Is the preservation of the left colic artery an ideal choice for colorectal cancer surgery? A meta-analysis

Ruize Qu
Peking University Third Hospital

Fei Li
Peking University Third Hospital

Bingyan Wang
Peking University Third Hospital

Siyi Lu
Peking University Third Hospital

Junren Ma
Peking University Third Hospital

Yanpeng Ma
Peking University Third Hospital

Yan Meng
Peking University Third Hospital

Junwei Wang
Peking University Third Hospital

Xin Zhou
Peking University Third Hospital

Wei Fu (fuwei@bjmu.edu.cn)
peking university third hospital

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Abstract

Background: Left colic artery (LCA) preservation or non-preservation in radical resection for colorectal cancer is still under debate. This study aimed to compare the perioperative and oncological outcomes between the two procedures.

Methods: Systematic search was performed in PubMed, Medline, Embase, Web of Science, and China National Knowledge Infrastructure databases for relevant randomized and non-randomized clinical trials published between 2011 and 2019. The primary endpoints were 5-year overall survival (OS), 5-year disease-free survival (DFS), total lymph nodes harvested, and anastomotic leakage. Secondary endpoints included the number of metastatic lymph nodes, intraoperative blood loss, urinary dysfunction, bowel obstruction, and operation time.

Results: Twenty-eight studies with 10545 patients (LCA non-preservation surgery, 4920; LCA preservation surgery, 5625) were included. Data of 7142 rectal cancer patients (LCA non-preservation surgery, 3468; LCA preservation surgery, 3674) were extracted for subgroup analysis. There was significantly lower incidence of anastomotic leakage (odds ratio=1.21; 95% confidence interval [1.04, 1.41]; P=0.015) in colorectal cancer patients with LCA preservation. When rectal cancer was independently analyzed, no significant difference was found in anastomotic leakage between the groups. There were significantly more metastatic lymph nodes and significantly shorter operation time in colorectal cancer and rectal cancer patients with LCA non-preservation. No significant difference was found regarding 5-year OS, 5-year DFS, total lymph nodes harvested, intraoperative blood loss, urinary dysfunction, and bowel obstruction for colorectal and rectal cancer.

Conclusions: LCA non-preservation was not proved to increase anastomotic leakage in rectal cancer surgery and was associated with more harvested metastatic lymph nodes and shorter operation time.

Trial registration: A review protocol was registered on PROSPERO (registration number: CRD42020183906) and http://www.researchregistry.com (registration number: reviewregistry841).

Background

Colorectal cancer (CRC) is the most common malignancy in the digestive system [1–3], and radical surgery is the first choice of treatment. Currently, there are two options in handling the left colic artery (LCA) that have caused endless debate in CRC surgery. For LCA non-preservation surgery, the inferior mesenteric artery (IMA) is ligated at its root with the apical lymph nodes dissected, and the LCA is ligated when handling the mesentery [4]. For LCA preservation surgery, the left colonic artery is exposed, and the IMA is ligated distal to the left colonic artery branch [5–7]. Many studies on this topic have been published, but a consensus has not been reached. Even meta-analyses regarding this topic still provide different opinions, in which studies across a long period were included, and surgeries for sigmoid colon cancer and rectal cancer (RC) were not analyzed separately [8–13]. With many new clinical trials published, these meta-analyses should be updated.

Thus, in this study, a meta-analysis was performed to determine whether the LCA should be preserved in CRC surgery, with RC surgery as an independent subgroup, comparing perioperative and oncological outcomes between LCA preservation and non-preservation procedures.

Methods

This meta-analysis was performed according to the Preferred Reporting items for systematic Reviews and Meta-Analyses (PRISMA) statement [14] and was registered in

Search Strategy

A systematic search was conducted in PubMed, Medline, Embase, Web of Science, and China National Knowledge Infrastructure databases for relevant studies that compare preservation and non-preservation of the LCA in RC surgery. Combinations of the following search terms were used: “left colic artery,” “left colic artery preservation,” “left colic artery non-preservation,” “high tie,” “high ligation,” “low tie,” “low ligation,” “rectum cancer,” “rectal cancer,” “rectal tumor,” “rectum cancer,” “rectum neoplasms,” “rectal neoplasms,” “colorectal neoplasms,” “colorectal cancer,” “colorectal tumor,” “colon neoplasms,” “colon cancer,” “colon tumor.” The search strategy for PubMed is displayed in the Appendix.

Inclusion criteria and exclusion criteria

The search findings were filtered and identified by two independent authors.

Criteria for inclusion: (1) studies published in English or Chinese; (2) studies of radical surgery comparing the preservation and non-preservation of the LCA; (3) studies including at least one of the required outcomes; and (4) randomized controlled trial (RCT), retrospective cohort (RC), prospective cohort (PC), and case-control (CC) studies of human CRC surgeries.

Criteria for exclusion: (1) studies such as case reports, editorial comments, letters, systematic review, and expert opinions; (2) studies including republished data; (3) studies without a control group; (4) studies performed on cadaver; and (5) animal trials.

Data Extraction
Primary relevant data were collected independently by two authors using standardized methods. The following data were extracted: first author, publication year, country, trial type, tumor location, the number of patients for each treatment method, patient recruitment period, and all outcomes of interest. When the required information is insufficient, the original authors were contacted to obtain the necessary data. The outcomes were categorized to primary and secondary observational endpoints. The primary observational endpoints included anastomotic leakage, total lymph node harvested, 5-year overall survival (OS), and 5-year disease-free survival (DFS), and the secondary observational endpoints included the number of metastatic lymph nodes, intraoperative blood loss, urinary dysfunction, bowel obstruction, and operation time.

Quality Assessment

The quality of each eligible RCT was assessed using the Cochrane scoring system [15]. Five quality items were included to evaluate the quality of an RCT, and each RCT was rated as having low, unclear, or high risk of bias. RC, PC, and CC studies were assessed using the Newcastle-Ottawa quality assessment scale [16]. The quality scale ranged from 0 to 9 points, and studies were considered of high quality when the NOS scale score was > 5. The quality of each study was assessed by two independent authors, with disagreements resolved via discussion.

Statistical Analyses

All statistical analyses were performed using Review Manager version 5.3 (Cochrane Collaboration, Oxford, UK) and STATA version 14 (StataCorp LP, College Station, Texas). The weighted mean difference (WMD) was applied to analyze continuous variables representing oncological, safety, and surgical outcomes. A reporting strategy was used for studies that did not report standard deviation (SD) values for the overall analysis [17]. For dichotomous variables, the odds ratio (OR) was calculated to identify the relative oncological and perioperative outcomes. Moreover, the Q test and the I^2 statistic were applied to estimate heterogeneity among studies. P < 0.05 and/or I^2 > 50% indicated heterogeneity, and a random-effect model was applied for the pooled analysis. A fixed-effect model was used if there was no heterogeneity. All statistical values were computed with 95% confidence intervals (CI), and P < 0.05 was considered statistically significant. Sensitivity analysis was performed to exclude potential heterogeneity-causing studies, including low quality studies and studies with extremely large sample sizes, to evaluate the disproportionate influence on the pooled results. Finally, publication bias was determined using funnel plots. Funnel plots and Begg’s test were applied to detect publication bias. P < 0.1 indicated statistical significance.

Results

Study Characteristics

After detailed evaluation, 28 studies were finally included (Fig. 1A). Details of the included studies were collected (Table 1). Seven RCTs [18–24], 19 RC/PC studies [25–43], and two CC studies [44, 45] published between 2011 and 2019 were analyzed, investigating 10,545 patients (including 4920 patients who underwent LCA non-preservation surgery and 5625 patients who underwent LCA preservation surgery) (CRC group). Additionally, 18 studies on RC alone (including 7 RCTs [18–24] and 11 RC/PC studies [25, 26, 28, 30–32, 35, 38, 39, 42, 43]) with 7142 patients (including 3468 patients who underwent LCA non-preservation surgery and 3674 who underwent LCA preservation surgery) were extracted for the subgroup analysis (RC group). Studies were assessed using the Cochrane and NOS scoring systems. Five RCTs have an unclear risk of bias [19, 20, 22–24], and two had a high risk of bias [18, 21]. In the RCT by Fujii et al. [18], the blinding of participants, personnel, and outcome assessors was not performed, and the RCT by Matsuda et al. [21] lacked the blinding of outcome assessment and had a high risk of bias. The other five studies did not adequately describe the allocation sequence concealment or lacked the blinding of participants, personnel, and outcome assessors. Therefore, these five studies had an unclear risk of bias (Fig. 1B). The NOS scale scores for observational studies were all higher than 6, indicating a high quality (Supplementary Table 1).
Table 1  
Characteristics of included studies in this meta-analysis

<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Country</th>
<th>Study Type</th>
<th>Study Type</th>
<th>Tumor Location</th>
<th>Surgical Method</th>
<th>Patient Recruitment Period</th>
<th>Involved Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charan</td>
<td>2015</td>
<td>India</td>
<td>RC</td>
<td>Rectum and colon</td>
<td>44</td>
<td>16</td>
<td>2007–2008</td>
<td>Total Lymph Nodes Harvested</td>
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<tr>
<td>Draganov</td>
<td>2019</td>
<td>Canada</td>
<td>RC</td>
<td>Rectum and colon</td>
<td>158</td>
<td>123</td>
<td>2002–2018</td>
<td>Anastomotic Leakage, Total Lymph Nodes Harvested</td>
</tr>
<tr>
<td>Guo</td>
<td>2017</td>
<td>China</td>
<td>RCT</td>
<td>Rectum</td>
<td>29</td>
<td>28</td>
<td>2013</td>
<td>Operation Time, Total Lymph Nodes Harvested</td>
</tr>
<tr>
<td>Kim</td>
<td>2019</td>
<td>Korea</td>
<td>CC</td>
<td>Rectum and colon</td>
<td>97</td>
<td>97</td>
<td>2011–2015</td>
<td>Anastomotic Leakage, Operation Time, Bowel Obstruction, Total Lymph Nodes Harvested, Metastatic Lymph Nodes</td>
</tr>
<tr>
<td>Komen</td>
<td>2011</td>
<td>Netherlands</td>
<td>PC</td>
<td>Rectum</td>
<td>16</td>
<td>17</td>
<td>2011</td>
<td>Anastomotic Leakage, Operation Time, Total Lymph Nodes Harvested, Metastatic Lymph Nodes</td>
</tr>
<tr>
<td>Kvemeng Hultberg</td>
<td>2016</td>
<td>Sweden</td>
<td>RC</td>
<td>Rectum</td>
<td>373</td>
<td>432</td>
<td>2011–2012</td>
<td>Anastomotic Leakage, Urinary Dysfunction</td>
</tr>
<tr>
<td>Lee</td>
<td>2018</td>
<td>Korea</td>
<td>RC</td>
<td>Rectum and colon</td>
<td>51</td>
<td>83</td>
<td>2008–2013</td>
<td>Anastomotic Leakage, Operation Time, Bowel Obstruction, 5-year Overall Survival, 5-year Disease-free Survival, Total Lymph Nodes Harvested, Metastatic Lymph Nodes</td>
</tr>
<tr>
<td>Mari</td>
<td>2019</td>
<td>Italy</td>
<td>RCT</td>
<td>Rectum</td>
<td>111</td>
<td>95</td>
<td>2014–2016</td>
<td>Anastomotic Leakage,</td>
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</tbody>
</table>

RC = Retrospective Cohort; PC = Prospective Cohort; RCT = Randomized Controlled Trial; CC = Case Control
<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Country</th>
<th>Study Type</th>
<th>Tumor Location</th>
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<th>Patient Recruitment Period</th>
<th>Involved Factors</th>
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<td>Park</td>
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<td>Korea</td>
<td>RC</td>
<td>Rectum and colon</td>
<td>613</td>
<td>163</td>
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<td>PC</td>
<td>Rectum</td>
<td>5</td>
<td>18</td>
<td>2012–2013</td>
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<tr>
<td>Tanaka</td>
<td>2015</td>
<td>Japan</td>
<td>CC</td>
<td>Rectum</td>
<td>16</td>
<td>341</td>
<td>2008–2013</td>
</tr>
<tr>
<td>Wang</td>
<td>2015</td>
<td>China</td>
<td>RCT</td>
<td>Rectum</td>
<td>63</td>
<td>65</td>
<td>2012–2013</td>
</tr>
<tr>
<td>Yasuda</td>
<td>2016</td>
<td>Japan</td>
<td>RC</td>
<td>Rectum and colon</td>
<td>42</td>
<td>147</td>
<td>1997–2007</td>
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<tr>
<td>Zedan</td>
<td>2016</td>
<td>Egypt</td>
<td>RC</td>
<td>Rectum</td>
<td>38</td>
<td>76</td>
<td>2007–2011</td>
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</table>

Primary Endpoints

Anastomotic Leakage

Twenty-five studies [18, 20–26, 28–35, 37–39, 41–46] compared anastomotic leakage between different surgical types. No heterogeneity was found among these studies; thus, a fixed-effects model was applied. The result showed that LCA preservation had a significantly lower incidence of anastomotic leakage than non-preservation surgery in the CRC group (OR = 1.21; 95% CI |1.04, 1.41|; P = 0.015) (Fig. 2A). For the RC group, no heterogeneity was found among these studies, and a fixed-effects model was employed. The meta-analysis implied no difference in anastomotic leakage between the preservation and non-preservation groups in RC, and the result was not altered in each subgroup of different experimental types (overall, OR = 1.16; 95% CI |0.986, 1.37|; P = 0.073; RCT, OR = 1.51; 95% CI |0.89, 2.56|; P = 0.128; non-RCT, OR = 1.13 95% CI |0.95, 1.34|; P = 0.164) (Fig. 2B).

Total Number of Lymph Nodes Harvested

For the CRC group, 15 studies [19, 21–23, 25, 27–29, 31, 33–35, 37, 43, 44] evaluated the total number of lymph nodes harvested. Heterogeneity was detected; thus, a random-effects model was employed. The analysis showed no significant difference between the two groups (WMD = 0.14; 95% CI |0.87, 0.59|; P = 0.707) (Fig. 2C). For the RC group, heterogeneity was found among studies reporting the total number of lymph nodes harvested; thus, a random-effects model was used. The result showed no significant difference in RC surgery between the two groups (WMD = -0.31; 95% CI |1.17, 0.54|; P = 0.472) (Fig. 2D).

5-year OS and 5-year DFS
For the CRC group, 10 studies [18, 25, 28, 33, 35–37, 41, 42, 46] assessed 5-year OS. No heterogeneity was detected in these studies; thus, a fixed-effects model was applied. No significant difference was found between LCA preservation and non-preservation in CRC surgery (OR = 0.98; 95% CI [0.89, 1.09]; P = 0.735) (Fig. 3A). Nine studies [18, 25, 33, 35–37, 41, 42, 46] analyzed 5-year DFS. No heterogeneity was found among these studies; thus, a fixed-effects model was applied. The result showed no significant difference between LCA and non-preservation in CRC surgery (OR = 0.95; 95% CI [0.85, 1.05]; P = 0.321) (Fig. 3B). For the RC group, no heterogeneity was found among the involved studies; thus, a fixed-effects model was applied. No significant difference was observed in both 5-year OS (OR = 0.94; 95% CI [0.82, 1.08]; P = 0.401) (Fig. 3C) and 5-year DFS (OR = 0.93; 95% CI [0.80, 1.09]; P = 0.377) (Fig. 3D) between LCA preservation and non-preservation in RC surgery.

Secondary Endpoints

Metastatic Lymph Nodes Harvested, Intraoperative Blood Loss, Urinary Dysfunction, Bowel Obstruction, and Operation Time

As secondary endpoints, the results of studies reporting the observation for perioperative outcomes were also analyzed. No heterogeneity was found among studies reporting the number of metastatic lymph nodes harvested, intraoperative blood loss (CRC group), urinary dysfunction, and bowel obstruction; therefore, a fixed-effects model was used for analysis. Heterogeneity was found among studies reporting intraoperative blood loss (RC group) and operation time; thus, a random-effects model was applied for analysis. The results showed no significant difference between the two procedures in both CRC and RC surgeries in terms of intraoperative blood loss (CRC group, WMD = 8.63; 95% CI [-1.30, 18.56]; P = 0.089; RC group, WMD = 5.41; 95% CI [-1.69, 12.50]; P = 0.135), urinary dysfunction (CRC group, OR = 1.09; 95% CI [0.66, 1.80]; P = 0.744; RC group, OR = 0.86; 95% CI [0.68, 1.10]; P = 0.232), and bowel obstruction (CRC group, OR = 1.00; 95% CI [0.73, 1.38]; P = 0.999; RC group, OR = 0.95; 95% CI [0.53, 1.71]; P = 0.857) (Table 2). The results also showed that more metastatic lymph nodes would be collected with the LCA non-preservation surgery in the CRC group and RC group (CRC group, WMD = 0.47; 95% CI [0.27, 0.68]; P < 0.001; RC group, WMD = 0.51; 95% CI [0.28, 0.73]; P < 0.001) (Fig. 3E and Sup Fig. 1A). Moreover, the operation time of LCA non-preservation surgery was significantly shorter than that of the preservation surgery in the CRC and RC groups (CRC group, WMD = -9.68; 95% CI [-13.04, -6.32]; P < 0.001; RC group, WMD = -14.61; 95% CI [-18.27, -10.95]; P < 0.001) (Fig. 3F and Sup Fig. 1B).
<table>
<thead>
<tr>
<th>Tumor Location</th>
<th>Outcomes</th>
<th>Involved Trials</th>
<th>Patient Number</th>
<th>Patient Number of Each Group</th>
<th>OR or WMD (95% CI)</th>
<th>P Value</th>
<th>p²</th>
<th>p value for heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC Group</td>
<td>Primary Observational Endpoints</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anastomotic Leakage</td>
<td>25</td>
<td>10116</td>
<td>4603 5513</td>
<td>1.21 (1.04, 1.41)</td>
<td>0.015*</td>
<td>0.0%</td>
<td>0.632</td>
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<tr>
<td></td>
<td>Total Lymph Nodes Harvested</td>
<td>15</td>
<td>4470</td>
<td>2385 2085</td>
<td>-0.14 (-0.87, 0.59)</td>
<td>0.707</td>
<td>62.3%</td>
<td>0.001</td>
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<tr>
<td></td>
<td>5-year Overall Survival</td>
<td>10</td>
<td>3864</td>
<td>2191 1673</td>
<td>0.98 (0.89, 1.09)</td>
<td>0.735</td>
<td>0.0%</td>
<td>0.937</td>
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<tr>
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<td>5-year Disease-free Survival</td>
<td>9</td>
<td>3748</td>
<td>2117 1631</td>
<td>0.95 (0.85, 1.05)</td>
<td>0.321</td>
<td>0.0%</td>
<td>0.789</td>
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<tr>
<td></td>
<td>Secondary Observational Endpoints</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metastatic Lymph Nodes</td>
<td>8</td>
<td>3552</td>
<td>1534 2018</td>
<td>0.47 (0.27, 0.68)</td>
<td>&lt; 0.001*</td>
<td>0.4%</td>
<td>0.426</td>
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<tr>
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<td>Operation Time</td>
<td>14</td>
<td>5707</td>
<td>2728 2979</td>
<td>-9.68 (-13.04, -6.32)</td>
<td>&lt; 0.001*</td>
<td>81%</td>
<td>&lt; 0.001</td>
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<td>Intraoperative Blood Loss</td>
<td>11</td>
<td>5192</td>
<td>2506 2686</td>
<td>8.63 (-1.30, 18.56)</td>
<td>0.089</td>
<td>70.3%</td>
<td>&lt; 0.001</td>
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<td>Urinary Dysfunction</td>
<td>10</td>
<td>3522</td>
<td>1589 1933</td>
<td>1.09 (0.66, 1.80)</td>
<td>0.744</td>
<td>51.7%</td>
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<td>Bowel Obstruction</td>
<td>10</td>
<td>3699</td>
<td>1549 2150</td>
<td>1.00 (0.73, 1.38)</td>
<td>0.999</td>
<td>25.3%</td>
<td>0.211</td>
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<td>RC-only Group</td>
<td>Primary Observational Endpoints</td>
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<tr>
<td></td>
<td>Anastomotic Leakage</td>
<td>18</td>
<td>7459</td>
<td>3434 4025</td>
<td>1.16 (0.99, 1.37)</td>
<td>0.073</td>
<td>0.0%</td>
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<tr>
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<td>Total Lymph Nodes Harvested</td>
<td>9</td>
<td>2163</td>
<td>1305 858</td>
<td>-0.31 (-1.17, 0.54)</td>
<td>0.472</td>
<td>59.4%</td>
<td>0.011</td>
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<td>5-year Overall Survival</td>
<td>5</td>
<td>1858</td>
<td>1155 703</td>
<td>0.94 (0.82, 1.08)</td>
<td>0.401</td>
<td>0.0%</td>
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<td>5-year Disease-free Survival</td>
<td>4</td>
<td>1742</td>
<td>1081 661</td>
<td>0.93 (0.80, 1.09)</td>
<td>0.377</td>
<td>0.0%</td>
<td>0.765</td>
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<td>Secondary Observational Endpoints</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Metastatic Lymph Nodes</td>
<td>5</td>
<td>2362</td>
<td>1269 1093</td>
<td>0.51 (0.28, 0.73)</td>
<td>&lt; 0.001*</td>
<td>34.1%</td>
<td>0.194</td>
</tr>
<tr>
<td></td>
<td>Operation Time</td>
<td>9</td>
<td>3055</td>
<td>1611 1444</td>
<td>-14.61 (-18.27, -10.95)</td>
<td>&lt; 0.001*</td>
<td>47.1%</td>
<td>0.057</td>
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<td>Intraoperative Blood Loss</td>
<td>8</td>
<td>2868</td>
<td>1537 1331</td>
<td>5.41 (-1.69, 12.50)</td>
<td>0.135</td>
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<td>Urinary Dysfunction</td>
<td>7</td>
<td>1695</td>
<td>817 878</td>
<td>0.86 (0.68, 1.10)</td>
<td>0.232</td>
<td>0.0%</td>
<td>0.522</td>
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<tr>
<td></td>
<td>Bowel Obstruction</td>
<td>4</td>
<td>1323</td>
<td>538 785</td>
<td>0.95 (0.53, 1.71)</td>
<td>0.857</td>
<td>9.9%</td>
<td>0.344</td>
</tr>
</tbody>
</table>

OR, odds ratio; WMD, weighted mean difference; 95% CI, 95% confidence interval; *Significantly Different
Risk of Publication Bias

Funnel plot analysis assessed the risk of bias of 5-year OS (Sup Fig. 2A), 5-year DFS (Sup Fig. 2B), and the total number of lymph nodes harvested (Sup Fig. 2C). No visual asymmetry was found in 5-year OS and 5-year DFS. However, the plot of the total number of lymph nodes harvested showed few points outside the limits of the 95% CI. Moreover, Begg's test showed no evidence of publication bias (P = 0.138 for the total number of lymph nodes harvested).

Sensitivity Analysis

Sensitivity analysis was performed for the analysis of anastomotic leakage, the total number of lymph nodes harvested, 5-year OS, 5-year DFS, the number of metastatic lymph nodes, and operation time in the CRC group. Studies were individually removed from the analysis to obtain new results, and no obvious bias was detected (Sup Fig. 3).

Discussion

In this meta-analysis, long-term outcomes of interest were generally comparable between LCA preservation and non-preservation in CRC surgery. The pooled results revealed that the rate of anastomotic leakage after LCA preservation surgery was slightly lower than that after non-preservation surgery. However, this difference became statistically insignificant in the pooled result of the subgroup analysis of RC alone. Moreover, LCA non-preservation surgery could dissect more metastatic lymph nodes than the LCA preservation surgery. The operative time was significantly shorter in LCA non-preservation surgery than in LCA preservation surgery.

Although some excellent meta-analyses have been published in the past few years, the optimal procedure for CRC in handling the LCA remains controversial [8–13]. To our knowledge, no published meta-analysis has compared the preservation and non-preservation of the LCA in RC alone. Therefore, we summarized previously reported data including more recently published and high-quality studies (especially RCTs), and to identify the optimal procedure for CRC, we compared the oncological and perioperative outcomes between LCA preservation and non-preservation in the surgical treatment of CRC and RC.

Anastomotic leakage is the most devastating complication in CRC surgery and one of the most important reasons why the optimization of the procedure in CRC is drawing so much attention. The reported postoperative occurrence risk is 2.2%-12% [47], despite the advancements in laparoscopic techniques and the well-accepted concept of total mesocolic excision. The blood supply and tension of the anastomosis are two major factors affecting the rate of anastomotic leakage [48]. In our opinion, for cancers located in the descending colon or the sigmoid colon, the ligation of the sigmoid artery and superior rectal artery would greatly compromise blood supply of the bowel distal to the anastomosis stoma. Meanwhile, blood supply from the pudendal artery system to the lengthy rectal stump is limited. Therefore, blood perfusion becomes a more important factor that could influence the healing of the anastomosis stoma. In RC, the rectal stump distal to the anastomosis stoma could be well perfused by blood supply from underneath. In this case, the relatively lower position of the anastomosis stoma may make the tension of the intestine a more dominant factor of anastomosis [49]. The conservation of the LCA would decrease the mobility of the proximal intestine by approximately 6–9 cm, which could increase the tension of the anastomotic stoma [50, 51], and this may balance out the benefit of better blood supply. Besides, a protective stoma of the distal ileum was more common in radical surgery for mid-low RC, which would also influence the diagnosis of anastomosis leakage [52]. To our knowledge, the balance between better perfusion provided by LCA preservation and the less tension of the colon limb proximal to the anastomotic stoma with LCA ligation should be determined by the location of the cancer and be evaluated according to the intraoperative circumstance of each case.

Lymph node dissection is a pivotal procedure in radical resection of CRC surgery [53]. The extent of lymph node involvement may be directly linked to the prognosis of CRC patients [54]. In LCA non-preservation surgery, the lymph nodes around the IMA should be removed as well, which could reportedly increase the number of lymph nodes harvested [55, 56]. In this case, regardless of whether the LCA should be preserved, the range of lymph node dissection would be theoretically the same and the number of the lymph nodes harvested would not differ, especially when new techniques to dissect the apical lymph node separately were introduced, as proved by our pooled results [56]. Regarding the number of metastatic lymph nodes harvested, our result showed that LCA non-preservation surgery can collect significantly more metastatic lymph nodes than LCA preservation surgery in both CRC and RC subgroups. This result might have been biased by non-RCTs on the assumption that high ligation tends to be performed in tumors with a higher N stage. However, detecting the difference in the N stage of cancers between the two groups was beyond the scope of this meta-analysis, which, we admit, is a limitation of this study.

Moreover, the 5-year OS rate and 5-year DFS rate are critical outcomes for evaluating the prognosis of patients with malignancy tumors including CRC [57]. OS and DFS are associated with postoperative complications and the number of total and metastatic lymph nodes collected [39]. Non-preservation of the LCA can reportedly benefit the 5-year OS and DFS rates of CRC patients [12, 21]. In this meta-analysis, no difference in these two outcomes was found between LCA preservation and non-preservation in both the CRC and RC subgroups. The reason might be the better prognosis of CRC after radical surgery, and apical lymph node metastasis is rarely seen in most colorectal tumors. Therefore, it is essential to identify CRC patients with apical lymph node metastasis during preoperative assessment.
In this meta-analysis, the operation time in non-LCA preservation surgery is statistically shorter in the CRC group and RC subgroup. The exposure of the LCA in LCA preservation surgery is very challenging, and the dissection of the mesentery distal to the left colon in laparoscopic surgery is also time-consuming. In comparison, direct ligation of the LCA during surgery is easier, with downregulated difficulty of separating blood vessels, which enables operators to perform the surgery more efficiently and conveniently. A higher incidence of urinary dysfunction is reportedly associated with LCA non-preservation surgery in CRC [8], but no statistical difference was found in our study. The related nerve is located around the root of the IMA and could be preserved from damage if dissection and ligation were done carefully 1–2 cm away from the root of the aorta.

Nevertheless, this meta-analysis still has some limitations. First, both RCTs and non-RCTs were included in the analysis, making it difficult to formulate a more comprehensive and rigorous conclusion [6]. In the future, extensive and well-designed clinical trials, especially multicenter RCTs, are required to resolve this dilemma. Second, the subgroup of colon cancer could not be evaluated independently. Some conclusions regarding colon cancer were a combination of overall results and results of the RC subgroup, which makes it less reliable. Finally, few studies are still focusing on the apical lymph node dissection in LCA preservation surgery; thus, further research is needed to provide better evidence.

**Conclusion**

No added risk of anastomotic leakage was found with LCA non-preservation surgery in RC. However, the preservation of the LCA tends to decrease anastomotic leakage in CRC surgery, and the difference may be linked to tumor location. Moreover, non-preservation of the LCA increased the number of potential metastatic lymph nodes collected and decreased the operation time, while the long-term prognosis was not affected, but further analysis is required. Therefore, LCA non-preservation surgery can be applied in low rectal carcinoma, depending on the condition of each patient. LCA preservation should be considered in high RC surgery and sigmoid or descending colon cancer surgery. Future studies should focus on low-lying RC and rectosigmoid cancer.

**Abbreviations**

CC: case-control
CI: confidence interval
CRC: colorectal cancer
DFS: disease-free survival
IMA: inferior mesenteric artery
LCA: left colic artery
NOS:
OR: odds ratio
OS: overall survival
PC: prospective cohort
RC: rectal cancer/retrospective cohort
RCT: randomized controlled trial
SD: standard deviation
WMD: weighted mean difference

**Declarations**

**Ethics approval and consent to participate**

This is not applicable as none of individual participants were included in this study.

**Consent for publication**

Not applicable.

**Availability of data and materials**
All data generated or analyzed during this study are included in this published article.

**Conflict of Interest**

The authors declare that they have no conflict of interest.

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**Authors’ contributions**

Study design: Wei Fu and Xin Zhou

Literature screening: Ruize Qu and Fei Li

Data analysis: Ruize Qu, Fei Li, Bingyan Wang, Siyi Lu, Junren Ma, Yanpeng Ma, Yan Meng, and Junwei Wang

Original draft writing: Fei Li and Ruize Qu

Review and editing: Xin Zhou and Wei Fu

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**References**


Supplementary Figure 2. Funnel plot for assessing the risk of bias: (A) 5-year overall survival, (B) 5-year disease-free survival, and (C) the total number of lymph nodes harvested.

Supplementary Figure 3. Sensitivity analysis for assessing the risk of bias. (A) Anastomotic leakage, (B) the total number of lymph nodes harvested, (C) 5-year overall survival, (D) 5-year disease-free survival, (E) the number of metastatic lymph nodes, and (F) operation time.

Figures

(A) Flow diagram depicting the process of the identification and inclusion of selected studies. (B) Cochrane risk of bias analysis for included randomized controlled trials.
Figure 2

Forest plot of the anastomotic leakage and total number of lymph nodes harvested. (A) Anastomotic leakage of the CRC group, (B) anastomotic leakage of the RC group, (C) the total number of lymph nodes harvested in the CRC group, and (D) the total number of lymph nodes harvested in the RC group. (CRC, colorectal cancer; LCA, left colic artery; RC, rectal cancer).
Figure 3

Forest plot of 5-year overall survival, 5-year disease-free survival, metastatic lymph nodes, and operation time. (A) 5-year overall survival of the CRC group, (B) 5-year disease-free survival of the CRC group, (C) 5-year overall survival of the RC group, and (D) 5-year disease-free survival of the RC group, (E) the number of metastatic lymph nodes, and (F) operation time. (CRC, colorectal cancer; LCA, left colic artery, RC, rectal cancer).

Supplementary Files

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