77068_Auto_Edited.docx

Name of Journal: *World Journal of Clinical Cases*

Manuscript NO: 77068

Manuscript Type: ORIGINAL ARTICLE

Observational Study

Clinical observation of laparoscopic cholecystectomy combined with endoscopic retrograde cholangiopancreatography or common bile duct lithotripsy

Abstract

BACKGROUND

The incidence of common bile duct (CBD) stones accounts for approximately 10%–15% of all CBD diseases. Approximately 8%–20% of these patients also have gallstones with heterogenous signs and symptoms.

AIM

To investigate the clinical effects of laparoscopic cholecystectomy (LC) combined with endoscopic retrograde cholangiopancreatography (ERCP) and LC with CBD excision and stone extraction in one-stage suture (LBEPS) for the treatment of gallbladder and CBD stones.

METHODS

Ninety-four patients with gallbladder and CBD stones were selected from our hospital from January 2018 to June 2021. They were randomly divided into study and control groups with 47 patients each. The study group underwent LC with ERCP, and the control group underwent LC with LBEPS. Surgery, recovery time of gastrointestinal function, complication rates, liver function indexes, and stress response indexes were measured pre- and postoperatively in both the groups.

RESULTS

The durations of treatment and hospital stay were shorter in the study group than in the control group. There was no significant difference between the one-time stone removal rate between the study and control groups. The time to anal evacuation, resumption of oral feeding, time to bowel sound recovery, and time to defecation were shorter in the study group than in the control group. The preoperative serum direct bilirubin (DBIL), total bilirubin (TBIL), and alanine aminotransferase (ALT) levels were insignificantly higher in the study group than that in the control group. A day after surgery, the postoperative serum DBIL, TBIL, and ALT levels were lower than their preoperative levels in both groups, and of the two groups, the levels were lower in the study group. Although the preoperative serum adrenocorticotrophic (ACTH), cortisol (COR), epinephrine (A), and norepinephrine (NE) levels were higher in the study group than that in the control group, these differences were not significant (P > 0.05). The serum ACTH, COR, A, and NE levels in both groups decreased one day after surgery compared to the preoperative levels, but the inter-group difference was statistically insignificant. Similarly, (91.79 ± 10.44) ng/mL, A, and NE levels were lower in the study group than in the control group. The incidence of complications was lower in the study group than in the control group.

CONCLUSION

LC combined with ERCP induces only a mild stress response; this procedure can decrease the risk of complications, improve liver function, and achieve and promote a faster recovery of gastrointestinal functions.

INTRODUCTION

The incidence of common bile duct (CBD) stones is approximately 10%–15% of the total incidence of all CBD diseases. Approximately 8%–20% of these patients also have gallstones, presenting with complex and diverse clinical manifestations[1,2]. If patients of gallstones with coexisting CBD stones do not receive timely and effective intervention, biliary obstruction may lead to severe infections and complications like toxic shock as well as many other threats to patients' life and health[3,4].

Traditionally, patients with gallbladder and CBD stones are treated by open surgery. This method can achieve good results but at the expense of being more traumatic, potentially more complicating, and with longer postoperative recovery times of bodily functions[5]. Laparoscopy is a modern and popular minimally invasive surgical technique. Laparoscopic cholecystectomy (LC) combined with endoscopic retrograde cholangiopancreatography (ERCP) and LC combined with choledochotomy and lithotomy (LBEPS) are very commonly used. Both procedures have their own unique characteristics and can achieve the treatment purpose[6-8].

To further explore the efficacy and safety of LC combined with ERCP and LC combined with LBEPS in gallbladder and CBD stones, 94 patients with this condition from our hospital were selected for this study, and the aforementioned contents were discussed in groups.

MATERIALS AND METHODS

General information

Ninety-four patients with gallbladder and CBD stones in our hospital from January 2018 to June 2021 were selected and randomly divided into a study group and a control group, with 47 cases in each. There were 26 men and 21 women in the study group; the age ranged from 46 to 76 years (average age: 55.97 ± 11.29 years). The number of CBD stones ranged from 1 to 4 (average: 2.41 ± 1.10), and the diameter of the CBD stones ranged from 3.1 to 8.6 mm (average: 5.89 ± 1.64 mm). There were 29 men and 18 women in the control group; the age ranged from 43 to 79 years (average: 60.44 ± 10.71 years); and the diameter of the CBD stones ranged from 3.1 to 8.6 mm (average: 5.89 ± 1.64 mm). The clinical data on sex, age, the diameter of the CBD stones, and the number of CBD stones were balanced and comparable between the two groups (P > 0.05). This study was approved by the ethics committee of our hospital.

Selection criteria

The inclusion criteria were: (1) diagnosis confirmed by abdominal computed tomography or hepatobiliary ultrasound; (2) age less than 80 years; (3) knowledge of the study and provision of signed informed consent; and (4) good compliance and cooperation, with an ability to understand and communicate for smooth conduction of the study.

The exclusion criteria were: (1) patients with coagulation and bleeding disorders; (2) patients unfit for carbon dioxide pneumoperitoneum and general anesthesia intubation; (3) patients with anomalous bile duct anatomy; (4) patients with severe acute pancreatitis and purulent obstructive cholangitis; and (5) patients with bile duct/gallbladder malignancy.

Study group

LC combined with ERCP was performed in this group. The patient was assisted to lie in a supine position under general anesthesia for 8 h. The patient's abdomen was assessed via a three-/four-hole approach. The gallbladder triangle was explored and separated, its artery and the cystic duct were clamped, and the gallbladder was removed from the gallbladder bed. After ensuring hemostasis, a Wen drain was left in place and the wound was sutured. The patient was then turned to the left lateral position. A duodenoscope was introduced through the mouth and *via* the esophagus and the duodenal papilla was identified in the duodenum. Selective intubation of the CBD was performed with a guidewire, a contrast medium was injected, and ERCP was completed. Endoscopic duodenal papillary sphincterotomy was performed at the 11 o'clock position of the duodenal papilla by the retracting knife method. The stones were then extracted and retrieved orally. Papillary balloon dilation was performed in accordance with the number, size, location, and softness of the stones. After the stone extraction, a cholangiogram was performed to check for residual stones, which if found, were managed by repeat duodenoscopic removal. A nasobiliary drainage tube was routinely left for flushing the bile duct and for draining the bile. If no abnormality was observed 6 h postoperatively, the patient was orally allowed to consume clear liquids. The patient was permitted to consume normal food 24 h postoperatively in case serum amylase and lipase levels were found to be in the normal range. The nasobiliary drainage tube was withdrawn one to two days postoperatively only after a normal nasobiliary ductography.

Control group

For the control group, LC combined with LBEPS was performed; LC was completed in the manner similar to that of the study group.

LBEPS was performed as follows: an incision was made, and the CBD was exposed; a 10-mm incision was made in the anterior wall of the CBD, and a fiberoptic choledochoscope was inserted in the subxiphoid process to investigate the upper and lower segments of the CBD; any bile duct stones detected were removed through a lithotripsy basket, while sediment-like stones and small stones that were difficult to remove by the basket were flushed out into the duodenum. The CBD incision was closed by a one-stage suture using 4-0 absorbable sutures (interrupted) after the following conditions were confirmed on examination: only a mild inflammation of the CBD; normally functioning sphincter of Oddi; and no residual stones in the CBD. A drain was placed in the gallbladder bed at the end of the surgery. The trocar subcutaneous tissues were sutured, the skin was glued with tissue glue, and the gastric tube was removed after surgery.

Observed indicators

Time durations of treatment, hospitalization, and primary stone extraction rate were documented to compare the two groups. The recovery times of gastrointestinal functions in both groups were documented, including the time to anal evacuation, resumption of oral feeding, time to recovery of bowel sounds, and the time to defecation. The levels of liver function indexes, including ALT, TBIL, and DBIL, were measured pre- and postoperatively in both groups; 4 mL of blood was drawn from the medial cubital vein, centrifuged, and the levels of the liver function indexes were measured by a Hitachi 7180 automatic biochemical analyzer. The levels of stress indicators, including ACTH, COR, A, and NE, were measured pre- and postoperatively in both groups by enzyme-linked immunosorbent assay of peripheral venous blood. Finally, the incidence of complications in both groups was counted.

Statistical analysis

Data were analyzed by SPSS 22.0, and the measured data (mean ± SD) were expressed by the t-test. The measured data n (%) were expressed by the χ^2 test, and $P < 0.05$ indicated statistical significance.

RESULTS

Comparison of surgical conditions between the study and control groups

The treatment time was 97.64 ± 17.51 min and the duration of hospital stay was 7.08 ± 1.82 d in the study group, which was significantly longer in the control group [119.62 ± 24.37 min and 9.33 ± 2.29 d, respectively ($P < 0.05$)]. There was no significant difference between the one-time stone retrieval rate in the study group (97.87%) and the control group (95.74%) ($P > 0.05$) (Table 1).

Comparison of the recovery of gastrointestinal function between the two groups

In the study group, the time to anal evacuation was 25.02 ± 3.68 h, time to resume oral feeding was 7.82 ± 3.44 h, time to recovery of bowel sounds was 16.56 ± 3.58 h, and time to defecation was 33.35 ± 6.07 h. These values were significantly longer in the control group [28.29 ± 4.11 h, 9.62 ± 4.09 h, 18.94 ± 4.29 h, 36.96 ± 7.11 h, respectively ($P < 0.05$)] (Table 2).

Comparison of liver function index levels before and after surgery between the two groups

The preoperative serum levels of DBIL, TBIL, and ALT were 182.10 ± 82.33 umol/L, 258.62 ± 100.54 umol/L, and 38.56 ± 7.18 U/L, respectively, in the study group. These were not significantly different from those of the control group [178.89 ± 79.59 umol/L, 261.45 ± 96.77 umol/L, and 40.04 ± 6.69 U/L, respectively ($P > 0.05$)]. The serum DBIL, TBIL, and ALT levels were significantly lower in both groups a day after surgery as compared to the levels before treatment ($P < 0.05$). The serum levels of DBIL, TBIL, and ALT were 93.37 ± 40.02 umol/L, 156.98 ± 83.31 umol/L, and 26.83 ± 6.65 U/L, respectively, in the study group. These values were significantly longer in the control group [111.51 ± 36.33 umol/L, 191.03 ± 72.12 umol/L, and 30.13 ± 7.92 U/L respectively ($P < 0.05$)] (Table 3).

Comparison of stress index levels before and after surgery between the two groups

Preoperative serum levels of ACTH, COR, A, and NE were 14.78 ± 2.28 ng/mL, 126.67 ± 11.59 ng/mL, 1.39 ± 0.15 nmol/L, and 3.68 ± 0.65 nmol/L, respectively, in the study group. These were not significantly different from those of the control group [15.36 ± 2.35 ng/mL, 130.68 ± 12.01 ng/mL, 1.42 ± 0.12 nmol/L, 3.83 ± 0.72 nmol/L, respectively ($P > 0.05$)]. The serum ACTH, COR, A, and NE levels in both groups decreased significantly one day after surgery compared to the levels measured before surgery ($P < 0.05$). The levels of serum ACTH, COR, A, and NE one day after surgery were 6.19 ± 2.05 ng/mL, 91.79 ± 10.44 ng/mL, 0.71 ± 0.24 nmol/L, and 1.41 ± 0.51 nmol/L, respectively, in the study group. These were significantly lower than that in the control group [8.68 ± 3.88 ng/mL, 105.32 ± 11.65 ng/mL, 0.96 ± 0.37 nmol/L, 2.21 ± 0.73 nmol/L, respectively ($P < 0.05$)] (Table 4).

Comparison of complications between the two groups

The complication rate was significantly lower in the study group (6.38%) than in the control group (21.28%) ($P < 0.05$) (Table 5).

DISCUSSION

Gallbladder and CBD stones have a high prevalence rate, with a recent increase in incidence due to several factors such as poor lifestyle habits and changes in dietary structure[9,10]. Patients with gallbladder and CBD stones require timely and effective intervention to prevent the disease from worsening and are thus more difficult to treat.

Open surgery, the traditional clinical treatment for gallbladder and CBD stones, though effective requires longer preoperative fasting and hospitalization. The T-tube-associated complications create both psychological and physical burdens for patients[11,12]. LC combined with either ERCP or LBEPS has changed the nature of treatment of gallbladder and bile duct stones because of their minimally invasive nature. LBEPS requires maximum placement of the choledochoscope into the gallbladder and CBD to assess the location, number, and volume of stones under direct vision. In a narrow biliary tract, it is difficult to maneuver the scope distally into the bile duct. This may be unfavorable for stone removal with LC[13,14]. Moreover, it has been reported that LBEPS requires T-tube drainage, which can cause serious invasive injury, including bile duct injury, which is not favorable for prognosis[15]. In contrast, ERCP provides information on the distribution, number, and morphology of stones even in a narrow bile duct. ERCP is simpler to perform, does not require a T-tube, and hence preserves the integrity and normal physiological function of the bile duct, which is more desirable and safe[16].

In this study, LC combined with ERCP and LC combined with LBEPS were used to treat patients with gallbladder and CBD stones in our hospital. The study results showed that the surgery and postoperative recovery of gastrointestinal functions in the study group were better than those of the control group. The complication rates were significantly lower in the study group (6.38%) than those in the control group (21.28% with $P < 0.05$), indicating that LC combined with ERCP was more effective than LC combined with LBEPS in reducing the number of gallstones and CBD stones. LC combined with ERCP was found to be more effective and safer as it reduced the likelihood of intraoperative injury, shortened postoperative gastrointestinal function recovery time, and reduced the risk of complications. The main reasons for this are as follows. (1) With dual-scope combined procedures, gallstones and CBD stones can be treated simultaneously. Cholecystectomy and LBEPS have similar operative duration; however, ERCP take significantly lesser time than choledochoscopy; (2) LC combined with LBEPS requires routine removal of the gallbladder, and parallel dissection of the CBD; and (3) LC combined with LBEPS requires routine removal of the gallbladder, separation, and dissection of the CBD and anterior choledochotomy. In contrast, choledochotomy requires a longer time to perform choledochoscopic stone extraction through the mouth, which can increase bleeding. Therefore, LC combined with ERCP overcomes these problems and ensures treatment safety[17,18].

Although LC combined with ERCP and LC combined with LBEPS are both minimally invasive procedures for gallbladder and CBD stones, they are nonetheless invasive, and can cause varying degrees of liver function derangements and trigger stress reactions. These factors negatively impact disease recovery and prognosis. In this study, serum DBIL, TBIL, and ALT levels were higher in the study group than in the control group. Conversely, serum ACTH, COR, A, and NE levels were lower in the study group than in the control group ($P < 0.05$), suggesting that LC combined with ERCP is more advantageous in reducing the stress response and liver function damage. This further supports the clinical efficacy of LC combined with ERCP therapy for the treatment of gallbladder and CBD stones from the perspective of serum markers. In addition, with dual-scope combination, after the resection of the gallbladder, the LC is immediately followed by ERCP. This shortens the duration of carbon dioxide pneumoperitoneum, thereby reducing the stress reaction in vivo. Liver function also improves due to smooth and rapid draining of bile, facilitated by placement of the biliary plastic stent or a nasobiliary tube. For LC combined with ERCP, if intraoperative CBD stones are difficult to remove, plastic biliary stents can be left in place to reduce the occurrence of vagal biliary fistula or obstructive purulent cholangitis. Furthermore, ERCP can be repeated safely in cases of residual removal or difficulty in stone removal and thus can prevent the trauma caused by reoperation[19,20].

Our study has some limitations. The sample size was not large enough; a larger multicenter study is needed to confirm these results. Moreover, long-term follow-up was not performed in this study.

CONCLUSION

In conclusion, the treatment of gallbladder and CBD stones by LC combined with ERCP is worth promoting because it can reduce trauma, decrease the risk of complications, reduce the impact on liver function, induce only a mild stress reaction, and promote a faster recovery of gastrointestinal function. A larger trial with longer follow-up is needed to confirm whether patients with gallbladder and CBD stones can benefit from LC combined with ERCP therapy in the long term.

REFERENCES

1 **Karpuz S**, Attaallah W. Could cholecystectomy be abandoned after removal of bile duct stones by endoscopic retrograde cholangio-pancreaticography? *Asian J Surg* 2021; **44**: 939-944 [PMID: 33573924 DOI: 10.1016/j.asjsur.2021.01.013]

2 **Giuseppe Tarantino,** Paolo Magistri,Roberto Ballarin,et al.Surgery in biliary lithiasis: from the traditional "open" approach to laparoscopy and the "rendezvous" technique MID: 29291778 DOI: 10.1016/S1499-3872(17)60031-6

3 **Garg PK**, Bansal VK. Intraoperative on-table endoscopic retrograde cholangiopancreatography (ERCP) is better than laparoscopic bile duct exploration for concomitant bile duct stones during emergency laparoscopic cholecystectomy. *Evid Based Med* 2017; **22**: 27 [PMID: 27836920 DOI: 10.1136/ebmed-2016-110549]

4 **He YG**, Gao MF, Li J, Peng XH, Tang YC, Huang XB, Li YM. Cystic duct dilation through endoscopic retrograde cholangiopancreatography for treatment of gallstones and choledocholithiasis: Six case reports and review of literature. *World J Clin Cases* 2021; **9**: 736-747 [PMID: 33553415 DOI: 10.12998/wjcc.v9.i3.736]

5 **Aleknaite A**, Simutis G, Stanaitis J, Jucaitis T, Drungilas M, Valantinas J, Strupas K. Comparison of Endoscopy First and Laparoscopic Cholecystectomy First Strategies for

Patients With Gallstone Disease and Intermediate Risk of Choledocholithiasis: Protocol for a Clinical Randomized Controlled Trial. *JMIR Res Protoc* 2021; **10**: e18837 [PMID: 33538700 DOI: 10.2196/18837]

6 **Vakayil V**, Klinker ST, Sulciner ML, Mallick R, Trikudanathan G, Amateau SK, Davido HT, Freeman M, Harmon JV. Single-stage management of choledocholithiasis: intraoperative ERCP versus laparoscopic common bile duct exploration. *Surg Endosc* 2020; **34**: 4616-4625 [PMID: 31617103 DOI: 10.1007/s00464-019-07215-w]

7 **Donoghue S**, Jones RM, Bush A, Srinivas G, Bowling K, Andrews S. Cost effectiveness of intraoperative laparoscopic ultrasound for suspected choledocholithiasis; outcomes from a specialist benign upper gastrointestinal unit. *Ann R Coll Surg Engl* 2020; **102**: 598-600 [PMID: 32538107 DOI: 10.1308/rcsann.2020.0109]

8 **Al-Temimi MH**, Kim EG, Chandrasekaran B, Franz V, Trujillo CN, Mousa A, Tessier DJ, Johna SD, Santos DA. Laparoscopic common bile duct exploration versus endoscopic retrograde cholangiopancreatography for choledocholithiasis found at time of laparoscopic cholecystectomy: Analysis of a large integrated health care system database. *Am J Surg* 2017; **214**: 1075-1079 [PMID: 28939251 DOI: 10.1016/j.amjsurg.2017.08.030]

9 **Di Mauro D**, Ricciardi E, Siragusa L, Manzelli A. Outcome of Laparoscopic Common Bile Duct Exploration After Failed Endoscopic Retrograde Cholangiopancreatography: A Comparative Study. *J Laparoendosc Adv Surg Tech A* 2019; **29**: 1391-1396 [PMID: 31355693 DOI: 10.1089/lap.2019.0383]

10 **Xu J**, Yang C. Cholecystectomy outcomes after endoscopic sphincterotomy in patients with choledocholithiasis: a meta-analysis. *BMC Gastroenterol* 2020; **20**: 229 [PMID: 32680467 DOI: 10.1186/s12876-020-01376-y]

11 **Gonzalez-Urquijo M**, Baca-Arzaga AA, Flores-Villalba E, Rodarte-Shade M. Laparoscopy-assisted transgastric endoscopic retrograde cholangiopancreatography for choledocholithiasis after Roux-en-Y gastric bypass: A case report. *Ann Med Surg (Lond)* 2019; **44**: 46-50 [PMID: 31312443 DOI: 10.1016/j.amsu.2019.06.008]

12 **Peponis T**, Panda N, Eskesen TG, Forcione DG, Yeh DD, Saillant N, Kaafarani HMA, King DR, de Moya MA, Velmahos GC, Fagenholz PJ. Preoperative endoscopic retrograde cholangio-pancreatography (ERCP) is a risk factor for surgical site infections after laparoscopic cholecystectomy. *Am J Surg* 2019; **218**: 140-144 [PMID: 30473225 DOI: 10.1016/j.amjsurg.2018.09.033]
13 **Thacoor A**, Pike TW, Pathak S, Dixon J, Macutkiewicz C, Smith AM. The role of intraoperative cholangiography in patients undergoing laparoscopic cholecystectomy for acute gallstone pancreatitis: is magnetic resonance cholangiopancreatography needed? *Ann R Coll Surg Engl* 2019; **101**: 428-431 [PMID: 31155897 DOI: 10.1308/rcsann.2019.0049]
14 **Şenocak R**, Çelik SU, Kaymak Ş, Hançerlioğullari O. Perioperative outcomes of the patients treated using laparoscopic cholecystectomy after emergent endoscopic retrograde cholangiopancreatography for bile duct stones: Does timing matter? *Ulus Travma Acil Cerrahi Derg* 2020; **26**: 396-404 [PMID: 32436986 DOI: 10.14744/tjtes.2020.94401]
15 **Lee HW**, Park DH, Lee JH, Oh DW, Song TJ, Lee SS, Seo DW, Lee SK, Kim MH, Moon JE. Prevalence and Predictors of Unnecessary Endoscopic Retrograde Cholangiopancreatography in the Two-Stage Endoscopic Stone Extraction Followed by Laparoscopic Cholecystectomy. *J Gastrointest Surg* 2019; **23**: 1578-1588 [PMID: 30671794 DOI: 10.1007/s11605-018-04090-z]
16 **Gomez D**, Cabrera LF, Villarreal R, Pedraza M, Pulido J, Sebastián S, Urrutia A, Mendoza A, Zundel N. Laparoscopic Common Bile Duct Exploration With Primary Closure After Failed Endoscopic Retrograde Cholangiopancreatography Without Intraoperative Cholangiography: A Case Series from a Referral Center in Bogota, Colombia. *J Laparoendosc Adv Surg Tech A* 2020; **30**: 267-272 [PMID: 32053025 DOI: 10.1089/lap.2019.0547]
17 **Singh AN**, Kilambi R. Single-stage laparoscopic common bile duct exploration and cholecystectomy versus two-stage endoscopic stone extraction followed by laparoscopic cholecystectomy for patients with gallbladder stones with common bile duct stones:

systematic review and meta-analysis of randomized trials with trial sequential analysis. *Surg Endosc* 2018; **32**: 3763-3776 [PMID: 29603004 DOI: 10.1007/s00464-018-6170-8]
18 **Ricci C**, Pagano N, Taffurelli G, Pacilio CA, Migliori M, Bazzoli F, Casadei R, Minni F. Comparison of Efficacy and Safety of 4 Combinations of Laparoscopic and Intraoperative Techniques for Management of Gallstone Disease With Biliary Duct Calculi: A Systematic Review and Network Meta-analysis. *JAMA Surg* 2018; **153**: e181167 [PMID: 29847616 DOI: 10.1001/jamasurg.2018.1167]
19 **Vettoretto N**, Arezzo A, Famiglietti F, Cirocchi R, Moja L, Morino M. Laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy in people undergoing laparoscopic cholecystectomy for stones in the gallbladder and bile duct. *Cochrane Database Syst Rev* 2018; **4**: CD010507 [PMID: 29641848 DOI: 10.1002/14651858.CD010507.pub2]
20 **Pan L**, Chen M, Ji L, Zheng L, Yan P, Fang J, Zhang B, Cai X. The Safety and Efficacy of Laparoscopic Common Bile Duct Exploration Combined with Cholecystectomy for the Management of Cholecysto-choledocholithiasis: An Up-to-date Meta-analysis. *Ann Surg* 2018; **268**: 247-253 [PMID: 29533266 DOI: 10.1097/SLA.0000000000002731]

Table 1 Comparison of surgical conditions between the two groups

Groups	**Treatment time (min)**	**Length of hospitalization (d)**	**One-time stone retrieval rate, *n* (%)**
Research Group (*n* = 47)	97.64 ± 17.51	7.08 ± 1.82	46 (97.87)
Control group (*n* = 47)	119.62 ± 24.37	9.33 ± 2.29	45 (95.74)
χ^2/t value	5.022	5.273	0.344

P value	0.000	0.000	0.556

Table 2 Comparison of recovery of gastrointestinal function between the two groups (mean ± SD, h)

Groups	Anal venting time	Time to start eating	Recovery time of bowel sounds	Defecation time
Research Group (*n* = 47)	25.02 ± 3.68	7.82 ± 3.44	16.56 ± 3.58	33.35 ± 6.07
Control group (*n* = 47)	28.29 ± 4.11	9.62 ± 4.09	18.94 ± 4.29	36.96 ± 7.11
t value	4.064	2.309	2.920	2.647
P value	0.000	0.023	0.004	0.010

Table 3 Comparison of liver function index levels before and after surgery between the two groups (mean ± SD)

Groups	DBIL (umol/L)	TBIL (umol/L)	ALT (U/L)
Pre-operative			
Research Group (*n* = 47)	182.10 ± 82.33	258.62 ± 100.54	38.56 ± 7.18
Control group (*n* = 47)	178.89 ± 79.59	261.45 ± 96.77	40.04 ± 6.69
t value	0.198	0.139	1.034
P value	0.844	0.890	0.304
1 d after surgery			
Research Group (*n* = 47)	93.37 ± 40.02[a]	156.98 ± 83.31[a]	26.83 ± 6.65[a]

Control group (*n* = 47)	111.51 ± 36.33[a]	191.03 ± 72.12[a]	30.13 ± 7.92[a]
t value	2.301	2.118	2.188
P value	0.024	0.037	0.031

[a]$P < 0.05$ *vs* this group preoperatively.

DBIL: serum direct bilirubin; TBIL: total bilirubin; ALT: alanine aminotransferase.

Table 4 Comparison of stress response index levels before and after surgery between the two groups (mean ± SD)

Groups	ACTH (ng/ml)	COR (ng/ml)	A (nmol/L)	NE (nmol/L)
Pre-operative				
Research Group (*n* = 47)	14.78 ± 2.28	126.67 ± 11.59	1.39 ± 0.15	3.68 ± 0.65
Control group (*n* = 47)	15.36 ± 2.35	130.68 ± 12.01	1.42 ± 0.12	3.83 ± 0.72
t value	1.214	1.647	1.071	1.060
P value	0.228	0.103	0.287	0.292
1 d after surgery				
Research Group (*n* = 47)	6.19 ± 2.05[a]	91.79 ± 10.44[a]	0.71 ± 0.24[a]	1.41 ± 0.51[a]
Control group (*n* = 47)	8.68 ± 3.88[a]	105.32 ± 11.65[a]	0.96 ± 0.37[a]	2.21 ± 0.73[a]
t value	3.890	5.929	3.886	6.159
P value	0.000	0.000	0.000	0.000

[a]$P < 0.05$ *vs* this group preoperatively.

ACTH: Serum adrenocorticotrophic; COR: Cortisol; A: Epinephrine; NE: Norepinephrine.

Table 5 Comparison of complications between the two groups, *n* (%)

Groups	Hemorrhage	Biliary tract infection	Bile leak	Pancreatitis	Total incidence
Research Group (n = 47)	0 (0.00)	1 (2.13)	0 (0.00)	2 (4.26)	3 (6.38)
Control group (n = 47)	5 (10.64)	3 (6.38)	1 (2.13)	1 (2.13)	10 (21.28)
χ^2 value					4.374
P value					0.036

77068_Auto_Edited.docx

ORIGINALITY REPORT

5%
SIMILARITY INDEX

PRIMARY SOURCES

1	www.wjgnet.com Internet	69 words — 2%
2	www.science.gov Internet	30 words — 1%
3	www.hindawi.com Internet	26 words — 1%
4	zenodo.org Internet	21 words — 1%

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 1%
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 10 WORDS