1.18-11.75; *P* = 0.025) and intraoperative blood transfusion (OR = 3.50, 95%CI: 1.11-10.97 *P* = 0.032). The most powerful predictor was preoperative AP (OR = 4.70, 95%CI: 1.48-14.96; *P* = 0.009).

## DISCUSSION

This retrospective analysis was performed using data from 58 consecutive patients with periampullary tumors and concomitant PAP from January 2009 to December 2013. The preoperative waiting time was significantly shorter for the patients who underwent resection (22.4 d vs 54.6 d, *P* < 0.001) compared to those who did not. In the present study, 183 consecutive patients

**Table 4 Risk factors influencing pancreatic fistula after pancreaticoduodenectomy by univariate and multivariate logistic regression analyses**

Parameter	Univariate <sup>1</sup>		Multivariate <sup>1</sup>	
	OR (95%CI)	P value	OR (95%CI)	P value
Age ( $\geq 70$ yr <i>vs</i> $< 70$ yr)	0.74 (0.24-2.30)	0.738		
Sex (male <i>vs</i> female)	0.57 (0.23-1.43)	0.228		
Weight loss (yes <i>vs</i> no)	1.10 (0.48-2.51)	0.821		
Preoperative jaundice (yes <i>vs</i> no)	1.55 (0.64-3.76)	0.334		
Acute pancreatitis (yes <i>vs</i> no)	3.14 (1.28-7.67)	0.012	2.91 (1.10-7.68)	0.032
Blood transfusion (yes <i>vs</i> no)	1.23 (0.53-2.81)	0.632		
Comorbid disease (yes <i>vs</i> no)	1.36 (0.58-3.19)	0.485		
Preoperative biliary drainage (yes <i>vs</i> no)	4.97 (1.70-14.54)	0.003	3.40 (1.05-10.99)	0.041
Intraoperative blood transfusion (yes <i>vs</i> no)	2.28 (0.99-5.24)	0.052	2.69 (1.08-6.71)	0.034
Histopathologic diagnosis		0.090		NS
Pancreatic carcinoma	1.0			
Ampullary carcinoma	1.86 (0.53-6.53)	0.333		
Duodenal carcinoma	2.54 (0.83-7.73)	0.022		
Distal bile duct carcinoma	3.83 (1.28-11.45)	0.016		
Pancreatic texture (soft <i>vs</i> hard)	9.29 (1.22-70.68)	0.031	9.82 (1.22-79.31)	0.032
Pancreatic duct ( $< 3$ mm <i>vs</i> $\geq 3$ mm)	2.22 (0.85-5.82)	0.105		

<sup>1</sup>Logistic regression. NS: Not significant.**Table 5 Risk factors influencing severe complications after pancreaticoduodenectomy by univariate and multivariate logistic regression analyses**

Parameter	Univariate <sup>1</sup>		Multivariate <sup>1</sup>	
	OR (95%CI)	P value	OR (95%CI)	P value
Age ( $\geq 70$ yr <i>vs</i> $< 70$ yr)	0.68 (0.15-3.17)	0.623		
Sex (male <i>vs</i> female)	2.46 (0.67-9.06)	0.175		
Weight loss (yes <i>vs</i> no)	1.14 (0.40-3.28)	0.810		
Preoperative jaundice (yes <i>vs</i> no)	0.85 (0.29-2.49)	0.762		
Preoperative acute pancreatitis (yes <i>vs</i> no)	3.87 (1.30-11.46)	0.015	4.70 (1.48-14.96)	0.009
Preoperative biliary drainage (yes <i>vs</i> no)	2.55 (0.65-10.1)	0.181		
Comorbid disease (yes <i>vs</i> no)	2.78 (0.95-8.07)	0.061	3.72 (1.18-11.75)	0.025
Intraoperative blood transfusion (yes <i>vs</i> no)	2.92 (0.99-8.61)	0.052	3.50 (1.11-10.97)	0.032
Histology (pancreatic <i>vs</i> other)	0.74 (0.26-2.13)	0.578		

<sup>1</sup>Logistic regression. NS: Not significant.

underwent PD following our standard protocol of digestive reconstruction<sup>[13]</sup>. After the resection, the incidence of tumor-positive lymph nodes (N1) was significantly higher in the AP group (53.3% *vs* 30.2%,  $P = 0.017$ ). There was a significant difference in the frequency of overall POPF between the AP and non-AP groups (29.4% *vs* 11.7%,  $P = 0.009$ ). Moreover, the frequency of severe complications (Clavien grade 3 or higher) in the AP group was significantly higher than that in the non-AP group (17.6% *vs* 4.8%,  $P = 0.019$ ). The development of preoperative AP has been recognized as an important risk factor for both POPF and severe complications (Clavien grade 3 or higher) after PD.

When considered in connection with periampullary tumors, PAP may considerably influence the patient's management<sup>[5]</sup>. There is often an immediate and lasting inflammatory response that may induce pancreatic or fatty necrosis and other fluid collection. The resulting adhesion between the parenchyma of the pancreas and the peripancreatic tissues can blur tissue boundaries,

making the surgical procedure more difficult. As a result, the association that exists should initially be managed conservatively. In contrast, surgical resection is the sole curative measure for periampullary tumors. A prolonged delay in surgery may result in a missed opportunity for radical resection of malignancies, especially pancreatic adenocarcinoma, which is generally a very aggressive, fast growing tumor<sup>[1]</sup>. Therefore, a dilemma arises: Can an operation successfully be performed in a patient with periampullary tumors in the setting of AP?

The management decisions related to patients requiring PD following AP include (1) determining the timing of the operation; (2) maximizing the curability of any surgical resection; and (3) avoiding complications, such as POPF and intra-abdominal infections. In our cohort, the mean interval from the diagnosis of AP to the operation was 33.4 d in our 58 cases. This is consistent with the report by Erkan *et al*<sup>[5]</sup>, in which the median interval from the diagnosis of AP to the operation was 34 d in four patients with periampullary tumors followed by mild to moderate AP

who underwent PD, while the median time was 31 d in six patients who underwent TP. In contrast, the median time was 111 d in six patients with periampullary tumors followed by severe AP who underwent PD<sup>[4]</sup>. According to Tummala's<sup>[2]</sup> study of 218 patients with AP who underwent endoscopic ultrasound-guided FNA, 38 pancreatic cancer cases were diagnosed, and their resection rate was 39%. This is consistent with the report by Mujica *et al.*<sup>[1]</sup>, with a curative resection rate of 27%. In contrast, the number of patients found to have a lesion considered to be resectable for cure at the time of surgery was more than 50% in our series (resection rate, 38 of the 58 cases, 65.5%). This finding may account for the timely operation (mean 18.4 d) or the pathological entity, with only 61.8% of pancreatic carcinoma cases, leading to a delay in the resection of these tumors with a lower resection rate. After resection, the incidence of tumor-positive lymph nodes (N1) was significantly higher in the AP group. This finding may account for a longer delay in surgery, leading to the delayed resection of these tumors with a greater number of tumor-positive lymph nodes (N1). Moreover, in the mouse model, AP can accelerate the initiation and progression to pancreatic cancer<sup>[14,15]</sup>. Therefore, a timely diagnosis and the proper treatment of pancreatic cancer with AP may potentially reduce the morbidity and complications and may likely also improve the oncological outcomes<sup>[1,2]</sup>.

In the present study, the PAP and pancreatic texture have been recognized as important risk factors for POPF. It is clear that the pancreatic texture is a major contributing factor, especially when trying to perform a fine duct to mucosa anastomosis on a soft pancreatic remnant. A soft pancreas is very vulnerable to ischemia and actively produces exocrine secretions<sup>[16]</sup>. Patients with PAP generally have a softer/fragile pancreatic texture. In 4 cases from the AP group, the texture of the gland was not suitable (*e.g.*, fragile pancreas due to inflammation) for a safe pancreaticojejunostomy; therefore, the procedure was converted from PD to TP during the surgery. Conversely, in 34 patients, the texture of the pancreas appeared to be safe for an anastomosis. The frozen section analysis of the resection margins of these 34 patients showed varying degrees of inflammation but no necrosis. Erkan *et al.*<sup>[5]</sup> demonstrated that the intraoperative findings of the pancreatic texture determine whether or not a pancreaticojejunostomy should be performed. It could also be theorized that the pancreatic duct diameter might contribute to POPF formation. Our data indicate no difference in the pancreatic duct diameter between the two cohorts. This finding may account for the fact that patients with PAP generally have a softer/fragile pancreatic texture, although they have a large pancreatic duct diameter.

The occurrence of preoperative AP was clarified to be the independent risk factor for severe complications after PD. Two previous studies reported that the occurrence of preoperative AP significantly increased the postoperative

complications, including pancreatic fistula<sup>[4,5]</sup>. In our present study, preoperative AP significantly increased the occurrence of POPF, postpancreatectomy hemorrhage and intra-abdominal infection. The increased postpancreatectomy hemorrhage rate in the AP group compared to the controls indicates that recent pancreatic inflammation may increase the postoperative bleeding in general<sup>[5]</sup>. Many pancreatic surgeons believe that postpancreatectomy hemorrhage after PD is a secondary effect caused by POPF or intra-abdominal abscess<sup>[17,18]</sup>.

Nevertheless, the presence of PAP increased the severe complications and extended the hospitalization time, but there was no mortality. This rate was well within the range seen in previous studies in the literature, where POPF rates ranged from 10% to 28.5%<sup>[19]</sup>, and severe postpancreatectomy hemorrhage rates from 5.8% to 9.2%<sup>[18,20]</sup>. Patients with PAP can be managed conservatively until the timely operation. Therefore, PD may be safely performed in highly selective patients with PAP, although the absence of necrosis or inflammation at the pancreatic resection margin should be evaluated in a larger group of patients to assess its value in predicting anastomotic insufficiency.

In conclusion, PAP significantly increases the incidence of POPF and severe complications after PD. PD can be safely performed in highly selective patients with PAP.

## COMMENTS

### Background

It is well known that acute pancreatitis (AP) may occur in association with a periampullary neoplasm. However, to date, it remains unclear how preoperative AP (PAP) affects the surgical management of periampullary tumors.

### Research frontiers

The current research hotspot is how to manage periampullary tumors with PAP.

### Innovations and breakthroughs

In the present study, the authors showed that PAP delays the resection of periampullary tumors. PAP significantly increases the incidence of postoperative pancreatic fistula and severe complications after pancreaticoduodenectomy (PD).

### Applications

The study results suggest that PD can be safely performed in highly selective patients with PAP.

### Terminology

Idiopathic AP is a term commonly used to describe patients with AP after the common etiologies of AP have been excluded, such as alcohol and gallstones.

### Peer-review

This is an interesting study in which the authors analyzed the effect of PAP on tumors.

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