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## International Journal of Surgery

journal homepage: www.journal-surgery.net



#### Review

# Enhanced recovery after surgery programs versus traditional perioperative care in laparoscopic hepatectomy: A meta-analysis



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#### HIGHLIGHTS

- We summarized that the application of ERAS in laparoscopic hepatectomy is safe and effective, and it could accelerate the postoperative recovery and lighten the financial burden of patients.
- According to our study, ERAS could accelerate the time to first diet and first flatus, and decrease duration of the postoperative hospital stay, the cost of hospitalization, postoperative complication rate after surgery.
- ERAS have the potential to replace CTL as the gold standard perioperative care for patients undergoing laparoscopic hepatectomy.

#### ARTICLE INFO

# Article history: Received 28 September 2016 Received in revised form 30 October 2016 Accepted 4 November 2016 Available online 10 November 2016

Keywords: Laparoscopy Hepatectomy Enhanced recovery after surgery Meta-analysis

#### ABSTRACT

Objective: Enhanced recovery after surgery (ERAS) programs are a series of measures being taken during the perioperation to alleviate surgical stress and accelerate the recovery rate of patients. Although several studies reported the efficacy of ERAS in liver surgery, the role of ERAS in laparoscopic hepatectomy is still unclear. This meta-analysis is aimed to evaluate the efficacy and safety of ERAS programs versus traditional care in laparoscopic hepatectomy.

Methods: We searched PubMed, EMBASE, the Cochrane Library, CNKI, Wang Fang Database and VIP Database for randomized controlled trials (RCTs) or clinical controlled trials (CCTs) concerning using ERAS in laparoscopic hepatectomy. Data collection ended in June 1st, 2016. The main end points were intraoperative blood loss, intraoperative blood transfusion, operative time, the cost of hospitalization, time to first flatus, the time to first diet after surgery, duration of postoperative hospital stay, total postoperative complication rate, gradelcomplication rate, grade II-Vcomplication rate.

Results: 8 studies with 580 patients were eligible for analysis. There were 292 cases in ERAS group and 288 cases in traditional perioperative care (CTL) group. Compared with CTL group, ERAS group was associated with significantly accelerated of time to first diet after surgery (SMD = -1.79, 95% CI:  $-3.19 \sim -0.38$ , P = 0.01), time to first flatus (MD = -0.51, 95%CI:  $-0.91 \sim -0.12$ , P = 0.01). Meanwhile, it was associated with significantly decreased of duration of the postoperative hospital stay (MD = -3.31, 95%CI:  $-3.95 \sim -2.67$ , P < 0.0001), cost of hospitalization (MD = -1.0, 95%CI:  $-1.49 \sim -0.51$ , P < 0.0001), total postoperative complication rate (OR = 0.34, 95%CI: 0.15 - 0.75, P = 0.008), gradelcomplication rate (OR = 0.37, 95%CI: 0.22 - 0.64, P = 0.0003) and gradell-Vcomplication rate (OR = 0.49, 95%CI: 0.32 - 0.77, P = 0.002). Whereas there was no significantly difference in intraoperative blood loss (P > 0.05), intraoperative blood transfusion (P > 0.05), operative time (P > 0.05) between ERAS group and CTL group. Conclusion: Application of ERAS in laparoscopic hepatectomy is safe and effective, and it could accelerate the postoperative recovery and lighten the financial burden of patients.

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#### 1. Introduction

The enhanced recovery after surgery (ERAS) was first introduced by Kehlet's team [1] in 1991. It was aimed at optimizing the traditional perioperative care to alleviate the patients' pathophysiologic reactions after surgery, improve patients' physical and psychological recovery, and reduce the surgical stress, then led to fast recovery [2]. It contains following measures that have been proven to optimize the perioperative strategies effectively: preoperative patient education, optimized anesthesia, preoperative and postoperative medicine with acetaminophen, postoperative antiemetic, early oral intake and early mobilization [3].

During the past two decades, numerous articles have reported that ERAS was safe and effective in gastrectomy for gastric cancer [4], colorectal [5], liver [6] and biliary tract [7] surgery. A recent meta-analysis demonstrated that ERAS for liver surgery contributed to a significant decrease in postoperative complications and length of hospital stay compared to standard care [8]. However, the evidence of using ERAS in laparoscopic hepatectomy remains insufficient. With the rapid development of laparoscopy in recent years, laparoscopic hepatectomy has obtained good clinical efficacy. Laparoscopic hepatectomy is a minimally invasive surgery that causes less stress and trauma compared with open surgery. Meanwhile, it is widely used for the treatment of both benign and malignant liver diseases with lower morbidity and mortality. But despite this, laparoscopic hepatectomy is still a difficult surgery with high risks nowadays, which may result from poorly operative techniques in primary-level hospitals, uncontrolled bleeding and air embolism [9]. It is necessary to optimize the traditional care to accelerate patients' recovery and reduce the complications after laparoscopic hepatectomy. Thus, we conducted a meta-analysis of published articles to assess the effects of ERAS versus traditional care in patients undergoing laparoscopic hepatectomy.

#### 2. Methods

#### 2.1. Search strategy

Publications were selected by searching the major medical databases, including PubMed, EMBASE, the Cochrane Library, Chinese Biological and Medical Database, CNKI (China National Knowledge Infrastructure), Wang Fang and VIP Database. The searching was ended in June 1st, 2016. The following key words: "fast track surgery", "enhanced recovery of surgery program", "enhanced recovery after surgery", "accelerated recovery", "laparoscopy", "hepatectomy", "liver surgery" were used for searching eligible articles. Then the references of the retrieved articles were also browsed to broaden the search range.

#### 2.2. Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) RCTs or CCTs that compared ERAS with conventional perioperative care in patients undergoing laparoscopic hepatectomy; (2) publications available with full text in English or Chinese; (3) studies that reported at least one of the outcomes mentioned below; and (4) if there was any overlap between authors or institutions, the higher-quality or more recent studies would be selected. The exclusion criteria were: (1) reports that ERAS and traditional perioperative care were not compared; (2) the studies that did not provide an ERAS protocol or patients without laparoscopic hepatectomy; (3) case reports or Reviews; (4) studies that were not full text; and (5) studies on the same patient cohorts that were reported in more than one article.

#### 2.3. Data extraction, outcome and assessment of risk of bias

Data were extracted independently by two reviewers from the full text eligible articles. If there were any disagreements, the article would be presented to a third author and discussed among the investigators. The outcomes for analysis were total postoperative complication rate, gradelcomplication rate and gradell-Vcomplication rate, the postoperative hospital stay, the hospitalization expenses, the time to first diet after surgery, the time to first flatus after surgery and in intraoperative blood loss, intraoperative blood transfusion and operative time. The quality of eligible articles was assessed using the Cochrane risk of bias tool [10], including the following items: random sequence generation, allocation concealment, blinding of participants, incomplete outcome data, selective outcome reporting and other biases.

#### 2.4. Statistical analysis

This meta-analysis was performed by Review Manager Software, RevMan version 5.3 Cochrane Collaboration (http://tech. cochrane.org/revman). If the results were dichotomous variables, the risk ratio (RR) or odds ratio (OR) would be used for statistical analysis. Whereas if the results were continuous variables, the weighted mean difference (WMD) or Standard Mean Difference (SMD) would be applied instead. Results were presented with 95% confidence intervals (CIs). Heterogeneity was determined using the  $\chi^2$  test, and  $I^2$  was used to quantify heterogeneity. A p value of <0.10 with an  $I^2$  value of >50% was considered significant heterogeneity between the articles, and a random-effects model was used in this case. Whereas in opposite cases, it was thought of no heterogeneity and a fixed-effects model was adopted. P < 0.05 was considered as statistically significant. For continuous variables, if the study provided medians and interquartile ranges instead of means and standard deviations, medians and ranges would be converted to the means and standard deviations according to the Cochrane handbook [11].

#### 3. Results

#### 3.1. Search results

#### 3.1.1. Eligible studies

A total of 111 trails were identified in this study. The flow diagram of study is shown in Fig. 1. By searching the key words mentioned above, three RCTs [12–14] and five CCTs [15–19] were considered to be eligible for the meta-analysis. Analyses were conducted on 580 patients in the ERAS group (n = 292) as well as traditional care group (n = 288). Among the eight researches, the items such as Type of surgery, Study design, No., Gender, Age, ASA score, benign or malignant liver lesions were extracted. Detailed characteristics of patients are listed in Table 1.

#### 3.1.2. Methodological quality of studies

The methodological quality of studies was determined using the RevMan bias assessment tool which was shown in Fig. 2. Three studies [12–14] reported detailed randomization methods. And three studies [17–19] mentioned randomization without a description of the methods. There was only one study [12] which used sealed envelopes for allocation. Five studies [13,14,17–19] reported allocation concealment without a detailed description. Only one of the RCTs [13] blinded the patients and personnel as well as outcome assessors, the rest of the included studies reported blind methods without a detailed description. All trails had a low risk of bias for incomplete outcome data and selective reporting. Other biases were unclear.

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