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Laparoscopic versus open left hemicolectomy for left-sided colon cancer: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Laparoscopic colectomy has been widely used clinically due to its minimally invasive advantages, and many studies have also demonstrated its safety and efficacy. However, the efficacy of laparoscopic left hemicolectomy remains unclear due to the differences in pathogenesis and surgical details between left and right colon cancers. Therefore, we plan to conduct a systematic review and meta-analysis to investigate whether laparoscopic techniques can be safely used in left hemicolectomy.

Method and analysis This meta-analysis protocol will be completed and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidelines. A systematic search was performed for all articles related to laparoscopic left hemicolectomy in PubMed, Web of Science, Medline, EMBASE and the Cochrane Library from inception to 5 November 2021. Article screening and data extraction were performed independently by two authors and cross-checked after completion. The literature to be included will use corresponding tools for bias risk assessment. Subgroup analyses and sensitivity analyses will be used to explore potential heterogeneity.

Ethics and dissemination Because this systematic review is based on studies with published results and does not involve intervention in patients, no ethical review is required. The results of this study will be published in a peer-reviewed journal.

PROSPERO registration number CRD42022291526.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ To the best of our knowledge, this will be the first meta-analysis to compare surgical approaches for left hemicolectomy.
⇒ Subgroup and sensitivity analyses will be used to explore potential heterogeneity.
⇒ Both the quality of the included literature and the final outcomes will be evaluated.
⇒ Restriction of publication language to English only is a limitation of this study.

INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed malignant tumour and the third leading cause of tumour-related deaths worldwide.[1 2] At present, surgery is still the main treatment for CRC, and laparoscopic surgery has become widely accepted due to its minimally invasive advantages. Although laparoscopic rectal cancer surgery remains controversial, laparoscopic colon cancer surgery has been recommended early by the National Comprehensive Cancer Network guidelines,[3] mainly based on several large multicentre randomised controlled trials (RCTs), including the Australasian Laparoscopic Colon Cancer Study (ALCCaS) Trial,[4] the Clinical Outcomes of Surgical Therapy (COST) study,[5] the Medical Research Council Conventional vs Laparoscopic-Assisted Surgery In Colorectal Cancer (CLASICC) trial and the Colon Cancer Laparoscopic or Open Resection (COLOR) Study.[6 7] These trials have demonstrated that laparoscopic colectomy is superior to conventional open surgery in terms of short-term outcomes, such as surgical incision length, intraoperative bleeding, and postoperative functional recovery, while also demonstrating that the adequacy of tumour removal is not threatened and that tumour-related long-term outcomes are not significantly different from those of open surgery.[8–11] In addition, these results have also been verified by the Cochrane Database of Systematic Reviews.[12 13]

However, left-sided colon cancer has been underrepresented in these trials, as the patients who underwent left hemicolectomy accounted for a very low proportion in the included cases, such as 113 (10.4%) in the COLOR study,[10] 59 (7.4%) and 64 (7.4%) in the CLASICC trial and COST study,[5 7] respectively, and even fewer in the ALCCaS and Barcelona trials, with only 22 (3.7%) and 5 (2.3%),[11 14] respectively. Compared

with right hemicolectomy or transverse colectomy, left hemicolectomy has quite different anatomic features and surgical procedures, with a challenge in the mobilisation of splenic flexure. Furthermore, it has been widely accepted that right and left colon cancers are two different diseases based on their differences in embryonic origin, genetic characteristics and biological behaviours, and therefore, may have different survival outcomes.[15–18] Therefore, the safety and prognosis of the treatment of left and right colon cancer should be evaluated separately by site, but the existing clinical trials are not representative of left hemicolectomy, so there is an urgent need to study this topic.

At present, several clinical trials have been conducted specifically on laparoscopic left hemicolectomy,[19 20] and even results from RCTs have been published,[21 22] but these results lack a pooling to form evidence-based medical evidence. Therefore, the purpose of this study was to synthesise the published results to fill the evidence gap for laparoscopic techniques for left hemicolectomy and to remind future investigators conducting colon cancer-related studies to stratify the final results based on the different locations of the tumour if there are inconsistencies between the results of this study and those of the whole colon.

MATERIALS AND METHODS

This meta-analysis protocol will be completed and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidelines.[23 24] According to the guidelines, our study has been registered on the website of the International Prospective Register of Systematic Reviews.[25]

Inclusion criteria

Population

All patients with left-sided colon cancer confirmed by preoperative imaging and pathology who underwent left hemicolectomy with mobilisation of splenic flexure were the target population of our study.

Intervention

The intervention in the experimental group was laparoscopic left hemicolectomy. In this meta-analysis, the definition of left hemicolectomy mainly included four aspects. First, ligation of the corresponding vessels, such as the inferior mesenteric vein, was performed. Second, mobilisation and pull-down of splenic flexure were observed. Third, resection of the distal transverse colon, splenic flexure, descending colon, sigmoid, etc. Finally, either an intracorporeal anastomosis or an extracorporeal anastomosis is performed for colocolonic anastomosis or colorectal anastomosis. Slight adjustments during the procedure to suit the actual situation are considered acceptable.

Comparison

Traditional open left hemicolectomy.

Outcome

The outcomes assessed in this systematic review and meta-analysis included perioperative outcomes (operative time, estimated blood loss, length of incision, time to resume oral diet, time to peristalsis), postoperative outcomes (length of hospital stay, number of harvested lymph nodes, 30-day mortality, postoperative complications) and oncological outcomes (tumour recurrence, 5-year overall survival and 5-year disease-free survival). In this study, 5-year disease-free survival which was defined as the duration from the date of surgery to confirmed recurrence or death from any cause was considered primary outcome, with tumour recurrence, 5-year over survival, perioperative outcomes and postoperative outcomes as secondary outcomes. In this study, tumour recurrence was defined as any recurrence confirmed by imaging or pathology, including local recurrence and systemic recurrence. OS was defined as the duration from the date of surgery to the date of proven death from any cause.

Study design

All randomised controlled and non-randomised controlled clinical studies comparing laparoscopic left hemicolectomy with open left hemicolectomy for which full text was available were included.

Exclusion criteria

1. Studies that included tumours from other colorectal locations but did not analyse the left hemicolectomy separately or for which data from the left hemicolectomy were not extractable were not included.
2. Benign colorectal disease or emergency surgery will be excluded.
3. No splenic flexure mobilisation will also be excluded.
4. Non-comparative studies and non-English publications were excluded.

Study selection

We systematically searched the PubMed, Web of Science, Medline, EMBASE and Cochrane Library databases for all literature comparing laparoscopic and open surgical approaches for left hemicolectomy from inception to 5 November 2021. Searches were carried out using medical subject headings and free text words in combination with the search strategy. We used the following keywords: “colon cancer”, “left hemicolectomy”, “laparoscopy” and “open”. All possible forms of these keywords will be used to ensure the comprehensiveness of the search. Additionally, we enriched our retrieval results with several methods, such as the similar articles function in PubMed, cross-checking references of the retrieved literature, searching ClinicalTrials (https://www.clinicaltrials.gov/), etc.

Search terms for PubMed

#1 ((((((((((((((((((((Colonic Neoplasms) OR (Neoplasm, Colonic)) OR (Neoplasms, Colonic)) OR (Colon Neoplasms)) OR (Colon Neoplasm)) OR (Neoplasm, Colon)) OR (Neoplasms, Colon)) OR (Cancer of Colon)) OR (Colon Cancers)) OR (Colon Cancer)) OR (Cancer, Colon)) OR (Cancers, Colon)) OR (Cancer of the Colon)) OR (Colonic Cancer)) OR (Cancer, Colonic)) OR (Cancers, Colonic)) OR (Colonic Cancers)) OR (Colon

Adenocarcinoma)) OR (Adenocarcinoma, Colon)) OR (Adenocarcinomas, Colon)) OR (Colon Adenocarcinomas)

#2 open surgery

#3 ((((((((((((((Laparoscopy) OR (Celioscopy)) OR (Peritoneoscopy)) OR (Surgical Procedures, Laparoscopic)) OR (Laparoscopic Surgical Procedure)) OR (Procedure, Laparoscopic Surgical)) OR (Procedures, Laparoscopic Surgical)) OR (Surgery, Laparoscopic)) OR (Laparoscopic Surgical Procedures)) OR (Laparoscopic Surgery)) OR (Laparoscopic Surgeries)) OR (Surgeries, Laparoscopic)) OR (Laparoscopic Assisted Surgery)) OR (Laparoscopic Assisted Surgeries)) OR (Surgeries, Laparoscopic Assisted)) OR (Surgery, Laparoscopic Assisted)) OR (Surgical Procedure, Laparoscopic)

#4 (left hemicolectomy) OR (left colectomy)

#5 #2 AND #3

#6 #1 AND #4 AND #5

The management of the literature search records will be carried out in EndNote V.X9.1. Two authors (QD and JZ) independently performed an initial screening of the titles and abstracts of the search results and assessed the eligibility of the articles. After removing duplicates and irrelevant literature, the two authors will assess the eligibility of the articles according to the inclusion criteria after reading the full text of the remaining articles separately. Any controversial points arising during this process will be referred to a third author (LY) and discussed until the dispute is resolved. The specific literature screening process will be summarised in a flow diagram.

Data extraction

Data to be collected, such as study details (first author, year of publication, study design, follow-up period, type of outcome), patient demographics (age, sex, American Society of Anesthesiologists score, tumour stage, etc), and the outcomes of interest mentioned above will be consolidated into a piloting spreadsheet. Additionally, we will extract the effect estimates of the outcome of interest for statistical analysis. If there were multiple representations of the data, we preferred to use the data after adjusting for confounding factors. To reduce bias and reduce errors in data extraction, the same two investigators (QD and JZ) independently extracted data from the included literature, cross-checked after extraction and disagreements were resolved by discussion and, if necessary, by asking a third author (LY) to resolve. Because this analysis was based on the intention-to-treat principle, all patients who were converted from the laparoscopic group to the conventional open surgery group remained in the laparoscopic group for analysis. We will also use sensitivity analyses to assess the impact of including studies that do not report intention-to-treat on overall outcomes.

There are currently several RCTs, such as COST, CLASICC, ALCCaS and COLOR, comparing laparoscopic and open colectomy, and we believe that inclusion of their data would enhance the quality of our evidence for this study. We will be sending emails to the authors of these trials asking for stratified data on left hemicolectomy. Meanwhile, for the missing data of other studies, we will also send an email to ask for.

Statistical analysis

Statistically, it is not possible to combine the median with the mean value, and only data expressed as the mean and SD can be used for meta-analysis. In this study, we will not use the median to estimate the mean, as other studies have done, because we believe this would not be worth the cost. The weighted mean difference or standardised mean difference and corresponding 95% CI were used for the analysis of continuous variables. The dichotomous variables were analysed using risk ratio values with 95% CIs. Considering the characteristics of survival analysis, we will first attempt to extract survival analysis-related data from the included studies and then calculate the pooled HR. HR and 95% CI will be extracted directly from the article, and if not reported in the article, we consider using software such as Engauge Digitizer to obtain the required data from Kaplan–Meier curves following the method provided by Parmar *et al*.[26] Finally, the obtained data will be integrated into the spreadsheet designed by Tierney *et al*[27] to calculate the HR and 95% CI. If the data were insufficient or the HR was not available for other reasons, then the pooled OR values of OS and DFS were calculated separately.

Statistical heterogeneity among the studies was calculated by χ^2 test and I^2 test.[28] We considered that high heterogeneity existed if the value of $p<0.1$ or $I^2>50\%$. When the heterogeneity was 0, the fixed-effects model was used, and when the heterogeneity was between 0% and 50%, the random-effects model was used. We will conduct subgroup analyses, based on different study design types and meta-regression so that we can explore the potential causes of heterogeneity and reduce it as accurately as possible when heterogeneity exceeded 50%. If the heterogeneity is too high, then qualitative analysis was performed. Sensitivity analysis will be performed to determine the robustness of the results by sequentially excluding one study at a time. A $p<0.05$ was considered statistically significant. Software such as RevMan V.5.4 and STATA V.16 will be used for statistical processing. Publication bias will be estimated by visual assessment of funnel plots if ≥10 studies are available. If the extracted data are not suitable for pooling, a systematic narrative synthesis will be presented in textual form.

Risk of bias assessment

Quality assessment will be carried out by two authors (QD and JZ), and discrepancies will be resolved through discussion. If consensus was not reached, then the third author (LY) was consulted for arbitration. The risk of bias in RCTs will be assessed using the Cochrane Risk of Bias Tool,[29] which includes six aspects: randomisation, allocation concealment, application of blinding, integrity of outcome data, selective reporting, and other biases. For each, we will use high risk, low risk or unclear risk to assess the results. The methodological quality of non-randomised controlled trials will be evaluated using the Newcastle-Ottawa Scale,[30] which consists of three aspects: patient selection, comparability of cohorts, and assessment of outcome. The total score is 9 stars, and each article is classified as low quality (0–5 stars) or high

quality (6–9 stars). The final results will be summarised in a table.

Evidence quality evaluation

The quality of evidence for each outcome will be evaluated using the Grading of Recommendations Assessment, Development and Evaluation system,[31] with four levels: high, moderate, low and very low.

Patient and public involvement

Since this study is a secondary study based on other studies, there will be no direct patient or public involvement in this study.

Ethics and dissemination

Because no patients were involved, ethical approval was not required. The final results of this research will be submitted to a peer-reviewed journal or presented at relevant conferences, and any deviations from this protocol will be recorded and explained in the final report.

Contributors The original idea was conceived by LY. QD and YY drafted the manuscript for this protocol. QD, YY, JZ, YW and LY participated in the design of the study and the setting of the inclusion and exclusion criteria. QD and YY design the search strategy, and XL will be responsible for the modifications. QD and JZ will perform the literature screening and data extraction. YW and LY will review the overall work. All authors read and approved the publication of the protocol.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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