



Review

Laparoscopic versus open surgery for rectal cancer: A meta-analysis of classic randomized controlled trials and high-quality Nonrandomized Studies in the last 5 years



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HIGHLIGHTS

- RCTs and NRCTs were combined.
- Literature within last 5 years were selected.
- The difference in distal resection margin (DRM) was statistical clear.
- Safe and reliable method for rectal cancer.

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ABSTRACT

Objective: To present a meta-analysis of high-quality published reports comparing laparoscopic rectal resection (LRR) and open rectal resection (ORR) for rectal cancer.

Methods: Studies that compared LRR and ORR and were published within the last 5 years were identified. All eligible randomized controlled trials (RCTs) and non-randomized comparative trials (NRCTs) were evaluated based on the Jadad score, the Cochrane risk of bias assessment tool and modified Methodological Indices for Nonrandomized Studies (MINORS). The mean differences (MD) and odds ratios (OR) were used to compare the operative time, blood loss, mortality, complications, harvested lymph nodes, hospital stay, distal resection margin, and circumferential resection margin. The risk ratio (RR) method was used to examine recurrence and survival.

Results: Fourteen studies were identified and included 7 RCTs and 7 NRCTs and 4353 patients (2251 LRR, 2102 ORR). Although the operation time of the LRR group was obviously longer than that of the conventional surgery group (MD = 25.64, 95%CI = [5.17,46.10], $P = 0.01$), LRR was associated with fewer overall complications (OR = 0.67, 95%CI = [0.52,0.87], $P = 0.002$), less blood loss (MD = -66.49, 95%CI = [-88.31, -44.66], $P < 0.00001$), shorter postoperative hospital stays (OR = -1.26, 95%CI = [-2.45, -0.07], $P = 0.004$) and shorter bowel function recovery times (MD = -0.93, 95%CI = [-1.27, -0.58], $P < 0.00001$). Moreover, the difference in the DRM was statistically clear (MD = 0.14, 95%CI = [0.02,0.27], $P = 0.03$). However, no significant differences between the LRR and ORR groups were observed in terms of the number of lymph nodes harvested, mortality, positive CRM, local and distal recurrence, or overall and disease-free survival.

Conclusions: This study indicates that there are no significant differences between LRR and ORR in terms of survival and pathological outcomes with the exception of the DRM. Moreover, this study suggests that LRR can be performed safely and elicits faster recovery times compared with conventional surgery.

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1. Introduction

1.1. Background

Colorectal cancer, including rectal cancer, is the third most

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common cancer in the world, and approximately one-third of these cancers are localized to the rectum. Nearly 39220 new cases occurred in America in 2015 [1]. Since Jacobs reported the first minimally invasive resection in 1991 [2], this treatment has been considered a landmark in the progress of surgical treatment, although arguments have existed since that time. The controversial points include the intraoperative and postoperative complications, lymphadenectomy, postoperative outcomes, long-term quality of life, and over-all and disease-free survivals. There are numerous publications from the past 25 years that have evaluated and compared laparoscopic and open surgery for rectal cancer including the United Kingdom Medical Research Council trial of Conventional versus Laparoscopic-Assisted Surgery In Colorectal Cancer (CLASICC), the Comparison of Open versus laparoscopic surgery for mid- and low-Rectal cancer After Neoadjuvant chemoradiotherapy (COREAN) trial, and the Colorectal cancer Laparoscopic or Open Resection (COLOR) II trial.

Since its appearance 22 years ago, laparoscopy has brought enormous changes to rectal cancer surgery and has become the best choice for some diseases, such as inflammatory bowel disease and diverticulitis, due to its benefits in terms of recovery and the complication rate as well as its minimally invasive nature. With the development of equipment and techniques in recent years, research into rectal cancer has been extensive, and growing numbers of clinical doctors and patients have come to comprehend and welcome laparoscopic rectal resection. However, the laparoscopic approach differs from classic open surgery in rectal cancer not only due to the strict indications for laparoscopy but also due to concerns about its security and effectiveness.

In recent years, many scholars have attempted to solve the problem, and meta-analysis is one of the significant methods that have been directed toward this goal. Meta-analyses are being used not only to increase the total sample size and estimate bias in every single field of research to increase the consistency of the evaluation of results but are also being used to discover the imperfections of past studies to create new issues and mentalities.

Over the last 10 years, a number of meta-analyses on this topic have been published. Some have included few of the available RCTs or antiquated RCTs, and the unreliable results and little strong evidence have been presented [3–5]. Some of the included small RCTs are more likely to exhibit potential publication and study biases due to the different levels of surgical techniques [5–7]. For example, one previous study did not use original data [8], one meta-analysis only described the short-term outcomes [9], and another study included only long-term results [10]. Jiang [5] made an excellent meta-analysis of mid-low rectal cancer on short- and long-term outcomes. This paper includes 13 trials, however, only 3 literature was published within last 3 years, on the other hand, the RCTs and NRCTs were not divided from each other, as for result, “it failed to provide statistical evidence for a significant difference in the DRMs between two groups ($WMD = -0.21$, $P = 0.22$)”, Moreover, few of the meta-analyses included studies published after 2012, and it is well known that the laparoscopic equipment and surgical techniques have changed rapidly, particularly in recent years.

The study included NRCTs, which is a well-known argumentative problem in the field of evidence-based medicine because NRCTs are considered to increase the effects due to intrinsic flaws or publication bias. There is evidence suggesting that the data derived from high-quality NRCTs may be similar to those derived from RCTs [11]. Moreover, the inclusion of NRCTs may help to overcome the problems associated with a paucity of randomized evidence. Furthermore, the pooling of high-quality NRCTs may be as accurate as the pooling RCTs when surgical procedures are compared [12], which the authors of other similar analyses did not

notice. Therefore, the present meta-analysis combined RCTs and NRCTs.

We selected the latest trials from within the last 5 years for this meta-analysis of rectal cancer. The aim of this study was to perform an updated evaluation of all of the available high-quality published trials to compare laparoscopic surgery and the conventional approach.

2. Methods

2.1. Eligibility criteria

2.1.1. Types of studies

All published RCTs and high-quality NRCTs comparing laparoscopic and open approaches for rectal cancers with curative intent including early and advanced studies were evaluated. There were no limitations regarding language or publication status. If the research population included diseases other than rectal cancer, e.g., gastrointestinal stromal tumors (GISTs) and colorectal cancers, the trial was excluded unless two or more groups of data were counted separately. The included trials were required to discuss the clinical and pathological data from at least 50 patients to reduce the potential publication and study biases to the fullest extent possible. If 2 studies from the same author or the same institution were found, we first selected the more informative or more recent study unless the studies were conducted over different periods, the data from overlapping patients could be removed, or the data types that we required from the 2 studies were different; however, the total sample size was calculated only once.

2.1.2. Types of interventions

The RCTs and NRCTs were performed subgroup analysis to describe their characters, the data derived from high-quality NRCTs may be similar to those derived from RCTs and the inclusion of NRCTs may help to overcome the problems associated with a paucity of randomized evidence, the subgroup analysis may lead the results more credible.

The documents were required to clearly describe the rectal cancer surgery as either “anterior resection” (AR), “low anterior resection” (LAR), “abdominoperineal resection” (APR) or TME and to definitely describe the technique as “laparoscopic” or “open”. Laparoscopy-assisted and hand-assisted laparoscopic surgeries, including those performed with the Davic system, were permitted. Regarding open surgery, we considered all procedures that were described as “open” or “conventional open”. On Pubmed, we use “anterior resection OR AR OR low anterior resection OR LAR OR abdominoperineal resection OR APR OR TME” AND “laparoscopic OR open OR laparoscopy-assisted OR hand-assisted laparoscopic OR Davic” AND “rectal OR bowel OR recta OR straight intestine OR anus” AND “cancer OR carcinoma OR adenocarcinoma”.

2.2. Types of outcome measures

The outcomes measured were as follows:

- 1 Primary:** operative mortality, overall complications, number of harvested lymph nodes, distal resection margin, circumferential resection margin, local and distant recurrence or metastasis, and disease-free and overall survival within 1, 3, and 5 years.
- 2 Secondary:** Operative time (min), blood loss (mL), time to bowel function recovery (days), time of hospital stay (days).

2.2.1. Search process

To identify all of the relevant trials that compared laparoscopic

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