Safety and Efficacy of Enhanced recovery after laparoscopic cholecystectomy surgery: a single-center randomized controlled study

Ming-zhe Li (li_mingzhe2020@163.com)
The Seventh Affiliated Hospital, Sun Yat-sen University

Xin Chen
The People's Hospital of Fengqing

Chen Wang
The Seventh Affiliated Hospital, Sun Yat-sen University

Shi-zeng Li
The People's Hospital of Fengqing

Bin Xia
The Seventh Affiliated Hospital, Sun Yat-sen University

Wen-hui Wu
The Seventh Affiliated Hospital, Sun Yat-sen University

Chang-hua Zhang
The Seventh Affiliated Hospital, Sun Yat-sen University

Yu-long He
The Seventh Affiliated Hospital, Sun Yat-sen University

Research Article

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Abstract

Background: The role of Eintraoperative joint organ removal or transit abdominal surgery recovery after surgery (ERAS) in reducing hospital stay time and perioperative hospitalization costs have been proven. However, most studies have been carried out in areas rich in medical resources. In this study, we evaluated the safety and efficacy of ERAS compared with traditional perioperative period care for laparoscopic cholecystectomy (LC) in areas poor in medical resources in China.

Methods: A randomized controlled trial on laparoscopic cholecystectomy was conducted at The People's Hospital of Fengqing from July 2020 to March 2021. Patients were randomly divided into an ERAS group and a traditional care group. The main outcome was the length of hospital stay after surgery. The secondary outcomes included hospitalization costs and visual analogue scale (VAS) scores for postoperative pain, first exhaust time, and first semi-liquid diet time after surgery. The ERAS group was provided with perioperative education, nutritional support, preoperative 2 h oral carbohydrates, restricted rehydration, intraoperative insulation, no drainage tubes, wound hemp, early mobilization postoperative nausea and vomiting (PONV) prevention and multi-modal analgesia, early activity.

Results: The study was conducted on a total of 140 patients with 70 patients each in the ERAS group and traditional care groups. In the ERAS group, The length of hospital stay after surgery was shorter (4.06 vs.4.61 days, $P<0.05$), the average hospitalization cost (CNY 7900 vs. 8470, $P<0.05$),and VAS score (3.10 vs. 3.57 points, compared to the eraser group $P<0.001$) was lower, the first exhaust time was shorter (12.2 vs. 14.2 hours, $P<0.001$), the first semi-liquid diet time after surgery was shorter(14.5 vs. 16.8 hours, $P<0.001$), and the incidence of major postoperative complications was lower (bile leakage, postoperative bleeding, bile duct damage) (0% vs. 12.9%, $P<0.05$). No significant difference in surgery time (57.8 vs. 54.6 min, $P>0.05$) was observed between the two groups.

Conclusion: Even in areas poor in medical resources in China, the use of the ERAS concept for LC surgery can reduce the length of hospital stay, cut down the cost of hospitalization, and lessen the pain of patients after surgery and accelerate postoperative recovery.

Introduction

Chronic cholecystitis is caused by repeated attacks of acute or subacute cholecystitis, or long-standing gallbladder stones caused by abnormal gallbladder function. About 25% of patients are affected by bacterial infections, which causes gallbladder tube or bile duct obstruction[1]. Based on the presence or absence of stones in the gallbladder, chronic cholecystitis can be divided into stone cholecystitis and non-stone cholecystitis. Non-stone cholecystitis is chronic cholecystitis that is caused by bacteria, viral infection, or bile salt and trypsin[2]. Laparoscopic cholecystectomy is the gold standard for the treatment of chronic cholecystitis, with the advantages of being minimally invasive, short hospital stay, fewer postoperative complications, and the rapid recovery of patients.

The concept of accelerated rehabilitation surgery (enhanced recovery after surgery, ERAS) was proposed by Professor Kehlet in 1997 and included the implementation of proven and effective methods to reduce stress and complications in surgical patients[3], curb physical and psychological trauma and stress, lessen fatalities and the length of hospital stay, and speed up the recovery of patients. The main components of ERAS include preoperative education of patients, optimization of anesthesia, reduction of stress response, intraoperative insulation and deep vein thrombosis prevention, effective analgesia, intensive postoperative rehabilitation treatment, including early bed-leaving activities and early intestinal nutrition, with the aim of practicing patient-centered consultation and treatment. Accelerated rehabilitation involves physicians, anesthesiologists, surgical nurses, and other nursing staff, nutrition, rehabilitation, hospital management and other links, at the same time requires the cooperation of patients and their families.

At present, ERAS is widely practiced in elective surgery and has achieved good results, especially in elective colorectal surgery[4]. ERAS can significantly decrease the length of hospital stay, lessen complications, prejudice re-hospitalization rate and cut down hospitalization costs. A few retrospective studies have suggested that the use of ERAS strategy is effective and safe for laparoscopic cholecystectomy. It has been reported that the time of hospitalization after surgery can be shortened by 1–2 days following laparoscopic cholecystectomy and ERAS strategy for chronic gallbladder inflammation[5, 6], but the safety and effectiveness of the application of ERAS for laparoscopic cholecystectomy still lacks high-level evidence.

This study was carried out at The People's Hospital of Fengqing, which is located in a poor area that lacks medical resources. In this study, we aimed to explore the safety and effectiveness of the used ERAS after laparoscopic cholecystectomy in a poor area that lacked medical resources.

Method

Participants and recruitment

Randomly classified clinical data on 70 patients (ERAS group) treated under the ERAS concept following LC at The People's Hospital of Fengqing from July 2020 to March 2021, and 70 patients (traditional group) who were treated under the traditional care concept at the hospital during the same period. The ERAS group (computer software was used to produce random sequences without hiding the groupings) comprised of 25 males and 45 females, aged 19–70 years, with an average age of 48.8 years. All 70 cases were affected by gallbladder stones associated with cholecystitis. The traditional group comprised of 15 males and 55 females, aged 21 to 70 years, with an average age of 50.4 years, and included 58 patients affected by gallbladder stones with cholecystitis, 2 patients with gallbladder polyps, and 10 patients with gallstones in the traditional group. The preoperative diagnosis was based on medical history, physical examination, and imaging examination (ultrasound, CT, and MRCP). There was no statistical difference between the basic demographic data of the two groups of patients ($P > 0.05$) (Table 1).

Table 1
Basic demographic data

	Total group population	Traditional control group	ERAS group	p
	(N = 140)	(N = 70)	(N = 70)	
Mean (SD) age	49.6 (12.1)	50.4 (11.9)	48.8 (12.4)	0.425
Gender				
Male	40 (28.6%)	15 (21.4%)	25 (35.7%)	
Female	100 (71.4%)	55 (78.6%)	45 (64.3%)	0.092
Mean (SD) BMI, kg/m2	23.8 (3.71)	24.1 (3.77)	23.4 (3.66)	0.316
Mean (SD) ASA score	1.98(0,15)	1.96(0.20)	2.00 (0)	0.083
Diagnosis				
Gallbladder stones are associated with chronic cholecystitis	128 (91.4%)	58 (82.9%)	70 (100%)	
Gallbladder polyps	2 (1.4%)	2 (2.9%)	0 (0%)	
Gallstones	10 (7.1%)	10 (14.3%)	0 (0%)	0.001
Complication, N(%)				
Not	131 (93.6%)	61 (87.1%)	70 (100%)	
Yes	9 (6.4%)	9 (12.9%)	0 (0%)	0.006
Mean (SD) albumin	43.7 (5.46)	43.8 (6.44)	43.5 (4.30)	0.669
Mean(SD) Cereal-to-amenase,	33.2 (27.0)	35.0 (35.0)	31.3 (15.3)	0.421
Mean (SD) ALT	46.3 (55.4)	53.8 (74.3)	38.9 (23.4)	0.111
Mean (SD) Total bilirubin,	13.6 (10.1)	12.9 (12.6)	14.4 (6.76)	0.392
Mean (SD) Direct bilirubin,	4.10 (5.72)	4.59 (7.78)	3.61 (2.21)	0.314
Mean (SD) Indirect bilirubin,	9.72 (5.52)	8.67 (5.88)	10.8 (4.94)	0.023

Inclusion criteria

(1) Patients diagnosed with chronic cholecystitis and proposed to undergo laparoscopic cholecystectomy; (2) age 18–75 years old, regardless of sex; (3) ASA score 1–2 points; (4) no history of abdominal surgery (5) no chronic liver and kidney diseases; (6) informed consent of patients was obtained.

Case exclusion criteria

(1) Age < 18 years old or > 75 years old; (2) a previous history of upper abdominal surgery that affects recovery; (3) the need for joint organ removal; (4) severe mental illness; diabetes, poor blood sugar control; severe emphysema, interstitial pneumonia or ischemic heart disease; (5) pregnancy or lactation; (6) patients or family members that cannot comprehend the condition and the purpose of this study

Exit criteria

(1) intraoperative and postoperative confirmation as a gallbladder malignancy; (2) Intraoperative joint organ removal or intraoperative conversion to open surgery conducted after selection for the study due to a combination of acute inflammation and emergency surgery; (3) withdrawal from the research study due to various reasons; (4) inability to complete the study plan due to various reasons.

Clinical pathways

Three-hole LC was performed on both groups of patients, but the perioperative procedures of treatment followed were different. The ERAS team made a series of optimizations and adjustments in preoperative, intraoperative and postoperative treatment measures based on the latest China Expert Consensus and Guidelines for Accelerated Rehabilitation Surgery (Table 2). The development and implementation of the program required multidisciplinary collaboration between surgeons, caregivers, anesthesiologists, pharmacists, operating room staff, clinics and pre-hospital service personnel.

Preoperative care

The preoperative care of the traditional care group included routine mission, routine preoperative non-smoking alcohol prohibition, the prohibition of eating for 12 hours, and the prohibition of drinking for 6 hours. Alternatively, the ERAS group was provided with ERAS concept education, preoperative nutrition assessment and nutritional support, prohibition of eating 6 hours prior to the operation, prohibition of drinking 2 hours prior to the operation, and 250 ml of oral 5% GS was administered 2 h before the surgery. Both groups were given prophylactic antibiotics, without urethra retention and without intestinal preparation.

Intraoperative care

Both groups of patients were administered general anesthesia through tracheal intubation and the same surgical method, three-hole LC was performed. Patients in the ERAS group were treated with restrictive rehydration (target-oriented fluid therapy), insurgence during surgery, without placing a drainage tube, and

the wound was treated with 10 ml of 0.5% Bupivacaine, a local immersion anesthetic. Rehydration was not strictly controlled and there was no insulation during surgery for patients in the traditional treatment group.

Table 2
Two groups of perioperative period treatment

	ERAS group	Traditional control group
Preoperative		
Preoperative mission	Conduct ERAS concept mission	General mission
Quit smoking and alcohol before surgery	Yes	
Preoperative Nutrition Assessment and Nutritional Support	NSR2002 Nutritional Risk > 3 lines of nutritional support	Not
Fasting Time	Fast for 6 hours, drink 2h, take 2h orally 5% GS 250ml before surgery	Regular fasting 12h, fasting 6h
Leave the urethra	Not	
Intestinal preparation	Not	
Preventive antibiotics	Yes	
in surgery		
Anaesthetic	Tracheal intubation general anaesthetic	
Liquid management	Restrictive rehydration (target-oriented fluid therapy).	No, rehydration is not strictly controlled
The way of surgery	Three-hole method LC	
Keep warm during surgery	Keep warm during surgery	No, keep warm during non-operation
Drainage tube	Do not place the drainage tube	Place the drainage as appropriate
Wound treatment	0.5% Bupivacaine 10ml partial immersion anaesthetic	No special treatment
After surgery		
Stop gagging	Preventive intravenous drop 5-HT3 receptor antagonists on the day after surgery	No special treatment
relieve pain	Regular use of oral/intravenous NSAID painkillers	If, VAS > 3, give pain relief to the disease
Eat early	Encourage early eating, start a fluid diet at 6h after surgery, and a half-stream diet for 1–2 days	No, give a fluid diet after exhaust

	ERAS group	Traditional control group
Early activities	Encourage early bed-out activities, after surgery 6h can get out of bed activities	No, as the patient wishes

Postoperative

Patients in the ERAS group were provided with postoperative vomiting and nausea (POVN) prevention care. Patients were provided preventive intravenous dropped 5-HT3 receptor antagonists anti-spitting drugs and routinely used oral/intravenous NSAID painkillers on the day after surgery. Patients were encouraged to eat early, start on a fluid diet 6 h after surgery and a half-stream diet 1–2 days after surgery. Patients in the traditional care group didn't receive any special POVN treatment. If the patient had a VAS > 3, pain relief was provided. The patients were given a fluid diet if they were exhausted.

Observe the indicator

(1) Preoperative observation indicators: BMI for patients, anaesthetic risk ASA score, diagnosis of the disease, liver function (albumin, glutamate transaminase AST, glutamate transaminase ALT total bilirubin, direct bilirubin, indirect bilirubin).

(2) Postoperative observation index: postoperative hospital stay (days), total hospital stay time (days), surgery time (minutes), vas-score on the first day after surgery, first exhaust time (hours), first half-stream time (days), complications, mortality, hospitalization costs.

Discharge criteria

(1) Stable vital signs;

(2) Oral half-stream diet, no nausea, vomiting and other symptoms;

(3) Oral painkillers, VAS score < 2 points

(4) Ability to get out of bed

Follow-up

Both groups were followed up for 7–30 days after surgery. Postoperative complications, readmission rate and the re-surgery rate were recorded.

Outcome measure

The main outcome measured in this study was the length of hospital stay after surgery, which was measured from the beginning of surgery until the patient was discharged. The secondary outcomes measured the cost of hospitalization and VAS scores for postoperative pain, first exhaust time, and first half-flow time after surgery.

Statistical analysis

Based on a previous study[23], SPSS 19.0 software was used to determine the mean (group A, 4.5; group B, 5.5; SD = 2; sampling ratio, 1; α, 0.05; β, 0.2) The total number of cases required was 128, and the study included a total of 140 patients, including 70 patients in the ERAS group and 70 in the regular control group, based on a 5–10% rate of missed visits.

Measurements are presented as (± s). t-tests and count data usage rates were determined. Comparisons between the two groups were made using $\chi 2$ tests. $P < 0.05$ was considered to indicate statistical significance.

Results

After informed consent was obtained, a total of 140 patients were included in this study, None the patients that were enrolled withdrew until the end of the trial (Fig. 1). The two groups of patients were similar in terms of age, gender, ASA, and BMI. After correcting for factors including age, sex, BMI, diagnosis, complications, indirect bilirubin and the following results were obtained from the covariance analysis. The ERAS group showed significantly better improvement based on the recorded postoperative first-time eating and exhaust time in the ERAS group. VAS scores and the length of hospital stay on the first day after surgery were significantly reduced, the total cost of hospitalization was significantly reduced, and the difference was statistically significant ($P < 0.05$), while the difference in surgical time was not statistically significant ($P > 0.05$) (Table 3).

Table 3
Comparison of postoperative rehabilitation and economic indicators between the two groups of patients

	Traditional control group	ERAS group	One-factor analysis of p-values	p' (p-value of covariance analysis corrects age, sex, BMI, diagnosis, complications, indirect bilirubin)
Mean (SD) hospital stay after surgery, days	4.61 (1.34)	4.06 (0.961)	0.005	0.005
Mean (SD) Total hospitalization time, day	8.43 (2.22)	7.79 (1.70)	0.056	0.036
Mean (SD) surgery time, minutes	54.6 (22.0)	57.8 (28.5)	0.461	0.418
Mean (SD) scores VAS on the first day after surgery	3.57 (0.579)	3.10 (0.515)	< 0.001	< 0.001
Mean (SD) first exhaust time, hours	14.2 (4.90)	12.2 (2.56)	0.002	< 0.001
Mean (SD) first half-stream time, hours	16.8 (4.97)	14.5 (2.39)	0.001	< 0.001
Mean (SD) hospitalization costs, yuan	8470 (1710)	7900 (922)	0.015	0.007

Discussion

The study showed that even in underdeveloped areas, the implementation of ERAS can significantly reduce the length of hospital stay (7.79 d vs. 9.43 d, $P < 0.05$) and treatment costs (CNY 7900 vs. CNY 8470, $P < 0.05$). Thanks to the division of labor of surgeons, anesthesiologists, and responsible nurses, patients and their families were provided with detailed ERAS interventions and laparoscopic cholecystectomy techniques to mobilize patients and help them achieve their nutritional goals.

The nutritional status of the ERAS perioperative period was assessed and improved by the dietitian according to NRS2002 guidelines. Patients were given 400 ml of carbohydrate solution 2 hours before surgery to reduce feelings of anxiety, hunger, and insulin resistance, which promotes the restoration of cell function during tissue damage, while the oral preoperative carbohydrates minimize postoperative insulin resistance[7]. Intraoperative restriction of body fluid supplementation, starting a fluid diet 6 h after surgery, starting a half-stream diet 1–2 days after surgery, encouraging early postoperative activities, and the ability to practice out of bed activities 6 h after surgery. Early activity and early feeding are key factors in ERAS. Several studies on open colon surgery have observed a substantial reduction in the incidence of postoperative complications and have considered fluid restriction[8], functional exometrophic[9], and

preoperative carbohydrate intake[10, 11] as key factors of success. Previous studies have found that early oral feeding can reduce stress, energy consumption, and complications such as vomiting, nausea, or bowel paralysis[12, 13].

In the ERAS group attention was paid to the patient's body temperature during surgery to avoid an increase in the stress response caused by accidental heat loss. Previous studies have also shown that as long as heat loss is expected[14, 15], body temperature protection and prevention of hypothermia during surgery should be provided to reduce stress response to reheating, increase oxygen consumption, the breakdown of hormone secretion and nitrogen loss. Prevention of hypothermia during surgery can reduce the rate of wound infections and the length of hospital stay.

Postoperative nausea and vomiting PONV is often considered as common after surgery[16], including laparoscopic surgery[17, 18]. To prevent PONV in the ERAS group in this study, the number of preventive intravenous dropped 5-H T3 receptor antagonists provided on the day after surgery was increased, compared with the traditional treatment group, and the use of opioid painkillers was avoided after surgery.

Postoperative pain may amplify the patient's endocrine metabolic response, as well as autoreflections, nausea, intestinal obstruction, and muscle spasms, delaying the recovery of bodily functions[19]. Good postoperative pain control can promote recovery and reduce morbidity[20]. The ERAS group of this study was mainly provided with nonsteroidal anti-inflammatory drugs to reduce the inflammatory response to control postoperative pain, along with early postoperative feeding to ensure energy intake, to achieve optimal pain control to avoid stress and insulin resistance. The reduction in VAS scores on the first day after surgery also showed the effectiveness of the ERAS group.

The ERAS group also avoided certain traditional care elements that have been proven to be harmful, such as the routine use of nasal gastric tubes, prolonged urination, and prolonged or inappropriate use of abdominal drainage tubes[21]. Navigators set up by nurses in this study can help patients and their families by mentoring them on how to provide patient-centered care. The best results are received when the level of cooperation between all who are concerned is good, and can also alleviate the patient's anxiety, fear and stress, which further improves patient compliance, so that the study can be carried out smoothly. Further data on more than 900 consecutive colorectal cancer patients highlighted the import role played by compliance in ERAS: the better compliance, the better the results in terms of complications, initial and total hospital stays, and re-admission[11, 22]. This study also confirmed the view that better compliance not only reduces overall complications, emphasizing the importance of compliance.

Conclusion

Compared with ERAS-related studies on laparoscopic cholecystectomy conducted in areas rich in medical resources in China and abroad, the length of stay in this study was lower than that of these areas rich in medical resources, considering that this study was carried out in The People's Hospital of Fengqing, which has limited medical resources, even though challenges were faced in providing patients with a high

level of postoperative care and follow-up. However, it is also in these poor areas where the level of care is low that ERAS can significantly shorten hospital stays and reduce the cost of hospitalization. In addition, there are still significant limitations in this study.

This study did not use a postoperative nausea and vomiting (PONV) score to assess the preoperative baseline, and the ERAS group used only a single anti-spitting drug compared with the traditional group, resulting in the control group of patients being more likely to develop PONV. The study relied only on VAS scores to measure postoperative pain intensity. Finally, a detailed analysis of the postoperative complications in the traditional care group was not conducted, which resulting in it not being possible to prove the effectiveness of interventions during the ERAS perioperative period to reduce postoperative complications.

Declarations

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Data availability: The Datasets generated and/or analyzed in the current study are not publicly available due to the individuals privacy issue but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate**:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was a single-center randomized controlled trial conducted between July 2020 and March 2021. The trial was approved by the Ethics Committee of The People's Hospital of Fengqing. The study was registered at the Chinese Clinical Trial Registry (02/07/2020 ChiCTR2000034331).

Consent for publication: Not applicable.

Conflict of Interest Disclosures: None reported

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Figures

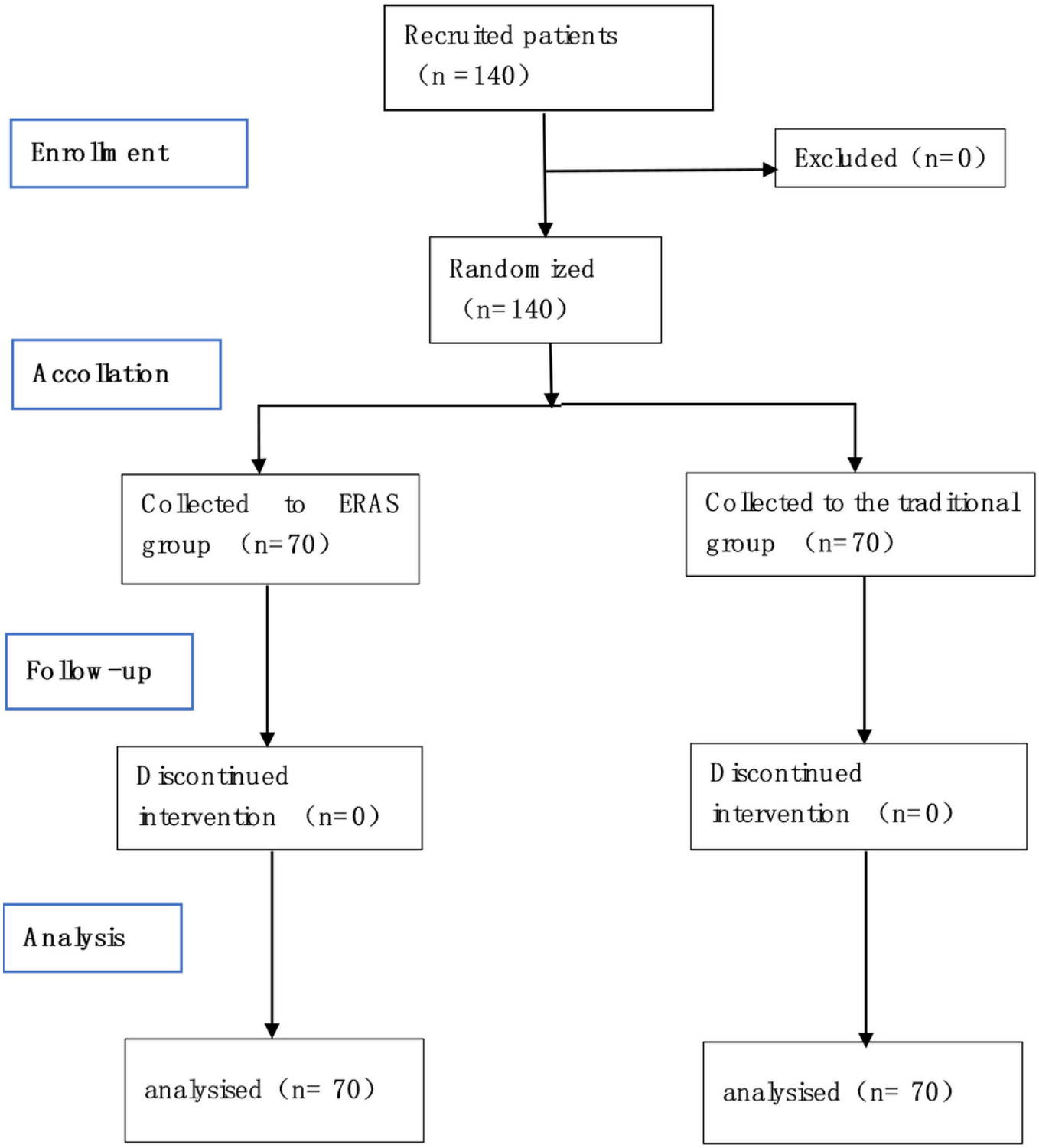

Figure 1

CONSORT diagram for the trial. ERAS enhanced recovery after surgery

Supplementary Files

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- CONSORT2010FlowDiagram.doc