Original Article

Cholecystectomy reduces the severity of subsequent idiopathic acute pancreatitis

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Abstract

Background: Acute pancreatitis (AP) is a common digestive system disease, and its incidence is increasing year by year. Although some clinical studies have indicated that cholecystectomy can reduce the risk of recurrent pancreatitis after acute biliary pancreatitis (ABP), it is not clear whether cholecystectomy would affect the severity of subsequent AP.

Methods: In this study, we combined computed tomography scoring index (CTSI), bedside index for severity in AP (BISAP), and clinical manifestations grading of AP with propensity score matching (PSM), after correction for baseline confounding factors, to respectively explore the influence of cholecystectomy on the severity of subsequent pancreatitis in 527 AP patients.

Results: The results showed that ABP (231/527) is more common in female patients and elderly patients ($P < 0.001$). Age, amylase, creatinine, blood urea nitrogen, and aspartate aminotransferase levels of patients with ABP at admission were higher than those of non-biliary pancreatitis (296/527), and the levels of albumin, hematocrit, and blood glucose were lower ($P < 0.050$). Further, compared with the unresected group (458/527), patients after cholecystectomy (69/527) had less white blood cells and higher level of albumin ($P < 0.050$). Patients had lower clinical manifestation grade ($P = 0.019$) and CTSI grade ($P < 0.008$) after cholecystectomy. After PSM correction, there was no difference in biochemical parameters between the cholecystectomy group and the non-cholecystectomy group, but differences in clinical manifestation grade ($P = 0.039$) and CTSI grade ($P = 0.013$) remained. We also found that cholecystectomy reduced the frequency of biliary pancreatitis (30.4% vs. 45.9%, $P < 0.050$). Finally, we found that cholecystectomy could reduce the severity of subsequent idiopathic AP.

Conclusion: Cholecystectomy could reduce the severity of subsequent idiopathic AP and the frequency of biliary pancreatitis.

Keywords: Acute Pancreatitis, cholecystectomy, effect, severity, subsequent

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INTRODUCTION

Acute pancreatitis (AP) is an inflammatory injury such as pancreatic edema, hemorrhage, and necrosis caused by the self-digestion of pancreatic tissue.[1] It has become one of the major diseases endangering human health and life and also brings serious economic burden. Clinically, AP is characterized by acute upper abdominal pain and elevated blood/urine amylase or lipase. According to different grading standards, AP can be divided into mild AP (MAP), moderately severe AP (MSAP), and severe AP (SAP). MAP has mild clinical symptoms, short treatment time, and good prognosis. The clinical manifestations of MSAP may be more severe, with a risk of transient organ failure and severe development. SAP is characterized by severe complications, rapid changes in the condition, long hospitalization, high treatment costs, and high mortality.[2] The overall fatality rate of AP is about 5%, and the mortality of patients with SAP dramatically increases to 30%.[1,3]

According to the etiology, AP can be divided into biliary, alcoholic, hyperlipidemic, and idiopathic pancreatitis. Acute biliary pancreatitis (ABP) accounts for 30–60% of AP,[4,5] and is more severe than acute alcoholic pancreatitis and post-endoscopic retrograde cholangiopancreatography pancreatitis.[6] Major guidelines and a large number of clinical studies have indicated that cholecystectomy can reduce the risk of recurrent pancreatitis after ABP.[3,7-10] However, it is not well demonstrated whether cholecystectomy would affect the severity of subsequent AP. In this study, we combined computed tomography severity index (CTSI), bedside index for severity in AP (BISAP), and clinical manifestation grading of AP to respectively explore the influence of cholecystectomy on the severity of subsequent pancreatitis, so as to provide evidence in early judgment of the severity of subsequent pancreatitis and reduce hospitalization costs and mortality.

PATIENTS AND METHODS

Case inclusion

Inclusion criteria: Patients diagnosed with AP at the Second Affiliated Hospital of Chongqing Medical University, from January 01, 2018 to December 31, 2018. *Exclusion criteria*: (1) patients with malignant tumor and severe liver and kidney function impairment; (2) pregnant women; (3) post-endoscopic retrograde cholangiopancreatography pancreatitis; (4) patients diagnosed with chronic pancreatitis; (5) drug-induced and traumatic AP; and (6) patients who left hospital without cure. This study protocol was reviewed and approved by the Ethics Committee of the Second Affiliated Hospital of Chongqing Medical University, approval number 92.

Observation indicators and grouping

General information of patients including gender, age, consciousness, basic diseases, and so on was collected. Clinical data including gallbladder status, severity of pancreatitis, complications, computed tomography (CT), and other imaging data was recorded. Relevant biochemical indicators, such as white blood cells, blood calcium, blood glucose, creatinine, urea nitrogen, aspartate aminotransferase, and amylase, were collected.

According to the etiology, AP was divided into biliary pancreatitis and non-biliary pancreatitis. Also, patients were divided into unresected group and resected group according to whether the patients have undergone cholecystectomy. According to the World Health Organization age classification, patients were divided into three groups: young group <45 years old, middle-aged group 45–59 years old, and elderly group >60 years old.

Diagnostic and grading criteria

According to the Atlanta AP guidelines revised in 2012,[11] the diagnosis of AP requires at least two of the following three characteristics: (1) persistent severe upper abdominal pain of acute onset, usually radiating to the shoulder and back; (2) serum lipase activity (or amylase activity) is at least three times of the normal upper limit; and (3) CT or magnetic resonance imaging or transabdominal ultrasound shows the typical findings of AP.

ABP was defined as[12] (1) gallstones and/or sludge diagnosed on transabdominal ultrasound or CT performed on admission or (2) dilated common bile duct on ultrasound or CT (diameter: >8 mm for age ≤75 years and >10 mm for age >75 years) or (3) two of the following three laboratory abnormalities: (a) serum bilirubin level >1.3 mg/dL (40 μmol/L); (b) alanine aminotransferase level >100 U/L, with the level of alanine aminotransferase being greater than the level of aspartate aminotransferase; and (c) alkaline phosphatase level >195 U/L with a gamma-glutamyltransferase level >45 U/L. Other causes of AP (e.g., alcohol abuse) and signs of chronic pancreatitis (history and CT) had to be absent.

Hyperlipidemic AP was diagnosed if serum triglycerides (TGs) reached 11.3 mmol/L or TG was more than 5.56–11.3 mmol/L accompanied by chylemia, excluding other etiologies of AP (gallstone, drug, infection, etc.)[13]

Alcohol pancreatitis was considered if there was consumption of more than 50 g per day of alcohol for more than 5 years or the patient had consumed excessive

alcohol shortly before the onset of AP and other possible causes had been excluded.[4]

If the etiology of AP remained unknown (initially), the disease was referred to as idiopathic AP (IAP).[14]

Clinical manifestation grading criteria for AP are as follows:[3] (1) MAP: with the clinical manifestations and biochemical changes of AP, without organ failure and local or systemic complications, usually recovers within 1–2 weeks; (2) MSAP: with the clinical manifestations and biochemical changes of AP, accompanied by transient organ failure (can be recovered within 48 h), or with local or systemic complication; and (3) SAP: with the clinical manifestations and biochemical changes of AP, and must be accompanied by continuous (>48 h) organ failure.

BISAP grading criteria:[15] (1) blood urea nitrogen >25 mg/dl; (2) impaired mental state (glass score <15); (3) systemic inflammatory response syndrome (at least two of the following): body temperature >38°C or <36°C, breathing >20 beats/min or PCO_2 <32 mmHg, heart rate >90 beats/min, white blood cells <4000 or >12,000 cells/mm^3, or naive neutrophils >10%; (4) age >60 years; and (5) pleural effusion found in imaging examination. Each item is scored as 1 point, with <3 points as MAP and cumulatively ≥ 3 points as MSAP.

CTSI grading criteria are as follows:[16] (1) grade of AP: grade A- normal pancreas, 0 points; grade B- localized or diffused enlargement of the pancreas (including irregular contour, uneven density, dilatation of the pancreatic duct, and localized effusion), 1 point; grade C- in addition to grade B lesions, also had peripancreatic inflammatory changes, 2 points; grade D- except pancreatic lesions, the pancreas has a single effusion area, 3 points; grade E pancreas or peripancreatic- two or more effusion gas areas, or abscess, 4 points; (2) degree of pancreatic necrosis: no necrosis, 0 points; necrosis area ≤30%, 2 points; necrosis area ≤50%, 4 points; and necrosis range >50%, 6 points. Combined with CT AP grade, and assessment of degree of pancreatic necrosis: grade I, 0–3; grade II, 4–6; and grade III, 7–10. Grade II or above is severe.

Statistical analysis

All data were statistically analyzed by Statistical Package for the Social Sciences (SPSS) 22.0. Propensity score matching (PSM) was used to match patients with cholecystectomy and without cholecystectomy in a 1:3 ratio, and gender and age were used as independent variables to model the events affecting the two groups' outcome. Logistic regression model was used to estimate the propensity value. The carboplatin value of PSM was 0.05. The measurement data were in accordance with the use of *t*-test for normal distribution and rank sum test for non-normal distribution. The data were expressed by mean ± standard deviation or median (interquartile interval); the count data were expressed by quantity and percentage. Chi-square test was used for comparison in the count data. *P* value less than 0.050 indicates that the difference is statistically significant.

RESULTS

Clinical baseline characteristics

A total of 527 cases of AP were included in this study, including 231 cases of biliary pancreatitis, 50 cases of hyperlipidemic pancreatitis, 32 cases of alcohol pancreatitis, and 214 cases of idiopathic pancreatitis. Of them, 458 cases belonged to unresected gallbladder group and 69 cases to resected group; 286 cases were males and 241 cases were females. The average age of patients was 53 years. According to the classification of clinical manifestations, 417 cases had MAP and 110 cases had MSAP and SAP. According to BISAP rating, 502 cases were MAP and 25 cases were MSAP and SAP. According to the CTSI score, 428 cases were mild and 99 cases were severe [Table 1].

Comparison between biliary and non-biliary pancreatitis

Among all patients, biliary pancreatitis was more common in female AP patients (55% vs. 45%) and in elder patients ($P < 0.001$) (Supplementary Table). The ratio of biliary pancreatitis was significantly lower in patients with cholecystectomy than in patients without gallbladder resection (30.4% vs. 45.8%, $P < 0.050$) [Table 1]. As per BISAP grade, pancreatitis was more severe in patients with biliary pancreatitis than in patients with non-biliary pancreatitis ($P < 0.050$) (Supplementary Table 1). However, there was no significant difference in clinical grade and CTSI. Patients with non-biliary pancreatitis had higher albumin, blood glucose, and hematocrit than those with biliary pancreatitis, while patients with biliary pancreatitis were older and had increased amylase, creatinine, blood urea nitrogen, and aspartate aminotransferase than non-biliary pancreas at the time of admission ($P < 0.050$) (Supplementary Table 1).

Comparison of patients with and without cholecystectomy

At the time of admission, patients without cholecystectomy had higher white blood cells than those in the resected group ($P < 0.050$) [Table 1]. The level of albumin in the resected group was higher than that in the unresected

Table 1: Clinical baseline characteristics of patients enrolled

Clinical features	No. of patients (%)	Before PSM		*P*	No. of patients (%)	After PSM		*P*
		Unresected (*n*=458) No. of patients (%)	Resected (*n*=69) No. of patients (%)			Unresected (*n*=207) No. of patients (%)	Resected (*n*=69) No. of patients (%)	
Gender								
Male	286 (54.3)	261 (57.0)	25 (36.2)	**0.001**	104 (37.7)	78 (37.7)	26 (37.7)	1.000
Female	241 (45.7)	197 (43.0)	44 (63.8)		172 (62.3)	129 (62.3)	43 (62.3)	
Age (years)								
<45	178 (33.8)	166 (36.2)	12 (17.4)	**<0.001**	61 (22.1)	49 (23.7)	12 (17.4)	0.110
45–59	169 (32.1)	131 (28.6)	38 (55.1)		122 (44.2)	84 (40.6)	38 (55.1)	
>60	180 (34.2)	161 (35.2)	19 (27.5)		93 (33.7)	74 (35.7)	19 (27.5)	
Cause of pancreatitis								
Biliary	231 (43.8)	210 (45.8)	21 (30.4)	**0.010**	122 (44.2)	101 (48.8)	21 (30.4)	**0.011**
Hyperlipidemic pancreatitis	50 (9.5)	42 (9.2)	8 (11.6)		23 (8.3)	15 (7.2)	8 (11.6)	
Alcoholic pancreatitis	32 (6.1)	31 (6.8)	1 (1.4)		11 (4.0)	10 (4.9)	1 (1.5)	
Idiopathic pancreatitis	214 (40.6)	175 (38.2)	39 (56.5)		120 (43.5)	81 (39.1)	39 (56.5)	
CTSI grade								
Mild	428 (81.2)	364 (79.5)	64 (92.8)	**0.008**	227 (82.2)	163 (78.7)	64 (92.8)	**0.008**
Severe	99 (18.8)	94 (20.5)	5 (7.2)		49 (17.8)	44 (21.3)	5 (7.2)	
Clinical manifestation grade								
Mild	417 (79.1)	355 (77.5)	62 (89.9)	**0.019**	222 (80.4)	160 (77.3)	62 (89.9)	**0.023**
Moderate and severe	110 (20.9)	103 (22.5)	7 (10.1)		54 (19.6)	47 (22.7)	7 (10.1)	
BISAP grade								
Mild	502 (95.3)	437 (95.4)	65 (94.2)	0.555	265 (96.0)	200 (96.6)	65 (94.2)	0.284
Moderate and severe	25 (4.7)	21 (4.6)	4 (5.8)		11 (4.0)	7 (3.4)	4 (5.8)	
WBC ($\times 10^9$/L)	11.17±4.82	11.35±4.88	9.99±4.22	**0.029**	10.80±4.57	11.06±4.66	9.99±4.22	0.093
Albumin (g/L)	37.58±5.78	37.40±5.92	38.74±4.61	**0.034**	38.55 (34.00, 41.70)	37.9 (33.5, 41.5)	39.60 (35.90, 42.25)	0.058
Serum calcium (mmol/L)	2.26 (2.14, 2.37)	2.25 (2.14, 2.37)	2.29 (2.19, 2.39)	0.062	2.27 (2.15, 2.37)	2.26 (2.14, 2.37)	2.29 (2.19, 2.39)	0.127
Age (years)	51 (42, 65)	50 (40, 65)	53 (48, 62)	0.116	54.00 (46.00, 63.75)	54 (45, 64)	53 (48, 62)	0.911
Creatinine (μmol/L)	58.8 (48.7, 72.4)	58.80 (49.78, 72.4)	58.60 (44.75, 71.85)	0.334	55.60 (45.83, 70.48)	54.80 (46.10, 70.40)	58.60 (44.75, 71.85)	0.908
Blood urea nitrogen (mmol/L)	4.78 (3.72, 6.20)	4.81 (3.70, 6.21)	4.65 (3.73, 5.71)	0.541	4.69 (3.73, 5.97)	4.72 (3.73, 6.15)	4.65 (3.73, 5.71)	0.759
Hematocrit (%)	40.44±5.95	40.50±6.05	40.08±5.28	0.592	39.70±5.70	39.57±5.83	40.08±5.28	0.521
Amylase (U/L)	253 (120, 863)	259.50 (117.75, 908.25)	205.00 (128.00, 544.00)	0.656	297.00 (120.25, 1011.50)	320.00 (118.00, 1159.00)	205.00 (128.00, 544.00)	0.314
Blood glucose (mmol/L)	7.20 (5.76, 10.13)	7.18 (5.76, 10.37)	7.29 (5.77, 9.50)	0.671	7.28 (5.85, 10.02)	7.26 (5.89, 11.00)	7.29 (5.77, 9.50)	0.528
Aspartate aminotransferase (U/L)	29 (19, 85)	29 (19, 85.25)	28 (19, 88)	0.999	33.5 (19.0, 114.5)	36.0 (19.0, 120.0)	28.0 (19.0, 88.0)	0.342

BISAP=bedside index for severity in acute pancreatitis, CTSI=computed tomography severity index, PSM=propensity score matching, WBC=white blood cells

group ($P < 0.050$) [Table 1]. There were more patients with moderate and severe pancreatitis in the group without gallbladder resection than in the resection group as per the clinical manifestation grade and CTSI grade ($P < 0.050$) [Table 1]. After PSM correction, there was no difference in biochemical parameters between the cholecystectomy group and the non-cholecystectomy group, but moderate and severe pancreatitis were more common in the unresected gallbladder group compared to the resected group, and the differences in clinical manifestation grade ($P = 0.039$) and CTSI grade ($P = 0.013$) were statistically significant [Table 1].

Analysis of biliary pancreatitis patients

There was no statistically significant difference in age, leukocyte, transaminase, and other biochemical indexes between the cholecystectomy group and the non-cholecystectomy group [Table 2]. Moreover, in the three scales of pancreatitis severity, there was no significant difference between the cholecystectomy group and the unresected group [Table 2]. The results were the same after PSM correction.

Analysis of non-biliary pancreatitis patients

We further analyzed the non-biliary pancreatitis, in which alcoholic pancreatitis accounted for 6.1%, hyperlipidemic pancreatitis accounted for 9.5%, and idiopathic pancreatitis accounted for 40.6% [Table 1]. In alcoholic pancreatitis and hyperlipidemic pancreatitis, cholecystectomy does not reduce the severity of pancreatitis and there was no significant difference in related biochemical indexes [Tables 3 and 4]. We also found that among idiopathic pancreatitis cases, there were more patients with moderate and severe pancreatitis in the group without gallbladder resection than in the resection group, according to the clinical manifestation grade and CTSI grade (P < 0.050) [Table 5]. Also, patients without cholecystectomy had higher white blood cells than those in the resected group ($P < 0.050$) [Table 5]. The levels of albumin and serum calcium in the resected group were higher than those in the unresected group ($P < 0.050$) [Table 5].

DISCUSSION

AP is a common digestive system disease, which is mainly caused by gallstones, cholestasis, and alcohol.[7] Many guidelines[2,7,17,18] recommend cholecystectomy to reduce recurrent biliary pancreatitis, as it could solve cholelithiasis, microlithiasis, cholestasis, and other biliary diseases.[8,14,19] There is also a study showing that laparoscopic cholecystectomy can effectively prevent the recurrence of

Table 2: Analysis of biliary pancreatitis patients

Clinical features	Total	Before PSM		*P*	Total	After PSM		*P*
		Unresected (*n*=210) No. of patients (%)	Resected (*n*=21) No. of patients (%)			Unresected (*n*=63) No. of patients (%)	Resected (*n*=21) No. of patients (%)	
CTSI grade								
Mild	189 (81.8)	170 (81.0)	19 (90.5)	0.282	68 (81.0)	49 (77.8)	19 (90.5)	0.336
Severe	42 (18.2)	40 (19.0)	2 (9.5)		16 (19.0)	14 (22.2)	2 (9.5)	
BISAP grade								
Mild	215 (93.1)	196 (93.3)	19 (90.5)	0.624	79 (94.0)	60 (95.2)	19 (90.5)	0.595
Moderate and severe	16 (6.9)	14 (6.7)	2 (9.5)		5 (6.0)	3 (4.8)	2 (9.5)	
Clinical manifestation grade								
Mild	181 (78.4)	164 (78.1)	17 (81.0)	0.762	64 (76.2)	47 (74.6)	17 (81.0)	0.554
Moderate and severe	50 (21.6)	46 (21.9)	4 (19.0)		20 (23.8)	16 (25.4)	4 (19.0)	
Aspartate aminotransferase (U/L)	70 (28, 194)	70.00 (28.00, 182.50)	185.00 (25.50, 332.00)	0.312	77.50 (27.75, 267.00)	74.00 (31.00, 207.00)	185.00 (25.50, 332.00)	0.542
Hematocrit (%)	39.68±5.58	39.76±5.64	38.86±4.97	0.482	39.50 (35.38, 42.33)	39.20 (35.30, 41.90)	39.80 (35.35, 43.00)	0.616
WBC (×10^9/L)	10.92±5.13	10.98±5.18	10.27±4.69	0.544	9.59 (6.53, 12.88)	9.68 (6.29, 12.91)	9.41 (7.52, 12.11)	0.820
Blood urea nitrogen (mmol/L)	4.91 (3.85, 6.86)	4.92 (3.87, 6.87)	4.56 (3.01, 6.96)	0.567	4.48 (3.61, 6.40)	4.27 (3.82, 5.96)	4.56 (3.01, 6.96)	0.901
Age (years)	57.92±15.64	57.82±15.78	58.90±14.45	0.763	57.55±12.30	57.10±11.58	58.90±14.45	0.562
Creatinine (μmol/L)	59.4 (50.9, 77.2)	59.00 (50.90, 77.28)	62.20 (50.60, 76.20)	0.795	56.55 (48.28, 70.40)	54.10 (45.50, 66.00)	62.20 (50.60, 76.20)	0.160
Albumin (g/L)	36.44±5.87	36.41±5.96	36.71±5.07	0.825	38.10 (32.50, 40.88)	38.40 (31.80, 40.90)	38.10 (32.55, 40.05)	0.861
Amylase (U/L)	508 (157, 1610)	511.50 (154.25, 1657.00)	477.00 (214.50, 1447.50)	0.843	496.00 (178.00, 1572.75)	515.00 (134.00, 1863.00)	477.00 (214.50, 1447.50)	0.816
Blood glucose (mmol/L)	6.95 (5.68, 9.00)	6.91 (5.66, 9.25)	7.29 (5.70, 8.88)	0.934	7.30 (5.74, 9.48)	7.44 (5.73, 9.63)	7.29 (5.70, 8.88)	0.661
Serum calcium (mmol/L)	2.27 (2.14, 2.36)	2.26 (2.14, 2.37)	2.29 (2.16, 2.32)	0.975	2.29 (2.16, 2.34)	2.28 (2.16, 2.35)	2.29 (2.16, 2.32)	0.877

BISAP=bedside index for severity in acute pancreatitis, CTSI=computed tomography severity index, PSM=propensity score matching, WBC=white blood cells

Table 3: Analysis of hyperlipidemic pancreatitis patients

Clinical features	No. of patients (%)	Unresected (*n*=42) No. of patients (%)	Resected (*n*=8) No. of patients (%)	*P*
CTSI grade				
Mild	40 (80.0)	32 (76.2)	8 (100.0)	0.184
Severe	10 (20.0)	10 (23.8)	0 (0.0)	
BISAP grade				
Mild	50 (100.0)	42 (100.0)	8 (100.0)	_
Moderate and severe	0 (0.0)	0 (0.0)	0 (0.0)	
Clinical manifestation grade				
Mild	38 (76.0)	30 (71.4)	8 (100.0)	0.173
Moderate and severe	12 (24.0)	12 (28.6)	0 (0.0)	
Aspartate aminotransferase (U/L)	23.14±9.23	23.52±9.87	21.13±4.49	0.506
Hematocrit (%)	43.40±4.90	43.52±4.39	42.78±7.42	0.699
WBC (×10⁹/L)	12.80±3.33	12.93±3.55	12.11±1.82	0.527
Blood urea nitrogen (mmol/L)	4.19 (3.51, 5.09)	4.17 (3.51, 5.09)	4.70 (3.28, 5.15)	0.958
Age (years)	41.66±10.71	40.98±10.99	45.25±8.83	0.306
Creatinine (μmol/L)	53.82±18.65	53.16±17.81	57.26±23.67	0.574
Albumin (g/L)	41.86±4.66	42.10±4.90	40.58±3.02	0.401
Amylase (U/L)	165.50 (95.75, 310.75)	181.50 (92.25, 334.25)	134.50 (108.00, 185.50)	0.597
Blood glucose (mmol/L)	11.57±4.79	12.02±5.00	9.17±2.50	0.124
Serum calcium (mmol/L)	2.17±0.26	2.16±0.27	2.25±0.24	0.342

BISAP=bedside index for severity in acute pancreatitis, CTSI=computed tomography severity index, WBC=white blood cells

IAP.[20] However, AP still happens to some patients after cholecystectomy and complications such as bile duct injury, bile leakage, bile duct stricture, and post-cholecystectomy syndrome may occur after cholecystectomy. Therefore, whether to perform cholecystectomy is still controversial. Also, it remains unknown whether cholecystectomy would affect the severity of subsequent AP.

At present, many scoring systems, such as Acute Physiology and Chronic Health Evaluation (APACHE) score, glass score, and BISAP score, have been developed for the severity classification of AP by combining clinical, imaging, and laboratory examination results in various combinations. In this study, the simple BISAP score combined with imaging score was selected to evaluate the severity of AP, as some studies have shown that BISAP scores have a prediction accuracy similar to that of the more complex APACHE-II scores[13,15] and Ranson scores.[13,21] In addition, our study combines the clinical manifestations of the patients' general conditions and the clinical manifestations of the disease changes to comprehensively and accurately evaluate the severity of AP. At the same time, we also used PSM to correct the relevant baseline level, reducing the error caused by the uneven baseline.

The present study found that the proportion of biliary pancreatitis was higher in women and elderly people, which is in accordance with the results of previous related studies conducted in the Netherlands,[22,23] and it may be related to the higher prevalence of gallstones in the elderly

Table 4: Analysis of alcoholic pancreatitis patients

Clinical features	No. of patients (%)	Unresected (*n*=31) No. of patients (%)	Resected (*n*=1) No. of patients (%)	*P*
CTSI grade				
Mild	27 (84.4)	26 (83.9)	1 (100.0)	0.662
Severe	5 (15.6)	5 (16.1)	0 (0.0)	
BISAP grade				
Mild	32 (100.0)	31 (100.0)	1 (100.0)	_
Moderate and severe	0 (0.0)	0 (0.0)	0 (0.0)	_
Clinical manifestation grade				
Mild	25 (78.1)	24 (77.4)	1 (100.0)	0.591
Moderate and severe	7 (21.9)	7 (22.6)	0 (0.0)	
Aspartate aminotransferase (U/L)	37.34±31.26	37.87±6.47	_	0.603
Hematocrit (%)	40.50±6.20	40.45±6.30	_	0.810
WBC (×10⁹/L)	12.30±6.78	12.55±6.73	_	0.242
Blood urea nitrogen (mmol/L)	4.44±1.88	4.49±1.89	_	0.457
Age (years)	47.56±11.67	47.45±11.85	_	0.770
Creatinine (μmol/L)	61.00 (56.63, 73.10)	60.9 (56.50, 70.70)	_	0.357
Albumin (g/L)	37.93±6.41	37.80±6.47	_	0.548
Amylase (U/L)	124.5 (63.5,211.5)	131 (65,212)	_	0.129
Blood glucose (mmol/L)	7.63±2.39	7.61±2.43	_	0.773
Serum calcium (mmol/L)	2.22±0.20	2.21±0.20	_	0.192

BISAP=bedside index for severity in acute pancreatitis, CTSI=computed tomography severity index, WBC=white blood cells

Table 5: Analysis of idiopathic pancreatitis patients

Clinical features	No. of patients (%)	Unresected (*n*=175) No. of patients (%)	Resected (*n*=39) No. of patients (%)	*P*
CTSI grade				
Mild	172 (80.4)	136 (77.7)	36 (92.3)	**0.038**
Severe	42 (19.6)	39 (22.3)	3 (7.7)	
BISAP grade				
Mild	204 (95.3)	167 (95.4)	37 (94.9)	0.882
Moderate and severe	10 (4.7)	8 (4.6)	2 (5.1)	
Clinical manifestation grade				
Mild	171 (79.9)	135 (77.1)	36 (92.3)	**0.033**
Moderate and severe	43 (20.1)	40 (22.9)	3 (7.7)	
Aspartate aminotransferase (U/L)	23.5 (17.0, 38.0)	22 (17, 38)	25 (19, 38)	0.206
Hematocrit (%)	40.42±6.37	40.48±6.66	40.14±4.93	0.762
WBC (×10^9/L)	11.12±4.68	11.47±4.72	9.56±4.21	**0.021**
Blood urea nitrogen (mmol/L)	4.92 (3.73, 6.11)	4.96 (3.63, 6.20)	4.80 (3.88, 5.68)	0.624
Age (years)	51.23±16.75	50.51±17.69	54.49±11.22	0.079
Creatinine (μmol/L)	60.40 (47.18, 72.08)	61.40 (49.00, 72.70)	52.80 (43.30, 69.50)	0.091
Albumin (g/L)	37.73±5.46	37.37±5.62	39.37±4.39	**0.037**
Amylase (U/L)	208.50 (113.75, 546.00)	232 (102, 588)	179 (123, 479)	0.925
Blood glucose (mmol/L)	6.91 (5.70, 10.38)	6.90 (5.70, 10.64)	6.96 (5.68, 9.40)	0.794
Serum calcium (mmol/L)	2.26 (2.15, 2.37)	2.25 (2.14, 2.36)	2.28 (2.21, 2.40)	**0.036**

BISAP=bedside index for severity in acute pancreatitis, CTSI=computed tomography severity index, WBC=white blood cells

and women.[23] In addition, the ratio of biliary pancreatitis was significantly lower in patients after cholecystectomy than in patients without gallbladder resection, which is consistent with the current clinical research and guidelines' recommendations.[1,3,7,14]

Of all enrolled pancreatitis patients, the number of patients with moderate and severe pancreatitis in the unresected group was more than that in the resected group, as per the CTSI and clinical manifestation grade. Cholecystectomy can remove gallstone-derived gallbladder, reduce biliary obstruction, bile reflux, and pancreatic duct hypertension,[14] and reduce the secretion of cholecystokinin (CCK). On the other hand, cholecystectomy can also reduce pancreatic self-digestive injury caused by obstruction and reduce the inflammatory response, which may be the reason why the severity of pancreatitis in patients with cholecystectomy is lower than that in patients without cholecystectomy. It has been found that the level of serum CCK in patients with gallstone[24] and biliary pancreatitis[25] is higher than that in ordinary people, which may be due to the high cholesterol concentration and the downregulation of CCK receptor expression in these patients.[26,27] Thus, CCK may stimulate Oddi sphincter spasm[28] and affect pancreatic secretion,[29-32] thus aggravating pancreatitis.[33] Inhibiting CCK can reduce the occurrence and severity of pancreatitis.[25,34-36]

It is reported that IAP accounts for about 16%–27% of AP.[37] In this study, ABP accounted for 43.8% of AP, idiopathic pancreatitis for 40.6%, alcoholic pancreatitis for 6.1%, and hyperlipidemic pancreatitis for 9.5%. The high proportion of idiopathic pancreatitis in this study may be related to undetected small biliary stones and cholestasis.[14] At present, it is considered that microlithiasis, sludge, and other occult biliary diseases are the important causes of IAP.[14] We suppose that this might explain the reason why cholecystectomy reduces the severity of IAP. Furthermore, this study found that compared with the resected group, patients without gallbladder resection had lower albumin, indicating poor nutritional status, which may also affect the severity of pancreatitis.

Our results revealed that there was no significant difference between patients with biliary pancreatitis after cholecystectomy and those without cholecystectomy, based on the three criteria grading the severity of pancreatitis, due to the fact that biliary pancreatitis is caused by gallstones from other biliary sources, or it is associated with high risk factors of choledocholithiasis after cholecystectomy, such as cholesterol stones, choledocholithiasis >2, choledocholithiasis >10 mm, endoscopic mechanical lithotripsy, open surgery, and heredity,[38-40] or because the sample size is small. Patients with high risk factors of recurrent choledocholithiasis after cholecystectomy should be followed up carefully and treated in time.

In summary, we found that cholecystectomy may reduce the severity of subsequent IAP and the ratio of biliary pancreatitis. The present study provides evidence for cholecystectomy and has a certain clinical significance for early judgment of the severity of subsequent pancreatitis. This conclusion should be tested by conducting prospective, multicenter clinical trials. Meanwhile, the underlying mechanism needs further demonstration.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Comparison between biliary pancreatitis patients and non-biliary pancreatitis patients

Clinical features	Total	Biliary (*n*=231) No. patients (%)	Non-biliary (*n*=296) No. patients (%)	*P*
Gender				
Male	286 (54.3)	104 (45.0)	182 (61.5)	**<0.001**
Female	241 (45.7)	127 (55.0)	114 (38.5)	
Age (years)				
<45	178 (33.8)	52 (22.5)	126 (42.6)	**<0.001**
45–59	169 (32.1)	68 (29.4)	101 (34.1)	
＞60	180 (34.2)	111 (48.1)	69 (23.3)	
State of the gallbladder				
Resected	69 (13.1)	21 (9.1)	48 (16.2)	**0.016**
Unresected	458 (86.9)	210 (90.9)	248 (83.8)	
CTSI grade				
Mild	428 (81.2)	189 (81.8)	239 (80.7)	0.754
Severe	99 (18.8)	42 (18.2)	57 (19.3)	
Clinical manifestation grade				
Mild	417 (79.1)	181 (78.4)	236 (79.7)	0.700
Moderate and severe	110 (20.9)	50 (21.6)	60 (20.3)	
BISAP grade				
Mild	502 (95.3)	215 (93.1)	287 (97.0)	**0.037**
Moderate and severe	25 (4.7)	16 (6.9)	9 (3.0)	
Age (years)	51 (42, 65)	58 (46,68)	47.5 (37, 57)	**<0.001**
Albumin (g/L)	37.58±5.78	36.44±5.87	38.46±5.55	**<0.001**
Aspartate aminotransferase (U/L)	29 (19, 85)	71 (28, 194)	22 (17,34)	**<0.001**
Amylase (U/L)	253 (120, 863)	508.00 (157.00, 1610.00)	188.00 (102.25, 469.50)	**<0.001**
Hematocrit (%)	40.44±5.95	39.68±5.58	41.04±6.17	**0.009**
Blood glucose (mmol/L)	7.20 (5.76, 10.13)	6.95 (5.68, 9.00)	7.47 (5.95, 11.00)	**0.014**
Blood urea nitrogen (mmol/L)	4.78 (3.72, 6.20)	4.91 (3.85, 6.86)	4.63 (3.60, 5.88)	**0.027**
Creatinine (μmol/L)	58.8 (48.7, 72.4)	59.40 (50.90, 77.20)	57.90 (46.63, 70.15)	**0.028**
WBC ($\times 10^9$/L)	11.17±4.82	10.92±5.13	11.37±4.55	0.279
Serum calcium (mmol/L)	2.26 (2.14, 2.37)	2.27 (2.14, 2.36)	2.25 (2.14, 2.37)	0.91

tomography severity index, WBC = white blood cells