

# Clinical efficacy of duodenoscopy combined with laparoscopy in the treatment of patients with severe acute pancreatitis and pancreatic pseudocyst, and the effects on IL-6 and CRP

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**Abstract.** The study aimed to investigate the clinical efficacy of duodenoscopy combined with laparoscopy in the treatment of patients with severe acute pancreatitis (SAP) and pancreatic pseudocyst (PP), and its effects on serum inflammatory factors. Altogether 94 patients complicated with SAP and PP who were admitted to Weifang People's Hospital (Weifang, China) from September 2015 to December 2018 were included. Based on the different operation methods, 49 patients who underwent traditional laparotomy under laparoscopic surgery were included in group A, and 45 patients who underwent duodenoscopy and laparoscopy under duodenoscope to treat the drainage of nipple and pancreatic pseudocysts were included in group B. The expression levels of related serum indexes and serum stress indexes before and at 48 h after surgery, the postoperative nausea, vomiting and abdominal pain scores, as well as the clinical efficacy, perioperative related indexes, recovery and complications were compared between the two groups. The prognostic factors in both groups were assessed via Logistic univariate and multivariate analyses. C-reactive protein (CRP), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), interleukin- $\beta$  (IL- $\beta$ ), endotoxin and nuclear factor  $\kappa$ B (NF- $\kappa$ B) were significantly lower in group B than those in group A ( $P < 0.001$ ). Upregulating cortisol and norepinephrine in group B was lower than that in group A ( $P < 0.001$ ). The total effective rate in group B was higher than that in group A ( $P < 0.05$ ). The perioperative related indexes, recovery,

and postoperative complications in group B were better than those in group A ( $P < 0.05$ ). Scores of abdominal pain, nausea and vomiting in group B were markedly lower than those in group A ( $P < 0.001$ ). Multivariate Logistic regression analysis showed that CRP, TNF- $\alpha$ , IL-6, IL- $\beta$  and surgical methods were independent risk factors for the prognosis of patients with SAP and PP. In conclusion, the combined treatment with duodenoscopy and laparoscopic surgery has little inflammatory and stress reaction, and it is highly safe, worthy to be popularized.

## Introduction

Severe acute pancreatitis (SAP) is a common disease of the digestive system. It is characterized by acute onset and rapid course of disease (1,2). Worldwide, the mortality of patients with SAP is as high as 20-30% every year (3,4). Pancreatic pseudocyst (PP) is a common local complication of SAP which aggravates the condition of patients with SAP and seriously affects prognosis (5). If SAP complicated with PP is not treated in time, the aggravation of the disease will lead to pancreatic necrosis or multiple organ failure, causing renal failure, respiratory failure and shock, which greatly affect the health and life of patients (6). With the development of social economy and the bad living habits of people, the annual incidence of SAP complicated with PP is increasing year by year, with a younger trend (7). Moreover, the pathogenesis is relatively complex. Clinically, there is still a lack of accurate and better treatment standard (8).

In addition to conventional drug therapy, traditional laparotomy is currently the most commonly used treatment clinically for patients complicated with SAP and PP. However, traditional laparotomy causes great damage to tissues around the pancreas of patients, as well as inflammation and stress reaction of wounds, and the safety performance still needs to be improved (9,10). With the rapid development of minimally invasive techniques, duodenoscopy and laparoscopy have been applied to pancreatitis surgery. It has been reported that, compared with traditional open surgery, duodenoscopy and laparoscopy can reduce the damage to tissues around pancreas and the risk of infection during surgery (11). At present, the clinical research on the application of holmium

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*Abbreviations:* ELISA, enzyme-linked immunosorbent assay; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; CRP, C-reactive protein; IL-6, interleukin-6; IL- $\beta$ , interleukin- $\beta$ ; NF- $\kappa$ B, nuclear factor  $\kappa$ B

*Key words:* severe acute pancreatitis complicated with pancreatic pseudocyst, duodenoscopy, laparoscopy, IL-6, CRP, TNF- $\alpha$

laser lithotripsy under electronic soft mirror to patients with renal calculi is limited. The present study assessed the clinical efficacy and value of a minimally invasive technique on patients complicated with SAP and PP by comparing the efficacy of traditional laparotomy with that of the combined treatment with duodenoscopy and laparoscopy, and investigating the related serum inflammatory, stress and prognosis factors.

## Patients and methods

**Patient characteristics.** From September 2015 to December 2018, 94 patients with SAP and PP were selected as the research subjects. Based on the different operation methods, 49 patients who underwent traditional laparotomy under laparoscopic surgery were included in group A (31 males and 18 females, with an average age of  $45.30 \pm 3.79$  years) and 45 patients who underwent duodenoscopy and laparoscopic duodenoscopy for the nipple and pancreatic pseudocyst drainage treatment were included in group B (30 males and 15 females, with an average age of  $44.94 \pm 3.89$  years). Inclusion criteria: Participants were all patients in Weifang People's Hospital (Weifang, China); the diagnostic criteria were in accordance with the diagnostic criteria for clinical SAP (12); patients were diagnosed with SAP complicated with PP by abdominal Doppler ultrasound, CT and other imaging examinations, and all of them presented secondary infection of acute PP before treatment; patients did not receive relevant antibacterial, anti-inflammatory or glucocorticoid treatment before surgery. Exclusion criteria: Patients complicated with severe liver and kidney dysfunction, coagulation disorders, or cognitive impairment and communication impairment; patients who had received treatment that could influence the operation methods before surgery, or those who did not cooperate with the examination. All subjects voluntarily participated in the study and provided a signed informed consent, and cooperated with the medical staff to complete the relevant diagnosis and treatment (medical research ethics approval no. WFRM1509PRC).

**Surgical methods.** Patients in group A received traditional laparotomy and surgical strategies, such as cystic jejunum Roux-en-Y, cystectomy and external drainage, whereas those in group B were treated with duodenoscopy when the main pancreatic duct was connected with the pancreatic cyst. Surgical drainage was conducted through nipple and PP. If ultrasonic endoscopy of patients showed that the cyst was not obviously compressing the stomach, cyst puncture stent implantation guided by the ultrasonic endoscope was adopted for treatment. If the ultrasonic results revealed an adhesion between the stomach wall and the capsule wall, the stomach tension was relatively high, then the treatment of electroacupuncture fenestration cyst drainage and stent implantation under gastroscope was adopted. If the implementation of duodenoscopy and laparoscopy was ineffective or failed, group A scheme was adopted for treatment. Preoperative evaluation and surgical indications of patients in groups A and B were evaluated in strict conformity with APACHE II scoring system. The preoperative condition evaluation and surgical indications of groups A and B were strictly in accordance with the clinical recommended APACHE II scoring system.

**Determination of indicators.** Venous blood was collected from the patients before surgery and at 48 h after surgery. The serum was separated and stored in a refrigerator at  $80^{\circ}\text{C}$  for testing. Enzyme-linked immunosorbent assay (ELISA) was used to determine tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), C-reactive protein (CRP), interleukin-6 (IL-6), interleukin- $\beta$  (IL- $\beta$ ), endotoxin and nuclear factor  $\kappa\text{B}$  (NF- $\kappa\text{B}$ ) in serum.

The collected venous blood to be tested was put into a centrifuge, and the serum was separated at  $1,500 \times g$  at  $4^{\circ}\text{C}$  for 10 min. The concentrations of CRP, TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin and NF- $\kappa\text{B}$  in serum were tested by ELISA, with reference to human CRP (cat. no. ZK-H911), TNF- $\alpha$  (cat. no. ZK-R6070), IL-6 (cat. no. ZK-B7099), IL- $\beta$  (cat. no. ZK-B7085), endotoxin (cat. no. ZK-M5161) and NF- $\kappa\text{B}$  (cat. no. ZK-R4608). Each kit was taken out from the refrigerator 30 min in advance in order to balance the room temperature with that of the sample to be tested. The sample well, standard well and blank well were set up. A total of  $50 \mu\text{l}$  of sample diluent were added to the blank well,  $100 \mu\text{l}$  of sample or standard substance to be tested were added to the other wells, the enzyme standard plate was covered with a film after being evenly mixed, and the wells were incubated for 2 h at  $37^{\circ}\text{C}$ . The liquid was discarded from each well and spin-dried. Next,  $100 \mu\text{l}$  of working liquid A were added to each well, and they were filmed and incubated for 1 h at  $37^{\circ}\text{C}$ . The liquid was discarded from each well and spin-dried, and the plate was washed 3 times with automatic plate washer. Next,  $100 \mu\text{l}$  of working solution B were added to each well, and they were filmed and incubated for 1 h at  $37^{\circ}\text{C}$ . The liquid was discarded from each well, spin-dried and the plate was washed for 3 times. Afterwards,  $90 \mu\text{l}$  of substrate solution were added to each well, and they were filmed and developed for 20 min at room temperature under dark conditions. Finally,  $50 \mu\text{l}$  termination solution was added to each well, and the OD value was immediately detected at a wavelength of 450 nm using an enzyme-labeled analyzer. The concentrations of CRP, TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin and NF- $\kappa\text{B}$  were determined.

**Outcome measures.** The changes of related serum indexes (CRP, TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin and NF- $\kappa\text{B}$ ) and serum stress indexes (cortisol and norepinephrine) before and at 48 h after surgery, the clinical efficacy (13), perioperative related indexes (duration of surgery, intraoperative blood loss, hospital stay, and recovery time of gastrointestinal function) and recovery conditions (exhaust time, time of body temperature recovery and relief time of abdominal pain) were compared between the two groups. The scores of postoperative nausea, vomiting and abdominal pain (14) were assessed. The complications (cyst infection, incision infection, pancreatic fistula, and gastrointestinal hemorrhage) 7 days after surgery were evaluated as well. The prognostic factors for patients were assessed via Logistic univariate and multivariate analyses. Clinical efficacy and postoperative prognosis were diagnosed by the clinical attending physician and relevant medical staff.

**Determination of cortisol and norepinephrine.** Cortisol and norepinephrine were determined by chemiluminescence. Cortisol chemiluminescence immunoassay kit was purchased from Shanghai Huzhen Industrial Co., Ltd. (cat. no. hz-0012c) and norepinephrine chemiluminescence immunoassay kit was

Table I. General clinical data of patients in groups A and B [mean  $\pm$  SD, n (%)].

Characteristics	Group A (n=49)	Group B (n=45)	t/ $\chi^2$	P-value
Age (years)	45.30 $\pm$ 3.79	44.94 $\pm$ 3.89	0.454	0.651
Sex			0.119	0.730
Male	31 (63.27)	30 (66.67)		
Female	18 (36.73)	15 (33.33)		
Course of disease (days)	7.60 $\pm$ 1.20	7.80 $\pm$ 1.40		
Size of cysts (cm)	4.10 $\pm$ 1.20	4.30 $\pm$ 1.10		
Smoking			0.327	0.568
Yes	29 (59.18)	24 (53.33)		
No	20 (40.82)	21 (46.67)		
Drinking			0.010	0.921
Yes	30 (61.22)	28 (62.22)		
No	19 (38.78)	17 (37.78)		
Education background			0.000	1.000
Bachelor's degree or above	49 (100.00)	45 (100.00)		
Below bachelor's degree	0 (0.00)	0 (0.00)		
Household registration			0.000	0.979
Town	23 (46.94)	21 (46.67)		
Countryside	26 (53.06)	24 (53.33)		
Aetiological agent			0.576	0.966
Biliary tract disease	13 (26.53)	13 (28.89)		
Overeating	8 (16.33)	5 (11.11)		
Pancreatic duct obstruction	10 (20.41)	9 (20.00)		
Endocrine and metabolic disorders	8 (16.33)	8 (17.78)		
Other	10 (20.41)	10 (22.22)		

purchased from Shanghai Xinyu Biological Technology Co., Ltd. (cat. no. xy-CL-0030c).

**Statistical analysis.** SPSS 17.0 (Beijing Boyi Zhixun Information Technology Co., Ltd.) was used for statistical analysis. The counting data between the two groups were tested by  $\chi^2$  test, and the risk factors related to the prognosis after surgery were assessed by single factor logistic regression analysis and multivariate logistic regression analysis. The normally distributed data were expressed as the mean  $\pm$  standard deviation (SD). The measurement data between groups were compared using independent samples t-test, and those of multiple time points were compared by repeated measures analysis of variance (ANOVA) and Bonferroni post hoc test. The comparison of mean values between groups was performed using one-way ANOVA and LSD-t test post hoc test.  $P < 0.05$  was considered to indicate a statistically significant difference.

## Results

**General clinical data.** There was no significant difference between the two groups in general clinical data ( $P > 0.05$ ). Details are presented in Table I.

**Changes of serum inflammatory factors in groups A and B before and at 48 h after surgery.** CRP in group A was

27.53 $\pm$ 3.28 and 21.85 $\pm$ 2.39 mg/l before surgery and 48 h after surgery, respectively; whereas CRP in group B was 28.10 $\pm$ 3.02 and 16.34 $\pm$ 2.62 mg/l before surgery and 48 h after surgery, respectively. TNF- $\alpha$  in group A was 16.22 $\pm$ 2.68 and 8.39 $\pm$ 2.56 pg/ml before surgery and 48 h after surgery, respectively; whereas TNF- $\alpha$  in group B was 17.01 $\pm$ 2.14 and 4.33 $\pm$ 1.68 pg/ml before surgery and 48 h after surgery, respectively. IL-6 in group A was 43.26 $\pm$ 2.15 and 37.09 $\pm$ 2.24 ng/l before surgery and 48 h after surgery, respectively; whereas IL-6 in group B was 43.29 $\pm$ 2.04 and 24.88 $\pm$ 1.36 ng/l before surgery and 48 h after surgery, respectively. IL- $\beta$  in group A was 52.10 $\pm$ 3.42 and 39.08 $\pm$ 2.09 ng/l before surgery and 48 h after surgery, respectively; whereas IL- $\beta$  in group B was 51.19 $\pm$ 3.06 and 27.63 $\pm$ 1.27 ng/l before surgery and 48 h after surgery, respectively. Endotoxin levels in group A were 3.29 $\pm$ 1.28 and 2.59 $\pm$ 0.69 pg/ml before surgery and 48 h after surgery, respectively; whereas those in group B were 3.26 $\pm$ 1.29 and 2.00 $\pm$ 0.23 pg/ml before surgery and 48 h after surgery, respectively. NF- $\kappa$ B in group A was 93.01 $\pm$ 2.18 and 87.51 $\pm$ 2.04% before surgery and 48 h after surgery, respectively; whereas NF- $\kappa$ B in group B was 92.07 $\pm$ 2.49 and 81.06 $\pm$ 1.09%, respectively.

There was no marked difference in CRP, TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin, and NF- $\kappa$ B between the two groups before surgery ( $P > 0.05$ ). However, the levels of CRP, TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin and NF- $\kappa$ B in both groups after surgery were

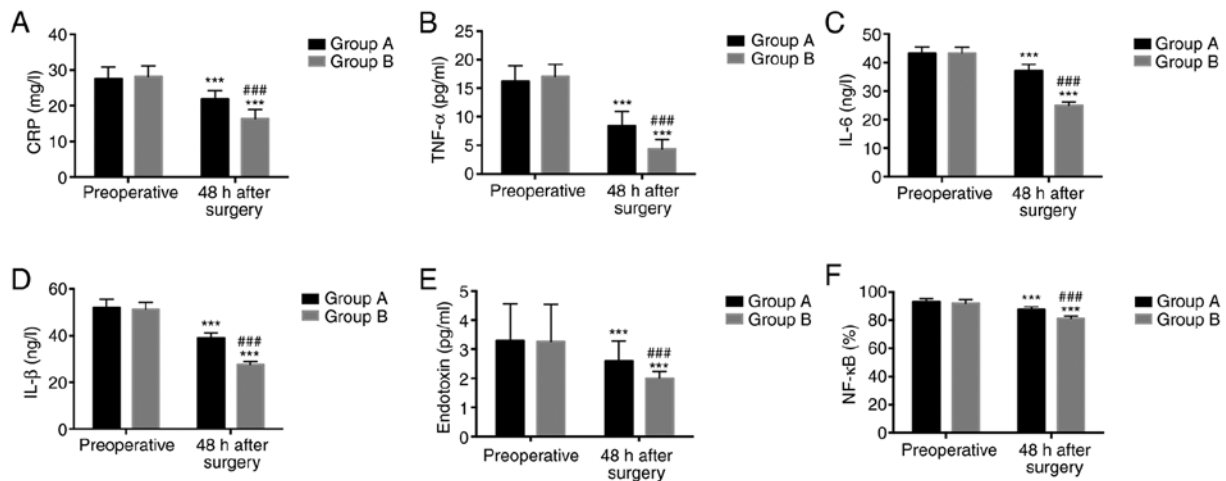


Figure 1. Changes of related serum indexes in groups A and B, before and at 48 h after surgery. Compared with before treatment, the concentrations of (A) CRP, (B) TNF- $\alpha$ , (C) IL-6, (D) IL- $\beta$ , (E) endotoxin and (F) NF- $\kappa$ B after treatment were significantly lower in both groups. After treatment, the concentrations of the serum indexes in group B were significantly lower than those in group A, with statistically significant differences. \*\*\* $P < 0.001$  and ### $P < 0.001$ . CRP, C-reactive protein; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; IL-6, interleukin-6; IL- $\beta$ , interleukin- $\beta$ ; NF- $\kappa$ B, nuclear factor  $\kappa$ B.

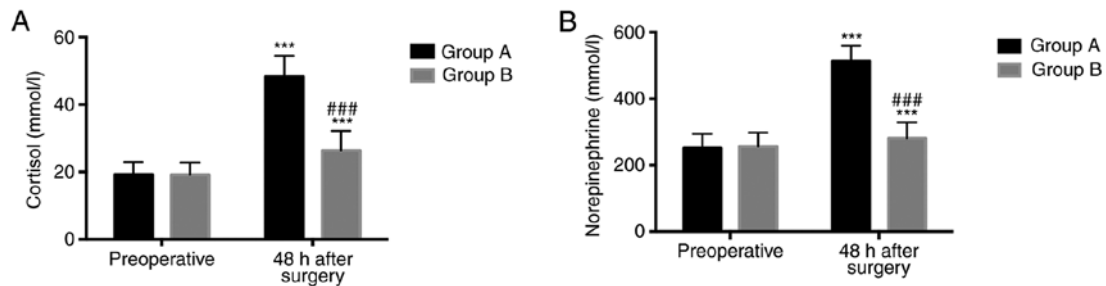


Figure 2. Changes of related serum stress indexes in groups A and B, before and at 48 h after surgery. Compared with before treatment, the concentrations of (A) cortisol and (B) norepinephrine after treatment were significantly higher in both groups, and the concentrations after treatment in group B were significantly lower than those in group A, with statistically significant differences. \*\*\* $P < 0.001$  and ### $P < 0.001$ .

significantly lower than those before surgery, and the levels in group B after surgery were significantly lower than those in group A ( $P < 0.001$ ) (Fig. 1).

*Changes of serum stress indexes before and 48 h after surgery in groups A and B.* Cortisol in group A was  $19.20 \pm 3.75$  and  $48.20 \pm 6.29$  mmol/l before surgery and 48 h after surgery, respectively; whereas, cortisol in group B was  $19.18 \pm 3.63$  and  $26.37 \pm 5.82$  mmol/l before surgery and 48 h after surgery, respectively. Norepinephrine in group A was  $251.47 \pm 42.92$  and  $513.20 \pm 45.94$  mmol/l before surgery and 48 h after surgery, respectively; whereas norepinephrine in group B was  $256.10 \pm 41.71$  and  $281.44 \pm 47.29$  mmol/l before surgery and 48 h after surgery, respectively.

There was no marked difference in cortisol and norepinephrine between the two groups before surgery ( $P > 0.05$ ). However, the levels of cortisol and norepinephrine in both groups after surgery were significantly higher than those before surgery, and the upregulation of the two in group B after surgery was lower than that in group A ( $P < 0.001$ ) (Fig. 2).

*Clinical efficacy in groups A and B.* In group A, there were 10 cases of patients with markedly effective treatment response, 24 with effective treatment response, 15 with

ineffective treatment response, and the total effective rate was 69.39%. In group B, there were 21 cases of patients with markedly effective response, 21 with effective treatment response, 3 with ineffective treatment response, and the total effective rate was 93.33%. The total effective rate in group B was higher than that of group A ( $P < 0.05$ ) (Table II).

*Perioperative related indexes in groups A and B.* The total duration of surgery in group A was  $148.02 \pm 28.39$  min, the amount of bleeding during surgery was  $350.89 \pm 34.90$  ml, the hospital stays was  $15.20 \pm 5.29$  days and the recovery time of gastrointestinal function was  $36.02 \pm 6.92$  h. The total duration of surgery in group B was  $102.29 \pm 26.04$  min, the intraoperative blood loss was  $163.29 \pm 31.28$  ml, the hospital stays was  $8.43 \pm 3.05$  days and the recovery time of gastrointestinal function was  $26.02 \pm 7.16$  h. The perioperative related indexes in group B were better than those in group A. Differences in total duration of surgery, intraoperative blood loss, hospital stay and recovery time of gastrointestinal function between the two groups were statistically remarkable ( $P < 0.001$ ) (Table III).

*Recovery of patients in the two groups.*

*Improvement of clinical symptoms of patients in groups A and B.* The exhaust time of patients in group A was

Table II. Clinical efficacy in groups A and B [n (%)].

Efficacy	Group A (n=49)	Group B (n=45)	$\chi^2$	P-value
Markedly effective	10 (20.41)	21 (46.67)	-	-
Effective	24 (48.98)	21 (46.67)	-	-
Ineffective	15 (30.61)	3 (6.67)	-	-
Total efficacy	34 (69.39)	42 (93.33)	8.688	0.003

Table III. Perioperative related indicators in groups A and B (mean  $\pm$  SD).

Indicators	Group A (n=49)	Group B (n=45)	t	P-value
Duration of surgery (min)	148.02 $\pm$ 28.39	102.29 $\pm$ 26.04	8.116	<0.001
Intraoperative blood loss (ml)	350.89 $\pm$ 34.90	163.29 $\pm$ 31.28	27.350	<0.001
Hospital stay (days)	15.20 $\pm$ 5.29	8.43 $\pm$ 3.05	7.513	<0.001
Recovery time of gastrointestinal function (h)	36.02 $\pm$ 6.92	26.02 $\pm$ 7.16	6.884	<0.001

Table IV. Improvement of clinical symptoms and signs in patients of groups A and B (mean  $\pm$  SD).

Variables	Group A (n=49)	Group B (n=45)	t	P-value
Anal exhaust time (days)	14.01 $\pm$ 2.31	12.62 $\pm$ 2.49	2.808	0.006
Body temperature recovery time (days)	8.20 $\pm$ 1.23	4.16 $\pm$ 1.52	14.22	<0.001
Abdominal pain relief time (h)	5.29 $\pm$ 0.93	2.82 $\pm$ 0.58	15.290	<0.001

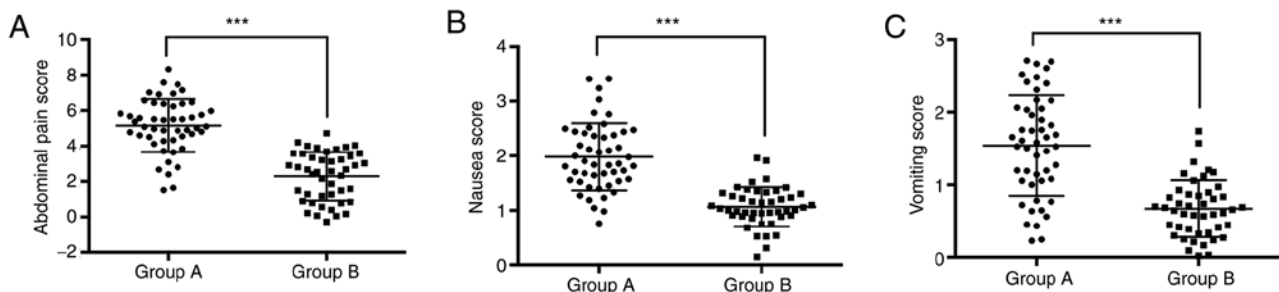


Figure 3. Score analysis of postoperative nausea, vomiting and abdominal pain in groups A and B. Compared with before treatment, (A) the abdominal pain score, (B) the nausea score and (C) the vomiting score in group B after treatment were significantly lower than those in group A, with statistically significant differences. \*\*\*P&lt;0.001.

14.01 $\pm$ 2.31 days, the recovery time of body temperature was 8.20 $\pm$ 1.23 days and the relief time of abdominal pain was 5.29 $\pm$ 0.93 h. The exhaust time of patients in group B was 12.62 $\pm$ 2.49 days, the recovery time of body temperature was 4.16 $\pm$ 1.52 days and the relief time of abdominal pain was 2.82 $\pm$ 0.58 h. Differences in exhaust time, body temperature recovery time and abdominal pain relief time between the two groups were markedly significant (P<0.05). Compared with the patients in group A, those in group B presented greater improvement as expressed by clinical symptoms (Table IV).

*Score analysis of postoperative nausea, vomiting, and abdominal pain in patients of groups A and B.* The

postoperative abdominal pain score in group A was 5.10 $\pm$ 1.49, nausea score was 1.98 $\pm$ 0.58 and vomiting score was 1.55 $\pm$ 0.78. The postoperative abdominal pain score in group B was 2.32 $\pm$ 1.10, nausea score was 0.94 $\pm$ 0.43 and vomiting score was 0.62 $\pm$ 0.46. The postoperative abdominal pain score, nausea score and vomiting score of patients in group B were significantly lower than those in group A (P<0.05) (Fig. 3).

*Analysis of complications of patients in groups A and B at 7 days after surgery.* The total complication rate due to cyst infection, incision infection, pancreatic fistula and gastrointestinal hemorrhage was lower in group B than that in group A; however, the differences were not statistically significant (P>0.05) (Table V).

Table V. Analysis of complications in groups A and B at 7 days after surgery [n (%)].

Complications	Group A (n=49)	Group B (n=45)	$\chi^2$	P-value
Cyst infection	2 (4.08)	1 (2.22)	-	-
Incision infection	2 (4.08)	1 (2.22)	-	-
Pancreatic fistula	2 (4.08)	0 (0.00)	-	-
Gastrointestinal hemorrhage	3 (6.12)	1 (2.22)	-	-
Total complications	9 (18.37)	3 (6.67)	2.884	0.090

Table VI. Univariate analysis of related factors for prognosis of patients [mean  $\pm$  SD, n (%)].

Factors	Good prognosis group (n=60)	Poor prognosis group (n=34)	$t/\chi^2$	P-value
Age (years)	45.40 $\pm$ 3.60	44.60 $\pm$ 3.40	1.056	0.294
Sex			1.223	0.346
Male	38 (63.33)	24 (70.59)		
Female	22 (36.67)	10 (29.41)		
Aetiological agent			0.370	0.985
Biliary tract disease	17 (28.33)	9 (26.47)		
Overeating	8 (13.33)	5 (14.71)		
Pancreatic duct obstruction	13 (21.67)	6 (17.65)		
Endocrine and metabolic disorders	10 (16.67)	6 (17.65)		
Other	12 (20.00)	8 (23.53)		
CRP (mg/l)	15.29 $\pm$ 2.01	20.73 $\pm$ 2.17	12.250	<0.001
TNF- $\alpha$ (pg/ml)	4.29 $\pm$ 1.22	9.13 $\pm$ 2.74	11.810	<0.001
IL-6 (ng/l)	25.10 $\pm$ 1.32	38.29 $\pm$ 2.54	33.170	<0.001
IL- $\beta$ (ng/l)	25.19 $\pm$ 1.31	39.05 $\pm$ 2.77	33.110	<0.001
Endotoxin (pg/ml)	1.97 $\pm$ 0.28	2.62 $\pm$ 0.71	6.299	<0.001
NF- $\kappa$ B (%)	78.23 $\pm$ 1.04	88.20 $\pm$ 2.52	26.94	<0.001
Surgical methods			48.920	<0.001
Duodenoscopy combined with laparoscopy	45 (75.00)	0 (0.00)		
Open surgery	15 (25.00)	34 (100.00)		
Abdominal pain score	2.01 $\pm$ 1.05	4.78 $\pm$ 1.13	11.960	<0.001
Nausea score	0.82 $\pm$ 0.26	1.73 $\pm$ 0.42	12.980	<0.001
Vomiting score	0.58 $\pm$ 0.27	1.53 $\pm$ 0.72	9.174	<0.001

CRP, C-reactive protein; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; IL-6, interleukin-6; IL- $\beta$ , interleukin- $\beta$ ; NF- $\kappa$ B, nuclear factor  $\kappa$ B.

*Analysis of prognostic factors of patients in groups A and B.* According to the prognosis of patients after 30 days, the patients were divided into two groups under the evaluation of the relevant attending doctors. Sixty patients with good prognosis were included in the good prognosis group and 34 with poor prognosis were included in the poor prognosis group. The prognostic factors related to SAP complicated with PP were assessed via Logistic univariate and multivariate analyses.

*i) Univariate analysis of prognostic factors in patients with SAP and PP.* Logistic univariate analysis of factors related to prognosis of patients with SAP and PP showed that CRP,

TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin, NF- $\kappa$ B, surgical methods, abdominal pain scores, vomiting scores and nausea scores had significant differences between the two groups ( $P < 0.05$ ). These factors were all related to the prognosis of patients with SAP and PP and were the risk factors for poor prognosis, as shown in Table VI.

*ii) Multivariate analysis of prognostic factors in patients with SAP and PP.* Risk factors related to the prognosis of patients were analyzed by multivariate conditional Logistic regression analysis. The results revealed that CRP, TNF- $\alpha$ , IL-6, IL- $\beta$  and the surgical methods were independent risk factors for the prognosis of patients with SAP and PP, as shown in Table VII.

Table VII. Multivariate analysis of related factors for prognosis of patients complicated with SAP and PP.

Factors	$\beta$	SE	Wald	P-value	Exp ( $\beta$ )	95% CI
CRP	2.170	1.065	4.003	0.039	8.206	0.392-48.397
TNF- $\alpha$	0.047	0.082	3.892	0.047	3.109	1.392-42.118
IL-6	2.368	1.692	5.090	0.021	9.145	0.089-39.950
IL- $\beta$	3.162	0.465	10.477	0.012	9.704	0.445-17.204
Endotoxin	3.006	2.089	8.028	0.398	6.154	1.778-23.326
NF- $\kappa$ B	3.129	2.765	8.753	0.440	7.093	1.924-21.372
Surgical methods	0.069	0.032	4.320	0.040	5.184	1.029-23.845
Abdominal pain score	1.093	1.114	4.082	0.239	4.112	0.054-29.357
Nausea score	1.823	1.659	4.376	0.301	4.276	1.104-20.659
Vomiting score	2.524	1.740	4.875	0.377	8.720	1.223-19.219

SAP, severe acute pancreatitis; PP, pancreatic pseudocyst; CRP, C-reactive protein; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; IL-6, interleukin-6; IL- $\beta$ , interleukin- $\beta$ ; NF- $\kappa$ B, nuclear factor  $\kappa$ B; CI, confidence interval.

## Discussion

PP is a pancreatic cyst lined by pancreatic epithelial cells gradually caused by adhesion of adjacent tissues around the pancreas in patients with acute or chronic pancreatitis (15). According to a previous study, if PP is not absorbed naturally or treated correctly, other complications, such as swollen bursa rupture and intracapsular hemorrhage, will occur which will aggravate the disease (16). At present, the continuous development of minimally invasive surgical techniques in clinical practice has diversified the surgical schemes for SAP complicated with PP (17).

Duodenoscopy combined with laparoscopic surgery is a combined method during which a support frame is implanted between the cyst and the stomach of the patient under the guidance of endoscopy so that the cyst can enter the stomach more smoothly, making its removal much more convenient, and greatly reducing the pain after surgery (18). This method plays an important role in the clinical treatment of SAP complicated with PP (19). In the present study, the clinical efficacy of duodenoscopy combined with laparoscopic surgery was higher than that of laparotomy alone. The perioperative indexes, such as total duration of surgery, intraoperative blood loss, hospital stay and recovery time of gastrointestinal function, were significantly better in patients receiving the combined treatment than those undergoing traditional laparotomy. The complications due to cyst infection, incision infection, pancreatic fistula and gastrointestinal hemorrhage were also less after the combined treatment. Moreover, postoperative nausea, vomiting, and abdominal pain scores in patients treated with the combination of duodenoscopy and laparoscopy were significantly lower than those of patients treated with traditional laparotomy. Therefore, we believe that the combination of duodenoscopy and laparoscopy is more reliable in ensuring the safety and clinical efficacy of SAP and PP treatment.

A recent study has reported that the prognosis of patients with SAP and PP is relevant to local or systemic stress reactions and inflammatory reactions induced during surgery. Further expression of a large number of cytokines can also cause pathological damage (20). TNF- $\alpha$  in serum is a vital

regulatory factor in the process of inflammatory reaction. TNF- $\alpha$  initiates the inflammatory effect in resection surgery and together with other inflammatory cytokines initiates and maintains inflammatory reaction (21). CRP is a sensitive indicator reflecting whether the body is infected or not. CRP has been reported to increase significantly when infection occurs after resection (22). A study has also shown that TNF- $\alpha$  is the initial factor of inflammatory response in SAP complicated with PP. Further expression of TNF- $\alpha$  can induce high expressions of IL-6, IL- $\beta$  and other cytokines, causing further damage to tissue and organs at the inflammatory site (23). Surgery activates the body's stress response. When the body is subjected to noxious stimulation, such as surgery, anesthesia and trauma, a series of neuroendocrine activities that cause metabolic changes appear in the body. Moreover, the more severe the surgical trauma is, the more intense the stress response of the body is, and the concentration of cortisol and norepinephrine in pituitary-adrenal cortex in circulating blood also increases suddenly (24). According to the results of the present study, there was no marked difference between the two groups in serum indexes and serum stress indexes before surgery. However, the levels of CRP, TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin and NF- $\kappa$ B in the two groups after surgery were significantly lower than those before surgery. The levels of cortisol and norepinephrine in both groups after surgery were significantly higher than those before surgery. CRP, TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin and NF- $\kappa$ B in group B after surgery were significantly lower than those in group A. As a result, the treatment plan of duodenoscopy combined with laparoscopic surgery for patients with SAP and PP has little effect on the inflammatory response and stress response of the body, which is conducive to the fast recovery of patients after surgery. Finally, according to the prognosis assessment of patients after 30 days, the relevant prognostic factors were investigated. It was shown that CRP, TNF- $\alpha$ , IL-6, IL- $\beta$ , endotoxin, NF- $\kappa$ B, surgical methods, abdominal pain score, vomiting score and nausea score were all related to the prognosis of patients with SAP and PP, and were the risk factors for poor prognosis. CRP, TNF- $\alpha$ , IL-6, IL- $\beta$  and surgical methods were independent risk factors for the prognosis of patients with SAP and



PP. Some studies have also reported that different surgical methods directly affect the prognosis of patients (25-27). A recent study has confirmed that the prognosis of patients with SAP also needs long-term monitoring of serum inflammatory factors (28).

The present study focused on the clinical efficacy of duodenoscopy combined with laparoscopy in the treatment of patients with SAP and PP. The results revealed that the safety of duodenoscopy combined with laparoscopy was high, and the influence on IL-6 and CRP was less volatile. However, there are still some limitations. For example, the relationship of different IL-6 and CRP fluctuations with the prognosis of patients, as well as the relationship between other routine biochemical indicators and the progress of surgery need to be further analyzed.

In conclusion, implementing duodenoscopy combined with laparoscopic surgery for SAP complicated with PP induces small inflammatory and stress response, and it is highly safe, worthy to be popularized.

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### Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

### Authors' contributions

LZ designed the study. SH performed the experiments. FL and SH measured outcomes and determined cortisol and norepinephrine. JY analyzed the data. SH wrote the manuscript. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Weifang People's Hospital (Weifang, China) (ethics approval no. WFRM1509PRC). Patients who participated in the study had complete clinical data. Signed written informed consents were obtained from the patients and/or guardians.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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