MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2020; 26: e924946
DOI: 10.12659/MSM.924946

Received: 2020.04.08
Accepted: 2020.07.13
Available online: 2020.07.17
Published: 2020.09.12

Use of Enhanced Recovery After Surgery (ERAS) in Laparoscopic Cholecystectomy (LC) Combined with Laparoscopic Common Bile Duct Exploration (LCBDE): A Cohort Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AEG **Nannan Zhang**
F **Gang Wu**
A **Yuanhang Zhou**
C **Zhiwei Liao**
F **Jinxing Guo**
B **Yongjun Liu**
B **Qi Huang**
F **Xiaodong Li**

Department of General Surgery, Baoshan Branch of Huashan North Courtyard Affiliated to Fudan University, (Renhe Hospital, Baoshan District, Shanghai), Shanghai, P.R. China

Corresponding Author: Gang Wu, e-mail: wugang66@aliyun.com
Source of support: We are grateful to the Program for Training Excellent Young Doctors in Baoshan, Shanghai for funding support (grant no. bswsyq-2017-A09) and the Special Fund Project for Science and Technology Innovation of the Science and Technology Commission in Shanghai Baoshan District (grant no. 18-E-15)

Background: The have been few reports on use of ERAS in LC combined with LCBDE to promote postoperative recovery of patients. Therefore, the purpose of this cohort study was to explore the use of ERAS in patients who underwent LC combined with LCBDE.

Material/Methods: We collected clinical data of 445 patients who underwent elective laparoscopic cholecystectomy combined with laparoscopic common bile duct exploration from January 2015 to February 2019 in our hospital and divided the patients into an E-LC group and an LC group. The stress response index, postoperative complication rate, and postoperative rehabilitation effect of the 2 groups were compared and analyzed.

Results: The WBC count and CRP levels in the E-LC group were significantly lower than those of the LC group 1 day after surgery ($p<0.05$). In terms of the postoperative complications, the incidence of nausea, incisional pain, and vomiting in the E-LC group were lower than in the LC group, and the differences were statistically significant ($p<0.05$). In terms of the postoperative rehabilitation efficacy, flatus time and length of hospital stay after surgery in the E-LC group were significantly shorter than those in the LC group ($p<0.05$).

Conclusions: Use of ERAS in the perioperative period in patients who underwent LC combined with LCBDE reduces the stress response and postoperative complications and accelerates postoperative rehabilitation.

Clinical trial registration number: ChiCTR1900024292, *http://www.chictr.org.cn/showprojen.aspx?proj=40785*

MeSH Keywords: **Cholecystectomy, Laparoscopic • Laparoscopy • Surgical Procedures, Minimally Invasive**

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/924946

2492 4 — 17

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

Laparoscopic cholecystectomy is considered to be the criterion standard procedure for treatment of benign gallbladder disease and, due to its minimal invasiveness, has the advantages of minor trauma, minor bleeding, low pain, and quick recovery. With the development of ERAS in recent years, many of these measures have been applied in clinical practice [1] because of their advantages in reducing the incidence of surgical stress and complications, accelerating postoperative rehabilitation, and shortening hospital stay [2–5]]. There have been many reports on the use of ERAS in surgery, but no reports on use of ERAS in LC combined with LCBDE, so it is necessary to assess its characteristics. Xiang et al. studied the effect of early resumption of eating on gastrointestinal function and concluded that early eating could increase abdominal distension, but they did not discuss other complications [6]. In the present study, the effects of ERAS on stress state and postoperative complication rates of patients undergoing LC with choledocholithotomy were investigated. The clinical data of 445 patients who underwent LC combined with LCBDE in our department from January 2015 to February 2019 were retrospectively studied to explore the value of ERAS in perioperative treatment of LC combined with LCBDE.

Material and Methods

Patient selection criteria

We collected clinical data of 445 patients who underwent elective laparoscopic cholecystectomy combined with laparoscopic common bile duct exploration from January 2015 to February 2019 in our hospital and divided them into an E-LC group (148 patients who voluntarily chose ERAS) and an LC group (297 who voluntarily chose the traditional perioperative treatment plan). Preoperative B-ultrasound, abdominal CT, or abdominal MRI was performed in all patients to confirm benign diseases of the gallbladder combined with common bile duct stones. The relevant conditions of common bile duct stones are shown in Table 1. The study design and data reporting were performed in accordance with the STROCSS guidelines for cohort studies [7].

The exclusion criteria were: complications of severe cardiopulmonary diseases and uncontrollable hypertension or severe diabetes, history of upper-abdomen surgery and severe local adhesions, intrahepatic bile duct stones confirmed before surgery, and a combination of other digestive tract cancers and diseases.

The indications for LCBDE were: preoperative imaging-confirmed choledocholithiasis and choledocholithiasis diameter ≥8 mm.

The discharge criteria were: able to move freely, normal body temperature and WBC count, absence of pain, no obvious discomfort after eating, flatus and bowel movements, and good healing of surgical sites.

Standard medical procedures

All operations were performed by the same surgeon and the same group of doctors. The anesthesia and surgical procedures were the same, and LC combined with LCBDE with a 4-hole method was performed. We dissected the gallbladder, fully exposed the gallbladder duct and gallbladder artery, clamped the gallbladder duct with a Hem-o-Lok clip and did not cut it temporarily, clamped and cut off the cystic artery, cut the anterior wall of the bile duct by 1.0~1.5 cm near the upper end of the common bile duct, put the choledochoscope into the puncture

Table 1. Comparison of baseline data between E-LC group and LC group.

Variable	Group		P value
	E-LC (n=148)	LC (n=297)	
Sex (M/F%)	64/84 (76.19%)	138/159 (86.79%)	0.52
Age (years)	54.47±1.12	55.01±0.77	0.68
Duration of disease (years)	5.61±0.17	5.98±0.14	0.11
Calculous cholecystitis (%)	104 (70.27%)	200 (67.34%)	0.53
Simple gallstone (%)	28 (18.92%)	61 (20.54%)	0.69
Gallbladder polypus (%)	16 (10.81%)	36 (12.12%)	0.69
Maximum diameter of stones in common bile duct (mm)	11.05±0.18	11.17±0.14	0.60
Number of stones in common bile duct	2.18±0.17	2.08±0.14	0.17

The E-LC group consisted of patients who were treated with an ERAS regimen. The LC group consisted of patients who were treated with a traditional perioperative regimen.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

hole under the xiphoid process, used a stone-collecting basket or flushing method to remove the stones, and used 4-0 absorbable line to suture the anterior wall of the bile duct continuously or discontinuously after choledochoscopy had confirmed there was no stenosis or residual stones in the lower part of the common bile duct. No bile leakage was found. The gallbladder was removed, the abdominal cavity was flushed, and the effusion was completely absorbed. The drainage tube was placed at the Winslow hole and exited from the sheath stuck hole at the junction of the right costal margin and the axillary front. When the bile duct wall is obviously edematous and the lower end of the common bile duct is narrow, the risk of bile leakage is high, and primary suturing of the common bile duct cannot be performed. In such situations, the T tube will remain in the common bile duct. About 5% of the patients in the 2 groups had a T tube placed. Cholangiography was performed 2 weeks after surgery. If there was no common bile duct stenosis, the T tube could be removed.

Patients in the E-LC group were treated with a standardized fast-rehabilitation surgical protocol in our hospital and received a fast-rehabilitation surgical nursing regimen. Preoperatively, in addition to routine preoperative conversations, the preoperative information and education informed the patients about the purpose and main measures of the ERAS program to increase compliance with the program, informed the patients about anesthesia and surgical methods, reduced their fears and anxiety about anesthesia and surgery, and informed them about discharge standards and related matters. Additionally, the patients fasted for 6 hours and receive a 250-ml oral 10% glucose solution 2 hours before surgery. Intraoperatively, patients were given general anesthesia combined with regional block anesthesia. The CO_2 pneumoperitoneum pressure was controlled at 10–12 mmHg. Postoperatively, patients could receive infiltration anesthesia with ropivacaine at the puncture site in combination with intramuscular injections of opioids (morphine or dezocine) to relieve pain after surgery. An antiemetic agent (metoclopramide) could also be used to prevent nausea and vomiting. The volume of fluid infusion was controlled at 1000–1500 mL/day until 1–2 days after surgery. The patients could drink water and consume liquid nutrients 6 hours after surgery and were gradually transitioned to a normal diet. After awakening from anesthesia, the patients began to move in bed and got out of bed 6–8 hours after surgery. The drainage tube was routinely placed during the operation until the volume of drainage fluid was less than 30 mL/day. The T tube was removed 2 weeks after the operation.

The patients in the LC group received routine LC combined with LCBDE treatment and preoperative information and surgical nursing. They fasted for 12 hours before surgery and abstained from water for 6 hours before surgery. During the operation, the patients were given general anesthesia. The CO_2 pneumoperitoneal pressure was intraoperatively controlled to be 13–15 mmHg. Postoperative analgesic pumps or intramuscular injections of opioids (morphine or dezocine) were used to relieve pain. Antiemetic agents were not routinely used to prevent nausea and vomiting. The volume of fluid infusion was controlled to be 1500–2000 mL/d until 1–2 days after the operation. After the operation, the patients fasted for approximately 24 hours, and then could drink water and eat, and were gradually transitioned to a normal diet after demonstrating flatus. The patients got out of bed 8–12 hours after the operation. The drainage tube was routinely placed during the operation until the volume of drainage fluid was less than 30 mL/day. The T tube was removed 2 weeks after the operation.

Observational indicators

To assess stress response indicators, venous blood was drawn from the elbow in the morning while the patient was in the fasting state 1 day before and after surgery to measure the white blood cell (WBC) count and C-reactive protein (CRP) levels.

To assess postoperative complications, the incidence of complications, including nausea and vomiting, incisional pain, abdominal distension, fever, urinary retention, abdominal infection, bile leakage, and bleeding, were noted. To assess postoperative rehabilitation, we recorded flatus time and length of hospital stay after the operation.

Statistical analyses

Statistical analysis was performed using SPSS 19.0 software. The mean±standard deviation (x±s) was used for the measurement data, the independent-sample *t* test was used for comparisons between groups, and the chi-square test was used for the comparison of count data. Differences were considered to be statistically significant at $p<0.05$.

Results

There were 64 males and 84 females in the E-LC group, with ages 15–82 years and a median age of 55 years. There were 138 males and 159 females in the LC group, with ages 27–85 years and a median age of 59 years. The patients were diagnosed by pathology as having benign gallbladder disease after the operation.

There were no significant differences between the 2 groups in sex ratio, age, duration of disease, disease type, maximum diameter, or number of stones in the common bile duct ($p>0.05$) (Table 1). There were also no significant differences in white blood cell (WBC) count or C-reactive protein (CRP) between the LC group and E-LC group 1 day before surgery. The WBC count

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 2. Comparison of stress response indexes between E-LC group and LC group 1 day before surgery and 1 day after surgery.

Variable		Group		P value
		E-LC (n=148)	LC (n=297)	
WBC count (×10^9/L)	1 day before surgery	8.38±0.16	8.46±0.09	0.63
	1 day after surgery	10.50±0.16	11.98±0.11	<0.05
CRP (mg/L)	1 day before surgery	7.42±0.20	7.93±0.18	0.07
	1 day after surgery	24.89±0.63	28.80±0.54	<0.05

WBC – white blood cell count; CRP – C-reactive protein.

Table 3. Comparison of postoperative complication rates between E-LC group and LC group.

Variable	Group		P value
	E-LC (n=148)	LC (n=297)	
Nausea and vomiting (%)	6 (4.05%)	35 (11.78%)	<0.05
Abdominal distension (%)	10 (6.76%)	24 (8.08%)	0.62
Incisional pain (%)	12 (8.11%)	55 (18.52%)	<0.05
Fever (%)	13 (8.78%)	25 (8.42%)	0.90
Urinary retention (%)	2 (1.35%)	5 (1.68%)	0.79
Abdominal infection (%)	3 (2.03%)	5 (1.68%)	0.78
Bile leakage (%)	0	2 (0.67%)	0.32
Bleeding (%)	2 (1.35%)	5 (1.68%)	0.79

Table 4. Comparison of postoperative rehabilitation between E-LC group and LC group.

Variable	Group		P value
	E-LC (n=148)	LC (n=297)	
Flatus time (hours)	19.36±0.10	23.84±0.08	<0.05
Hospital stay (days)	3.49±0.14	5.57±0.23	<0.05

and CRP levels in the E-LC group were significantly lower than those of the LC group 1 day after surgery (p<0.05) (Table 2). These results suggest that implementation of the ERAS recommendations can significantly reduce stress reactions.

The incidence of nausea, incisional pain, and vomiting in the E-LC group were lower than in the LC group, and the differences were statistically significant (p<0.05). There were no significant differences between the 2 groups in the incidence of abdominal distension, fever, urinary retention, abdominal infection, bile leakage, or bleeding (Table 3). The data in the tables indicate that use of ERAS reduced the incidence of postoperative complications in some patients in the LC group.

Flatus time and length of hospital stay after surgery in the E-LC group were significantly shorter than in the LC group (p<0.05) (Table 4). The data indicated that, compared with the conventional perioperative treatment methods of LC combined with LCBDE, the application of ERAS recommendations for LC combined with LCBDE reduced the impact of multiple stress factors on the body, reduced the length of postoperative hospital stay, accelerated recovery, and improved postoperative quality of life.

Discussion

LC combined with LCBDE, as a minimally invasive surgery, can effectively reduce surgical trauma to the body, but minor stimuli such as preoperative tension and anxiety, preoperative fasting, mechanical bowel preparation, intraoperative hypothermia, high intraoperative pneumoperitoneum pressure, and postoperative pain can still accumulate and create a strong stress response [8].

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Therefore, optimizing all perioperative treatment measures to reduce the impact of stress response on the body is of great significance for rapid recovery after surgery. At present, WBC count and CRP levels are the most commonly used indexes of stress response; when the body is stimulated by a stress response, the WBC count and CRP levels increase. In this study, the data showed that the WBC count and CRP levels of the E-LC group and LC group were similar 1 day before surgery, and the WBC count and CRP levels of the E-LC group were significantly lower than in the LC group 1 day after surgery, indicating that ERAS significantly reduced the perioperative stress response. In this study, the incidences of nausea, incisional pain, and vomiting in the E-LC group were lower than in the LC group, and the differences were statistically significant ($p<0.05$). There were no significant differences between the 2 groups in the incidence of abdominal distension, fever, urinary retention, abdominal infection, bile leakage, or bleeding. Our data showed that use of ERAS reduced the incidence of postoperative complications in patients in the LC group, and no deaths occurred in either group, thus confirming the safety of using ERAS technology in patients undergoing LC combined with LCBDE. Compared with conventional perioperative treatment methods for LC combined with LCBDE, the application of ERAS recommendations for LC combined with LCBDE reduces the impact of multiple stress factors on the body, thus reducing the length of postoperative hospital stay, speeding recovery, and improving postoperative quality of life. Our analysis shows that the reduction in stress response is related to the factors detailed below.

Improvements in the preoperative preparation effectively reduced the patients' stress response [9]. In the E-LC group, preoperative psychological counselling and education alleviated their fears and anxiety, thus reducing their psychological stress response to surgery. The patients were introduced to the surgical and postoperative procedures and precautions in detail so that they fully understood the LC combined with LCBDE surgery and fully cooperated with the doctors in the treatment plan to accelerate their recovery. Prolonged fasting and drinking water put patients in a state of metabolic stress, leading to insulin resistance, which is not conducive to prevention of postoperative complications. Consuming a small amount of carbohydrates 2 hours before surgery alleviates hunger, thirst and anxiety, reduces the incidence of postoperative insulin resistance and hyperglycemia, and promotes postoperative intestinal function recovery [10].

De'Angelis reported on use of an innovative surgical procedure in 14 cholelithiasis patients undergoing cholecystectomy using microlaparoscopic surgical instruments at low pneumoperitoneum pressure (8 mmHg) to minimize the surgical invasiveness and the risks related to CO_2 insufflation in the peritoneal environment. They reported that no conversions or intraoperative or postoperative complications occurred [11]. Thus, a low intraoperative pneumoperitoneum pressure reduced the effect of carbon dioxide on the body, leading to fast postoperative recovery.

Appropriate postoperative analgesia was beneficial in reducing psychological stress and reducing postoperative stress response. One study shows that long-acting anesthetics such as ropivacaine can achieve an analgesic effect for up to 16–24 hours [12]. At the end of the operation, ropivacaine was injected into the incision site, which effectively relieved puncture site pain after the operation. Preventive analgesia reduces postoperative pain and consumption of analgesics, and this appears to be the most effective means of decreasing postoperative pain [13] and limited the use rate of morphine analgesia in the E-LC group to only about 8%. Khatereh Isazadehfar et al. reported that muscular injection of 10 mg metoclopramide can effectively prevent gastrointestinal reactions and reduce the occurrence of nausea and vomiting, which is consistent with the results of the present study [14]. Early postoperative eating mechanically stimulated the intestinal wall, promoted bowel movements, shortened the flatus time, and reduced the amount of fluid infusion; early resumption of eating reduced the incidence of pulmonary, abdominal, and incisional infections and shortened the length of hospital stay. The early return to a normal diet did not increase the incidence of vomiting. Early postoperative resumption of eating was supplemented with sufficient glucose and amino acids to ensure normal protein synthesis, as adequate protein is required for the body to quickly repair wounds and restore physical fitness. Getting out of bed early prevented the formation of venous thrombosis and improved the patients' postoperative experience, and getting out of bed early and eating early shorten the postoperative recovery time [15]. Getting out of bed early for activities is beneficial to the recovery of gastrointestinal function, thereby reducing the incidence of postoperative complications [16]. A previous study reported that, compared with traditional care, ERAS programs were associated with significantly decreased overall complications and hospital length of stay [17], which is consistent with our research.

Conclusions

Use of ERAS provides positive psychological and physiological support and improves psychological and physiological stress levels, which in turn promotes better recovery. The combination of LC and LCBDE suggested by ERAS is safe and effective and can reduce the stress response generated by patients during the perioperative period, accelerate postoperative rehabilitation, and shorten hospital stay. Therefore, ERAS is a good perioperative treatment method worth implementing in patients who underwent LC combined with LCBDE. The sample size of our study was relatively small, and the benefits of ERAS for patients who underwent LC combined with LCBDE remains to be verified by future randomized, controlled, large-sample, clinical trials.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

References:

1. Kehlet H: Enhanced Recovery After Surgery (ERAS): Good for now, but what about the future? Can J Anaesth, 2015; 62(2): 99–104
2. De Groot JJ, Ament SM, Maessen JM et al: Enhanced recovery pathways in abdominal gynecologic surgery: A systematic review and meta-analysis. Acta Obstet Gynecol Scand, 2016; 95(4): 382–95
3. Madani A, Fiore JF Jr., Wang Y et al: An enhanced recovery pathway reduces duration of stay and complications after open pulmonary lobectomy. Surgery, 2015; 158(4): 899–908
4. Specht K, Kjaersgaard-Andersen P, Kehlet H et al: High patient satisfaction in 445 patients who underwent fast-track hip or knee replacement. Acta Orthop, 2015; 86(6): 702–7
5. Yip VS, Dunne DF, Samuels S et al: Adherence to early mobilisation: Key for successful enhanced recovery after liver resection. Eur J Surg Oncol, 2016; 42(10): 1561–67
6. Xiang Q, Yuan H, Cai W et al: Effect of early enteral nutrition on laparoscopic common bile duct exploration with enhanced recovery after surgery protocols. Eur J Clin Nutr, 2019; 73(9): 1244–49
7. Riaz A, Abdal-Razak A, Crossley E et al: STROCSS 2019 Guideline: Strengthening the reporting of cohort studies in surgery. Int J Surgery (London, England), 2019; 72: 156–65
8. Nelson G, Altman AD, Nick A et al: Guidelines for pre-and intraoperative care in gynecologic/oncology surgery: Enhanced Recover After Surgery(ERAS(R)) society Recommendations – Part I. Gynecol Oncol, 2016; 140: 313–22
9. Kim BJ, Aloia TA: What is “Enhanced Recovery”, and how can I do it? J Gastrointest Surg, 2018; 22(1): 164–71
10. Ljungqvist O, Scott M, Fearon KC: Enhanced recovery after surgery: A review. JAMA Surg, 2017; 152(3): 292–98
11. De'Angelis N, Petrucciani N, Giannandrea G, Brunetti F: The protocol of low-impact laparoscopic cholecystectomy: The combination of mini-laparoscopy and low-pressure pneumoperitoneum. Updates Surg, 2018; 70(4): 553–56
12. Gadsden J, Warlick A: Regional anesthesia for the trauma patient: Improving patient outcomes. Local Reg Anesth, 2015; 8: 45–55
13. Vadivelu N, Mitra S, Schermer E et al: Preventive analgesia for postoperative pain control: A broader concept. Local Reg Anesth, 2014; 7: 17–22
14. Isazadehfar K, Entezariasl M, Shahbazzadegan B et al: The comparative study of ondansetron and metoclopramide effects in reducing nausea and vomiting after laparoscopic cholecystectomy. Acta Med Iran, 2017; 55: 254–58
15. Sun JK, Mu XW, Li WQ et al: Effects of early enteral nutrition on immune function of severe acute pancreatitis patients. World J Gastroenterol, 2013; 19(6): 917–22
16. Stearns E, Plymale MA, Davenport DL et al: Early outcomes of an enhanced recovery protocol for open repair of ventral hernia. Surg Endosc, 2018; 32(6): 2914–22
17. Ni TG, Yang HT, Zhang H et al: Enhanced recovery after surgery programs in patients undergoing hepatectomy: A meta-analysis. World J Gastroenterol, 2015; 21(30): 9209–16

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]