



## Review

# The efficacy and safety of enhanced recovery after surgery (ERAS) program in laparoscopic digestive system surgery: A meta-analysis of randomized controlled trials



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## ARTICLE INFO

## Keywords:

Enhanced recovery after surgery  
Digestive system  
Laparoscopic surgery  
Meta-analysis

## ABSTRACT

**Background:** The enhanced recovery after surgery (ERAS) program has been applied to a variety of surgeries. However, the efficacy and safety of the ERAS program in laparoscopic digestive system surgery remain unclear. We conducted a meta-analysis to evaluate the ERAS program and traditional perioperative care (TPC) in laparoscopic digestive system surgery.

**Methods:** We searched five electronic databases for eligible trials. STATA version 14.0 and Revman version 5.3 were used to analyze the data. The results were presented and analyzed by weighted mean difference (WMD) and risk ratio (RR) at their 95% confidence interval (CI).

**Results:** Twenty-five randomized controlled trials (RCTs) of 2219 patients were included in our meta-analysis. The results revealed that the postoperative hospital stay (PHS) (WMD: 2.13 day, 95% CI: 2.56 to -1.70,  $p = 0.000$ ), time to first flatus (WMD: 12.68 h, 95% CI: 15.95 to -9.41,  $p = 0.000$ ), and time to defecation (WMD: 34.35 h, 95% CI: 46.82 to -21.88,  $p = 0.000$ ) were significantly shorter in the ERAS group compared to the TPC group. Additionally, the overall postoperative complication rate (RR: 0.66, 95% CI: 0.49 to 0.88,  $p = 0.000$ ) was markedly lower in patients using the ERAS program.

**Conclusion:** The results indicated that the ERAS program is associated with faster postoperative rehabilitation, shorter PHS, and better postoperative complication rates. The use of the ERAS program for laparoscopic digestive system surgery is more effective and safe than TPC, and it should be recommended. (PROSPERO registration number:CRD42018118551).

## 1. Introduction

Surgery of the digestive system is one of the most common abdominal surgeries. Since the operation involves the digestive tract or glands, the rates of postoperative complications are high and may prolong the postoperative hospital stay (PHS). Thus far, two new methods for reducing postoperative stress and helping postoperative recovery of digestive system surgery have been introduced. One method is laparoscopic surgery, which was first published by Jacobs et al. [1]. Many randomized controlled trials (RCTs) have proven that laparoscopic surgery can lead to shorter PHS, lower postoperative complication rates, and faster postoperative recovery than open surgery [2–6]. The other method is the enhanced recovery after surgery (ERAS) program. It was first introduced by Kehlet et al. [7] in 1995 and was later developed into an ERAS working group [8,9]. The program includes 17

different projects that include preoperative counseling and feeding, intraoperative epidural anesthesia, early postoperative mobilisation, postoperative pain management, postoperative fluid control, and early feeding [10–12]. This program aims to reduce patient stress response, improve postoperative recovery, and reduce the postoperative morbidity rate [13,14]. It has been adopted by many specialties, including colorectal surgery, urology, and gynecology [15,16]. In many relative studies, the program has shown shorter PHS, and some systematic reviews and meta-analyses indicate low overall morbidity rates after surgery [17–22]. However, such meta-analyses were performed with few RCTs, which results in poor study quality. To date, no similar meta-analyses have been reported on the ERAS program for laparoscopic digestive system surgery. The impact of the program in laparoscopic digestive system surgery still remains controversial. Thus, we conducted this meta-analysis of published RCTs to evaluate the efficacy and

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<https://doi.org/10.1016/j.ijisu.2019.07.034>

Received 25 January 2019; Received in revised form 20 July 2019; Accepted 25 July 2019

Available online 31 July 2019

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safety of the ERAS program in patients undergoing laparoscopic surgery of the digestive system.

## 2. Methods

This meta-analysis was performed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the methodological quality of systematic reviews) guidelines [23]. The PROSPERO registration number is CRD42018118551.

### 2.1. Literature search

PubMed, EMBASE, the Cochrane Library, Web of Science, and the [ClinicalTrials.gov](http://ClinicalTrials.gov) were searched for eligible records with no language restrictions. The last search was in November 2018. All included keywords are summarized in [Supplementary Table 1](#). Relevant publications were retrieved to identify additional references. Moreover, references from other meta-analyses of the same themes were searched.

### 2.2. Inclusion and exclusion criteria

Studies selected for this meta-analysis were based on the following inclusion criteria: 1) RCTs that compared the ERAS program with TPC in laparoscopic digestive system surgery; 2) for all parameters in ERAS protocol [24], the ERAS program included at least 10 items but not more than four in the TPC group; 3) the ERAS program protocol was clearly described; 4) studies reported at least three of the following outcomes: PHS, first time to flatus or defecation, rate of complications, readmission rate, or mortality rate; and 5) when duplicates of literature were retrieved, only the most recent publications were included. Exclusion criteria were as follows: 1) publications were case reports, reviews, letters, or bioinformatic analyses; 2) studies had insufficient data which could not extract useable information; 3) studies were not RCTs; and 4) studies only assessed single aspects of ERAS program.

### 2.3. Data extraction

Two reviewers (XFN and DJ) independently reviewed and extracted data from the included trials using standardized forms. When the results were inconsistent, it was resolved by consultation or by a third reviewer. The following data was extracted: name of the first author, publication year, the number of participants, PHS, first time to flatus and defecation, rates of complication, and some other details. If data could not be extracted from RCTs, the parameters were denoted as “NA”.

### 2.4. Assessment of risk of bias

Another two researchers evaluated the risk of bias of the identified RCTs using the Cochrane Collaboration Tool [25]. The quality assessment of each included RCT consisted of the following: bias of selection, performance, attrition, detection, reporting, and other items. The bias was divided into “low risk”, “high risk”, or “unclear risk” for each domain. When the results of the two researchers were different, all group members would discuss it together to reach a consensus.

### 2.5. Statistical analysis

Statistical analyses were conducted using STATA version 14.0 (STATA corp., College Station, TX.) and Review Manager version 5.3 (Nordic Cochrane, Copenhagen, Denmark). The WMDs and their 95% CIs were calculated to analyze continuous variables, and the overall RRs were calculated for analysis of dichotomous variables with their 95% CIs. For continuous variables, if means and standards were not directly provided in the articles, we extracted the available data

(medians and ranges) and transformed them to means and standards based on the methods provided by Hozo et al. and Luo et al. [26,27]. Heterogeneity among all trials was determined using the chi-squared test and the  $I^2$  statistic ( $P$  value  $< 0.1$  or  $I^2 > 50\%$  was considered as high heterogeneity). If there was high heterogeneity among trials, the random-effects model was utilized to analyze the trials [28]. Otherwise, a fixed-effects Mantel-Haenszel model was used. Sensitivity analysis was conducted to measure the impact on the reliability of the results by removing individual literatures. Publication bias was tested using Begg's and Egger's test with Egger's funnel plots [29,30].

## 3. Results

### 3.1. Study selection and characteristics

There were 1415 records retrieved through the five electronic databases, and two additional records were identified from other sources. There were 904 records that were screened after eliminating duplicates, and 804 records were excluded after screening the titles and abstracts. The full texts of the remaining 100 articles were screened, and 75 articles were eliminated after the full text was reviewed. Finally, twenty-five RCTs were selected in current study [31–55]. A flow chart of the research selection is summarized in [Fig. 1](#).

The characteristics of the included RCTs are shown in [Table 1](#). All RCTs were published between the years 2011 and 2018. All of the selected trials included a total of 1087 patients in ERAS group, and 1132 patients were in the TPC group. The number of patients in each trial ranged from 35 to 209. All twenty-five RCTs had an ERAS protocol that was clearly defined, and at least thirteen parameters were included in each trial. Relevant parameters involved in the studies were based on the new ERAS Society Recommendations published in 2018 [24], and they are summarized in [Table 2](#).

### 3.2. The efficacy outcomes of the ERAS program

Twenty-four trials, except Veenhof et al. [36], reported on the postoperative hospital stay (PHS) of 1068 patients undergoing the ERAS program and 1109 patients undergoing TPC. The results indicated that patients undergoing the ERAS program had significantly shorter PHS (WMD: 2.13 days, 95% CI: 2.56 to  $-1.70$ ,  $p = 0.000$ ) compared to patients undergoing TPC ([Fig. 2A](#)). Since there was high heterogeneity ( $I^2 > 80\%$ ) among the studies, the random-effects models were used. Sixteen studies reported time to first flatus, and ten studies reported time to defecation. In the random-effects models, the durations to first flatus (WMD: 12.68 h, 95% CI: 15.95 to  $-9.41$ ,  $p = 0.000$ ) and defecation (WMD: 34.35 h, 95% CI: 46.82 to  $-21.88$ ,  $p = 0.000$ ) were clearly shorter in patients undergoing the ERAS program compared to patients undergoing TPC ([Fig. 2B and C](#)). Both parameters had high heterogeneity ( $I^2 > 80\%$ ). To resolve the heterogeneity, we performed subgroup analyses for these three parameters by country and surgery type. The results showed no observable effect of any trials on heterogeneity.

### 3.3. The safety outcomes of the ERAS program

Twenty-four studies, except Wang et al. [52], were included in the analysis of the complication rates of 2174 patients. In total, 184 (17.3%) patients in the ERAS program group and 293 (26.4%) patients in the TPC group had complications. The meta-analysis revealed markedly lower complication rates in patients undergoing the ERAS program (RR: 0.66, 95% CI: 0.49 to 0.88,  $p = 0.000$ ) compared to patients undergoing TPC ([Fig. 3](#)). Because of the heterogeneity ( $I^2 = 57.5\%$ ), the random-effects models were applied. Nine studies contained 22 (4.4%) ERAS patients and 33 (6.2%) TPC patients that were readmitted within 30 days after surgery. No significant difference was observed in the readmission rates between the two programs (RR:

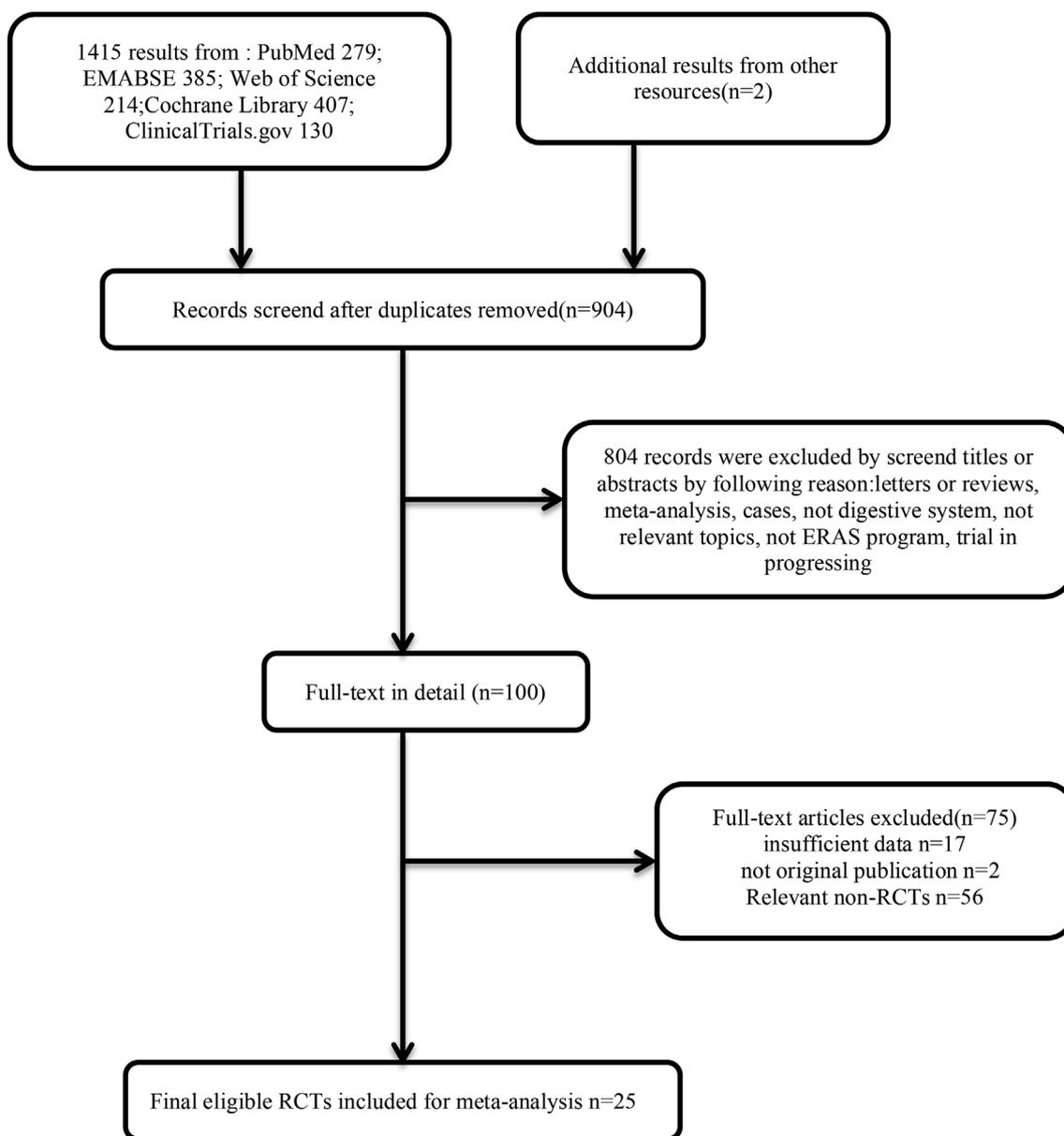


Fig. 1. Flow chart of study selection.

0.72, 95% CI: 0.43 to 1.20,  $p = 0.708$ ). Data for mortality rates were reported in four of the trials. The results of the analysis indicated that there was no obvious difference in mortality rates. The mortality rate was 4 (1.8%) in the ERAS program groups, and it was 6 (2.6%) in the TPC groups (RR: 0.75, 95% CI: 0.25 to 2.24,  $p = 0.526$ ). Since there was no heterogeneity in the readmission rates and the mortality rates ( $I^2 = 0.00\%$ ), the fixed-effect models were used.

### 3.4. Sensitivity analysis and publication bias

Sensitivity analysis was carried out to assess the stability and reliability of the results. The analysis results indicated that similar overall effects were observed with the removal of an individual study (Fig. 4A). Our meta-analysis was stable and credible.

Egger's and Begg's tests were conducted to evaluate the bias among the RCTs. No obvious dissymmetry was observed in the Egger's funnel plot for postoperative complication rates among the studies (Fig. 4B). The results of Egger's test were  $t = -1.28$  and  $p = 0.21$ . The results of Begg's test were  $z = 0.77$  and  $p = 0.44$ . There was no observable publication bias in this study.

### 3.5. Assessment of the risk of bias

Review Manger 5.3 was used to evaluate the risk of bias among the trials. It was difficult for surgeons and patients to abide to double blinding in such clinical trials. The performance bias in most of included trials was not evaluated as low-risk. The risk of overall bias was moderate to low risk, and the risk of bias graph and summary are shown in Fig. 5.

## 4. Discussion

Surgical operation is a major trauma to the human body, and it often leads to a range of psychological or physiological reactions, which are collectively known as the stress response [56]. Surgical rehabilitation is a complex process involving physiological, psychological, social, and economic factors [57]. Since the ERAS program and the laparoscopic techniques were introduced to surgical operations, these two methods have become the two major approaches to reduce the surgical stress response and enhance the postoperative recovery after surgery. In fact, there have been some short-term benefits observed in a number of

**Table 1**  
Characteristics of the included RCTs.

Study	Year	Sample size		Age (years) mean ± SD		Gender (M/F)		Type of surgery	Follow-up (days)
		ERAS	TC	ERAS	TC	ERAS	TC		
Lee,Taek-Gu	2011	46	54	61.9 ± 11.2	60.6 ± 0.0	26/20	30/24	Lap + colorectal	30
Van Bree,S.H.	2011	18	17	65.0 ± 9.4	66.0 ± 10.2	9/9	9/8	Lap + colorectal	30
Vlug,M.S.	2011	100	109	66.0 ± 8.6	68.0 ± 8.8	53/47	68/41	Lap + colorectal	28
Wang,Q.	2011	40	38	71.4 ± 3.7	72.3 ± 4.0	22/18	20/18	Lap + colorectal	30
Chen Hu,J.	2012	19	22	59.3 ± 6.0	61.4 ± 7.1	10/9	10/12	Lap + gastrectomy	28
Kim, J. W.	2012	22	22	52.6 ± 11.6	57.5 ± 14.5	13/9	15/7	Lap + gastrectomy	30
Veenhof,A.A.F.A.	2012	19	23	64.4 ± 9.2	66.1 ± 9.9	10/9	19/4	Lap + colorectal	30
Wang,G.	2012	40	40	55.7 ± 17.3	56.1 ± 14.6	27/13	26/14	Lap + colorectal	30
Lee,S.M.	2013	52	46	61.2 ± 10.8	61.7 ± 10.8	36/16	28/18	Lap + rectal	30
Mari,G.M.	2014	25	25	NA	NA	NA	NA	Lap + rectal	30
Taupyk,Y.	2015	31	39	58.5 ± 8.4	57.4 ± 10.1	22/9	20/19	Lap + colorectal	30
Abdikarim,I.	2015	30	31	63.0 ± 12.0	62.0 ± 11.0	21/9	20/11	Lap + gastrectomy	30
He,F.	2015	48	38	56.3 ± 16.3	60.4 ± 20.7	22/26	18/20	Lap + liver	30
Li,Y.	2016	67	60	72.9 ± 6.7	71.8 ± 8.0	49/18	47/13	Lap + gastrectomy	30
Liu,G.	2016	21	21	69.2 ± 5.1	70.3 ± 5.8	10/11	12/9	Lap + gastrectomy	30
Mingjie,X.	2016	73	76	60.5 ± 7.3	62.0 ± 8.3	48/25	50/26	Lap + gastrectomy	30
Liang,X.	2016	80	107	53.4 ± 13.5	55.5 ± 12.8	37/43	50/57	Lap + liver	30
Mari,G.M.	2016	70	70	63.8 ± 8.7	66.4 ± 10.1	39/31	35/35	Lap + colorectal	30
Shetiwy,M.	2017	35	35	48.5 ± 12.3	53.6 ± 11.5	21/14	14/11	Lap + colorectal	28
Xu,X.	2017	30	30	60.2 ± 8.1	60.1 ± 8.1	12/18	16/14	Lap + gastrectomy	30
Liang,X.	2017	56	58	56.4 ± 13.9	59.3 ± 10.4	32/24	37/21	Lap + liver	30
Ling,F.Y.	2017	50	50	56.0 ± 15.0	55.0 ± 14.0	37/13	33/17	Lap + esophagectomy	30
Zhang, Z.	2017	47	47	56.0 ± 6.6	55.9 ± 6.4	25/22	28/19	Lap + esophagectomy	90
Wang,C.G.	2017	22	23	40.9 ± 6.2	41.2 ± 5.6	13/9	14/9	Lap + cholecystectomy	30
Kang,S.H.	2018	46	51	56.3 ± 10.4	54.5 ± 12.6	33/13	38/13	Lap + gastrectomy	30

Lap: laparoscopic surgery, NA: not available.

studies. Numerous studies have looked at if combining the two methods leads to faster recovery. Thus, we performed the current meta-analysis to evaluate the safety and efficacy of the ERAS program combined with laparoscopic techniques. The main outcome parameters of certain trials reflected the advantages of the ERAS program; however, other trials did

not demonstrate these benefits.

In this study, we combined useable data to evaluate the effectiveness of the ERAS program. The results of our analysis revealed that patients undergoing laparoscopic digestive system surgery with the ERAS program had a shorter length of PHS (2.13 days), time to first

**Table 2**  
ERAS items in each RCTs.

Study	a	b	c	d	e	f	g	h	i	j	k	l	m	n	o	p	q	r	s	t	u	v	w	x	y	Items
Lee,Taek-Gu (2011)	✓	✓	✓				✓		✓	✓	✓	✓	✓		✓	✓	✓	✓		✓		✓		✓	✓	17
van Bree,S.H.(2011)		✓			✓	✓	✓		✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	16
Vlug,M.S.(2011)		✓			✓	✓			✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	15
Wang,Q.(2011)	✓			✓		✓		✓		✓	✓			✓	✓		✓	✓	✓	✓	✓		✓		✓	14
Chen Hu,J.(2012)	✓		✓		✓				✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	15
Kim, J. W.(2012)	✓		✓		✓				✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	14
Veenhof,A.A.F.A.(2012)		✓	✓		✓				✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	13
Wang,G.(2012)	✓			✓	✓			✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	17
Lee,S.M.(2013)	✓	✓	✓				✓		✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	17
Mari,G.M.(2014)		✓		✓	✓			✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	17
Taupyk,Y.(2015)				✓	✓	✓			✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	14
Abdikarim,I.(2015)	✓			✓					✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	13
He,F.(2015)	✓			✓	✓				✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	14
Li,Y.(2016)	✓			✓	✓				✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	15
Liu,G.(2016)	✓	✓			✓				✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	14
Mingjie,X.(2016)	✓	✓	✓		✓				✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	16
Liang,X.(2016)	✓	✓	✓	✓					✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	17
Mari,G.M.(2016)	✓	✓		✓	✓				✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	15
Shetiwy,M.(2017)	✓	✓		✓		✓			✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	18
Xu,X.(2017)	✓								✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	16
Liang,X.(2017)	✓	✓	✓	✓					✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	18
Ling,F.Y.(2017)	✓	✓		✓				✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	17
Zhang,Z.(2017)	✓		✓				✓		✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	13
Wang,C.G.(2017)	✓	✓	✓						✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	14
Kang,S.H.(2018)	✓	✓			✓			✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓		✓	17

**The ERAS parameters were numbered in (a–y):** a: Preadmission information, education and counseling; b: Preoperative optimization; c: Prehabilitation; d: Preoperative nutritional care; e: Management of Anaemia; f: Prevention of nausea and vomiting (PONV); g: Pre-anaesthetic medication; h: Antimicrobial prophylaxis and skin preparation; i: Bowel Preparation; j: Preoperative fluid and electrolyte therapy; k: Preoperative fasting and carbohydrate loading; l: Standard Anaesthetic Protocol; m: Intraoperative fluid and electrolyte therapy; n: Preventing intraoperative hypothermia; o: Surgical access; p: Drainage of the peritoneal cavity and pelvis; q: Nasogastric Intubation; r: Postoperative analgesia; s: Thromboprophylaxis; t: Postoperative fluid and electrolyte therapy; u: Urinary drainage; v: Prevention of postoperative ileus; w: Postoperative glycaemic control; x: Postoperative nutritional care; y: Early Mobilisation.

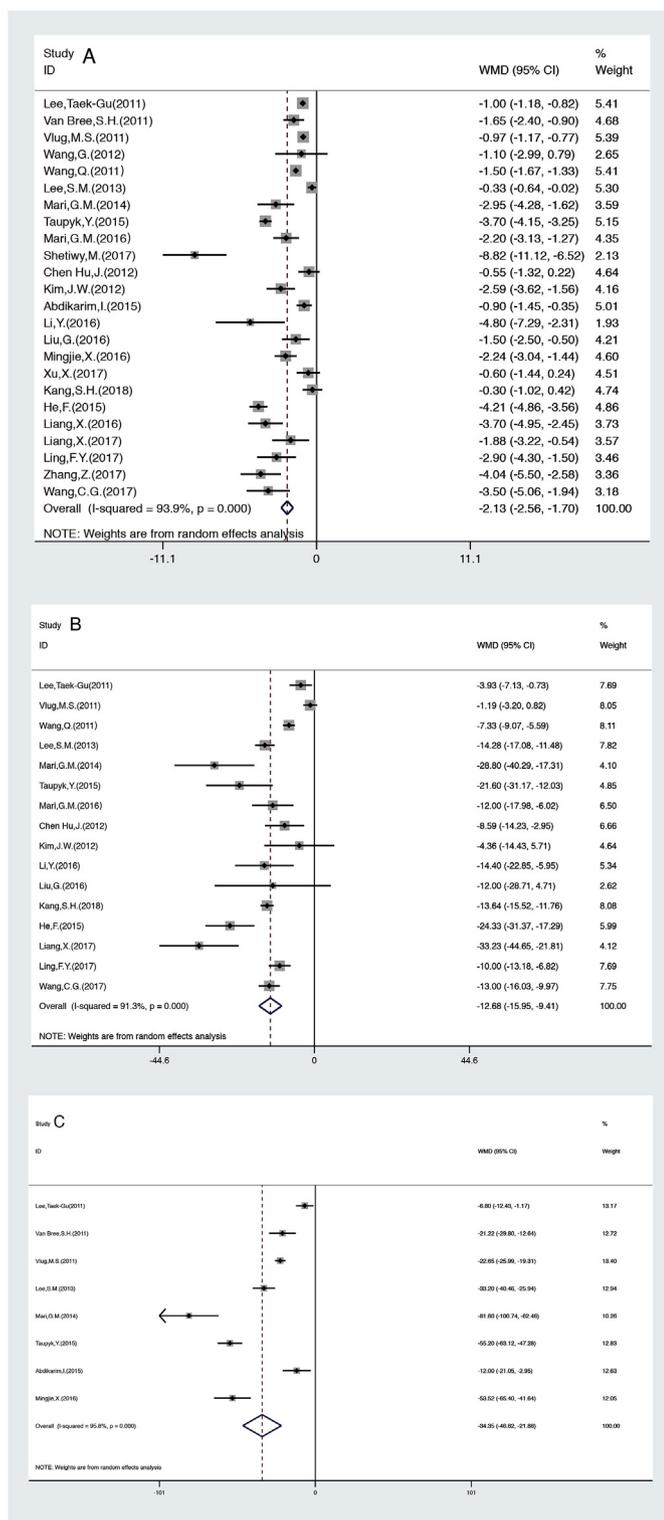


Fig. 2. Forest plot for the efficacy outcomes compared the ERAS program with the TPC: A) PHS; B) first time to flatus; C) first time to defecation.

flatus (12.68 h), and defecation (34.35 h) compared to the TPC group. Meanwhile, the safety of the ERAS program was also assessed. Our study indicated that the ERAS program group had lower postoperative complication rates (RR = 0.66), but there were no significant differences found in the mortality and readmission rates. The ERAS program was generally considered to accelerate postoperative recovery, but it might cause higher rates of complications and readmission. However, the analyses showed that the ERAS program had shorter PHS, and it did

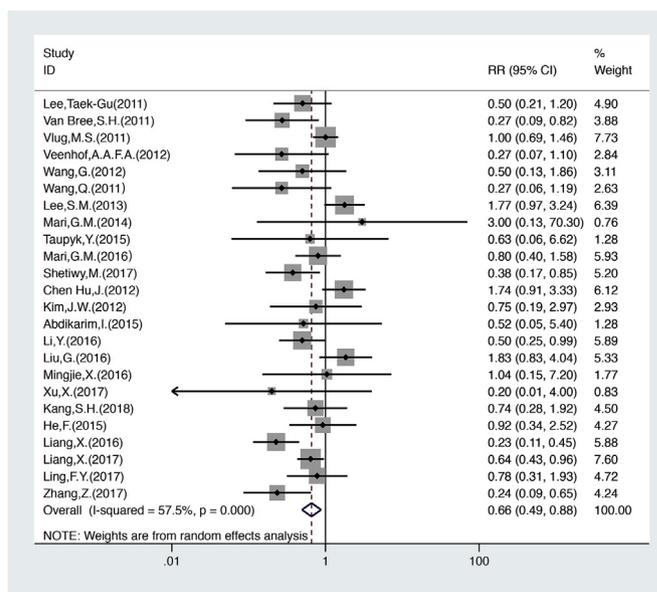


Fig. 3. Forest plot for the ERAS program compared with the TPC in overall complication rates.

not increase the risk of complications and the readmission rates. In summary, the ERAS program is helpful for rapid recovery after digestive system surgery.

In the current study, we primarily focused on the digestive system surgeries of colorectal surgery, gastrectomy, liver surgery, cholecystectomy, and esophagectomy. All results were obtained by analyzing these types of laparoscopic surgeries. To make the results more accurate, we selected RCTs as the inclusion criteria. However, there are few RCTs for certain types of surgery, such as laparoscopic cholecystectomy (1 RCT) and esophagectomy (2 RCTs). The results of the included RCTs showed that the ERAS program could reduce the PHS of laparoscopic cholecystectomy without increasing complications and readmission rates. Moreover, some studies that involved the ERAS program items also indicated that the ERAS program had better postoperative benefits compared to TPC in laparoscopic cholecystectomy [58,59]. The RCT cases of laparoscopic esophagectomies indicated that the ERAS program can accelerate postoperative rehabilitation and shorten PHS. Moreover, several comparative studies revealed the same results as the included RCTs above [60,61]. These results suggest that the ERAS program could shorten PHS, reduce complication rates, and promote postoperative fast recovery in laparoscopic cholecystectomy and esophagectomy. Furthermore, high-quality RCTs are required to confirm the results of our study.

In recent years, a limited number of meta-analyses were conducted to assess the efficacy and safety of the ERAS program in patients undergoing laparoscopic surgery. In 2014 and 2016, Zhao's and Yang's studies [22,62] evaluated ten (including five RCTs) and eight studies on laparoscopic colorectal and liver surgery, respectively. In 2017 and 2018, two meta-analyses performed by Li et al. [63] and Liu et al. [64] evaluated the program in laparoscopic gastrectomy. Compared to these studies, this meta-analysis has certain advantages. The current study included a large number of RCTs, and the previous meta-analyses included only a limit number of RCTs or even no RCT. Our meta-analysis is also the first to evaluate the ERAS program in laparoscopic digestive system surgery; other studies only assessed one type of digestive system surgery. Compared to previous studies, our conclusions are more accurate and reliable because we included the latest trials that met the inclusion criteria. Moreover, our study included the most comprehensive parameters, such as time to first defecation and mortality rates. Furthermore, this meta-analysis was strictly screened to meet the inclusion criteria.

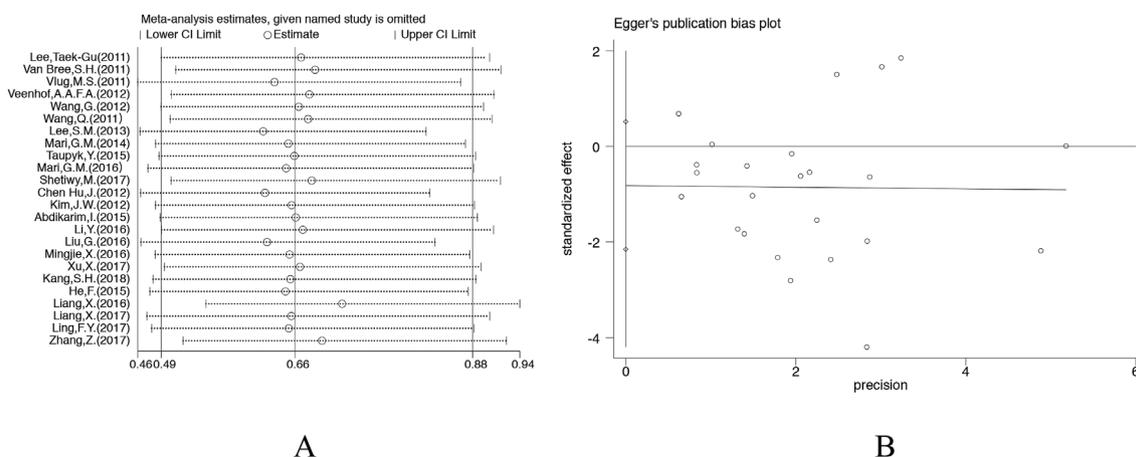


Fig. 4. Sensitivity analysis of the pooled RR (A); Egger's funnel plot of the publication bias (B).

Significant heterogeneity was detected for some outcomes among the studies. Thus, we performed sensitivity and subgroup analyses to evaluate the cause of heterogeneity. However, the sensitivity analyses indicated the results are stable and reliable, and the subgroup analyses of country and type of surgery did not eliminate the sources of heterogeneity. No individual trials affected the overall outcomes. Therefore, the heterogeneity in our meta-analysis may be due to the clinical heterogeneity, such as the ERAS items used, the various patient demographics, the inclusion criteria, the surgical technique, and the TPC approach that varied in different countries. Another concern is the publication bias because studies with positive results are more likely to be published in journals. Thus, we tried to develop a more comprehensive search strategy to minimize the possible bias. No obvious bias was identified in our study.

5. Conclusion

In conclusion, this meta-analysis indicated that ERAS programs significantly shortened PHS, accelerated gastrointestinal function recovery, and reduced overall postoperative complication rates without

affecting the readmission rates in laparoscopic digestive system surgery. The ERAS programs are effective and safe in laparoscopic digestive system surgery. Further high-quality, multicenter RCTs are needed to provide more evidence.

Ethical approval

This is a meta-analysis, and no need for ethical approval.

Sources of funding

No.

Author contribution

Xiaofei Ni and Jian Suo designed the study, Xiaofei Ni, Dan Jia searched databases and collected full-text papers, Xuan Sun and Yuchen Guo performed statistical analysis. Xiaofei Ni and Jian Suo wrote the manuscript. All authors screened the final version of the manuscript.

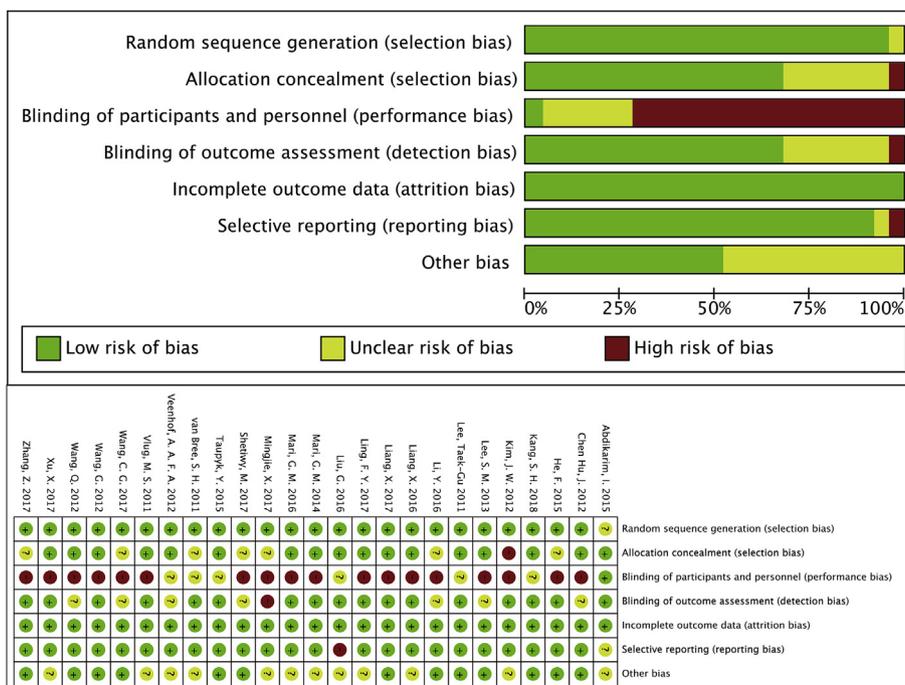


Fig. 5. The risk of bias graph and the risk of bias summary.

**Conflicts of interest**

No.

**Research registration number**

CRD42018118551.

Registration link: [www.crd.york.ac.uk/PROSPERO/](http://www.crd.york.ac.uk/PROSPERO/) - recordDetails**Guarantor**

Jian Suo.

**Provenance and peer review**

Not commissioned, externally peer-reviewed.

**Acknowledgements**

None.

**Appendix A. Supplementary data**Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijso.2019.07.034>.**References**

- [1] M. Jacobs, J.C. Verdeja, H.S. Goldstein, Minimally invasive colon resection (laparoscopic colectomy), *Surg. Laparosc. Endosc.* 1 (1991) 144–150 <http://europepmc.org/abstract/MED/1688289>.
- [2] J.K. Noel, K. Fahrbach, R. Estok, et al., Minimally invasive colorectal resection outcomes: short-term comparison with open procedures, *J. Am. Coll. Surg.* 204 (2007) 291–307 <https://doi.org/10.1016/j.jamcollsurg.2006.10.002>.
- [3] B. Kaltoft, I. Gogenur, J. Rosenberg, Reduced length of stay and convalescence in laparoscopic vs open sigmoid resection with traditional care: a double blinded randomized clinical trial, *Color, Dis* 13 (2011) e123–130 <https://doi.org/10.1111/j.1463-1318.2011.02550.x>.
- [4] Y.W. Kim, Y.H. Baik, Y.H. Yun, et al., Improved quality of life outcomes after laparoscopy-assisted distal gastrectomy for early gastric cancer: results of a prospective randomized clinical trial, *Ann. Surg.* 248 (2008) 721–727 <https://doi.org/10.1097/SLA.0b013e318185e62e>.
- [5] G. Ding, W. Cai, M. Qin, Pure laparoscopic versus open liver resection in treatment of hepatolithiasis within the left lobes: a randomized trial study, *Surg. Laparosc. Endosc. Percutaneous Tech.* 25 (2015) 392–394 <https://doi.org/10.1097/sle.0000000000000120>.
- [6] W. Ji, L.T. Li, Z.M. Wang, et al., A randomized controlled trial of laparoscopic versus open cholecystectomy in patients with cirrhotic portal hypertension, *World J. Gastroenterol.* 11 (2005) 2513–2517 <https://doi.org/10.3748/wjg.v11.i16.2513>.
- [7] L. Bardram, P. Funch-Jensen, P. Jensen, et al., Recovery after laparoscopic colonic surgery with epidural analgesia, and early oral nutrition and mobilisation, *Lancet* 345 (1995) 763–764 [https://doi.org/10.1016/S0140-6736\(95\)90463-6](https://doi.org/10.1016/S0140-6736(95)90463-6).
- [8] K. Lassen, M. Soop, J. Nygren, et al., Consensus review of optimal perioperative care in colorectal surgery: enhanced Recovery after Surgery (ERAS) Group recommendations, *Arch. Surg.* 144 (2009) 961–969 <https://doi.org/10.1001/archsurg.2009.170>.
- [9] H. Kehlet, D.W. Wilmore, Multimodal strategies to improve surgical outcome, *Am. J. Surg.* 183 (2002) 630–641 [https://doi.org/10.1016/S0002-9610\(02\)00866-8](https://doi.org/10.1016/S0002-9610(02)00866-8).
- [10] A. Arroyo, J.M. Ramirez, D. Callejo, et al., Influence of size and complexity of the hospitals in an enhanced recovery programme for colorectal resection, *Int. J. Colorectal Dis.* 27 (2012) 1637–1644 <https://doi.org/10.1007/s00384-012-1497-4>.
- [11] H. Kehlet, Fast-track colonic surgery: status and perspectives, *Rectal Cancer Treat.* vol. 165, 2005, pp. 8–13 <https://doi.org/10.1007/3-540-27449-9-2>.
- [12] D.W. Wilmore, H. Kehlet, Management of patients in fast track surgery, *Br. Med. J.* 322 (2001) 473–476 <https://doi.org/10.1136/bmj.322.7284.473>.
- [13] K.C.H. Fearon, O. Ljungqvist, M. Von Meyenfeldt, et al., Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection, *Clin. Nutr.* 24 (2005) 466–477 <https://doi.org/10.1016/j.clnu.2005.02.002>.
- [14] H. Kehlet, Fast-track colorectal surgery, *Lancet* 371 (2008) 791–793 [https://doi.org/10.1016/S0140-6736\(08\)60357-8](https://doi.org/10.1016/S0140-6736(08)60357-8).
- [15] G. Nelson, E. Kalogera, S.C. Dowdy, Enhanced recovery pathways in gynecologic oncology, *Gynecol. Oncol.* 135 (2014) 586–594 <https://doi.org/10.1016/j.ygyno.2014.10.006>.
- [16] E.L. Jones, T.W. Wainwright, J.D. Foster, et al., A systematic review of patient reported outcomes and patient experience in enhanced recovery after orthopaedic surgery, *Ann. R. Coll. Surg. Engl.* 96 (2014) 89–94 <https://doi.org/10.1308/003588414x13824511649571>.
- [17] M. Adamina, H. Kehlet, G.A. Tomlinson, et al., Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery, *Surgery* 149 (2011) 830–840 <https://doi.org/10.1016/j.surg.2010.11.003>.
- [18] L. Zorcolo, A.S. Rosman, M. Pisano, et al., A meta-analysis of prospective randomized trials comparing minimally invasive and open distal gastrectomy for cancer, *J. Surg. Oncol.* 104 (2011) 544–551 <https://doi.org/10.1002/jso.21980>.
- [19] M.Z. Li, L.B. Xiao, W.H. Wu, et al., Meta-analysis of laparoscopic versus open colorectal surgery within fast-track perioperative care, *Dis. Colon Rectum* 55 (2012) 821–827 <https://doi.org/10.1097/DCR.0b013e31824bd31e>.
- [20] P. Li, F. Fang, J.X. Cai, et al., Fast-track rehabilitation VS conventional care in laparoscopic colorectal resection for colorectal malignancy: a meta-analysis, *World J. Gastroenterol.* 19 (2013) 9119–9126 <https://doi.org/10.3748/wjg.v19.i47.9119>.
- [21] T.G. Ni, H.T. Yang, H. Zhang, et al., Enhanced recovery after surgery programs in patients undergoing hepatectomy: a meta-analysis, *World J. Gastroenterol.* 21 (2015) 9209–9216 <https://doi.org/10.3748/wjg.v21.i30.9209>.
- [22] R. Yang, W. Tao, Y.Y. Chen, et al., Enhanced recovery after surgery programs versus traditional perioperative care in laparoscopic hepatectomy: a meta-analysis, *Int. J. Surg.* 36 (2016) 274–282 <https://doi.org/10.1016/j.ijso.2016.11.017>.
- [23] A. Liberati, D.G. Altman, J. Tetzlaff, et al., The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration, *J. Clin. Epidemiol.* 62 (2009) e1–34 <https://doi.org/10.1016/j.jclinepi.2009.06.006>.
- [24] U.O. Gustafsson, M.J. Scott, M. Hubner, et al., Guidelines for perioperative care in elective colorectal surgery: enhanced recovery after surgery (ERAS®) society recommendations: 2018, *World. J. Surg.* 43 (2019) 659–695 <https://doi.org/10.1007/s00268-018-4844-y>.
- [25] J.P.T. Higgins, D.G. Altman, P.C. Gotzsche, et al., The Cochrane Collaboration's tool for assessing risk of bias in randomised trials, *BMJ* 343 (2011) d5928 <https://doi.org/10.1136/bmj.d5928>.
- [26] S.P. Hozo, B. Djulbegovic, I. Hozo, Estimating the mean and variance from the median, range, and the size of a sample, *BMC Med. Res. Methodol.* 5 (2005) 13 <https://doi.org/10.1186/1471-2288-5-13>.
- [27] D. Luo, X. Wan, J. Liu, et al., Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range, *Stat. Methods Med. Res.* 27 (2018) 1785–1805 <https://doi.org/10.1177/0962280216669183>.
- [28] R. DerSimonian, N. Laird, Meta-analysis in clinical trials revisited, *Contemp. Clin. Trials* 45 (2015) 139–145 <https://doi.org/10.1016/j.cct.2015.09.002>.
- [29] C.B. Begg, M. Mazumdar, Operating characteristics of a rank correlation test for publication bias, *Biometrics* 50 (1994) 1088–1101 <https://doi.org/10.2307/2533446>.
- [30] A.E. Stuck, L.Z. Rubenstein, D. Wieland, Bias in meta-analysis detected by a simple, graphical test. Asymmetry detected in funnel plot was probably due to true heterogeneity, *BMJ* 316 (1998) 469 author reply 470–461 <https://doi.org/10.1136/bmj.316.7129.469>.
- [31] T.G. Lee, S.B. Kang, D.W. Kim, et al., Comparison of early mobilization and diet rehabilitation program with conventional care after laparoscopic colon surgery: a prospective randomized controlled trial, *Dis. Colon Rectum* 54 (2011) 21–28 <https://doi.org/10.1007/DCR.0b013e3181fcd3e>.
- [32] S. Van Bree, M. Vluc, W. Bemelman, et al., Faster recovery of gastrointestinal transit after laparoscopy and fast-track care in patients undergoing colonic surgery, *Gastroenterology* 141 (2011) 872–880 e871–874 <https://doi.org/10.1053/j.gastro.2011.05.034>.
- [33] M.S. Vluc, J. Wind, M.W. Hollmann, et al., Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFa-study), *Ann. Surg.* 254 (2011) 868–875 <https://doi.org/10.1097/SLA.0b013e31821fd1ce>.
- [34] J. Chen Hu, L. xin Jiang, L. Cai, et al., Preliminary experience of fast-track surgery combined with laparoscopy-assisted radical distal gastrectomy for gastric cancer, *J. Gastrointest. Surg.* 16 (2012) 1830–1839 <https://doi.org/10.1007/s11605-012-1969-4>.
- [35] J.W. Kim, W.S. Kim, J.H. Cheong, et al., Safety and efficacy of fast-track surgery in laparoscopic distal gastrectomy for gastric cancer: a randomized clinical trial, *World, J. Surg.* 36 (2012) 2879–2887 <https://doi.org/10.1007/s00268-012-1741-7>.
- [36] A.A.F.A. Veenhof, M.S. Vluc, M.H.G.M. Van Der Pas, et al., Surgical stress response and postoperative immune function after laparoscopy or open surgery with fast track or standard perioperative care: a randomized trial, *Ann. Surg.* 255 (2012) 216–221 <https://doi.org/10.1097/SLA.0b013e31824336e2>.
- [37] G. Wang, Z. Jiang, K. Zhao, et al., Immunologic response after laparoscopic colon cancer operation within an enhanced recovery program, *J. Gastrointest. Surg.* 16 (2012) 1379–1388 <https://doi.org/10.1007/s11605-012-1880-z>.
- [38] Q. Wang, J. Suo, J. Jiang, et al., Effectiveness of fast-track rehabilitation vs conventional care in laparoscopic colorectal resection for elderly patients: a randomized trial, *Color, Dis* 14 (2012) 1009–1013 <https://doi.org/10.1111/j.1463-1318.2011.02855.x>.
- [39] S.M. Lee, S.B. Kang, J.H. Jang, et al., Early rehabilitation versus conventional care after laparoscopic rectal surgery: a prospective, randomized, controlled trial, *Surg. Endosc.* 27 (2013) 3902–3909 <https://doi.org/10.1007/s00464-013-3006-4>.
- [40] G.M. Mari, A. Costanzi, D. Maggioni, et al., Fast-track versus standard care in laparoscopic high anterior resection: a prospective randomized-controlled trial, *Surg. Laparosc. Endosc. Percutaneous Tech.* 24 (2014) 118–121 <https://doi.org/10.1097/SLE.0b013e3182a50e3a>.
- [41] I. Abdikarim, X.Y. Cao, S.Z. Li, et al., Enhanced recovery after surgery with laparoscopic radical gastrectomy for stomach carcinomas, *World J. Gastroenterol.* 21 (2015) 13339–13344 <https://doi.org/10.3748/wjg.v21.i47.13339>.

- [42] F. He, X. Lin, F. Xie, et al., The effect of enhanced recovery program for patients undergoing partial laparoscopic hepatectomy of liver cancer, *Clin. Transl. Oncol.* 17 (2015) 694–701 <https://doi.org/10.1007/s12094-015-1296-9>.
- [43] Y. Taupyk, X. Cao, Y. Zhao, et al., Fast-track laparoscopic surgery: a better option for treating colorectal cancer than conventional laparoscopic surgery, *Oncol. Lett.* 10 (2015) 443–448 <https://doi.org/10.3892/ol.2015.3166>.
- [44] Y. Li, J. Qiu, H. Cao, Application of enhanced recovery after surgery for patients with laparoscopic radical gastrectomy, *Chinese J. Gastrointest. Surg.* 19 (2016) 269–273 <https://doi.org/10.3760/cma.j.issn.1671-0274.2016.03.009>.
- [45] X. Liang, H. Ying, H. Wang, et al., Enhanced recovery program versus traditional care in laparoscopic hepatectomy, *Med. (United States)* (2016) 95 <https://doi.org/10.1097/MD.0000000000002835>.
- [46] G. Liu, F. Jian, X. Wang, et al., Fast-track surgery protocol in elderly patients undergoing laparoscopic radical gastrectomy for gastric cancer: a randomized controlled trial, *OncoTargets Ther.* 9 (2016) 3345–3351 <https://doi.org/10.2147/OTT.S107443>.
- [47] G. Mari, J. Crippa, A. Costanzi, et al., ERAS protocol reduces IL-6 secretion in colorectal laparoscopic surgery: results from a randomized clinical trial, *Surg. Laparosc. Endosc. Percutaneous Tech.* 26 (2016) 444–448 <https://doi.org/10.1097/SLE.0000000000000324>.
- [48] X. Liang, H. Ying, H. Wang, et al., Enhanced recovery care versus traditional care after laparoscopic liver resections: a randomized controlled trial, *Surg. Endosc.* 32 (2018) 2746–2757 <https://doi.org/10.1007/s00464-017-5973-3>.
- [49] F.Y. Ling, J.W. Xiong, D.L. Yu, et al., Value of enhanced recovery after surgery in perioperative period of minimally invasive esophagectomy for esophageal carcinoma, *World Chin. J. Dig.* 25 (2017) 1491–1496 <https://doi.org/10.11569/wcjd.v25.i16.1491>.
- [50] X. Mingjie, Z. Luyao, T. Ze, et al., Laparoscopic radical gastrectomy for resectable Advanced gastric cancer within enhanced recovery programs: a prospective randomized controlled trial, *J. Laparoendosc. Adv. Surg. Tech.* 27 (2017) 959–964 <https://doi.org/10.1089/lap.2016.0057>.
- [51] M. Shetiwy, T. Fady, F. Shahatto, et al., Standardizing the protocols for enhanced recovery from colorectal cancer surgery: are we a step closer to ideal recovery? *Ann. Coloproctol.* 33 (2017) 86–92 <https://doi.org/10.3393/ac.2017.33.3.86>.
- [52] C.G. Wang, Q.S. Jiang, N.H. Zhu, et al., Effect of fast track surgery on clinical efficacy of laparoscopic common bile duct exploration combined with choledochoscopy, *World Chin. J. Dig.* 25 (2017) 1083–1087 <https://doi.org/10.11569/wcjd.v25.i12.1083>.
- [53] X. Xu, J. Xu, Application of enhanced recovery after surgery in laparoscopy-assisted distal gastrectomy, *Cancer Res. Clin.* 29 (2017) 180–183 <https://doi.org/10.3760/cma.j.issn.1006-9801.2017.03.009>.
- [54] Z. Zhang, H. Li, C. Yan, et al., A comparative study on the efficacy of fast-track surgery in the treatment of esophageal cancer patients combined with metabolic syndrome, *Oncol. Lett.* 14 (2017) 4812–4816 <https://doi.org/10.3892/ol.2017.6759>.
- [55] S.H. Kang, Y. Lee, S.H. Min, et al., Multimodal enhanced recovery after surgery (ERAS) program is the optimal perioperative care in patients undergoing totally laparoscopic distal gastrectomy for gastric cancer: a prospective, randomized, clinical trial, *Ann. Surg. Oncol.* 25 (2018) 3231–3238 <https://doi.org/10.1245/s10434-018-6625-0>.
- [56] F. Carli, Physiologic considerations of Enhanced Recovery after Surgery (ERAS) programs: implications of the stress response, *Can. J. Anesth.* 62 (2015) 110–119 <https://doi.org/10.1007/s12630-014-0264-0>.
- [57] J.M. Blazeby, Systematic review of outcomes used to evaluate enhanced recovery after surgery (*Br J Surg* 2014; 101: 159-170, *Br. J. Surg.* 101 (2014) 171 <https://doi.org/10.1002/bjs.9378>.
- [58] G.S. Murphy, J.W. Szokol, S.B. Greenberg, et al., Preoperative dexamethasone enhances quality of recovery after laparoscopic cholecystectomy: effect on in-hospital and postdischarge recovery outcomes, *Anesthesiology* 114 (2011) 882–890 <https://doi.org/10.1097/ALN.0b013e3181ec642e>.
- [59] B.N. Singh, D. Dahiya, D. Bagaria, et al., Effects of preoperative carbohydrates drinks on immediate postoperative outcome after day care laparoscopic cholecystectomy, *Surg. Endosc.* 29 (2015) 3267–3272 <https://doi.org/10.1007/s00464-015-4071-7>.
- [60] H. Pan, X. Hu, Z. Yu, et al., Use of a fast-track surgery protocol on patients undergoing minimally invasive oesophagectomy: preliminary results, *Interact. Cardiovasc. Thorac. Surg.* 19 (2014) 441–447 <https://doi.org/10.1093/icvts/ivv172>.
- [61] A.F. Khasanov, E.I. Sigal, V.R. Trifonov, et al., The program of accelerated rehabilitation after esophagoplasty (fast track surgery) in esophageal cancer surgery, *Khirurgiia* (2015) 37–43 <https://doi.org/10.17116/hirurgia2015237-43>.
- [62] J.H. Zhao, J.X. Sun, P. Gao, et al., Fast-track surgery versus traditional perioperative care in laparoscopic colorectal cancer surgery: a meta-analysis, *BMC Canc.* 14 (2014) 607 <https://doi.org/10.1186/1471-2407-14-607>.
- [63] Z. Li, Q. Wang, B. Li, et al., Influence of enhanced recovery after surgery programs on laparoscopy-assisted gastrectomy for gastric cancer: a systematic review and meta-analysis of randomized control trials, *World J. Surg. Oncol.* 15 (2017) 207 <https://doi.org/10.1186/s12957-017-1271-8>.
- [64] Q. Liu, L. Ding, H. Jiang, et al., Efficacy of fast track surgery in laparoscopic radical gastrectomy for gastric cancer: a meta-analysis of randomized controlled trials, *Int. J. Surg.* 50 (2018) 28–34 <https://doi.org/10.1016/j.ijso.2017.12.026>.