Journal of Gastrointestinal Surgery (2019) 23:1502–1512
https://doi.org/10.1007/s11605-019-04170-8

REVIEW ARTICLE

Is the Enhanced Recovery After Surgery (ERAS) Program Effective and Safe in Laparoscopic Colorectal Cancer Surgery? A Meta-Analysis of Randomized Controlled Trials

Xiaofei Ni[1] · Dan Jia[2] · Yan Chen[1] · Lei Wang[1] · Jian Suo[1]

Received: 26 December 2018 / Accepted: 12 February 2019 / Published online: 11 March 2019

Abstract

Background Enhanced recovery after surgery (ERAS) program has shown a few advantages in colorectal cancer surgery. However, the effectiveness of the ERAS program in laparoscopic colorectal cancer surgery is still unclear. We performed a meta-analysis of randomized controlled trials (RCTs) to evaluate the effect of ERAS program in laparoscopic colorectal cancer surgery compared with traditional perioperative care (TC).

Methods PubMed, EMBASE, Web of Science, The Cochrane Library, and ClinicalTrials.gov were searched for eligible RCTs comparing ERAS program with TC in laparoscopic colorectal cancer surgery. The main outcomes included the average length of postoperative hospital stay (PHS), time to first flatus and defecation, overall complication, readmission, and mortality rates were undertaken.

Results Thirteen RCTs involving 1298 patients were included in our study (639 in ERAS group and 659 in TC group). ERAS group had shorter average length of PHS (weighted mean difference [WMD] − 2.00 day, 95% confidence interval [CI] − 2.52 to − 1.48, $p = 0.00$), time to first flatus (WMD − 12.18 h, 95%CI − 16.69 to − 7.67, $p = 0.00$), and time to first defecation (WMD − 32.93 h, 95%CI − 45.36 to − 20.50, $p = 0.00$) than TC group. In addition, the overall complication rates (risk ratio [RR] 0.59, 95%CI 0.40 to 0.86, $p < 0.01$) were significantly lower in ERAS group compared with TC group.

Conclusions The results indicated that ERAS program is a much better effective and safe protocol for laparoscopic colorectal cancer surgery compared with TC. Hence, ERAS program should be recommended in laparoscopic colorectal cancer surgery.

Keywords Enhanced recovery after surgery · Laparoscopic surgery · Colorectal cancer · Meta-analysis

Introduction

Colorectal cancer (CRC) is the third most common cancer in men and women.[1] There are 1.4 million cases previously diagnosed with CRC, and an additional 134,490 patients are diagnosed in 2016 in USA.[1,2] Surgery is the most common treatment for CRC, as the intestinal tract is involved in the process of surgery, the postoperative morbidity rate is high and the average length of postoperative hospital stay (PHS) may be prolonged.[3] To avoid these problems, many new techniques and methods have been introduced into colorectal cancer surgery. Laparoscopic (assisted) surgery for colorectal resection has been first described by Jacobs et al.[4] in 1991. Laparoscopic colorectal cancer surgery shows some advantages in reducing the average length of PHS and postoperative morbidity.[5–8]

Enhanced recovery after surgery (ERAS) program is first introduced by Kehlet et al.[9] in the mid 1990s, which aims to reduce surgery stress, accelerate the average length of postoperative functional recovery, and lower postoperative morbidity.[10–12] This program developed into ERAS working group to recommend standard protocol for ERAS program.[13] It contains 17 different items, including preoperative counseling, optimal intraoperative

✉ Jian Suo
suojian24@hotmail.com

[1] Department of Gastrointestinal Surgery, First Hospital of Jilin University, 71Xinmin Street, Chaoyang District, Changchun 130021, Jilin Province, China

[2] Department of Third Operation Room, First Hospital of Jilin University, 71Xinmin Street, Chaoyang District, Changchun, Jilin Province, China

epidural anesthesia, postoperative fluid limitation, early recovery mobilization, postoperative pain control, and early feeding.[14,15] Some RCTs have proven that ERAS program is associated with shorter average length of PHS, lower postoperative morbidity, and faster gastrointestinal function recovery.[16,17] But in other studies, there is no significant difference between ERAS group and traditional care (TC) group.[18] A few meta-analyses have been published about ERAS program in laparoscopic colorectal cancer surgery.[19,20] However, such meta-analyses have been conducted on a limited number of RCTs and most of them have been regarded as poor quality. It is necessary to perform a meta-analysis with a large number of RCTs. The impact of ERAS program in laparoscopic colorectal cancer surgery is still controversial. Therefore, we collected and extracted data from relevant RCTs and performed the present meta-analysis to evaluate the effects of ERAS program in laparoscopic colorectal cancer surgery.

Methods

This meta-analysis was conducted in accordance with the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta Analyses).[21] This study has been registered in the PROSPERO register (CRD42019118565).

Literature Search

We searched the PubMed, EMBASE, Cochrane Library, Web of Science, and ClinicalTrials.gov for relevant results (last search, October 2018). There were no language restrictions in our study. The following keywords were used: ("fast track" OR "enhanced recovery" OR "FTS" OR "ERAS" OR "accelerated rehabilitation" OR "multimodal perioperative care" OR "enhanced recovery after surgery" OR "enhanced recovery of surgery program" OR "enhanced recovery of surgery program" OR "clinical pathway" OR "critical pathway" OR "perioperative protocol" OR "evidence-based medicine" AND "colectomy" OR "colorectal" OR "colon" OR "rectal" OR "sigmoid" OR "rectum" OR "colonic" OR "colorectal cancer" OR "colorectal diseases" OR "intestines" OR "intestinal diseases" OR "rectal surgery" OR "sigmoidectomy" AND "laparoscopy" OR "laparoscopic" OR "minimally invasive" OR "laparoscopic surgery" AND "randomized" OR "randomly" OR "RCT" OR "trial" OR "control"). Furthermore, relevant literature was evaluated for additional references on the same subject.

Data Extraction and Quality Assessment

Data were selected and extracted by two independent reviewers with standardized forms. For each RCT, the following data were extracted: the number of participants, the average length of PHS, complications, readmissions, mortality, and other parameters. Quality assessment was evaluated using the Cochrane Collaboration's risk of bias tool.[22] The tools included an assessment of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other items. The risk of each parameter was graded as "low risk," "high risk," or "unclear risk," respectively.

Inclusion and Exclusion Criteria

Relevant RCTs for our meta-analysis met the following inclusion criteria: (1) RCTs comparing the ERAS group with TC group in patients undergoing laparoscopic colorectal cancer surgery; (2) studies describing the ERAS program with a clear protocol; (3) studies including at least three of the following parameters—the average length of PHS, duration of flatus or defecation, rates of complications, readmissions, or mortality; and (4) studies describing an ERAS program at least 13 parameters in the ERAS group.[23] The exclusion criteria were as follows: (1) studies were reviews, letters, cases, or bioinformatics; (2) studies were not RCTs; (3) studies only had the abstracts presented at national or international conferences without full-text articles; (4) studies reported ERAS program without laparoscopic colorectal cancer surgery; (5) when duplicate publications were extracted, only the latest one was included.

Statistical Analysis

For dichotomous variables, overall RRs and their corresponding 95%CIs were used to analyze the pool results. For continuous variables, the WMDs with 95%CIs were calculated for analysis of the included studies. When articles only provided medians and ranges of the continuous variables, we converted them into means and standard with the methods provided by Hozo et al. and Luo et al..[24,25] The chi-squared test and I^2 statistic were used to assess the heterogeneity among all studies. A random-effects model was used to calculate the parameters when there was statistically high heterogeneity (P value < 0.1 or $I^2 > 50\%$).[26] Otherwise, we selected a fixed-effects model. Sensitivity analysis was performed to test the reliability of present meta-analysis by eliminating individual studies. Egger's test and funnel plot asymmetry were measured to evaluate the publication bias.[27,28] All statistical analyses were conducted with STATA version 14.0 (STATA corp., College

Station, TX) and Review Manger version 5.3 (Nordic Cochrane, Copenhagen, Denmark).

Results

Study Selection and Characteristics

By searching the five electronic databases, 834 publications were identified. And one additional publication was retrieved from other sources. Two hundred ninety-eight publications were eliminated because of duplication. The remaining 537 publications were screened by the titles and abstracts, and 474 records were excluded. Subsequently, 50 publications were excluded after full-text reading. Eventually, 13 studies including 13 RCTs were enrolled in the present meta-analysis.[16–18,29–38] A flowchart meeting the research selection is summarized in Fig. 1.

The 13 studies included 639 ERAS patients, and 659 TC patients, from China, Korea, Netherland, Italy and Egypt. All trials were published between 2011 and 2017. The number of participants in each RCT ranged from 35 to 210. General characteristics of the included trials are summarized in Table 1. All 13 trials covered in this meta-analysis had a clear ERAS protocol. Each trial had at least 13 items which described the ERAS program in the ERAS group. Table 2 summarizes the relevant elements involved in these trials according to the new Enhanced Recovery After Surgery (ERAS) Society Recommendations published in 2018.[23]

The Average Length of Postoperative Hospital Stay

Twelve studies, except Veenhof et al.,[33] reported the average length of PHS including 620 patients in ERAS group and 636 patients in TC group. The results indicated that ERAS group has a significant shorter average length of PHS (WMD −2.00 day, 95%CI −2.52 to −1.48, p = 0.00) than TC group (Fig. 2). As a high heterogeneity ($I^2 > 50\%$) was observed in the analysis, a random-effects model was selected. To clear the heterogeneity, subgroup analyses of countries and surgery types were performed. The results of the subgroup analyses revealed that no significant heterogeneity was affected by any single trial.

Time to First Flatus and Defecation

Nine RCTs and seven RCTs, involving 1071 and 678 patients, reported time to first flatus and time to first defecation,

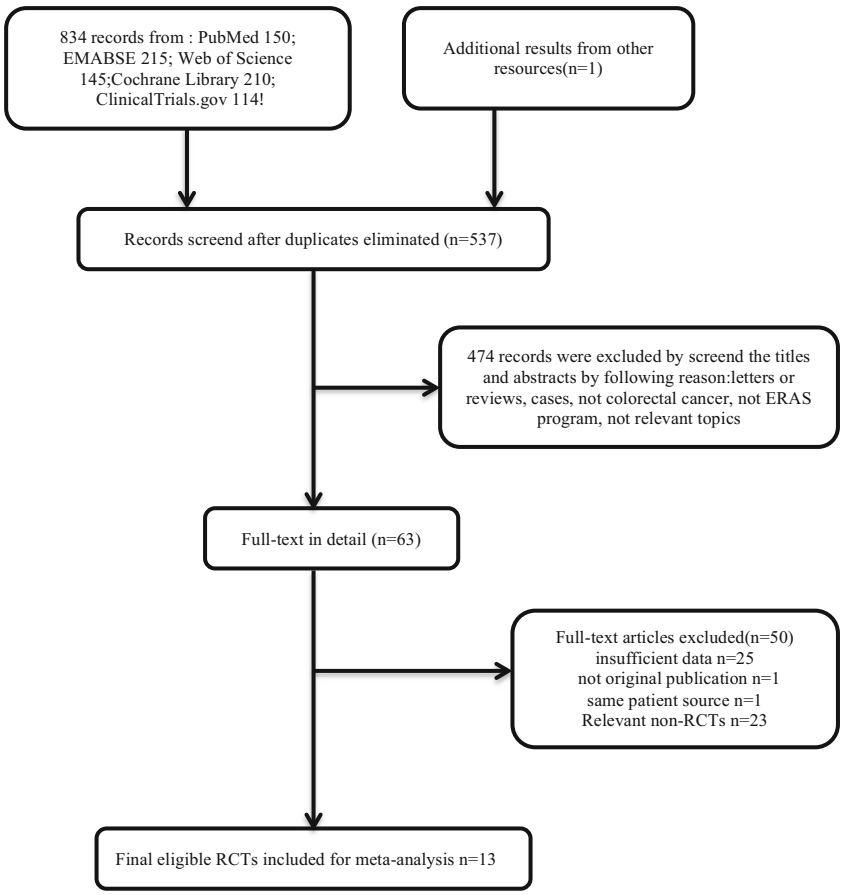

Fig. 1 Flowchart meeting the study selection

Table 1 General characteristics of the included RCTs

Study	Year	Country	Sample size		Age (years), mean ± SD		Gender (M/F)		Types of surgery	Follow-up (days)
			ERAS	TC	ERAS	TC	ERAS	TC		
Lee, Taek-Gu	2011	Korea	46	54	61.9 ± 11.2	60.6 ± 0.0	26/20	30/24	Lap + colorectal	30
Van Bree, S.H.	2011	Netherlands	18	17	65.0 ± 9.4	66.0 ± 10.2	9/9	9/8	Lap + colorectal	30
Vlug, M.S.	2011	Netherlands	100	109	66.0 ± 8.6	68.0 ± 8.8	53/47	68/41	Lap + colorectal	28
Veenhof, A.A.F.A.	2012	Netherlands	19	23	64.4 ± 9.2	66.1 ± 9.9	10/9	19/4	Lap + colorectal	30
Wang, G.	2012	China	40	40	55.7 ± 17.3	56.1 ± 14.6	27/13	26/14	Lap + colorectal	30
Wang, Q.	2011	China	40	38	71.4 ± 3.7	72.3 ± 4.0	22/18	20/18	Lap + colorectal	30
Lee, S.M.	2013	Korea	52	46	61.2 ± 10.8	61.7 ± 10.8	36/16	28/18	Lap + rectal	30
Feng, F.	2014	China	57	59	54.0 ± 12.0	56.3 ± 11.5	36/21	40/19	Lap + rectal	30
Mari, G.M.	2014	Italy	25	25	NA	NA	NA	NA	Lap + rectal	30
Taupyk, Y.	2015	China	31	39	58.5 ± 8.4	57.4 ± 10.1	22/9	20/19	Lap + colorectal	30
Mari, G.M.	2016	Italy	70	70	63.8 ± 8.7	66.4 ± 10.1	39/31	35/35	Lap + colorectal	30
Wang, G.	2011	China	106	104	56.6 ± 6.2	54.8 ± 5.4	65/41	60/44	Lap + colorectal	30
Shetiwy, M.	2017	Egypt	35	35	48.5 ± 12.3	53.6 ± 11.5	21/14	14/11	Lap + colorectal	28

Lap laparoscopic surgery, *NA* not available

respectively. In random-effects models, the results indicated that significant shorter in time to first flatus (WMD − 12.18 h, 95%CI − 16.69 to − 7.67, $p = 0.00$) and time to first defecation (WMD − 32.93 h, 95%CI − 45.36 to − 20.50, $p = 0.00$) in ERAS group compared with TC group, respectively (Fig. 3a, b). Subgroup analyses of countries and surgery types showed no significant effect of any trials on heterogeneity.

Complication, Readmission, and Mortality

All included RCTs reported the postoperative complication rates in patients undergoing laparoscopic colorectal cancer surgery. Postoperative complications occurred in 114 (17.84%) ERAS patients and 178 (27.01%) TC patients. The forest plot showed that there is a significant lower

Table 2 Relevant ERAS elements involved in these RCTs

Trials	Year	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
Veenhof, A.A.F.A.	2012		✓	✓		✓				✓	✓	✓	✓			✓	✓			✓			✓		✓	✓	13
Wang, G.	2012	✓			✓	✓			✓	✓	✓	✓	✓	✓		✓		✓	✓		✓	✓	✓		✓	✓	17
Wang, Q.	2011	✓			✓		✓		✓		✓	✓			✓	✓		✓	✓		✓			✓	✓	✓	13
Lee, S.M.	2013	✓	✓	✓				✓		✓	✓	✓	✓	✓		✓	✓	✓	✓		✓		✓		✓	✓	17
Feng, F.	2014	✓				✓				✓	✓		✓		✓	✓		✓	✓		✓	✓		✓	✓	✓	14
Mari, G.M.	2014		✓		✓	✓			✓	✓	✓	✓	✓	✓		✓	✓	✓	✓		✓	✓			✓	✓	17
Taupyk, Y.	2015				✓	✓	✓				✓	✓	✓	✓		✓		✓	✓		✓	✓	✓			✓	14
Mari, G.M.	2016		✓		✓	✓				✓	✓	✓	✓	✓		✓	✓	✓	✓		✓				✓	✓	15
Wang, G.	2011	✓			✓	✓				✓	✓	✓	✓	✓		✓		✓	✓		✓	✓	✓		✓	✓	16
Shetiwy, M.	2017	✓		✓	✓		✓			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓			✓	18

The ERAS elements were labeled as A–Y: A, preadmission information, education, and counseling; B, preoperative optimization; C, prehabilitation; D, preoperative nutritional care; E, management of anemia; F, prevention of nausea and vomiting (PONV); G, preanesthetic medication; H, antimicrobial prophylaxis and skin preparation; I, bowel preparation; J, preoperative fluid and electrolyte therapy; K, preoperative fasting and carbohydrate loading; L, standard anesthetic 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 mobilization

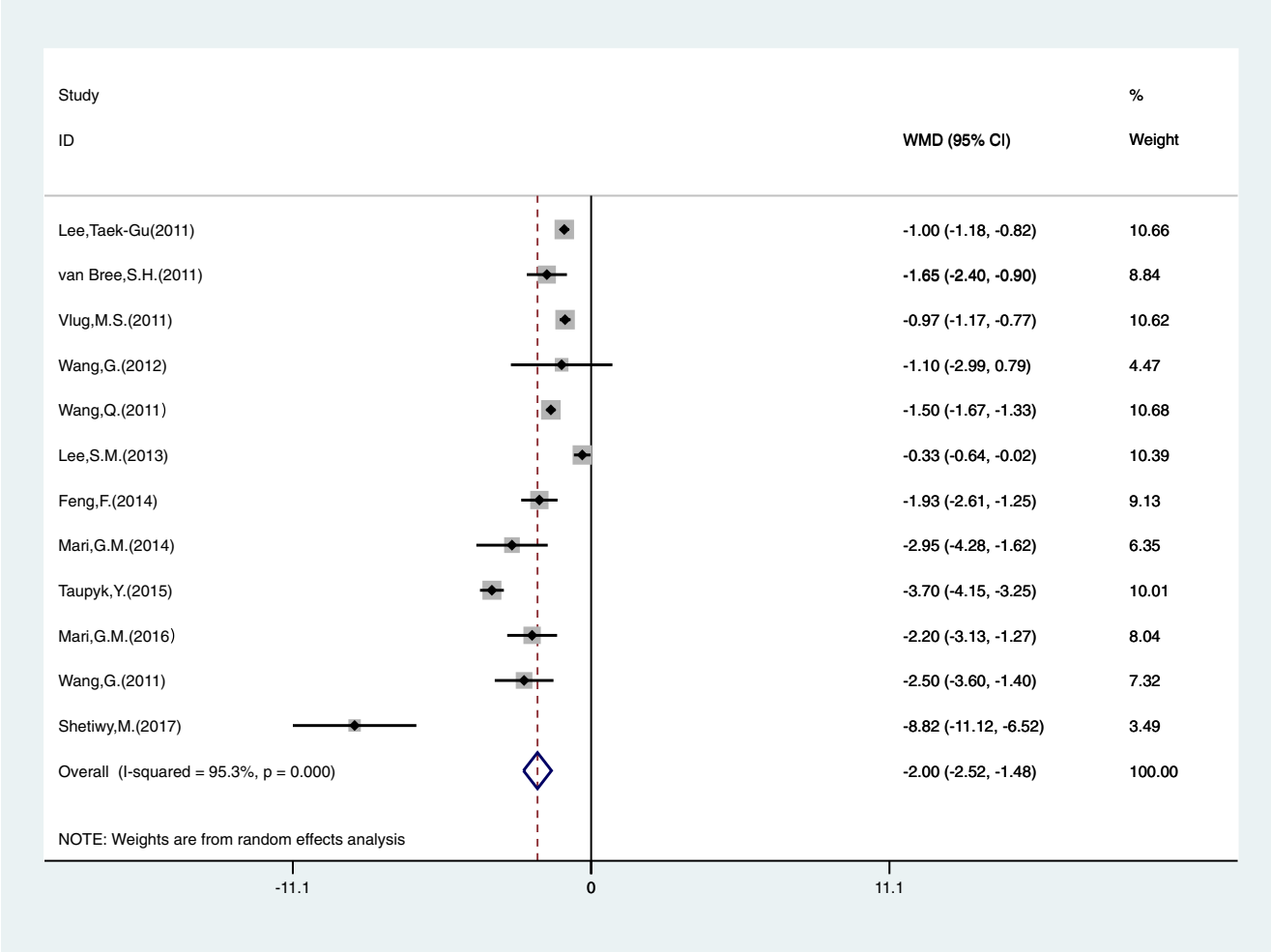

Fig. 2 Forest plot for the PHS compared ERAS program with TC

postoperative complication rates in EARS group (RR 0.59, 95%CI 0.40 to 0.86, $p < 0.01$) compared with TC group, with high heterogeneity ($I^2 = 56.6\%$) (Fig. 4). A random-effects model was used due to the high heterogeneity. The 30-day readmission rates and mortality rates were presented in five studies. The results indicated no significant differences in 30-day readmission rates (RR 0.65, 95%CI 0.35 to 1.20, $p = 0.77$) and mortality rates (RR 0.89, 95%CI 0.34 to 2.38, $p = 0.61$) between two groups. Both parameters had no heterogeneity ($I^2 = 0.00\%$) and fix-effects models were used.

Inflammatory Response Indicators

Two trials (220 patients) and three trials (290 patients) reported interleukin-6 (IL-6) and C-reactive protein (CRP) levels after laparoscopic colorectal cancer surgery, respectively. IL-6 and CRP levels were used as parameters to observe the degree of inflammation and tissue damage, and the level may reflect the extent of each surgery and trauma. The results indicated that ERAS group has lower levels for CRP (WMD = − 24.72 mg/L, − 25.98 mg/L, and − 30.34 mg/L on days 1, 3, and 5 after surgery, respectively) and for IL-6 (WMD = − 26.45 pg/L, − 24.21 pg/L, and − 18.33 pg/L on days 1, 3, and 5 after surgery, respectively) compared with TC group. Due to the heterogeneity ($I^2 = 0.00\%$), a fixed-effects model was applied for the analysis of the IL-6 levels on postoperative day 3. For the rest analyses, random-effects models were used. Details are shown in Table 3.

Assessment of Study Quality

The risk of bias in this meta-analysis was evaluated by using Review Mange 5.3. For such clinical trials, it was hard to comply with blinding of the surgeons and participants. The performance bias was considered as high risk in most included RCTs. All RCTs had a low risk in attrition bias and reporting bias. The overall risk of bias was defined as moderate to low risk. The risk of bias graph and summary are presented in Fig. 5.

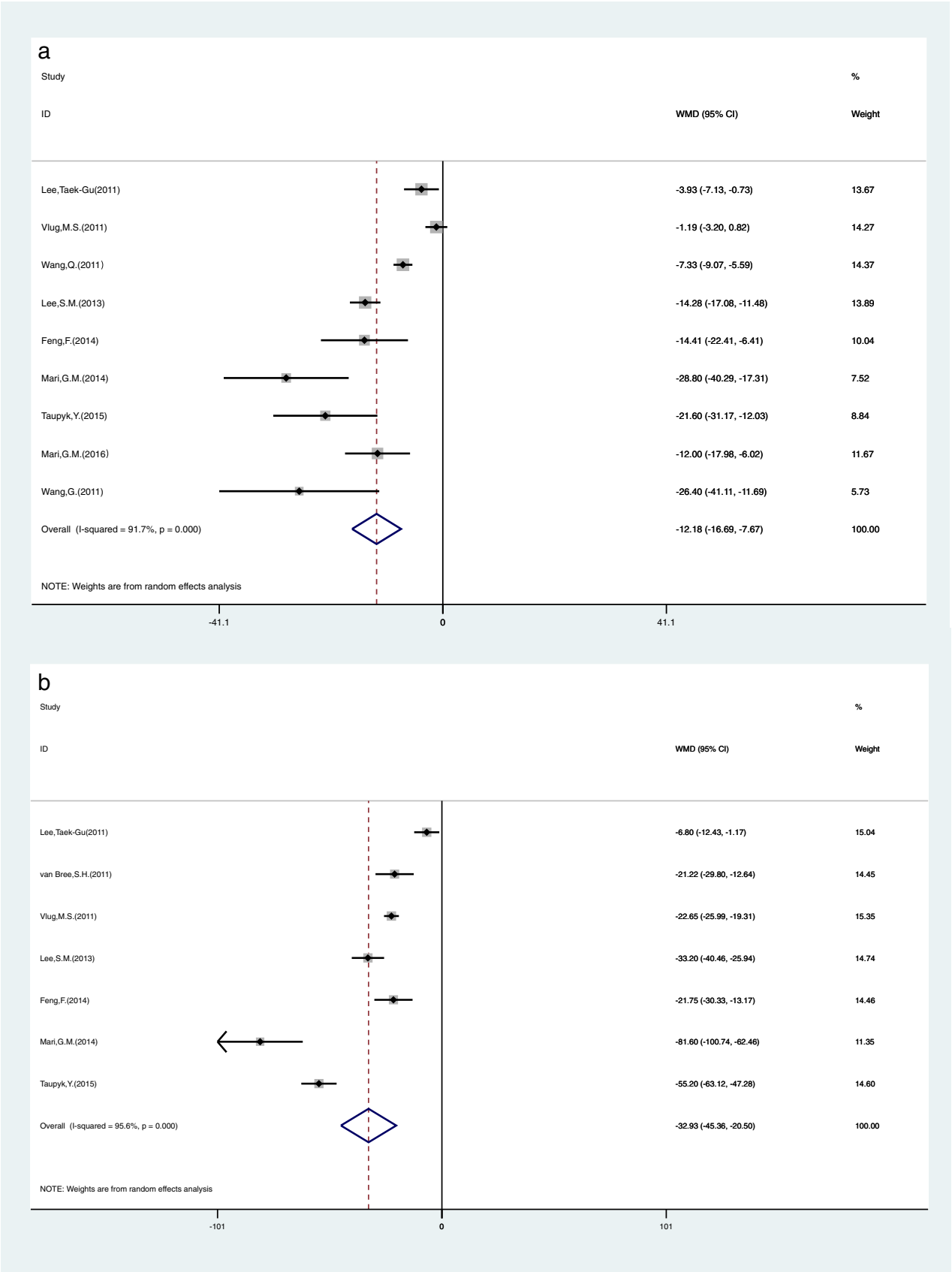

Fig. 3 Forest plot for gastrointestinal function recovery outcomes compared ERAS program with TC. **a** First time to flatus. **b** First time to defecation

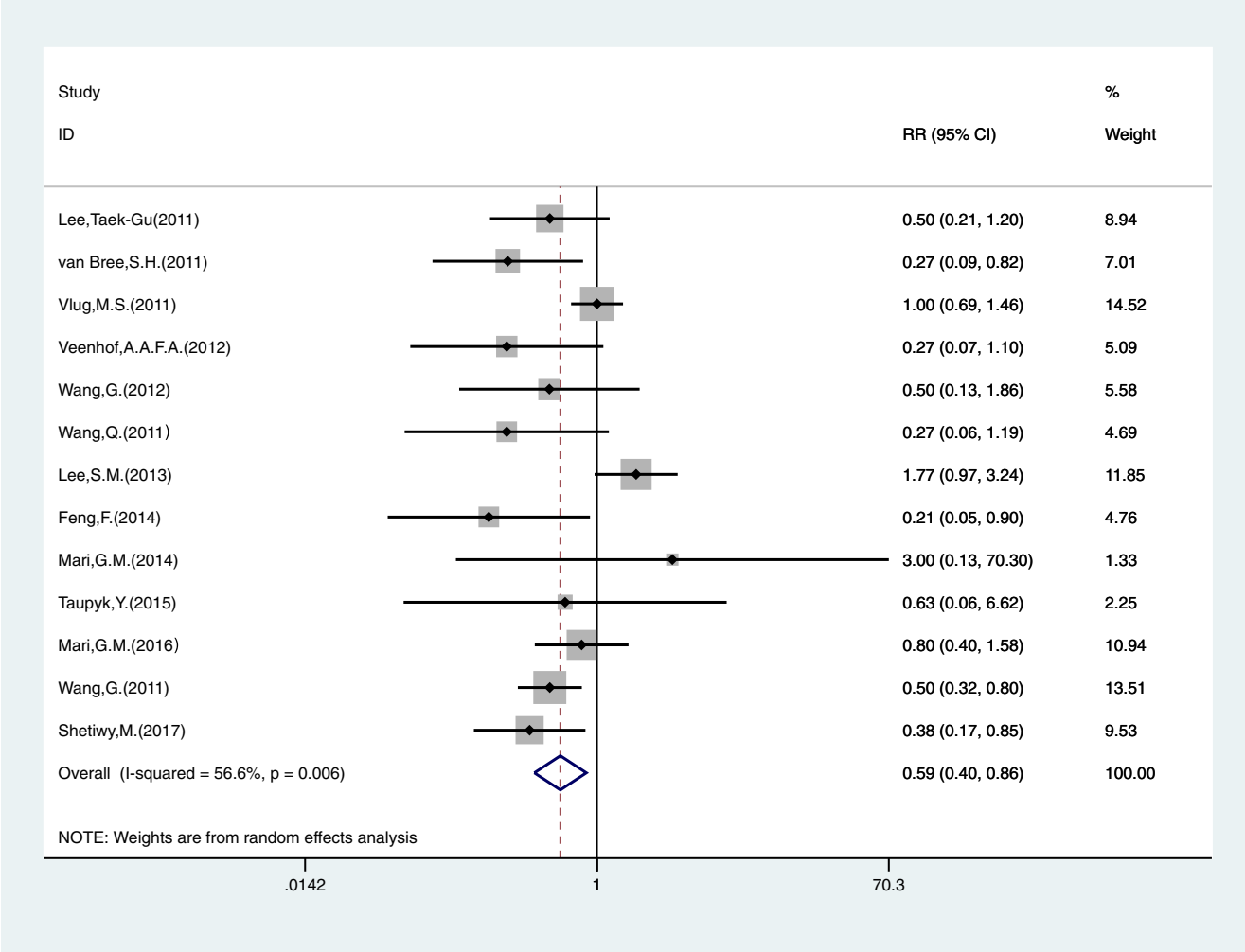

Fig. 4 Forest plot for the overall complication rates compared ERAS program with TC

Publication Bias and Sensitivity Analysis

The publication bias about included RCTs was assessed through Begg's test, Egger's test, and Egger's funnel plot. The Egger's funnel plot showed no obvious asymmetry is revealed for postoperative complications among all trials (Fig. 6a). The results of Begg's and Egger's tests indicated that there were no significant publication bias in current meta-analysis ($p = 0.86$ and $p = 0.14$, respectively).

The stability of our study was evaluated by using sensitivity analysis. No individual study had a significant effect among all studies (Fig. 6b). The results of our study were stable.

Discussion

Surgery can cause a series of physiological or psychological stress response, resulting in major trauma to the human body. Postoperative rehabilitation is related to physiological, psychological, economic, social, and other factors.[39,40] Over the past two decades, ERAS program and laparoscopic techniques have become two major approaches in accelerating postoperative recovery and reducing surgical stress response after colorectal surgery. Many trials have reported short-time benefits of combining these two approaches in colorectal cancer surgery.[16,32] We conducted this meta-analysis to evaluate ERAS program versus TC in patients undergoing laparoscopic colorectal cancer surgery. The present study is the largest meta-analysis to date, involving 13 RCTs, which reported related parameters about rapid recovery.

In current meta-analysis, we merged all available information to assess the efficacy and safety of ERAS program. The analyses indicated that patients undergoing laparoscopic colorectal cancer surgery in ERAS group significantly shorten the average length of PHS (2.00 days), duration of first time to flatus (12.18 h), and duration of first time to defecation (32.93 h) compared with TC group. In the meantime, the ERAS group had lower overall complication rates (RR = 0.59) but no obvious differences in readmission and mortality

Table 3 Inflammatory response indicators in ERAS program versus TC

Factors	studies, *n*	Patients, *n*		WMD and 95%CI	Heterogeneity test (I^2, P bias)	Statistical model
		ERAS	TC			
IL-6						
PROD	2	110	110	3.00 (− 1.25 to 7.24)	72.6%, 0.06	Random
POD 1	2	110	110	− 26.45 (− 42.57 to − 10.34)	93.2%, 0.00	Random
POD 3	2	110	110	− 24.21 (− 27.31 to − 21.10)	0.00%, 0.84	Fixed
POD 5	2	110	110	− 18.33 (− 25.00 to − 11.65)	84.7%, 0.01	Random
CRP						
PROD	3	141	149	− 1.23 (− 3.53 to 1.08)	84.3%, 0.00	Random
POD 1	3	141	149	− 24.72 (− 49.64 to 0.19)	98.5%, 0.00	Random
POD 3	2	110	110	− 25.98 (− 47.05 to − 4.91)	96.4%, 0.00	Random
POD 5	2	110	110	− 30.34 (− 53.96 to − 6.72)	96.9%, 0.00	Random

PROD preoperative day, *POD* postoperative day

rates in comparison with TC group. The ERAS program can accelerate surgical recovery, but a main problem is that the program might cause higher readmission rates. Nevertheless, our study revealed that ERAS program shortened the average length of PHS and did not increase in readmission rates. Besides, we also found out that ERAS group has lower IL-6 and CRP level on postoperative days 1, 3, and 5 than TC group. Inflammatory factors such as IL-6 and CRP can reflect

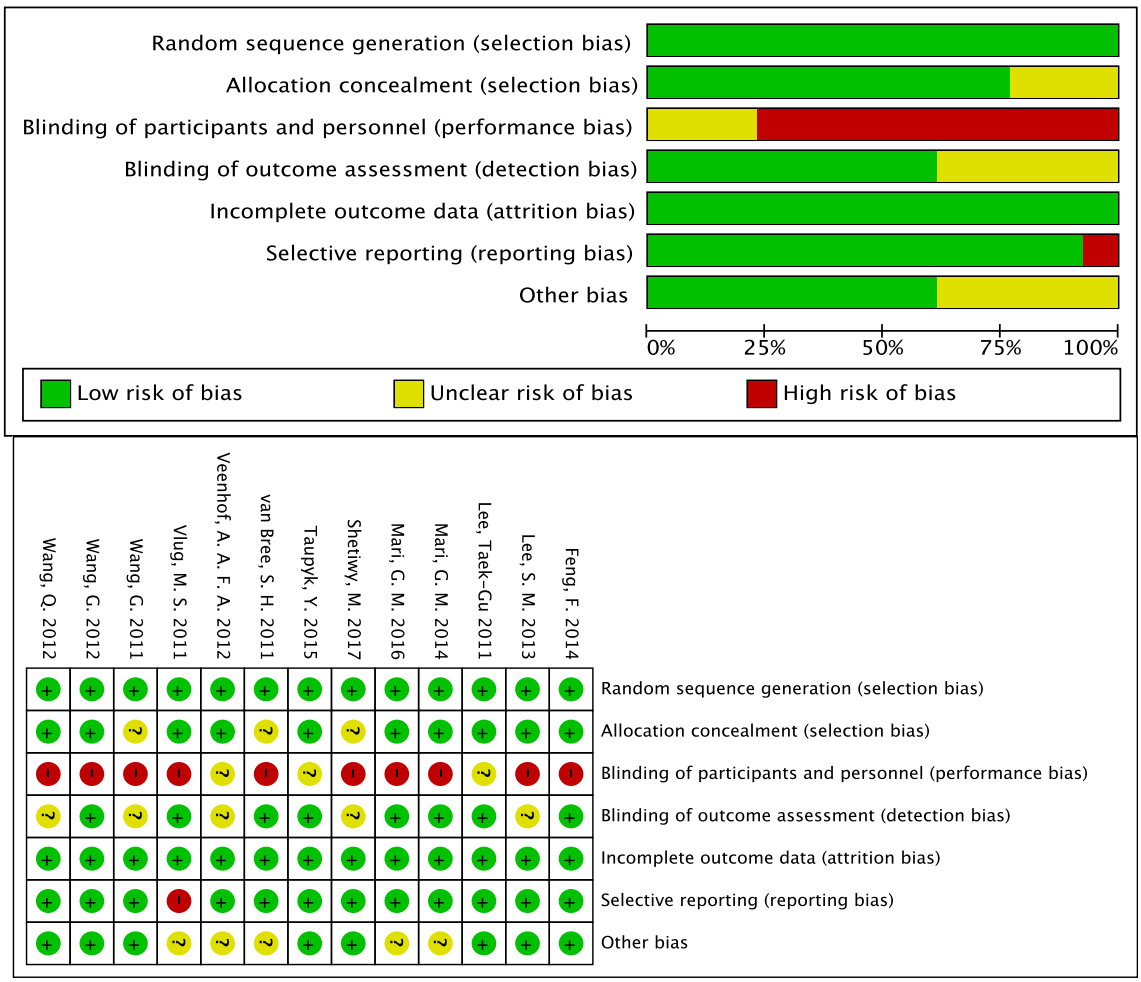

Fig. 5 The risk of bias graph and the risk of bias summary

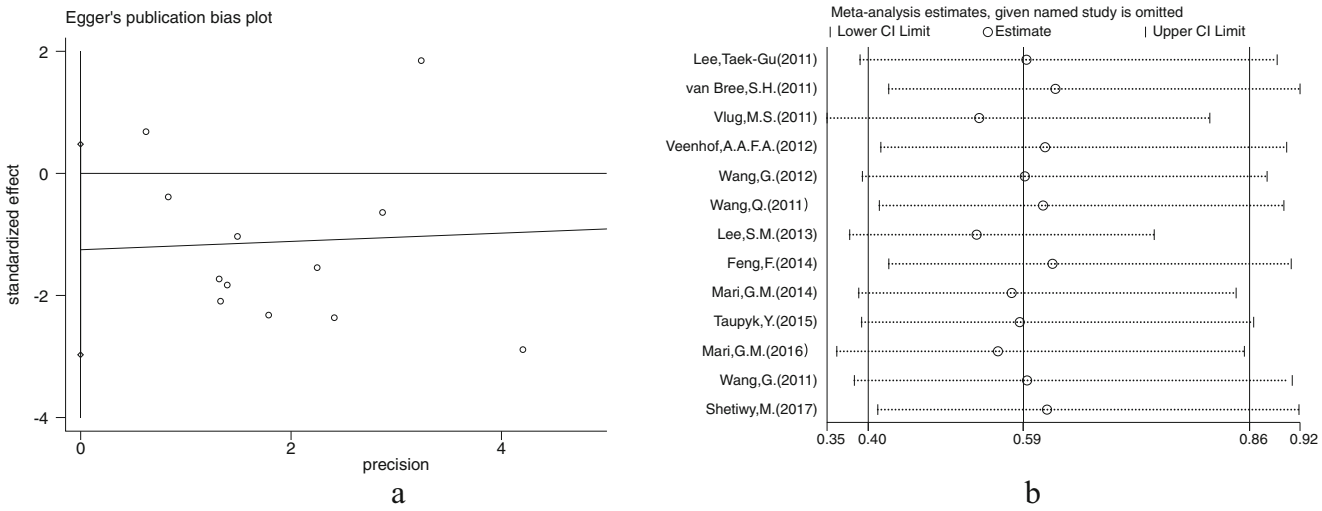

Fig. 6 Egger's funnel plot of the publication bias (**a**). Sensitivity analysis of the overall complication rates (**b**)

the degree of tissue damage caused by surgery.[41] Our results indicated ERAS program reduced the levels of IL-6 and CRP in comparison with TC after laparoscopic colorectal cancer surgery, which in accordance with the accelerated recovery process. In a word, ERAS program is an effective and safe strategy for postoperative recovery of the colorectal cancer surgery.

To date, several meta-analyses have been published to evaluate the ERAS program in laparoscopic colorectal cancer surgery. In 2013, Li et al.[42] reported six RCTs of ERAS program in laparoscopic colorectal cancer surgery. In 2014, Tan et al.[43] and Zhao et al.[19] assessed four RCTs and 10 studies (included 5 RCTs) of ERAS program in surgery, respectively. Compared with these meta-analyses, our study has certain advantages. Firstly, our results are more rigorous and reliable than previous meta-analyses because we include the latest studies that meet the inclusion criteria. Secondly, compared with previous studies, our study include a larger number of RCTs. Thirdly, our study is the first one to assess inflammatory response indicators (IL-6 and CRP levels) in ERAS patients undergoing laparoscopic colorectal cancer surgery. Fourthly, some RCTs had low quality in previous meta-analyses. But in our study, we tried our best to include high-quality studies based on Cochrane Collaboration's risk of bias tool.

Significant heterogeneity was observed in some analyses across the involved studies. Subgroup analyses and sensitivity analyses were performed to assess the source of heterogeneity. However, subgroup analyses of countries could not explain the source of the heterogeneity. The sensitivity analyses showed that no single trials affected the overall WMDs, and the results were stable. Hence, the cause of heterogeneity may be due to various sources, including ERAS elements used, accurate surgical procedures, inclusion criteria, and TC standards which vary across countries. Meanwhile, to minimize publication bias, we conducted an extensive search strategy. No significant publication bias was found in this meta-analysis.

Conclusion

In conclusion, the results showed a significant shorter the average length of PHS, faster to functional recovery, lower overall postoperative complication rates, and lower IL-6 and CRP levels in ERAS group versus TC group in patients undergoing laparoscopic colorectal cancer surgery. The ERAS program is an efficacy and safety strategy and should be recommended for laparoscopic colorectal cancer surgery.

Author Contributions XFN and JS: designed the study. XFN and DJ: searched the databases and collected full-text papers. LW and YC: performed statistical analysis. XFN and JS: wrote the manuscript. All authors read the final version of the manuscript.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Research Involving Human Participants and/or Animals The article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent For this type of study, formal consent is not required.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin* 2018; **68**: 7–30.
2. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, Stein KD, Alteri R, Jemal A. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin* 2016; **66**: 271–289.

3. Allaix ME, Furnee EJ, Mistrangelo M, Arezzo A, Morino M. Conversion of laparoscopic colorectal resection for cancer: What is the impact on short-term outcomes and survival? *World J Gastroenterol* 2016; **22**: 8304–8313.
4. Jacobs M, Verdeja JC, Goldstein HS. Minimally invasive colon resection (laparoscopic colectomy). *Surgical laparoscopy & endoscopy* 1991; **1**: 144–150.
5. Noel JK, Fahrbach K, Estok R, Cella C, Frame D, Linz H, Cima RR, Dozois EJ, Senagore AJ. Minimally invasive colorectal resection outcomes: short-term comparison with open procedures. *J Am Coll Surg* 2007; **204**: 291–307.
6. Junghans T, Raue W, Haase O, Neudecker J, Schwenk W. Value of laparoscopic surgery in elective colorectal surgery with "fast-track"-rehabilitation. *Zentralblatt fur chirurgie* 2006; **131**: 298–303.
7. Kaltoft B, Gogenur I, Rosenberg J. Reduced length of stay and convalescence in laparoscopic vs open sigmoid resection with traditional care: a double blinded randomized clinical trial. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland* 2011; **13**: e123–130.
8. Coratti F, Coratti A, Malatesti R, Testi W, Tani F. Laparoscopic versus open resection for colorectal cancer: meta-analysis of the chief trials. *Il Giornale di chirurgia* 2009; **30**: 377–384.
9. Bardram L, Funch-Jensen P, Jensen P, Crawford ME, Kehlet H. Recovery after laparoscopic colonic surgery with epidural analgesia, and early oral nutrition and mobilisation. *Lancet* 1995; **345**: 763–764.
10. Fearon KC, Ljungqvist O, Von Meyenfeldt M, Revhaug A, Dejong CH, Lassen K, Nygren J, Hausel J, Soop M, Andersen J, Kehlet H. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clinical nutrition (Edinburgh, Scotland)* 2005; **24**: 466–477.
11. Kehlet H. Fast-track colorectal surgery. *Lancet* 2008; **371**: 791–793.
12. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth* 1997; **78**: 606–617.
13. Lassen K, Soop M, Nygren J, Cox PB, Hendry PO, Spies C, von Meyenfeldt MF, Fearon KC, Revhaug A, Norderval S, Ljungqvist O, Lobo DN, Dejong CH. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Archives of surgery (Chicago, Ill : 1960)* 2009; **144**: 961–969.
14. Wilmore DW, Kehlet H. Management of patients in fast track surgery. *BMJ (Clinical research ed)* 2001; **322**: 473–476.
15. Kehlet H. Fast-track colonic surgery: status and perspectives. *Recent results in cancer research Fortschritte der Krebsforschung Progres dans les recherches sur le cancer* 2005; **165**: 8–13.
16. Feng F, Li XH, Shi H, Wu GS, Zhang HW, Liu XN, Zhao QC. Fast-track surgery combined with laparoscopy could improve postoperative recovery of low-risk rectal cancer patients: a randomized controlled clinical trial. *Journal of digestive diseases* 2014; **15**: 306–313.
17. Taupyk Y, Cao X, Zhao Y, Wang C, Wang Q. Fast-track laparoscopic surgery: a better option for treating colorectal cancer than conventional laparoscopic surgery. *Oncology Letters* 2015; **10**: 443–448.
18. Lee SM, Kang SB, Jang JH, Park JS, Hong S, Lee TG, Ahn S. Early rehabilitation versus conventional care after laparoscopic rectal surgery: a prospective, randomized, controlled trial. *Surgical Endoscopy* 2013; **27**: 3902–3909.
19. Zhao JH, Sun JX, Gao P, Chen XW, Song YX, Huang XZ, Xu HM, Wang ZN. Fast-track surgery versus traditional perioperative care in laparoscopic colorectal cancer surgery: a meta-analysis. *BMC Cancer* 2014; **14**: 607.
20. Song MX, Li XR. Efficacy of fast track surgery in elderly patients with colorectal cancer undergoing laparoscopic treatment: A meta-analysis. *World Chinese Journal of Digestology* 2015; **23**: 3960–3966.
21. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009; **62**: e1–34.
22. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ (Clinical research ed)* 2011; **343**: d5928.
23. Gustafsson UO, Scott MJ, Hubner M, Nygren J, Demartines N, Francis N, Rockall TA, Young-Fadok TM, Hill AG, Soop M, de Boer HD, Urman RD, Chang GJ, Fichera A, Kessler H, Grass F, Whang EE, Fawcett WJ, Carli F, Lobo DN, Rollins KE, Balfour A, Baldini G, Riedel B, Ljungqvist O. Guidelines for Perioperative Care in Elective Colorectal Surgery: Enhanced Recovery After Surgery (ERAS((R))) Society Recommendations: 2018. *World J Surg* 2018.
24. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005; **5**: 13.
25. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res* 2018; **27**: 1785–1805.
26. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin Trials* 2015; **45**: 139–145.
27. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994; **50**: 1088–1101.
28. Stuck AE, Rubenstein LZ, Wieland D. Bias in meta-analysis detected by a simple, graphical test. Asymmetry detected in funnel plot was probably due to true heterogeneity. *BMJ (Clinical research ed)* 1998; **316**: 469; **author reply 470-461**.
29. Lee T-G, Kang S-B, Kim D-W, Hong S, Heo SC, Park KJ. Comparison of Early Mobilization and Diet Rehabilitation Program With Conventional Care After Laparoscopic Colon Surgery: A Prospective Randomized Controlled Trial. *Diseases of the Colon & Rectum* 2011; **54**: 21–28.
30. van Bree SH, Vlug MS, Bemelman WA, Hollmann MW, Ubbink DT, Zwinderman AH, de Jonge WJ, Snoek SA, Bolhuis K, van der Zanden E, The FO, Bennink RJ, Boeckxstaens GE. Faster recovery of gastrointestinal transit after laparoscopy and fast-track care in patients undergoing colonic surgery. *Gastroenterology* 2011; **141**: 872–880.e871–874.
31. Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF, Gerhards MF, van Wagensveld BA, van der Zaag ES, van Geloven AA, Sprangers MA, Cuesta MA, Bemelman WA. 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* 2011; **254**: 868–875.
32. Wang G, Jiang Z-W, Xu J, Gong J-F, Bao Y, Xie L-F, Li J-S. Fast-track rehabilitation program vs conventional care after colorectal resection: A randomized clinical trial. *World Journal of Gastroenterology* 2011; **17**: 671–676.
33. Veenhof AAFA, Vlug MS, Van Der Pas MHGM, Sietses C, Van Der Peet DL, De Lange-De Klerk ESM, Bonjer HJ, Bemelman WA, Cuesta MA. Surgical stress response and postoperative immune function after laparoscopy or open surgery with fast track or standard perioperative care: A randomized trial. *Annals of Surgery* 2012; **255**: 216–221.
34. Wang G, Jiang Z, Zhao K, Li G, Liu F, Pan H, Li J. Immunologic response after laparoscopic colon cancer operation within an enhanced recovery program. *Journal of gastrointestinal surgery* 2012; **16**: 1379–1388.

35. Wang Q, Suo J, Jiang J, Wang C, Zhao YQ, Cao X. Effectiveness of fast-track rehabilitation vs conventional care in laparoscopic colorectal resection for elderly patients: a randomized trial. *Colorectal disease* 2012; **14**: 1009–1013.
36. Mari GM, Costanzi A, Maggioni D, Origi M, Ferrari GC, De Martini P, De Carli S, Pugliese R. Fast-track versus standard care in laparoscopic high anterior resection: a prospective randomized-controlled trial. *Surgical laparoscopy, endoscopy & percutaneous techniques* 2014; **24**: 118–121.
37. Mari G, Crippa J, Costanzi A, Mazzola M, Rossi M, Maggioni D. ERAS Protocol Reduces IL-6 Secretion in Colorectal Laparoscopic Surgery: results From a Randomized Clinical Trial. *Surgical laparoscopy, endoscopy & percutaneous techniques* 2016; **26**: 444–448.
38. Shetiwy M, Fady T, Shahatto F, Setit A. Standardizing the protocols for enhanced recovery from colorectal cancer surgery: are we a step closer to ideal recovery? *Annals of coloproctology* 2017; **33**: 86–92.
39. Blazeby JM. Systematic review of outcomes used to evaluate enhanced recovery after surgery (Br J Surg 2014; 101: 159-170). *Br J Surg* 2014; **101**: 171.
40. Carli F. Physiologic considerations of Enhanced Recovery After Surgery (ERAS) programs: implications of the stress response. *Canadian journal of anaesthesia = Journal canadien d'anesthesie* 2015; **62**: 110–119.
41. Stowers MD, Lemanu DP, Hill AG. Health economics in Enhanced Recovery After Surgery programs. *Canadian journal of anaesthesia = Journal canadien d'anesthesie* 2015; **62**: 219–230.
42. Li P, Fang F, Cai JX, Tang D, Li QG, Wang DR. Fast-track rehabilitation VS conventional care in laparoscopic colorectal resection for colorectal malignancy: A meta-analysis. *World Journal of Gastroenterology* 2013; **19**: 9119–9126.
43. Tan SJ, Zhou F, Yui WK, Chen QY, Lin ZL, Hu RY, Gao T, Li N. Fast track programmes vs. traditional care in laparoscopic colorectal surgery: a meta-analysis of randomized controlled trials. *Hepato-gastroenterology* 2014; **61**: 79–84.