Review Article

Laparoscopic colectomy for colonic malignancy: review of literature

Charles Randall Cooper, Daniel L. Feingold

Division of Colorectal Surgery, Columbia University, New York, NY, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Charles Randall Cooper, MD. Division of Colorectal Surgery, Columbia University, 177 Fort Washington Avenue 7GS-313, New York, NY 10032, USA. Email: cc3773@cumc.columbia.edu.

Abstract: Despite advances in adjuvant and neoadjuvant chemotherapy for the treatment of colon cancer, complete surgical resection remains the mainstay of curative treatment. Laparoscopic surgery has been adopted to improve post-operative outcomes in comparison to open surgery. This review will examine and highlight the findings of several large, multicenter, randomized trials comparing open and laparoscopic colon resection. We will examine specifically the oncologic outcomes of the COLOR, CLASICC, COST, ALCCaS, and Barcelona trials as well as a large meta-analysis.

Keywords: Colectomy; colon cancer; minimally invasive colectomy; open versus laparoscopic colectomy

Received: 12 November 2018; Accepted: 28 December 2018; Published: 08 January 2019.
doi: 10.21037/ales.2018.12.12
View this article at: http://dx.doi.org/10.21037/ales.2018.12.12

Introduction

While laparoscopy for colon cancer, first reported in the early 1990's, demonstrated improved length of stay, less pain, reduced ileus and fewer surgical site infections, its adoption was slower than other laparoscopic procedures such as appendectomy or cholecystectomy due to concerns regarding oncologic adequacy and outcomes (1). In the early era of laparoscopy, there were concerns regarding surgical margins, lymph node harvest, and tumor recurrence, including port site recurrences. While there have been many small, single center studies looking at the outcomes of laparoscopic surgery, there are only a few large, multicenter, randomized trials examining oncologic outcomes; COST COLOR, CLASICC, and the ALCCaS (2-10) (*Table 1*). This review focuses on the major oncologic findings of these trials. We will also review the single center randomized Barcelona trial and a large meta-analysis. With regards to conversion, the trials all analyzed patient outcomes on an intent to treat basis. The majority of these trials were powered at 80%.

Methods

The above stated trials were reviewed and their findings summarized.

Discussion

Comparison of Laparoscopic Assisted and Open Colectomy for Colon cancer, the Clinical Outcomes of Surgical Therapy Study Group (COST) Trial (1,2)

The COST trial published in 2004 was a non-inferiority trial conducted at 48 institutions in the United States that randomized 872 patients with colon adenocarcinoma to either open (n=428) or laparoscopic assisted colectomy (n=435). All resections were performed by credentialed surgeons who performed at least 20 prior laparoscopic assisted colorectal operations. In this trial, laparoscopic assisted resections included laparoscopic mobilization and ligation of the vascular pedicle. The authors allowed for a small incision for bowel exteriorization, resection and anastomosis. Conversion was not clearly defined in

Table 1 Comparison of randomized trials

Trial	Single or multicenter	Patients analyzed	Disease-free survival laparoscopic, %	Disease-free survival open, %	Mean lymph node Lap, [range] or ± SD	Mean lymph node open, [range] or ± SD
COST (1,2)*	Multicenter	863	84	82	12	12
COLOR (3,4)*	Multicenter	1,082	74.2	76.2	10 [3–20]	10 [3–20]
CLASICC (5-7)*	Multicenter	794	66.3	67.74	12 [8–17]	13.5 [8–19]
ALCCaS (8,9)[&]	Multicenter	592	72.3	71.1	13 [1–74]	13 [1–51]
Barcelona (10)[&]	Single	206	83	73	11.1±7.9	11.1±7.4

*, 3-year follow up; [&], 5-year follow up.

this trial.

Median follow-up in the study was 4.4 years and the primary end point of the study was time to tumor recurrence. There were no differences in tumor location between the two groups; left, right or sigmoid colon. Rectal and transverse colon cancers were excluded from this trial. An intent to treat analysis was performed.

Oncologic and pathologic outcomes

In terms of specimen adequacy, resection margins in the open colectomy group had a median proximal margin of 12 cm (range, 3–50 cm) and the laparoscopic assisted group had a median margin of 13 cm (range, 2–7 cm), P=0.38. Regarding the distal margin, the open group had a median margin of 11 cm (range, 1–42 cm) and the laparoscopic group had a median distal margin of 10 cm (range, 2–40 cm), P=0.09. There was no difference in the percentage of resection margins less than 5 cm with 6% of the open colectomy patients having a close margin compared with 5% of the laparoscopic surgery patients (P=0.52). The median number of lymph nodes harvested in each group was 12.

After a median follow-up of 4.4 years there were 84 recurrences observed in the open colectomy group and 76 in the laparoscopic assisted group. There was no significant difference in time to recurrence in the laparoscopic compared to the open group with a hazard ratio of 0.86 (95% CI: 0.63–1.17, P=0.32). Overall survival rate of the two groups was similar, with a hazard ratio for death in the laparoscopic group of 0.91 (95% CI: 0.68–1.21, P=0.51). At follow up, 186 patients had died including 95 in the open group and 91 in the laparoscopic group (P=0.51).

The disease-free survival rate was similar in both groups with 117 recurrences in the open group and 118 observed in the laparoscopic group (95% CI: 0.74–1.23, P=0.70). The authors concluded "the absence of a difference in time to recurrence, disease-free survival and overall survival persisted in multivariate analysis adjusted for stratification factors".

Subsequently, in 2007, Fleshman *et al.* reported the 5-year follow-up results with a median follow-up of 7 years with a range 5 to 10 years (2). Disease-free survival was not statistically different (open group 68.4% and laparoscopic group 69.2%, P=0.94). The overall 5-year survival was similar for both surgical approaches (open group 74.6% and laparoscopic group 76.4%, P=0.93). Recurrence rates were similar at 5 years (open group 21.8% and laparoscopic group 19.4%, P=0.25). Port site recurrences, a concern since the beginning of laparoscopic colectomy, occurred in 2 patients in the laparoscopic assisted group (0.5%) and in 1 patient in the open group (0.2%), P=0.50.

Colon cancer Laparoscopic or Open resection (COLOR) trial (3,4)

Published in 2005, the COLOR trial was designed to compare 3-year disease-free survival and overall survival after open and laparoscopic resection for colon cancer. From 1997 and 2003, patients from 29 European hospitals with right or left colon cancer with BMI up to 30 were randomized to open or laparoscopic resection. The exact definition of laparoscopic surgery was not detailed. All surgical teams were credentialed and had performed at least 20 prior laparoscopic assisted colectomies. The primary outcome was disease-free survival at 3 years. Conversion was defined as inability to complete all "intended laparoscopic steps laparoscopically" and patients were analyzed according to intent to treat.

The trial included 542 patients in the open group and 535 patients in the laparoscopic group and had a median follow up of 53 months. No significant differences were observed between the groups with regards to age, sex, BMI,

ASA, prior abdominal operations or cancer location (right *vs.* left *vs.* sigmoid).

Oncologic and pathologic outcomes

In terms of specimen adequacy, a positive resection margin was found in 20 of 1,059 patients (10 in each group, P=0.96). There were 9 positive circumferential resection margins and 1 positive distal longitudinal margin in the laparoscopic assisted group. In the open resection group, there were 8 circumferential margins that were positive, 1 positive proximal margin, and 1 positive distal margin. Median lymph node harvest was 10 (10th through 90th percentile reported as 3–20) in both groups (P=0.32).

The primary outcome of the study showed that for all cancer stages, 3-year disease-free survival was 74.2% (95% CI: 70.4–78%) in the laparoscopic group and 76.2% (95% CI: 72.6–79.8%) in the open group (P=0.70). The difference in 3-year disease free survival was 2.0% and was not significant (95% CI: −3.2 to 7). The overall 3-year survival for all stages in the laparoscopic group was 81.8% (95% CI: 78.4–85.1%) and 84.2% (95% CI: 81.1–87.3%) in the open surgery group (P=0.45). Comparative survival rates were seen in stage specific analysis, as well. The laparoscopic group had 26, 56, and 23 local, distant, and combined recurrences, respectively, compared with 26, 56, and 12 in the open group (P=0.24).

Interestingly, at 3 years 1.3% of patients (7/534) in the laparoscopic assisted group and 0.4% of patients (2/542) in the open surgery group had recurrence in the abdominal wall (P=0.09). Five of the 7 in the laparoscopic group were at trocar sites and 2 were at extraction sites. This laparoscopic abdominal wound recurrence rate was the highest among the studies included in this review.

Deijen *et al.* performed a 10-year review of the 329 Dutch patients originally included in the trial and reported for disease-free survival, overall survival or recurrence there were no significant differences observed (11). The disease-free survival rates were 45.2% in the laparoscopic group and 43.2% in the open group (P=0.96).

Conventional vs. Laparoscopic-Assisted Surgery in Patients with Colorectal Cancer (CLASICC) Trial (5-7)

The CLASICC trial, published in 2005, accrued 794 patients with colon and rectal cancer from 27 United Kingdom centers between 1996 and 2002 who were randomized to laparoscopic assisted (n=526) or open (n=268) surgery. Laparoscopic surgery was defined as laparoscopic mobilization of bowel and vascular ligation; a small incision was allowed for removal of the resected specimen. A total of 413 patients had colon cancer. Primary endpoints of the study were resection margins and in-hospital mortality. This trial differed from the others in that it included rectal cancer resections and used a centralized pathologic review process that reviewed 93% of the specimens. There were no differences in baseline characteristics such as BMI, sex, tumor stage or tumor location. Thirty-four patients died in the hospital after surgery, 13 (5%) in the open group and 21 (4%) in the laparoscopic group (P=0.57). Conversion was defined as a "vertical abdominal incision greater in size than that needed for specimen retrieval" and intent to treat analysis was performed.

Oncologic and pathologic outcomes

Median lymph node harvest was 13.5 (range, 8–19) in the open surgery group and 12 (range, 8–17) in the laparoscopic assisted group, but the nodal harvest numbers were not subdivided into colon or rectum groups.

In cases of colon cancer, positive circumferential resection margins were identified in 5% (6/131) of the open group and in 7% (16/246) of the laparoscopic group (P=0.45). There were no longitudinal resection margins that were positive in the open surgery group and only one was reported in the laparoscopic group (this was in a patient who underwent conversion). The median distance between tumor and resection margin on the mesentery in the open group was 9 cm (IQR 7–11 cm) and was 8 cm (IQR 6.5–10 cm) in the laparoscopic group.

Jayne *et al.* published a 3-year follow up to the CLASICC trial and found no significant differences in major oncologic outcomes (6). Overall survival rates differed by 1.8% (95% CI: −5.2% to 8.8%, P=0.55). The authors also reported no significant difference in disease-free-survival with a difference of only 1.4% (95% CI: −9.5% to 6.7%), P=0.70. At 3 years, the local recurrence rates differed by 0.8% (95% CI: −5.7% to 4.2%), P=0.76.

Green *et al.* reported 10 year follow up data with an overall median survival for patients with colon cancer of 85.1 months (open group 105.7 months *vs.* laparoscopic groups 81.9 (P=0.35) (7). Interestingly, overall survival in patients who underwent conversion to open surgery was significantly worse than patients completed in open fashion or laparoscopically. The median survival of the converted group was 59.2 months compared to 78.4 months in the open surgery group and 94.8 months in patients who had a laparoscopic assisted resection (P=0.001). Median disease-

free survival for patients with colon cancer was 94.8 months with no significant difference between open (106 months) and laparoscopic (86.6 months), P=0.438. No significant differences were noted in terms of local or distant recurrences comparing the two groups.

Australasian Randomized Clinical Study Comparing Laparoscopic and Conventional Open Surgical Treatments for Colon Cancer (ALCCaS) Trial (8,9)

In this study, 601 colon cancer patients were accrued from 31 Australian and New Zealand hospitals between 1998 and 2005. Patients were randomized to laparoscopic-assisted (n=294) or open (n=298) surgery. Laparoscopic surgery was defined as laparoscopic mobilization and division of the vascular pedicle. A small abdominal incision was allowed for specimen extraction. The primary aim of the study was to determine 3 and 5-year disease-free survival. Baseline characteristics between the two groups were similar with the exception that the laparoscopic group was older (mean age 71.7 *vs.* 69.4 years old, P=0.04). Conversion was defined as in incision longer or different than the planned incision. The authors subsequently published a 5-year follow up with primary end points of 5-year overall survival, recurrence-free survival, and freedom from recurrence rates using an intent to treat analysis (9). A total of 587 patients were followed for a median of 5.2 years with a confirmed follow up for 96.6% (n=567) patients at 5 years.

Oncologic and pathologic outcomes

The median lymph node harvest in both groups was 13 nodes (P=0.15). The distal resection margin was >5 cm in 77.6% of the laparoscopic group. This was more than the 86.6% reported in the open group (P=0.004). In the 5-year follow-up analysis, there were no significant differences seen between the laparoscopic resection and open colon resection in terms of overall survival (77.7% *vs.* 76.0%, respectively, P=0.64). There was also no difference in terms of recurrence free survival between the laparoscopic and open groups (72.7% *vs.* 71.2, respectively, P=0.70) or freedom from recurrence (86.2% *vs.* 85.6, respectively, P=0.85).

Laparoscopic-assisted colectomy vs. open colectomy for treatment of non-metastatic colon cancer: a randomized trial (Barcelona Trial) (10)

Published in 2002 by Lacy *et al.*, this study randomized 105 patients to laparoscopic-assisted colectomy and 101 patients to open colectomy between 1993 and 1998. The primary endpoint of the study was cancer-related survival. Laparoscopic assisted surgery was not clearly defined in the paper and neither was conversion. The baseline characteristics of age, tumor location, and procedure performed were similar between the groups. Median length of follow up was 44 (range, 27–85) in the laparoscopic-assisted group compared with 43 (range, 27–85) in the open colectomy group. Patients were analyzed according to the intent to treat.

Oncologic and pathologic outcomes

Average lymph node harvest was 11.1 in both groups. The primary endpoint and the most significant finding in the paper was cancer related mortality, which was significantly lower in the laparoscopic assisted group (9%) compared to the open surgery group (21%), P=0.03. This difference in cancer related survival was due to outcomes of patients with stage III cancer. Overall mortality was not significantly different between groups (18% in the laparoscopic group compared with 26% in the open group, P=0.14). Tumor recurrence rate was 17% in the laparoscopic group and 27% in the open surgery group (P=0.07). There were no statistically significant differences in type of recurrence such as distant, locoregional, peritoneal or port site metastasis. The mean time to recurrence was not significantly different between groups either, with 15 months observed in the laparoscopic group and 17 months in the open group, P=0.66).

Given the statistically significant cancer related survival benefit demonstrated in this trial related to laparoscopic colectomy, the study was criticized for not being generalizable, as it was a single-center study with highly experienced, expert laparoscopists and also included a relatively small number of patients (12). The trial also did not clearly define laparoscopy and had no definition of conversion.

Transatlantic laparoscopic assisted vs. open colectomy study group meta-analysis (12)

The pooled data of the Barcelona, COST, CLASICC, and COLOR trials were used in a large meta-analysis to determine whether laparoscopic colectomy was oncologically adequate. The meta-analysis focused on overall survival and disease-free survival 3 years after randomization and included 796 laparoscopic patients and

740 open surgery patients.

Oncologic and pathologic outcomes

The mean number of lymph nodes in laparoscopic resections was 11.8 and was 12.2 in the open group (P=0.40). Positive resection margins were found in 2.1% of the open group and 1.3% of the laparoscopic group (P=0.23). The 3-year disease-free survival was not significantly different between the 2 operative approaches (open group 75.3%, laparoscopic group 75.8%, P=0.83). Overall survival was also similar (open group 83.5%, laparoscopic group 82.2%, P=0.56). There were no significant differences noted comparing individual stages, either; 121 recurrences were noted in the in the open group compared with 113 in the laparoscopic group (P=0.43) and the types of recurrences (local, distant, or combined) were similar, as well.

Conclusions

Laparoscopic surgery for colon cancer is oncologically equivalent to open surgery in terms of long-term overall survival, disease specific survival and pathologic findings such as nodal harvest and margin negativity.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editors (Michael J Stamos and Mehraneh Dorna Jafari) for the series "Laparoscopic Colon Surgery" published in *Annals of Laparoscopic and Endoscopic Surgery*. The article has undergone external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ales.2018.12.12). The series "Laparoscopic Colon Surgery" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Clinical Outcomes of Surgical Therapy Study Group, Nelson H, Sargent DJ, et al. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 2004;350:2050-9.
2. Fleshman J, Sargent DJ, Green E, et al. Laparoscopic colectomy for cancer is not inferior to open surgery based on 5-year data from the COST Study Group trial. Ann Surg 2007;246:655-62; discussion 662-4.
3. Veldkamp R, Kuhry E, Hop WC, et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol 2005;6:477-84.
4. Colon Cancer Laparoscopic or Open Resection Study Group, Buunen M, Veldkamp R, et al. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. Lancet Oncol 2009;10:44-52.
5. Guillou PJ, Quirke P, Thorpe H, et al. MRC CLASICC trial group. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet 2005;365:1718-26.
6. Jayne DG, Guillou PJ, Thorpe H, et al. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. J Clin Oncol 2007;25:3061-8.
7. Green BL, Marshall HC, Collinson F, et al. Long-term follow-up of the Medical Research Council CLASICC trial of conventional versus laparoscopically assisted resection in colorectal cancer. Br J Surg 2013;100:75-82.
8. Hewett PJ, Allardyce RA, Bagshaw PF, et al. Short-term outcomes of the Australasian randomized clinical study comparing laparoscopic and conventional open surgical treatments for colon cancer: the ALCCaS trial. Ann Surg 2008;248:728-38.

9. Bagshaw PF, Allardyce RA, Frampton CM, et al. Long-term outcomes of the Australasian randomized clinical trial comparing laparoscopic and conventional open surgical treatments for colon cancer: the Australasian Laparoscopic Colon Cancer Study trial. Ann Surg 2012;256:915-9.
10. Lacy AM, García-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet 2002;359:2224-9.
11. Deijen CL, Vasmel JE, de Lange-de Klerk ESM, et al. Ten-year outcomes of a randomised trial of laparoscopic versus open surgery for colon cancer. Surg Endosc 2017;31:2607-15.
12. Bonjer HJ, Hop WC, Nelson H, et al. Transatlantic Laparoscopically Assisted vs. Open Colectomy Trials Study Group (2007) Laparoscopically assisted vs. open colectomy for colon cancer: a meta-analysis. Arch Surg 2007;142:298-303.

doi: 10.21037/ales.2018.12.12
Cite this article as: Cooper CR, Feingold DL. Laparoscopic colectomy for colonic malignancy: review of literature. Ann Laparosc Endosc Surg 2019;4:3.

