

Fast-track rehabilitation vs conventional care in laparoscopic colorectal resection for colorectal malignancy: A meta-analysis

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Abstract

AIM: To evaluate the fast-track rehabilitation protocol and laparoscopic surgery (LFT) vs conventional care strategies and laparoscopic surgery (LCC).

METHODS: Studies and relevant literature comparing the effects of LFT and LCC for colorectal malignancy were identified in MEDLINE, the Cochrane Central Register of Controlled Trials and EMBASE. The complications and re-admission after approximately 1 mo were

assessed.

RESULTS: Six recent randomized controlled trials (RCTs) were included in this meta-analysis, which related to 655 enrolled patients. These studies demonstrated that compared with LCC, LFT has fewer complications and a similar incidence of re-admission after approximately 1 mo. LFT had a pooled RR of 0.60 (95%CI: 0.46-0.79, $P < 0.001$) compared with a pooled RR of 0.69 (95%CI: 0.34-1.40, $P > 0.5$) for LCC.

CONCLUSION: LFT for colorectal malignancy is safe and efficacious. Larger prospective RCTs should be conducted to further compare the efficacy and safety of this approach.

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Key words: Laparoscopic surgery; Fast-track rehabilitation; Enhanced recovery; Colorectal surgery; Complications; Readmission

Core tip: Fast-track rehabilitation in laparoscopic colorectal resection has become the most fashionable way to treat colorectal malignancy. Complications after fast-track rehabilitation protocol and laparoscopic surgery (LFT) and conventional care strategies and laparoscopic surgery (LCC) of colorectal resection have generally been discussed in China, as well as in other countries. This study clarified that compared with LCC, LFT has fewer complications and has a similar incidence of re-admission after approximately 1 mo.

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INTRODUCTION

Fast-track rehabilitation in laparoscopic colorectal resection has become the most fashionable way of treating colorectal malignancy. During the mid-1990s, fast-track rehabilitation, involving dieticians, nurses, surgeons and anesthesiologists, was developed by Kehlet *et al.*^[1,2], Wilmore *et al.*^[3] and Basse *et al.*^[4]. Common to the other enhanced recovery rehabilitations, it is an attempt to reduce the stress response, decrease complications, speed up recovery, shorten the hospital stay and reduce health costs, all without compromising patient safety. The laparoscopic approach to colorectal surgery has been shown to accelerate dietary intake and return of bowel function^[5], to facilitate postoperative mobilization^[6], to reduce the length of stay in hospital^[5,7] and to have a positive effect on postoperative mortality^[5,7-9].

Recently, laparoscopic surgery has been generally applied in the treatment of gastrointestinal cancer, which can significantly attenuate trauma and accelerate the rehabilitation of patients after surgery. It was reported that the hospital stay time is shorter and the complication and readmission rate are lower after laparoscopic surgery^[10,11].

Despite all the major benefits of laparoscopy, elective colorectal resection is still associated with a morbidity rate between 20% and 30% and a postoperative hospital stay of 7-10 d^[12]. Both laparoscopic surgery and FT perioperative care have been reported to be safe and effective, and to result in a shorter hospital stay with earlier recovery of gastrointestinal function^[13-16] and lower morbidity than open colorectal surgery and standard care^[17-19]. Many recently published randomized controlled trials are available that have compared fast-track rehabilitation to conventional care in laparoscopic colorectal resection for colorectal malignancy. The safety after fast-track rehabilitation protocol and laparoscopic surgery (LFT) of colorectal resection has generally been discussed; therefore, this study analyzed and compared the complications and re-admission between LFT and conventional care strategies and laparoscopic surgery (LCC). The primary aim of this meta-analysis was to evaluate LFT *vs* LCC; the secondary aim was to assess LFT.

MATERIALS AND METHODS

Publication search

PubMed, the Cochrane Central Register of Controlled Trials and EMBASE were searched for all relevant literature, including articles referenced in the publications. The medical subject headings (MeSH) and keywords collected for individually and in combination were as follows: "laparoscopic surgery" "open surgery" and "fast track" or "enhanced recovery" and "colorectal". The last search was done on May 10th, 2013. References, lists of retrieved articles, reviews and meta-analyses were then scanned for

additional articles. Internet search engines were also used to perform a manual search for abstracts from international meetings, which were then downloaded and studied.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) randomized controlled trials; (2) studies that provided information on at least one of the outcome measures; (3) studies published in English. When a study reporting the same patient cohort was included in several publications, only the most recent or complete study was selected; and (4) detailed patient information provided. The exclusion criteria were as follows: (1) case reports; (2) articles that were not full text, or non-comparative studies; and (3) open operations, not by laparoscopic surgery.

Study selection

The inclusion criteria were met in studies if they involved LFT for colorectal malignancy in adult patients (*i.e.*, those 18 years and older) and used LCC as a control. All studies that used chemotherapy, or a rehabilitation protocol had to include less than seven of the seventeen FT items among the interventions in the FT group (programs using epidural or local anesthesia, minimally invasive techniques, optimal pain control and aggressive postoperative care) to achieve early recovery after colorectal surgery; and more than two of the conventional care strategies were included, were excluded. Studies that could not provide actual frequencies of complications or re-admission after approximately 1 mo were also excluded. Both full-length publications and abstract publications were selected. Letters, reviews without original data, non-English papers and animal studies were excluded. If any doubt regarding the suitability remained after the abstract was examined, the full manuscript was obtained.

Data extraction

All included studies were assessed for the quality of their methodology and relevance to the objective of our meta-analysis. Conduct and reporting were in accordance with the QUOROM statement. Data on complications or re-admission approximately 1 mo from each trial were extracted and compared independently by the two investigators.

Statistical analysis

In statistical analysis, Review Manager (RevMan) software version 5.0.0 was used (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). A pooled RR and a pooled Mean Difference with 95%CI were used to assess the outcomes of the studies. Statistical heterogeneity was tested by the χ^2 test. According to the forest plot, heterogeneity was limited, so the Mantel-Haenszel fixed effect model was adopted. The significance of the pooled RR was determined by the Z test and statistical significance was considered at $P < 0.05$. Publication bias was estimated by the use of a funnel plot with an Egger's linear regression test, and funnel plot

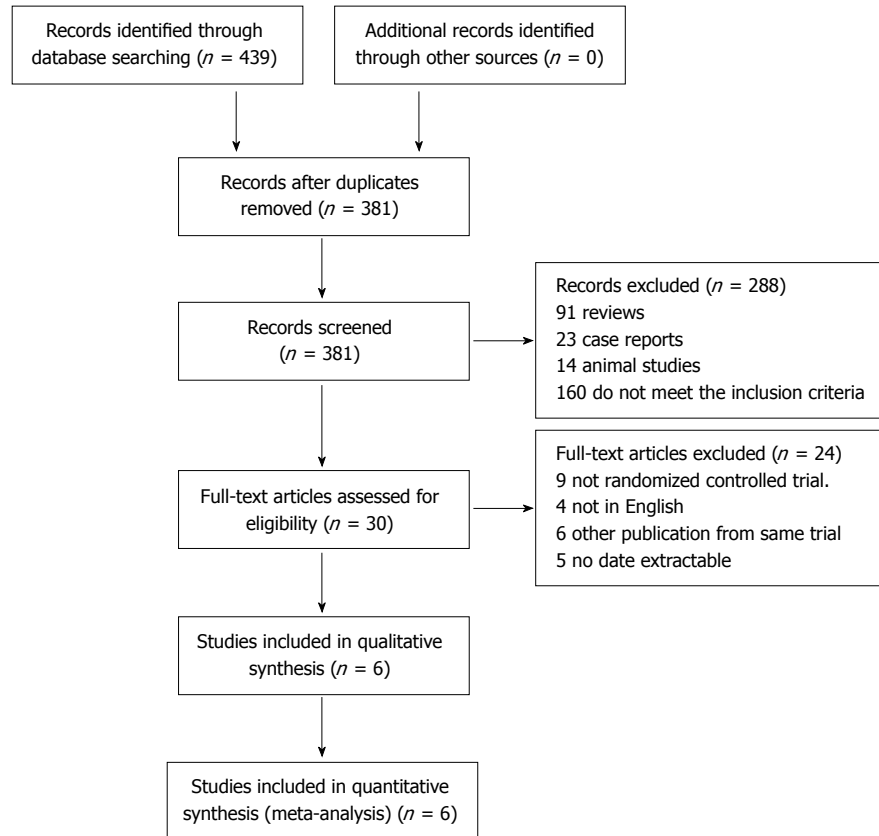


Figure 1 Selection of studies.

Table 1 Main characteristics of the six included studies

	<i>n</i>		Age (yr)		Sex (male/female)	
	LFT	LCC	LFT	LCC	LFT	LCC
Wang <i>et al</i> ^[20]	41	42	57.2 ± 18.1	55.4 ± 16.8	24/17	25/17
Vlug <i>et al</i> ^[21]	93	98	66 ± 10.3	66 ± 7.1	54/39	59/39
van Bree <i>et al</i> ^[22]	18	18	64 ± 10.1	66 ± 6.9	11/7	11/7
Veenhof <i>et al</i> ^[23]	17	20	65	68	9/8	14/6
Wang <i>et al</i> ^[24]	40	38	71	72	22/18	20/18
Wang <i>et al</i> ^[25]	106	104	57	55	65/41	60/44

LFT: Fast-track rehabilitation protocol and laparoscopic surgery; LCC: Conventional care strategies and laparoscopic surgery.

asymmetry on the natural logarithm scale of the RR was measured by a linear regression approach.

RESULTS

Search results

A total of 439 references were identified from medical journal databases. Upon examination of the abstracts, 409 articles were rejected based on the rejection criteria outlined in Figure 1. A study of the complete manuscripts for the 30 remaining articles led to elimination of 14 papers that contained no data pertaining to the outcome of LFT for colorectal resection, four papers not in English and six papers explaining the effect of analgesia. The remaining six non-duplicated randomized controlled trials (RCTs) that compared LFT with LCC were included

in the meta-analysis.

Characteristics of the selected RCTs

Characteristics of the six RCTs^[20-25] included in the meta-analysis are summarized in Table 1. These studies were published between 1985 and 2013 and investigated a total of 665 patients: 323 received LFT and 332 received LCC.

Meta-analysis results

Complication: Data were collected from six studies (655 patients) on complications for LFT *vs* LCC. In the LFT group, 19.81% patients (64/323) had complications, while in the LCC group, 33.13% patients (110/332) had complications. Pooling the results indicated that LFT could significantly reduce complications compared with LCC. The weighted mean difference (WMD) was 0.60 (95%CI: 0.46-0.79, $P < 0.05$), $\chi^2 = 12.33$ ($P = 0.03$) and $I^2 = 59\%$, indicating heterogeneity among the studies.

Anastomotic leak: Data were collected from four studies (497 patients) on anastomotic leak for LFT *vs* LCC. 4.94% (12/243 patients) had an anastomotic leak in the LFT group and 4.72% (12/254) in the LCC group. Pooling the results indicated that LFT and LCC had similar risks of anastomotic leak. The WMD was 1.07 (95%CI: 0.50-2.32, $P > 0.05$, Figure 2), $\chi^2 = 2.13$ ($P = 0.55$) and $I^2 = 0\%$, which excludes heterogeneity among the studies.

Wound infection: Data were collected from four stud-

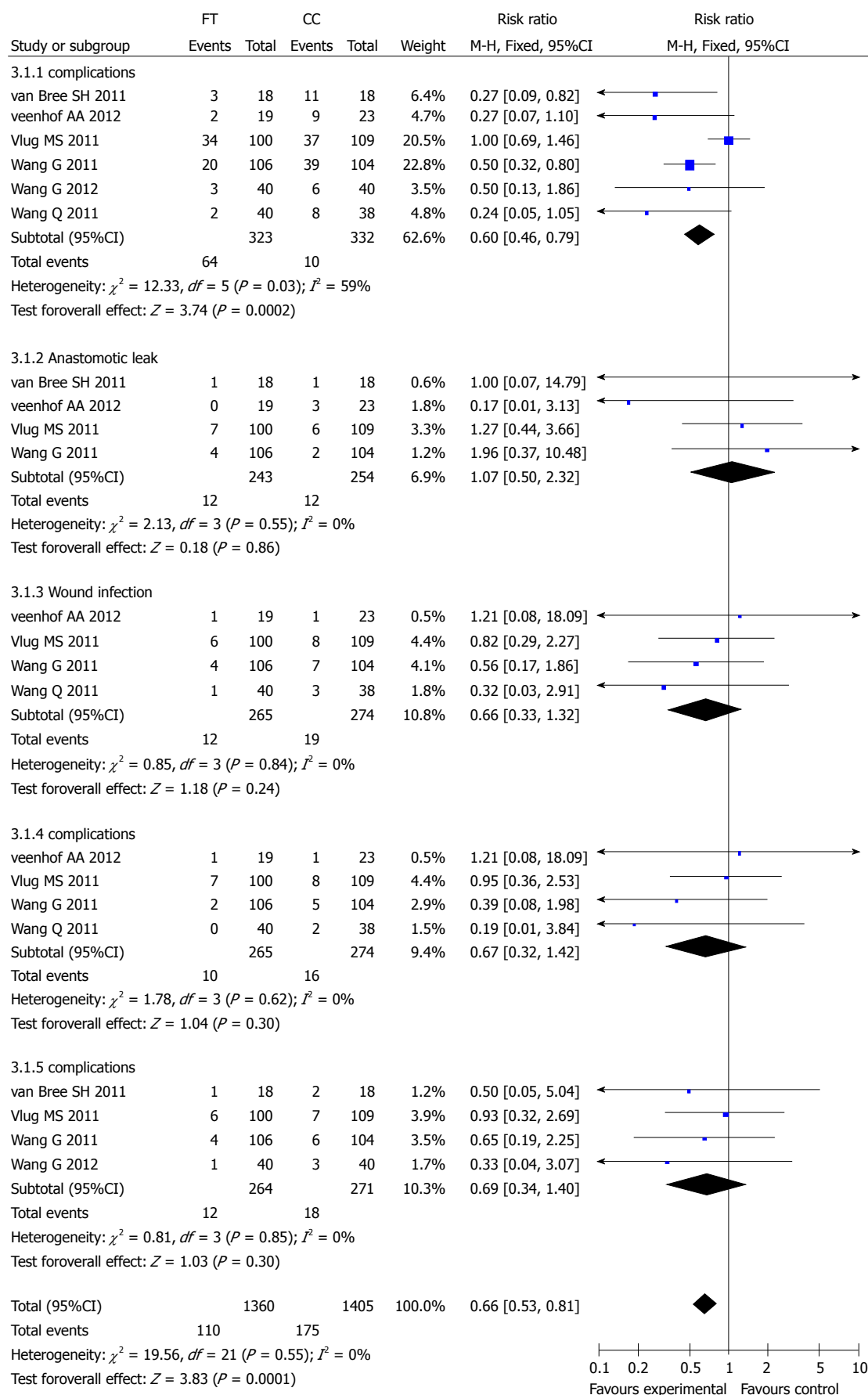


Figure 2 Forest plot comparing fast-track rehabilitation protocol and laparoscopic surgery vs conventional care strategies and laparoscopic surgery in colorectal resection, outcome: complications. LFT: Fast-track rehabilitation protocol and laparoscopic surgery; LCC: Conventional care strategies and laparoscopic surgery.

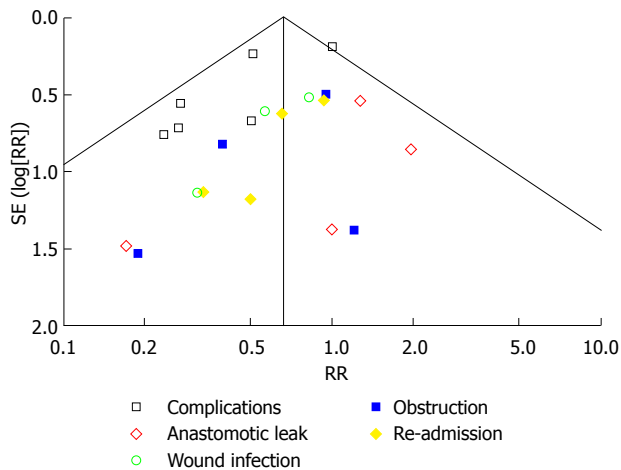


Figure 3 Comparison between the fast-track rehabilitation protocol and laparoscopic surgery, and conventional care strategies and laparoscopic surgery in laparoscopic colorectal resection for colorectal malignancy, outcome: complications.

ies (539 patients) on wound infection for LFT *vs* LCC; 4.53% (12/265 patients) had wound infection in the LFT group and 6.93% (19/274) in the LCC group. Pooling the results indicated that LFT did not significantly reduce wound infections compared with LCC. The WMD was 0.66 (95%CI: 0.33-1.32, $P > 0.05$), $\chi^2 = 0.85$ ($P = 0.84$) and $I^2 = 0\%$, which excludes statistical heterogeneity among the studies.

Obstruction: Data were collected from four studies (539 patients) on obstruction for LFT *vs* LCC. 3.77% (10/265 patients) had obstructions in the LFT group and 5.84% (16/274) in the LCC group. Pooling the results indicated no significant difference in the risk of obstruction. The WMD was 0.67 (95%CI: 0.32-1.42, $P > 0.05$), $\chi^2 = 1.78$ ($P = 0.62$) and $I^2 = 0\%$, which excludes heterogeneity among the studies.

Re-admission: Data were collected from four studies (535 patients) on re-admission for LFT *vs* LCC. 4.55% (12/264 patients) were readmitted in the LFT group and 6.64% (18/271) in the LCC group. Pooling the results indicated no apparent difference in re-admission. The WMD was 0.69 (95%CI: 0.34-1.4, $P > 0.05$), $\chi^2 = 0.81$ ($P = 0.85$) and $I^2 = 0\%$, which excludes heterogeneity among the studies.

Publication bias

Funnel plots were created to access the publication bias of the literature. The shapes of the funnel plots did not show any obvious asymmetry (Figure 3).

DISCUSSION

The straightforward conclusion from the six included studies is that LFT is a more reliable treatment for colorectal malignancy, compared with LCC. LFT reduced complications, but carried similar risks of anastomotic

leak, wound infection, obstruction and re-admission.

Complications after LFT and LCC of colorectal resection have generally been discussed in China, as well as in other countries. A recently published multivariate analysis identified male gender^[26], preoperative education, anesthesia^[27] and early postoperative oral nutrition^[28] as potential risk factors for complications after colorectal surgery. In addition, some studies have found an increased risk of anastomotic leaks in males, which is consistent with the results of this study (10.1% of the men required re-operation for anastomotic leak *vs* 3.3% of the women)^[29-32].

Preoperative education of patients has a crucial role in LFT. It is necessary to demonstrate the detailed treatment program, the different steps of fast-track rehabilitation program and relevant measures for the patients to make them better understand and accept the fast-track rehabilitation program.

Better cooperation of patients can bring better outcomes of LFT. Generally, since the gastric emptying time of solid meal and fluid are 6 and 2 h, respectively^[33], the patients should be encouraged to have liquid meal 2 h before the operation instead of fasting. It has been shown that preoperative oral carbohydrate is safe and can efficiently reduce complications^[34-36].

The role of epidural anesthesia or regional anesthesia in LFT should be stressed. Postoperative epidural analgesia can avoid stress-induced neurological, endocrinological and homeostatic changes or the blocking of sympathetic nerve-related surgical stress response, reduce complications such as nausea, vomiting and enteroparalysis after operation, promote early ambulation, improve the intestinal function and shorten the hospital stay time of patients after resection of colorectal cancer^[26,37-42].

Early postoperative oral nutrition is regarded as an essential part of LFT. Food intake can stimulate gastrointestinal peristalsis, and early feeding during the first 24 h after surgery promotes the recovery of an obstruction. It has been illustrated that early postoperative oral nutrition attenuates catabolism and potentially decreases infectious complications^[27,43].

Several studies have shown that American Society of Anesthesiologists grade III or higher is associated with increased postoperative morbidity^[44-46].

LFT can improve the rehabilitation of patients after resection of colorectal cancer better than LCC, thus benefiting their surgery, anesthesia, pain management, physical therapy and social work. The primary work of LFT is the preoperative education of patients to make them understand the whole plan and the aim of each stage. Therefore, it is vital to obtain cooperation from the nursing staff.

However, we should still regard these outcomes with caution and evaluate them critically for the following reasons. Firstly, although there was no detectable publication bias, as tested by the funnel plots, the overall methodological quality and reporting of the included studies were poor. Secondly, the number of studies found was relatively low, and the aforementioned quality issues may have biased the results significantly. Therefore, more

large trials with better separation between LFT and LCC for colorectal malignancy seem necessary. Furthermore, in light of current evidence, LFT should not yet be considered the new standard for colorectal malignancy. Long-term data on outcome, as well as important other factors in making a decision for an intervention, are also lacking. Quality of life data and data on physiological performance after 5 years have never been described, nor have data on cost-effectiveness or economic evaluations of LFT. These parameters may play an important part in recommending LFT treatment in colorectal resection. However, we believe that, with greater awareness and the increasing popularity of LFT, more long-term follow-up reports will eventually be published.

There have been eight previously published systematic reviews, including meta-analyses on this topic^[16,17,47-52]. These included three reviews of controlled clinical trials and randomized controlled trials^[17,47,49], and five reviews of randomized controlled trials only^[47,50-52]. The present study is the first meta-analysis to compare fast-track rehabilitation with conventional care in laparoscopic colorectal resection for colorectal malignancy. This also the first meta-analysis of patients undergoing elective colorectal surgery to demonstrate that LFT is associated with a significant reduction in postoperative complications, but no significant reduction in readmission rates. The increased number of included studies supported the quality of the evidence from the present study.

In conclusion, this meta-analysis demonstrated that LFT is safe and feasible for colorectal surgery. As LFT comes into even wider use, additional large, prospective RCTs should be conducted to further compare the efficacy and safety of this approach.

COMMENTS

Background

Fast-track rehabilitation in laparoscopic colorectal resection has become the most fashionable way of treating colorectal malignancy. Complications after fast-track rehabilitation protocol and laparoscopic surgery (LFT) and conventional care strategies and laparoscopic surgery (LCC) of colorectal resection have generally been discussed in China, as well as in other countries.

Research frontiers

Over the past three decades, many studies have assessed the performance of LFT. However, comparisons of LFT and LCC have not been published.

Innovations and breakthroughs

Based on this meta-analysis, LFT for colorectal malignancy is safe and efficacious. Similar associations were indicated in subgroup analyses of East Asian, Western, cohort, and high-quality studies. These findings were not presented clearly in previous systematic reviews.

Applications

LFT appears to be neither directly nor indirectly associated with risk. Further studies should seek to clarify this conclusion.

Peer review

LFT is rapidly becoming the focal point of attraction for specialists worldwide. This article shows the advantages of the procedure. This analysis has great practical value for clinicians.

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