A meta-analysis of short-term outcome of laparoscopic surgery versus conventional open surgery on colorectal carcinoma

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Abstract

Objective: The aim of this article is to study the superiority and safety of laparoscopic surgery for colorectal carcinoma.

Summary Background Data: Laparoscopy in rectal cancer is still not recommended as the treatment of choice by National Comprehensive Cancer Network guidelines. Laparoscopic rectal surgery is more complex and technically demanding, especially for mid and low rectal cancer.

Methods: A computer-based online research of retrospective or prospective studies addressing laparoscopic surgery versus conventional open surgery for colorectal carcinoma published in the last 11 years was performed in electronic database (Wangfang Database, China National Knowledge Infrastructure, Chinese Medical Current Contents, Pubmed, Medline, Ovid, Elsevier, ISI Web of Knowledge, Cochrane Database of Systematic Reviews). Selective trials were analyzed by the Review Manager 5.2 software.

Results: A total of 9 clinical trials, involving a total of 4747 patients, were identified. A meta-analysis showed that operating time was not significantly different between the 2 groups [WMD = 0.46, 95% confidence interval (95% CI): −55.68 to 56.60, P = 0.99], intraoperative blood loss in laparoscopic surgery group was less than conventional open surgery group [WMD = −64.66, 95% CI: −87.31 to 42.01, P < 0.01]; No significant difference in the number of lymph node retrieved from postoperative pathologic specimens was found between the 2 groups [WMD = 0.75, 95% CI: −1.72 to 0.23, P = 0.14]; Postoperative time to flatus in laparoscopic surgery group was earlier than that in open surgery significantly [WMD = −1.22, 95% CI: −1.53 to −0.91, P < 0.01]. The cases of postoperative complications were significantly different between the 2 groups, which showed that the cases of laparoscopic surgery group were less than those of open surgery group [odds ratio (OR) = 0.62, 95% CI: 0.52–0.72, P < 0.01]; Moreover, hospital stay of laparoscopic surgery group was shorter than that of open surgery that showed significant difference [WMD = −2.38, 95% CI: −3.30 to −1.46, P < 0.01].

Conclusion: Short-term outcomes of laparoscopic surgery are superior than conventional open surgery that include more safety and feasibility, and is expected to be a standardization operation method for colorectal carcinoma.

Abbreviations: CCT = clinical trials, CME = complete mesenteric excision, CRC = colorectal cancer, CVL = central vascular ligation, ERAS = enhanced recovery after surgery, LTME = laparoscopic mesorectal excision, MD = mean difference, NCCN = Comprehensive Cancer Network, NR = nonrandomized, OR = odds ratio, OTME = open mesorectal excision, RCT = randomized controlled trial, RNT = nonrandomized trials, TME = total mesorectal excision.

Keywords: colorectal carcinoma, laparoscopic surgery, meta-analysis, open surgery

1. Introduction

Colorectal cancer (CRC) is one of the most common malignancies in western countries,1 and its incidence is also increasing in Asian countries. At present, it is the second most common cancer, which in Hong Kong is the second cause of death cancer.2 With the introduction of total mesorectal excision (TME), laparoscopic
technique, as well as pre- and postoperative chemoradiotherapy, the local control rate and survival of rectal cancer patients have dramatically improved. The TME principles, which were first described by Heald et al., are currently considered the standard practice for mid and low rectal cancers, as local recurrence is reduced to less than 5%. A complete TME consists not only of the routine excision of intact mesorectum but also preservation of the autonomic nervous system and the sphincters. Although laparoscopy in colon cancer has gained acceptance due to its proven benefits, which include fewer perioperative complications, faster postoperative recovery, and comparable survival rates, laparoscopy in rectal cancer is still not recommended as the treatment of choice by National Comprehensive Cancer Network (NCCN) guidelines. Laparoscopic rectal surgery is more complex and technically demanding, especially for mid and low rectal cancer. As surgical techniques and equipment have developed, the feasibility and safety of laparoscopic TME (LTME) has been reported by many institutes. Moreover, long-term survival following LTME seems to be comparable to open TME (OTME). Laparoscopic surgery has been reported to improve postoperative short-term effects, with faster recovery and shorter hospital stay. But there are many reports of laparoscopic CRC surgery that had a high degree of difficulty especially in low and super-low rectal cancers and postoperative complications and high port recurrence, so its superiority and safety are still controversial.

So, we searched for nearly 11 years of laparoscopic CRC surgery compared with traditional open surgery, and the relevant indicators of the meta-analysis of the literature to further clarify the laparoscopic CRC surgery safety and feasibility.

2. Methods

We used (CBMDisc), PubMed, Medline, OVID, Elsevier, ISI Web of Knowledge platform and Cochrane, etc., to search randomized controlled trial (RCT) and retrospective nonrandomized trial (RNT) literature on laparoscopic CRC surgery and traditional open CRC surgery for nearly 10 years from 2005 to 2016. The main English search terms included CRC, colorectal carcinoma, laparoscopy, open surgery, short-term outcome, Chinese search term includes CRC, laparoscopic surgery, open surgery, short-term effect. Manual retrieval of relevant literature reference was available to expand the search and to determine no missing. This is a meta-analysis article, does not involve ethical review, and ethical approval is not necessary after inquiring the ethical review committee in our hospital.

2.1. Inclusion of studies

Both randomized clinical trials (CCT) and nonrandomized (NR) studies were included. The population of interest were confirmed as CRC by pathology or histology and undergoing radical surgery by means of laparoscopic surgery or conventional open surgery. The studies must include those indices: compared with the laparoscopic group and the traditional laparotomy group (operation time, surgical bleeding volume), postoperative complications (disease detection lymph count), recovery, complications, and length of hospital literature. Selected literature must indicate the surgical approach for the laparoscopic group and laparotomy group, and there are 2 sets of data comparison of the situation. The same author chose the literature as a recent one, and the original literature should provide complete data. The search process is depicted in Fig. 1.

2.2. Exclusion criteria

A single study of the uncontrolled group, comparative study of benign diseases, incidence of complicated bowel obstruction with emergency surgery, distant transfer of the literature, including tumor recurrence surgery and abdominal surgery history of the literature, nonradical surgery were excluded from our study. Statistical methods of violation of principles or unreasonable literature, repeated publication of the literature, failure to provide valid data, or no full text of the literature were also excluded from our study, as shown in Fig. 1.

2.3. Data extraction

Data extraction was independently performed by using specially designed data extraction sheets. After we collected nine qualified documents, the first author, published the year, the number of cases of surgery, operation time, intraoperative blood loss, postoperative lymph node count, postoperative anal exhaust time, total hospital stay, postoperative complications were summarized and data were recorded correctly.
2.4. Risk of bias assessment

Study quality was assessed using 2 methods. NR comparative trials were assessed using the Newcastle–Ottawa quality assessment scale,[17] as recommended in the Cochrane Handbook.[18,19] NR literature were assessed to 5 points or more qualified by NOS and included in the meta-analysis (as summarized in Table 1).[20–28] RCTs and NR comparative trial were all assessed as discussed in the Cochrane Handbook[18] as shown in Figs. 2 and 3.

2.5. Statistical analysis

The meta-analysis was performed using the Review Manager software (RevMan, version 5.2, Copenhagen: Nordic Cochrane Centre, Cochrane Collaboration, 2012) that was provided by the Cochrane Collaboration. Continuous variables were pooled using the mean difference (MD) with a 95% confidence interval (95% CI), and dichotomous variables were pooled using the odds ratio (OR) with a 95% CI. If studies reported only the median, range, and size of the trial, the means and standard deviations were calculated according to Hozo et al.[19] If data reported only the medians and range, this parameter was excluded, which we identified as 2 in Table 2. Each parameter 1 was included in the meta-analysis. Statistical heterogeneity was evaluated by $I^2$, and it was considered to be high if the $I^2$ statistic was greater than 50%. The fixed effects model was used for studies with low or moderate statistical heterogeneity, and the random effects model was used for studies with high statistical heterogeneity.

### Table 1

| First author     | NOS score | Author nationality | Type of study | Number of cases (endoscopy group/open group) | Total number of cases (n) |
|------------------|-----------|--------------------|---------------|---------------------------------------------|---------------------------|
| Jun et al[20]    | 5         | China              | NR            | 373/373                                     | 746                       |
| Laiyang et al[21]|           | China              | RCT           | 52/52                                       | 104                       |
| Law et al[22]    |           | China              | RCT           | 814/1197                                    | 2011                      |
| Bedirli et al[23]| 7         | Turkey             | NR            | 65/98                                       | 163                       |
| Chen et al[24]   | 7         | China              | NR            | 80/80                                       | 160                       |
| Jing et al[25]   | 6         | China              | NR            | 67/71                                       | 138                       |
| Yang et al[26]   | 6         | China              | NR            | 87/90                                       | 177                       |
| Cai et al[27]    |           | China              | NR            | 64/102                                      | 166                       |
| Veldcamp et al[28]|          | Canada             | RCT           | 536/546                                     | 1082                      |

Laparoscopic group: 2138 cases, 2609 cases of open group, total: 4747 cases.
NR = nonrandomized, RCT = randomized control trial.

RCT was assessed by the Cochrane Handbook according to risk of bias assessment; NR was assessed by NOS score and the Cochrane Handbook.

3. Results

3.1. Search results

The initial search resulted in 420 hits. After removal of duplicates, 310 remained. After screening hits on title, 110 hits
remained. After 50 of full-text articles were excluded with reasons, 60 of full-text articles assessed for eligibility and 28 of full-text articles excluded because of low quality, which led that 32 of studies included in qualitative synthesis remained. Twenty-three of full-text articles were excluded because of lack of parameters (e.g., blood loss, duration time) and 9[20–28] studies were included in quantitative synthesis for meta-analysis, of which 2[20,21] were the Chinese literature, and the other 7[22–28] were the English literature. In the English literature, the first authors[23,28] were Turks and Canadians. First authors of other English and Chinese literature[22,25–28] were the Chinese people. The total number of cases included 4747 cases, of which 2138 studies[21–27] were full-text articles excluded because of lack of full-text articles excluded because of low quality, which led that 60 of full-text articles assessed for eligibility and 28 of full-text articles included studies could be considered moderate to well (Fig. 3).

3.4. Primary outcome parameters
3.4.1. Surgery time. Nine articles recorded the amount of bleeding, but there were 2 articles[22,28] that did not use mean and standard deviation. We included the other 7 articles[20,21,23–27] for meta-analysis, the results were heterogeneous, and I² = 100%, using the random effect model. The results showed no significant difference between endoscopic surgery and open surgery (WMD = 0.46, 95% CI: −5.68 to 56.60, P = .99), see Fig. 4A.

3.4.2. Blood loss. Nine articles involved the amount of bleeding, but there were 2 literatures[22,28] demonstrating bleeding volume as mean and interval, so we did not include them in the study. The other 7 literature[20,21,23–27] meta-analyses results were heterogeneous, I² = 98%, showing that the laparoscopic group was significantly lower than the open group, a statistically significant difference (WMD = −64.66, 95% CI: −87.31 to 42.01, P < .01), see Fig. 4B.

3.4.3. Lymph node harvest (mean). There was 1 literature[20] not mentioned, and 2 articles[22,28] are expressed in terms of mean and interval. The other 6 cases were expressed as mean and standard deviation. We composed the 6 cases for meta-analysis. The results showed that the heterogeneity was significant, I² = 64%, and there was no significant difference between the laparoscopic group and the laparoscopic group (WMD = −0.75, 95% CI: −1.72 to 0.23, P = .14), see Fig. 4C.

3.4.4. Anal exhaust time. Postoperative exhaust time were converted to days as a unit (some in hours). There were 2 documents[20,22] that were not covered, and a document[27] was expressed in terms of intervals. The other 6 articles[21,23–26,28] were included in the meta-analysis. The results showed that the heterogeneity was significant, I² = 82% and the patients in the laparoscopic group were significantly earlier than those in the open group (WMD = −1.22, 95% CI: −1.53 to −0.91, P < .01), see Fig. 4D.

3.4.5. Postoperative complications. There were 2 articles[20,21] that did not address the parameters of the complication. Seven articles[22–28] recorded postoperative complications and expressed in the number of cases. So, we included in the 7 literature[22–28] using the ratio (OR) fixed model analysis. The results showed that the heterogeneity was significant, I² = 72% and that laparoscopic

### Table 2

**Information on the inclusion of indicators.**

| Author          | Intraoperative situation | Postoperative pathology and complications |
|-----------------|--------------------------|-------------------------------------------|
|                 | Surgery time, min        | Blood loss, mL                            | lymph node harvest mean (n) | Anal exhaust time, d | Postoperative complications | Duration, d |
| Jun et al [25]  | 1                        | 1                                         | 0                           | 0                    | 0                            | 1           |
| Laiyang et al [21] | 1                        | 1                                         | 1                           | 1                    | 1                            | 1           |
| Law et al [22]  | 2                        | 2                                         | 2                           | 0                    | 1                            | 2           |
| Bedirli et al [20] | 1                        | 1                                         | 1                           | 1                    | 1                            | 1           |
| Chen et al [24] | 1                        | 1                                         | 1                           | 1                    | 1                            | 1           |
| Jing et al 2012 [25] | 1                        | 1                                         | 1                           | 1                    | 1                            | 1           |
| Yang et al [26] | 1                        | 1                                         | 1                           | 1                    | 1                            | 1           |
| Cai et al [27]  | 1                        | 1                                         | 1                           | 1                    | 1                            | 1           |
| Veldcamp et al [28] | 2                        | 2                                         | 2                           | 1                    | 1                            | 1           |

0 = indicates that no reference is made, 1 = indicates the means and standard deviations, 2 = indicates data are expressed by means and range not by standard deviation. Each parameter 1 was included in the meta-analysis.
group was significantly lower than the open surgery group (OR = 0.62, 95% CI: 0.52–0.72, P < .01) (Fig. 4E). The funnel plot of standard of postoperative complications showed 2 of the studies lay outside the limits of the 95% CI, indicating some evidence of publication bias, see Fig. 5.

3.4.6. Duration. Nine articles were recorded in the number of hospital days, but 2 articles[22,27] were shown in terms of mean and interval, not included in the meta-analysis. Another 7 literature[20,21,23–26,28] analyses not only showed difference in heterogeneity, $I^2 = 94\%$, but also showed that laparoscopic...
hospital stay was significantly less than the laparotomy group (WMD = −2.38, 95% CI: −3.30 to −1.46, P < .01), see Figs. 4F, 5.

The detailed results of the meta-analysis of the 6 short-term efficacy indicators of the laparoscopic and open group are shown in Table 3.

4. Discussion

CRC was the second leading malignancy in western countries.129 With the changes in the dietary structure of our residents, especially in high-fat diet, the incidence of CRC had increased, and the patients tended to younger. In recent years, there had been a documented increase in the incidence of CRC in young patients.130 So far, surgery is still the main treatment of CRC. Since 1990, in the United States, Jacobs et al131 performed the first laparoscopic right hemicolectomy, laparoscopic colorectal surgery began extensive in the country experienced a hand-assisted laparoscopic CRC surgery to full-laparoscopic CRC surgery. The surgical stage, and the operation technique tended to be standardized, and the operation time was obviously close to the traditional open surgery. Many articles reported laparoscopic surgery with high-definition exposure, more conducive to the protection of autonomic nerve characteristics.132–135 Laparoscopic CRC surgery was favored by more surgeons.134,137 Laparoscopic colorectal surgery required not only the experience of CRC surgery but also the need for high laparoscopic skills and techniques. This article aims to explore the safety and superiority of laparoscopic CRC surgery compared with open surgery. At the same time through this study, let us have an ideal choice between laparoscopy and open surgery in CRC. We also want to use this analysis to improve the skills and techniques for anorectal surgeon during laparoscopic surgery.

Surgery time is not only related to the patient’s recovery but also related to the surgical experience of the surgeon. How to reduce the operation time under the premise of affecting the radical tumor, has been the most sought for surgeons. This meta-analysis showed no significant difference between laparoscopic CRC surgery and open surgery [MD = 0.46 (−55.68 to 56.60), Z = 0.02, P = .99]. Through the study of the original literature, we found that they were particularly demanding on surgical skills. In order to shorten the operation time, we summed up the “tumor and surrounding tissue block resection” concept: After the establishment of pneumoperitoneum, we first explore the liver, mesenteric lymph nodes, and pelvic cavity, and finally explore the tumor area of the intestine, and assess whether the radical surgery can be performed because the larger tumor (8–10 cm) is not recommended by laparotomy.138 To achieve complete resection of the tumor and surrounding tissue, we need to ensure that the visceral fascia integrity of the sharp free, and colorectal surgery called complete mesenteric excision (CME) and TME. Surgery must be accurately found Told fascia gap and sacral anterior space, the layer of thin for the loose connective tissue, no blood vessels to take shape. The sharp separation between these gaps can ensure complete removal of the tumor and surrounding tissue, and can shorten the operation time.

Surgery less bleeding can speed up the patient’s recovery and reduce complications.

It is associated with laparoscopic surgical techniques. The amount of bleeding will directly affect the surgical field of vision, and even the surgeon was forced into the abdominal surgery, which laparoscopic surgery failed. Our meta-analysis showed that blood loss was significantly lower in laparoscopic group than the open group [MD = −64.66 (−87.31 to 42.01), Z = 5.60, P < .01]. Laparoscopic surgery for CRC was superior to open surgery with high-definition, enlarged exposure characteristics. As mentioned above, the operation between the correct gap can not only clearly expose the blood vessels but also significantly reduce the amount of surgical bleeding.

The present study assessed the oncological safety by examining the postoperative results, such as the resection margin and the number of resected lymph node.24 Our paper showed that lymph node harvest number had no significance between laparoscopic surgery group and open surgery group [MD = −0.75 (−1.72 to 0.23), Z = 1.49, P = .14], which showed the oncological safety and was consistent with previous study.139–132 We summarize the points of laparoscopic CRC surgery for lymph

**Table 3**

| Indicators                  | Statistical results M (95% CI) | Statistical testing | Heterogeneity analysis |
|----------------------------|-------------------------------|---------------------|-----------------------|
|                            | Z    | P    | X²  | P   |
| Surgery time, min          | 0.46 | (−55.68 to 56.60) | 0.02 | .99 | 1300.1 | <.01 |
| Mean blood loss, mL        | −64.66 | (−87.31 to 42.01) | 5.60 | <.01 | 325.41 | <.01 |
| No. of lymph node sampled  | −0.75 | (−1.72 to 0.23)   | 1.49 | .14 | 14.05  | .02  |
| Anal exhaust time, d       | −1.22 | (−1.53 to −0.91)  | 7.78 | <.01 | 26.55  | <.01 |
| Postoperative complications | 0.62 | (0.52–0.72)      | 5.96 | <.01 | 21.66  | <.01 |
| Duration, d                | −2.38 | (−3.30 to −1.46) | 5.06 | <.01 | 99.95  | <.01 |

95% CI = 95% confidence interval.
node dissection. Colorectal lymphatic drainage has the characteristics of being covered by the visceral fascia in the mesentry and opening at the root of the blood vessel. Because of the presence of jump metastases in colorectal lymph node metastases, positive lymph nodes can also be found at station 3 when the first station is positive. In order to achieve maximum lymph node dissection, not only the need for tumor and surrounding tissue resection but also the need for central vascular ligation (CVL) was required. Because of laparoscopic high-definition vision and the amplification of vascular tissue effect, the root ligation of central blood vessels was safe and feasible, and would not increase the risk of intraoperative bleeding.

In order to maximize the effectiveness of laparoscopic CRC surgery, “no tumor” concept was equally important. The recurrence of CRC was related to the thoroughness of the first operation and the operation of the tumor-free technique. If the operation did not pay attention to the operation of the tumor-free technique, the patients who could cure the CRC could increase the chance of recurrence, implantation, and metastasis. The concept of tumor-free was not only vital to the surgeon but also vital to the equipment nurse. Nurses must be familiar with the cooperation of non-tumor technology, be ready for the necessary items to ensure timely and accurate delivery, and shorten the operation time to avoid the spread of cancer cells iatrogenic. Doctors in the operation should try to avoid the device to touch or grasp the tumor, because the puncture sheath and the incision in close contact and might adhere to tumor cells, so the operation of the puncture sheath up and down movement could increase the chance of harboring planting, or the use of threaded puncture sheath should be a good way to prevent accidental shedding of the casing. Once the pneumoperitoneum gradually disappeared, intra-abdominal shedding of tumor cells would pollute the wound and removing the tumor specimens might protect the incision. There were reports in the literature that laparoscopic CRC surgery in the intraperitoneal fluid free cancer cells might be caused by surgical procedures leading to tumor cell shedding or tumor invasion caused by serous membrane. So, we thought it was necessary to take measures to reduce the shedding of cancer cells, such as the use of diaphragm protection to take specimens of the incision, off the abdominal cavity pelvic distilled water rinse, and intra-abdominal anti-cancer drug use could reduce the proliferation of cancer cells.

The anal exhaust time was an important indicator of postoperative recovery. It was related to the surgical techniques described above. Our study showed that the anal exhaust time was significantly lower in the laparoscopic group than in the open group [MD = −1.22 (−1.53 to −0.91), Z = 7.78, P < .01]. The current popular enhanced recovery after surgery (ERAS) pathways could also promote bowel function recovery after laparoscopic surgery. It was a hot topic in CRC surgery. Laparoscopic CRC complications were usually urinary system damage, anastomotic leakage, intestinal obstruction, incision infection, and cardiovascular and cerebrovascular accident. With the laparoscopic surgeon technology increasingly skilled, significantly reduced the operation time, intraoperative blood loss decreased, the incidence of postoperative complications decreased significantly. The studies by Dasari et al,[65] Polle et al,[66] and Tilney et al[67] found no evidence of a difference in perioperative complications, while Rosman et al[68] and Tan et al[69] did find a significant difference. And because of the minimally invasive features of laparoscopic surgery, laparoscopic CRC surgery complications were lower than open surgery, which was consistent with our research [OR = 0.62 (0.52–0.72), Z = 5.96, P < .01]. Hospitalization time was not only an important indicator of patient rehabilitation but also an important part of ERAS. Because of the minimally invasive features of laparoscopic CRC, most patients had shorter hospital stay than open surgery. Our research also confirmed this [MD = −2.38 (−3.30 to −1.46), Z = 5.06, P < .01]. In order to reduce the complications of laparoscopic surgery patients and shorten the hospital stay, we referred to the relevant literature,[62–64,70] combined with our own surgical experience; we had made the following statements: First, Strict screening of surgical patients: if patients with severe cardiovascular disease and severe respiratory disease were expected to not tolerate abdominal high pressure CO₂, we decisively gave up laparoscopic surgery; Second, Preoperative examination and tumor staging: doing CT or MRI examination to understand the depth of the tumor invasion of patients and peripheral lymph node metastasis and distant organ metastasis; Third, Intraoperative specification: CME, TME, and CVL technology was important as mentioned above. Fourth, Postoperative care: the elderly, high-risk patients were placed on the ICU for observation treatment for about 1 to 2 days; after being transferred to the conventional ward, we paid attention to the detection of central venous pressure monitoring and liquid balance.

Our meta-analysis still had many shortcomings, such as the lack of comprehensive literature, the lack of the first author of the literature in Europe and the United States, some bias in part included studies, and only contained 2 languages in both English and Chinese; 2 literatures were published before 2010, relatively obsolete; The follow-up period was short, and the long-term efficacy was not analyzed, such as 3-year, 5-year survival rate, and recurrence.

5. Conclusion

The results of this study, compared with the traditional open surgery laparoscopic CRC surgery, do not increase the risk of surgery and postoperative complications, is a safe and feasible surgical approach, and is expected to become a standardized surgical approach to CRC. However, as there are limitations of this meta-analysis, conclusions should be regarded with some reservations. Better designed, large trials are needed, and 2 ongoing trials were identified.

Acknowledgment

We thank professor Licheng Dai and researcher Xuting Xu (Central Laboratory, Huzhou Central Hospital, Zhejiang province, China) for their critical revision of the meta-analysis section.

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