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Laparoscopic versus open colorectal surgery within enhanced recovery after surgery programs: a systematic review and meta-analysis of randomized controlled trials

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Abstract
Background Laparoscopic surgery and enhanced recovery after surgery (ERAS) programs were two major improvements for the management of colorectal diseases. The purpose of this systemic review was to examine whether laparoscopic colorectal surgery still improved short-term postoperative outcomes in comparison with open surgery when both groups of patients received ERAS programs.
Methods PubMed, Embase, the Cochrane Central Register of Controlled Trials, and reference lists of the identified studies were searched to identify randomized clinical trials that compared laparoscopic with open surgery in patients undergoing colorectal resection in the context of ERAS programs. The outcome measures were analyzed, and the quality of evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system.
Results Five randomized clinical trials encompassing 598 patients were included in the final analysis. Two of them were multicenter trials. The ERAS programs implemented in the five included trials cannot be classified as optimal ERAS programs, but suboptimal ERAS programs. Laparoscopic colorectal surgery significantly reduced total hospital stay (weighted mean difference (WMD) −1.92 days; 95 % confidence interval (CI) −2.61–−1.23 days; $P < 0.00001$) and number of complications (relative risk (RR) 0.78; 95 % CI 0.66–0.94; $P = 0.007$) compared with open surgery in the setting of ERAS programs. No significant differences were found between groups for primary hospital stay, number of patients with complications, readmission rates, and mortality. The quality of evidence for all outcomes was low-to-moderate on the GRADE scale, and none had high quality.
Conclusions Laparoscopic colorectal resection significantly reduced total hospital stay and number of complications when compared with open surgery in the setting of suboptimal ERAS programs, but the benefits of laparoscopic colorectal resection remain to be proved within optimal ERAS programs.

Keywords Laparoscopic · Enhanced recovery after surgery · Fast track · Colorectal surgery · Systematic review · Meta-analysis

Recovery from colorectal resection has traditionally been a prolonged and complicated affair, with a hospital stay of 6–12 days and an overall morbidity of 20–30 % [1, 2]. Over the past two decades, there have been two major improvements in the field of colorectal surgery; the introduction of laparoscopic surgery and the implementation of

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enhanced recovery after surgery (ERAS) programs, also referred to as "fast track" surgery, both focusing on minimizing the surgical stress to improve short-term outcomes [3, 4].

Since its introduction in 1991 [3], laparoscopic colorectal surgery has become increasingly popular. Evidence from randomized controlled trials and meta-analyses showed that laparoscopic colorectal surgery was associated with shorter hospital stay, less postoperative complications, and pain in comparison with open surgery [5–8]. The long-term oncological results were equivalent between laparoscopic and open surgery [6]. In parallel with the laparoscopic development, the ERAS programs, pioneered by Kehlet and coworkers in the mid-1990s [9], have been shown to improve markedly postoperative recovery of open and laparoscopic colorectal surgery [10]. The ERAS programs have been successfully adopted all over the world. These programs combine a number of evidence-based elements such as optimal postoperative analgesia, early oral feeding, and early mobilization [11]. Studies of ERAS programs have reported hospital stay of 2–3 days following open colorectal surgery which is comparable to any of the best laparoscopic trials in the literature [12, 13].

Although the feasibility and efficacy of laparoscopic colorectal surgery have been demonstrated, the technique is still not widely used and 68.6 % of cases are still performed open in the United States [14]. The laparoscopic colorectal resection procedure is technically demanding. The significant learning curve and prolonged operative times have made laparoscopic surgery for colorectal cancer more challenging [15, 16]. Moreover, a recent study reported that an operative duration >3 h was an independent risk factor for infectious complications in patients undergoing a laparoscopic right colectomy [17].

Therefore, if improvement in short-term postoperative results can be achieved using ERAS programs alone, then the perceived advantages of laparoscopic over open surgery may be less clear. The purpose of the present meta-analysis was to examine whether laparoscopic colorectal surgery still improved short-term postoperative outcomes in comparison with open surgery when both groups of patients received ERAS programs. The present meta-analysis was performed consistent with the recommendations of the Preferred Reporting items for systematic Reviews and meta-analyses (PRISMA) statement [18].

Materials and methods

Literature search

We searched MEDLINE via PubMed, EMBASE, and Cochrane Central Register of Controlled Trials for randomized controlled trials (RCTs) comparing laparoscopic with open surgery in patients undergoing colorectal resection in the context of ERAS programs. Sources were searched up to May 2014. No language restrictions were applied. To ensure that no clinical trials were overlooked, the reference lists of identified articles, previous review articles were manually searched to identify additional studies. The International Clinical Trials Registry Platform of the World Health Organization (www.who.int/trialsearch/) was also searched for any additional relevant registered trials. The full search strategy for PubMed is presented in Table 1.

Table 1 The full search strategy for PubMed

1. "fast track"
2. ERAS OR enhanced recovery
3. Multimodal[tiab] OR rehabilitation[tiab]
4. #1 OR #2 OR #3
5. Colorectal OR colon OR colonic OR Rectum OR Rectal OR Sigmoid OR intestinal
6. "Colorectal Neoplasms"[Mesh] OR "cecal neoplasms"[MeSH] OR "Laparotomy"[Mesh] OR "Colorectal Surgery"[MeSH] OR "Colectomy"[MeSH] OR "Colon/surgery"[MeSH] OR "Colonic Diseases/surgery"[Mesh] OR "Rectal Diseases/surgery"[Mesh] OR "Rectum/surgery"[Mesh]
7. #5 OR #6
8. minimal* invasive OR laparoscopic OR laparoscopically OR laparoscopy
9. "Surgical Procedures, Minimally Invasive"[Mesh] OR "laparoscopy"[MeSH]
10. #8 OR #9
11. #4 AND #7 AND #10
12. randomized controlled trial[pt] OR controlled clinical trial[pt]
13. randomized[tiab]
14. placebo[tiab]
15. clinical trials as topic [mesh:noexp]
16. randomly[tiab]
17. trial[ti]
18. #12 OR #13 OR #14 OR #15 OR #16 OR #17
19. animals[mh] NOT humans[mh]
20. #18 NOT #19
21. #11 AND #20

Inclusion and exclusion criteria

RCTs comparing laparoscopic with open surgery in adult patients (aged >18 years) undergoing colorectal resection for malignant or benign disease in the context of ERAS programs were eligible for inclusion. According to the guidelines of the ERAS group, there are more than 20 ERAS items in the ERAS programs [19, 20]. Because some items might have been implemented in modern traditional care, we made an arbitrary decision that ERAS programs study should include at least seven items. Studies were

required to report at least one of the outcome measures mentioned below. When more than one version of the same study was found, only the most recent version was included. When there was overlap between the results of studies reported by the same institution or authors, the larger, higher-quality study was included. Excluded studies (1) were not randomized controlled trials; (2) had <7 items applied; (3) had no documentation of individual items of the ERAS programs; (4) had no data available for the present meta-analysis; or (5) involved emergency surgery; (6) had only abstracts. Article titles and abstracts were screened, and full texts were reviewed independently by two reviewers (C.L.Z. and D.D.H.); discrepancies were resolved by discussion between the reviewers.

Data extraction and outcome measures

All eligible studies were reviewed, and all relevant data were extracted independently by two reviewers (C.L.Z. and D.D.H.) using a specifically designed data extraction form. Discrepancies were resolved by discussion between the reviewers and review of the original articles. Extracted information from each eligible study included (1) study information, including the name of the first author, year of publication, number of patients in each group, and number of ERAS items applied; (2) patient information including age, gender, and site of surgery; (3) follow-up time and outcome measures.

Primary outcome measures included (1) primary hospital stay (defined as the number of days in hospital after surgery until discharge); (2) total hospital stay (defined as primary hospital stay plus the additional hospital days for patients who were readmitted within 30 days after surgery); (3) number of complications; (4) number of patients with complications; (5) readmission rates; and (6) mortality. Secondary outcome measures included (1) operation time; (2) hospital costs; and (3) quality of life.

Considering that some ERAS items might be implemented but not reported in the final publication, investigators of all included trials were contacted to obtain the original protocols of ERAS programs. In addition, if the compliance of ERAS items was not reported, we also tried to contact the investigators to obtain the level of compliance.

Assessment of risk of bias

The quality of methodology of the included RCTs was assessed independently by two reviewers (C.L.Z. and D.D.H.) using the Cochrane Collaboration's risk of bias tool [21]. Discrepancies were resolved by discussion between the reviewers. The seven domains assessed were (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting, and (7) other bias. The risk of bias for each domain was rated as high (seriously weakens confidence in the results), low (unlikely to seriously alter the results), or unclear.

Statistical analysis

Meta-analyses were performed using relative risk (RR) for dichotomous outcomes and weighted mean difference (WMD) for continuous outcomes. Pooled estimates were presented with 95 % confidence interval (CI). Data reported as medians and interquartile ranges were converted to means and SDs [21]. The presence and amount of heterogeneity were assessed with Q test and I^2 index, and $P < 0.1$ was considered statistically significant [22, 23]. A random-effects model was used for pooling when there was evidence of heterogeneity; otherwise, a fixed-effects model was used. Funnel plots were created to determine the presence of publication bias, and asymmetry of each funnel plot was evaluated with Egger weighted linear regression test, with $P < 0.1$ considered significant [24]. For all other comparisons, $P < 0.05$ was used to determined statistical significance, and all tests were two-sided. The data analysis was performed with Review Manager software version 5.2 from the Cochrane Collaboration and STATA version 12.0 (StataCorp, College Station, TX). Some outcomes were not analyzed but were presented in a descriptive way.

Assessing quality of evidence

The quality of evidence for each outcome measure was rated with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system [25], as recommended by the Cochrane Collaboration. The quality of evidence for each outcome measure was rated as high (further research is very unlikely to change our confidence in the estimate of effect), moderate (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), low (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), or very low (any estimate of effect is very uncertain). The analyses were performed with GRADEpro software version 3.6 (http://ims.cochrane.org/revman/gradepro).

Results

The initial literature search yielded 290 potentially relevant studies. Five RCTs [26–30] (total, 598 patients) published between 2005 and 2014 were included in the meta-analysis (Fig. 1). There were two studies [26, 28] that included

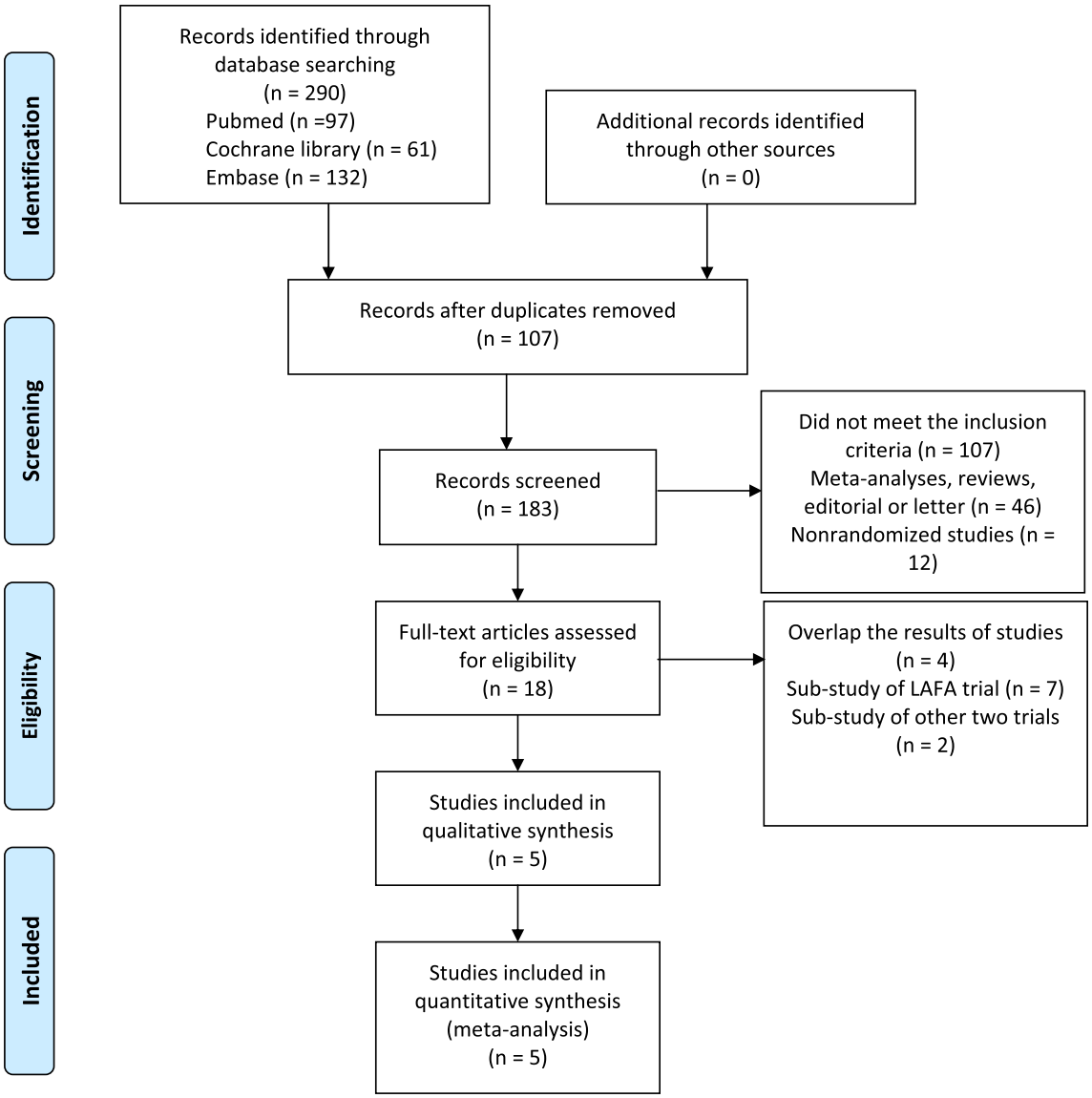

Fig. 1 PRISMA flow chart

patients treated in multiple centers, and the others were single-center studies.

Table 2 shows the characteristics of the included studies. The number of ERAS items applied in the five included studies contained a median of 16 (range 12–18). Some ERAS items which were actually used but not reported were obtained from authors of four included RCTs [26–28, 30]. The exact items used in each study are listed in Table 3. Figure 2 shows evaluation of risk of bias for the included trials. Three trials [26, 28, 29] used adequate methods for generating allocation sequence. In the other two trials [27, 30], the allocations were described as "randomized," but the detailed method was not specified. Adequate methods for allocating concealment were used in four trials [26–29], but concealment of the allocation sequence was not sufficiently described in one trial [30]. Patients and outcome assessors were effectively blinded in two trials [26, 30]. All included trials were at low risk of bias for incomplete outcome data and selective reporting. None of the included trials were completely free from other bias. Two large trials [26, 28] were at high risk for other bias because of the low compliance with ERAS items. Three other small trials did not report the compliance in the final publication, but we managed to obtain the original compliance level of two trials by contacting the investigators. According to their replies, the compliance level of these two trials [27, 30] was good. Thus, these two trials were at low risk of other bias. The risk of other bias in one trial [29] was unclear because the compliance with ERAS items was not successfully obtained from the investigator.

Table 2 Characteristics of the included studies

Studies	No. of patients		Age, y		Sex (M/F)		BMI		ASA[c]		Type of surgery
	Lap	Open	Lap	Open	Lap	Open	Lap	Open	Lap	Open	
Kennedy 2014 [26]	103	101	69.3 ± 9.4	70.1 ± 8.7	56/47	70/31	1/27/40/34[b]	3/24/45/29[b]	71[c]	77[c]	RH; LH; AR; APR; Other[d]
Wang 2012 [27]	40	41	55.7 ± 17.3	57.2 ± 18.1	27/13	24/17	21.8 ± 4.5	22.1 ± 4.2	83[c]	85[c]	RH; LH; SR
Vulg 2011 [28]	100	93	66 ± 8.6	66 ± 10.3	53/47	54/39	26.8 ± 4.0	26.3 ± 4.2	82[c]	81[c]	RH; LH
King 2006 [29]	41	19	72.3 ± 11.0	70.4 ± 10.5	23/18	8/11	26.1 ± 3.8	27.2 ± 4.6	80[c]	84[c]	RH; LH; SR; AR; APR; ST
Basse 2005 [30]	30	30	75.5 (58–85)[a]	75 (57–90)[a]	14/16	14/16	NR	NR	83[c]	63[c]	RH; SR

Lap laparoscopic surgery, *BMI* body-mass index, *ASA* American Society of Anesthesiologists, *NR* not reported, *RH* Right hemicolectomy, *LH* Left hemicolectomy, *AR* Anterior resection, *APR* Abdominoperineal resection, *SR* Sigmoid resection, *ST* Stoma created

[a] Median (range)

[b] Underweight/normal/overweight/obese

[c] Percentage of ASA I and II taken together

[d] Other colon and rectum surgery

Primary outcome measures

Laparoscopic colorectal surgery significantly reduced total hospital stay (WMD −1.92 days; 95 % CI −2.61–−1.23 days (Fig. 3); $P < 0.00001$; $I^2 = 0$ %; Fig. 4) and number of complications (RR 0.78; 95 % CI 0.66–0.94; $P = 0.007$; $I^2 = 15$ %; Fig. 5) compared with open surgery in the setting of ERAS programs. No significant differences were found between groups for primary hospital stay (WMD −1.01 days; 95 % CI −2.14–0.12 days; $P = 0.08$; $I^2 = 77$ %; Fig. 3), number of patients with complications (RR 0.81; 95 % CI 0.64–1.04; $P = 0.10$; $I^2 = 0$ %; Fig. 6), readmission rates (RR 0.73; 95 % CI 0.39–1.36; $P = 0.32$; $I^2 = 33$ %; Fig. 7), and mortality (RR 0.53; 95 % CI 0.19–1.44; $P = 0.21$; $I^2 = 0$ %; Fig. 8).

Secondary outcome measures

Operation time was assessed in four studies. Two of the studies did not report the mean and SD for this outcome. Thus, the meta-analysis was not done for operation time. However, all these four studies showed that operation time was significantly increased for the laparoscopic group.

Only two trials [28, 29] assessed the financial impact of laparoscopic colorectal surgery and consistently showed that hospital costs were similar between groups. The meta-analysis was not done for hospital costs due to the limited data available.

Quality of life was assessed in three studies [26, 28, 29] and consistently showed that the quality of life were similar in the two groups, although different quality of life questionnaires were used in these studies.

Publication bias

We used the Egger weighted linear regression test [24] to examine the asymmetry of funnel plots for all six meta-analysis outcomes and found that the funnel plots for primary hospital stay, total hospital stay, number of complications, number of patients with complications, operation time, and mortality were symmetrical ($P = 0.779$, 0.967, 0.778, 0.801 and 0.659). The funnel plots were asymmetrical for readmission rates ($P = 0.076$).

Discussion

The present systematic review and meta-analysis showed that laparoscopic colorectal surgery is associated with a significant reduction in total hospital stay and number of complications when compared with open surgery in the setting of ERAS programs. However, laparoscopic surgery significantly increased operation time. There were no significant differences in primary hospital stay, number of patients with complications, readmission rates, mortality, hospital costs, and quality of life between the groups. The quality of evidence was assessed using the GRADE approach (Fig. 9) [25].

The quality of evidence for all outcomes was low-to-moderate on the GRADE scale, and none had high quality. The reasons for the downgraded quality of evidence for each outcome are noted in Fig. 9. A high statistical heterogeneity was identified in the meta-analysis of primary hospital stay and readmission rates, which may have resulted in inconsistency. However, we did not downgrade the quality of evidence because of the heterogeneity, which

Table 3 ERAS items used in included studies (both groups)

ERAS items	Studies				
	Basse 2005	King 2006	Vulg 2011	Wang 2012	Kennedy 2014
Preoperative information, education, and counseling	√	√	√	√	√
Preoperative optimization	√	√	√	√	√
Preoperative bowel preparation			√	√	√
Preoperative fasting			√	√	√
Preoperative treatment with carbohydrates		√	√	√	√
Preanesthetic medication	√		√	√	√
Prophylaxis against thromboembolism					
Antimicrobial prophylaxis	√		√	√	√
Skin preparation					
Standard anesthetic protocol	√	√	√	√	√
Preventing and treating PONV	√		√		
Nasogastric intubation	√	√	√	√	√
Preventing intraoperative hypothermia	√		√		√
Perioperative fluid management	√	√	√	√	√
Drainage of peritoneal cavity		√	√	√	√
Urinary catheter	√	√	√	√	√
Chewing gum				√	
Postoperative laxatives and prokinetics	√	√	√		√
Postoperative analgesia	√	√	√	√	√
Early oral intake	√	√	√	√	√
Oral nutritional supplements					√
Postoperative glucose control					
Early mobilization	√	√	√	√	√
Number of ERAS items used	14	12	18	16	18

ERAS enhanced recovery after surgery, *PONV* postoperative nausea and vomiting

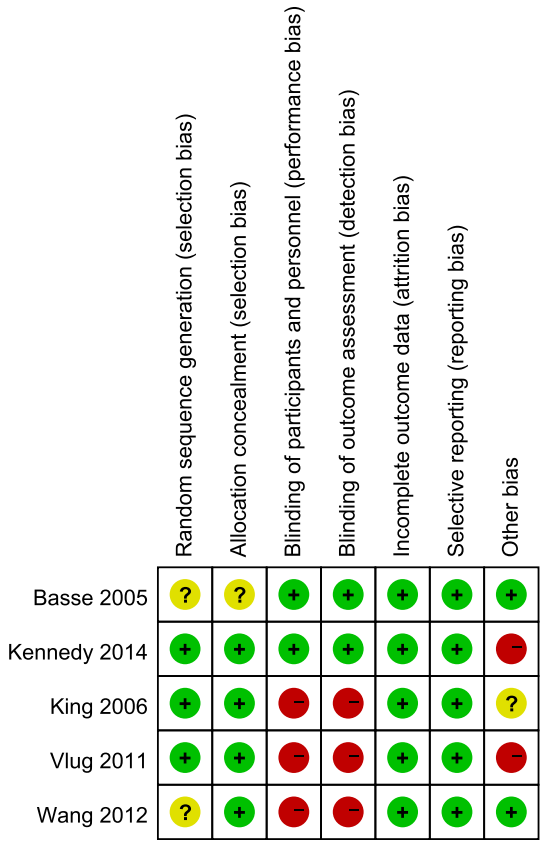

Fig. 2 Assessment of risk of bias in included studies

could be explained by the variation between studies in the experience of surgeons, the number of ERAS items incorporated, compliance with ERAS items, and definition of discharge criteria.

Despite the reduction in total hospital stay associated with laparoscopy, no significant benefit was identified in primary hospital stay. There are several possible explanations. Only the study by Basse et al. [30] showed no significant reduction in primary hospital stay, which was significantly shorter than that of the other studies. The results of this study are likely to be the most favorable because ERAS programs have been well developed in their hospital. However, the highest readmission rates (26.7 and 20 % for open and laparoscopic groups respectively) were reported in this study. In addition, results displayed a tendency toward lower readmission rates for the laparoscopic group, although pooled analysis failed to reach conventional levels of statistical significance. Moreover, the longer operative time in the included RCTs may offset the potential advantages of laparoscopy [15, 17].

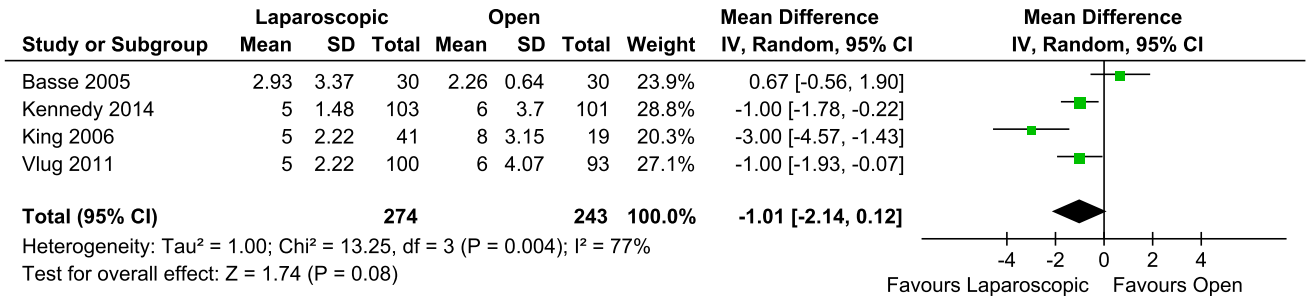

Fig. 3 Forest plot of laparoscopic versus open colorectal surgery for primary hospital stay

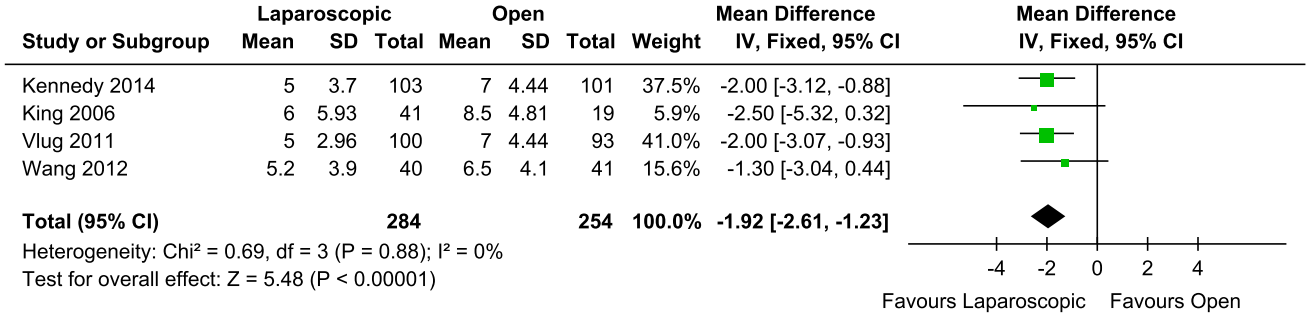

Fig. 4 Forest plot of laparoscopic versus open colorectal surgery for total hospital stay

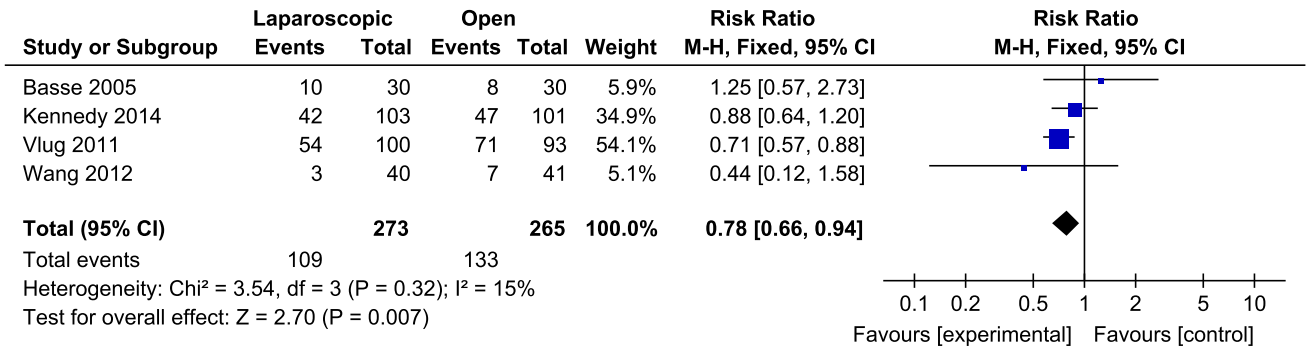

Fig. 5 Forest plot of laparoscopic versus open colorectal surgery for number of complications

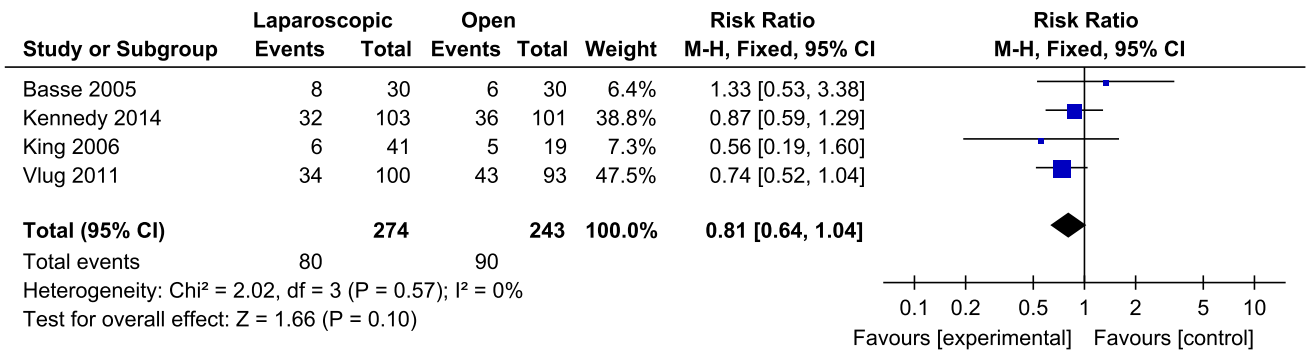

Fig. 6 Forest plot of laparoscopic versus open colorectal surgery for number of patients with complications

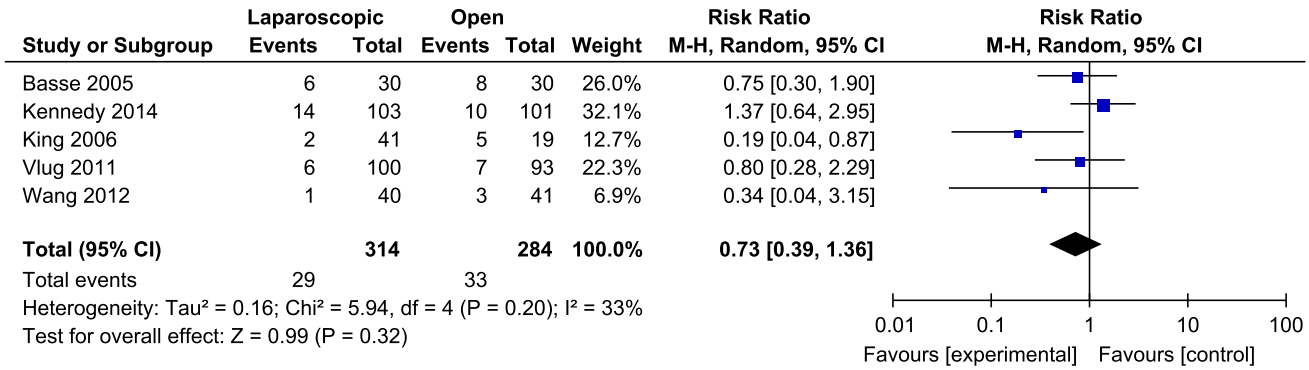

Fig. 7 Forest plot of laparoscopic versus open colorectal surgery for readmission rates

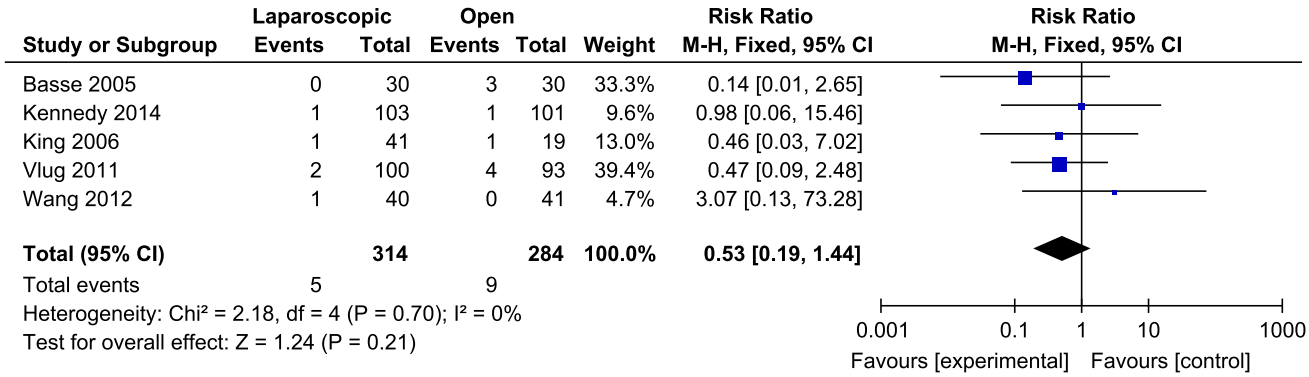

Fig. 8 Forest plot of laparoscopic versus open colorectal surgery for mortality

It has been demonstrated that improved adherence to the ERAS programs was significantly associated with improved clinical outcomes following major colorectal cancer surgery [31, 32]. However, the compliance of ERAS items in the two included large-scale multicenter trials was low. For example, the items of early oral feeding, early mobilization, and optimal analgesia were not well implemented in the EnROL trial [26]. Early oral feeding has been proved to reduce length of hospital stay and total postoperative complications [33]. Failure to mobilize was associated with prolonged length of hospital stay [34], while optimized pain relief, allowing early mobilization and early return of gut function, is a prerequisite for enhanced recovery [11]. Thus, the ERAS programs implemented in the five included RCTs cannot be classified as optimal ERAS programs, but suboptimal ERAS programs, and the role of laparoscopic colorectal surgery in the context of suboptimal ERAS programs is still uncertain in the present meta-analysis.

Apart from the above concerns, several additional limitations are associated with the included RCTs that warrant caution in the interpretation of the results of this meta-analysis. First, only two trials performed adequate blinding of assessors and patients; two of the included studies were unclear in randomization sequence generations; and concealment of the allocation sequence was not sufficiently described in one study; all of which may introduce biases. Second, the number of studies included in this meta-analysis was small. However, two of the included studies were large-scale multicenter trials, and the present meta-analysis was based on 598 patients. Third, the funnel plots were asymmetrical for readmission rates, which indicated the existence of publication bias. Finally, the meta-analysis was not done for hospital costs due to the limited data available. Thus, the effect of laparoscopic colorectal resection on hospital costs cannot be concluded in this meta-analysis.

In conclusion, laparoscopic colorectal resection significantly reduced total hospital stay and number of complications when compared with open surgery in the setting of suboptimal ERAS programs. However, the benefits of laparoscopic colorectal resection remain to be proved within optimal ERAS programs.

Question: Should laparoscopic colorectal surgery be used for patients received ERAS programs?
Bibliography: Laparoscopic versus Open for colorectal surgery in the setting of ERAS programs.

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Laparoscopic colorectal surgery		Risk with Control	Risk difference with Laparoscopic colorectal surgery (95% CI)
Primary hospital stay (CRITICAL OUTCOME; Better indicated by lower values)											
514 (4 studies) 30 days	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊖⊖⊖⊖ **MODERATE**[1] due to risk of bias	243	271	-		The mean primary hospital stay in the intervention groups was **1.01 lower** (2.14 lower to 0.12 higher)
Total hospital stay (CRITICAL OUTCOME; Better indicated by lower values)											
538 (4 studies) 30 days	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊖⊖⊖⊖ **MODERATE**[2] due to risk of bias	254	284	-		The mean total hospital stay in the intervention groups was **1.92 lower** (2.61 to 1.23 lower)
Number of complications											
538 (4 studies) 30 days	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊖⊖⊖⊖ **MODERATE**[1] due to risk of bias	133/265 (50.2%)	109/273 (39.9%)	**RR 0.78** (0.66 to 0.94)	Study population	
										502 per 1000	**110 fewer per 1000** (from 30 fewer to 171 fewer)
										Moderate	
										366 per 1000	**81 fewer per 1000** (from 22 fewer to 124 fewer)
Number of patients with complications (CRITICAL OUTCOME)											
517 (4 studies) 30 days	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊖⊖⊖⊖ **MODERATE**[1] due to risk of bias	90/243 (37%)	80/274 (29.2%)	**RR 0.81** (0.64 to 1.04)	Study population	
										370 per 1000	**70 fewer per 1000** (from 133 fewer to 15 more)
										Moderate	
										310 per 1000	**59 fewer per 1000** (from 112 fewer to 12 more)
Readmission rates (CRITICAL OUTCOME)											
598 (5 studies) 30 days	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias strongly suspected[3]	⊖⊖⊖⊖ **LOW**[2,3] due to risk of bias, publication bias	33/284 (11.6%)	29/314 (9.2%)	**RR 0.73** (0.39 to 1.36)	Study population	
										116 per 1000	**31 fewer per 1000** (from 71 fewer to 42 more)
										Moderate	
										99 per 1000	**27 fewer per 1000** (from 60 fewer to 36 more)
Mortality (CRITICAL OUTCOME)											
598 (5 studies) 30 days	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	undetected	⊖⊖⊖⊖ **LOW**[2,4] due to risk of bias, imprecision	9/284 (3.2%)	5/314 (1.6%)	**RR 0.53** (0.19 to 1.44)	Study population	
										32 per 1000	**15 fewer per 1000** (from 26 fewer to 14 more)
										Moderate	
										43 per 1000	**20 fewer per 1000** (from 35 fewer to 19 more)

[1] Patients and outcome assessors were not effectively blinded in 2 trials and low compliance of ERAS items was reported in 2 trials.
[2] Patients and outcome assessors were not effectively blinded in 3 trials and low compliance of ERAS items was reported in 2 trials.
[3] Egger weighted linear regression test showed that the funnel plot was asymmetric.
[4] Very small number of events, and 95% con dence interval was too wide.

Fig. 9 Grade profile for laparoscopic versus open colorectal surgery within ERAS programs

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