Colon and Rectal Cancer: Laparoscopic or Open?

Anne-Marie Boller and Heidi Nelson

Abstract Early experiences with laparoscopic colectomy were unfavorable, with higher than expected rates of wound tumor implants and concerns about short and long-term compromised oncologic outcomes. Several international randomized controlled trials were initiated to address concerns regarding compromised oncologic outcomes. Each of the trials was designed to test the hypothesis that level 1 evidence supports the general feasibility and recovery advantage as well as cancer equivalence of laparoscopic colectomy in curable colon cancer. The following four phase III randomized controlled trials have completed accrual and reported early data on recovery benefits for laparoscopic colectomy: Barcelona, Clinical Outcomes of Surgical Therapy Study Group (COSTSG), Colon Cancer Laparoscopic or Open Resection (COLOR), and Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASICC). These trials have uniformly and consistently shown a significant reduction in the use of narcotics and oral analgesics and length of hospital stay, as well as a faster return of diet and bowel function, with laparoscopic colectomy. Two of the trials, Barcelona and COSTSG, have sufficient maturation and follow-up to report recurrence and survival data, and neither has found a survival disadvantage in patients treated with laparoscopic colectomy. Results of the Barcelona trial suggest a cancer-related survival advantage in patients treated with laparoscopic colectomy, based solely on differences in patients with stage III disease; this is not confirmed by the COSTSG trial. Results of the CLASICC and COLOR trials, as well as 5-year data from the COSTSG trial, should definitively address survival results. The investigational experience with laparoscopic rectal cancer is not as mature; the subset of rectal cancer patients (n = 253) in the CLASICC trial provides the only available randomized controlled trial data. Laparoscopic colectomy in patients with curable cancer is accepted as an alternative to open colectomy, whereas the viability of laparoscopic rectal cancer resection requires further investigation.

Colorectal cancer is the third leading diagnosed cancer in the United States and the second leading cause of cancer-related deaths in Western countries (1). In 2004, an estimated 106,000 cases of colon cancer and 41,000 cases of rectal cancer were diagnosed in the United States, resulting in ~57,000 total deaths (1). Data from the United States Surveillance Epidemiology and End Results program indicate that the overall incidence of and mortality from colorectal cancer have been on the decline in the United States (2). Several factors, including surveillance and prevention programs, novel adjuvant and neoadjuvant therapeutic regimens, and the standardization of surgical techniques (e.g., total mesorectal excision), have contributed to the improved prognosis in colon and rectal cancer. Because surgery remains the primary treatment modality in colorectal cancer, the introduction of rapidly evolving laparoscopic techniques in the treatment of patients with colon and rectal cancer has been met with appropriate concern and resistance. Indeed, the advent and widespread acceptance of laparoscopic surgery for benign abdominal conditions has fueled the debate regarding the application of this technique in cases of cancer. Fortunately, many ongoing and future clinical trials will continue to define the role of laparoscopic surgery in the treatment of colon and rectal cancer.

Laparoscopic Colectomy in Colon Cancer

Laparoscopic resection of the colon was first described in 1990 (3). Although techniques and equipment were at first cumbersome, laparoscopic colectomy for benign and malignant conditions of the colon soon became a reality. Early reports regarding laparoscopic-assisted colectomy revealed a more rapid recovery from surgery and decreased surgical complications. Yet, wound site recurrence, which reached 21% in some studies, raised significant concerns about this technique (4). Ultimately, a virtual moratorium was placed on the laparoscopic-assisted method in colon cancer, as investigators awaited clinical evidence of its safety and feasibility. In response, four multi-institutional randomized controlled trials accrued patients to compare the effect of laparoscopic-assisted colectomy versus standard open resection on colon cancer recurrence and survival (5–8). Two trials, Barcelona and Clinical Outcomes of Surgical Therapy Study Group (COSTSG), have accrued long-term follow-up data (43 months and 3 years,

Authors' Affiliation: Division of Colon and Rectal Surgery, Mayo Clinic, Rochester, Minnesota
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Requests for reprints: Heidi Nelson, Division of Colon and Rectal Surgery, Mayo Clinic, Rochester, MN 55905. Phone: 507-284-3329; Fax: 507-284-1794; E-mail: Nelson.heidi@mayo.edu.

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respectively; refs. 7, 8). The Colon Cancer Laparoscopic or Open Resection (COLOR) and Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASICC) trials await such data (5, 6).

Results of Laparoscopic Colectomy in Colon Cancer

As a result of the above-mentioned randomized controlled trials, level 1 evidence is now available to support the advantages and to refute the disadvantages of laparoscopic colectomy in curable colon cancer. Morbidity and mortality rates were similar in the four trials, as were operative findings (5–8). Length of surgery in the laparoscopic-assisted arm in each of the trials ranged from 24 to 55 min and was consistently longer than that in the open arm; the incision was ~12 cm longer in the open arm than in the laparoscopic arm.

The four randomized controlled trials also revealed similar patient-related benefits (5–8). For example, the laparoscopic-assisted technique, compared with open surgery, caused a significant reduction in narcotic and oral analgesics requirements in the COSTSG trial. Similarly, the COLOR and CLASICC trials showed earlier resumption of fluid intake and a regular diet in laparoscopic colectomy than open surgery patients. Length of ileus, measured as time to first bowel movement, was significantly less (by 1 day) with laparoscopic colectomy in both the CLASICC and COLOR trials (7, 8). In COLOR, CLASICCC, and COSTSG, hospital stay was significantly reduced in laparoscopic patients (5, 6, 8).

Survival and long-term cancer outcome data are mature in the Barcelona and COSTSG trials. Barcelona trial investigators published the first long-term cancer outcome data (follow-up of 43 months) for laparoscopic colectomy (7). No difference in overall or disease-free survival was reported for any stage of disease, although cancer-related survival was significantly higher in the laparoscopic-assisted group than in the open surgery group (7). Analyzed individually, stage III cancer patients in the laparoscopic group had significantly improved overall and cancer-related survival, compared with patients in the open colectomy group (7). Similar differences were not observed in patients with stage I or II disease.

COSTSG investigators published long-term cancer outcome data (median follow-up of 4.4 years; ref. 8). Overall and disease-free survival and time to recurrence were similar in the laparoscopic-assisted and open surgery groups, establishing that the laparoscopic technique was not inferior to open surgery in the treatment of colon cancer. These findings were consistent in all stages of disease and persisted in multivariant analysis after adjustment for stratification factors. Tumor recurrence at the surgical wound was reassuringly rare throughout the study and without significant difference in the two study arms. Overall, there were only three total wound site recurrences (two in the laparoscopic surgery group and one in the open colectomy group; ref. 8).

Current Indications for Laparoscopic Colectomy in Colon Cancer

Despite early concerns regarding the use of the laparoscopic-assisted technique in the removal of colon cancer, solid level 1 evidence now exists to support its equivalence to the standard open approach. Multiple clinical studies have established the general feasibility of the laparoscopic approach in the management of colon cancer. Data presented above from the four prospective randomized controlled trials are convincing. The CLASICC and COLOR trials, as well as 5-year data from the COSTSG trial, should definitively address survival results. There is no reason not to offer laparoscopic colectomy in all stages of colon cancer in contemporary clinical practice.

Laparoscopic Proctectomy in Rectal Cancer

Although clinical trials have established the safety and feasibility of laparoscopic colectomy in colon cancer with rates of recurrence and survival that are equivalent to open surgery, no equivalent evidence exists for the laparoscopic approach in the treatment of rectal cancer. Although laparoscopic colectomy for colon cancer continues to gain acceptance, laparoscopic resection for rectal cancer remains controversial. Only one of the four randomized controlled trials mentioned above evaluated a subset of patients with rectal cancer (5–8).

Numerous issues unique to rectal cancer and its resection have contributed to its exclusion from recent prospective clinical trials. Surgical resection is the most important treatment modality for rectal cancer in terms of cure, staging, prognosis, and subsequent therapeutic decision-making. Additionally, the surgical integrity and pathologic staging of the resection is the most important prognostic factor in recurrent rectal cancer. Laparotomy and meticulous total mesorectal excision, as advocated by Heald et al. (9), is currently the accepted standard of care for middle and low rectal cancers. This technique has consistently been associated with low recurrence and optimal survival (10–12). Laparoscopic resection of rectal cancer must duplicate these oncologic results and show equivalence with open surgery through solid level 1 evidence to become an accepted surgical modality for rectal cancer.

Results of Laparoscopic Proctectomy in Rectal Cancer

Several single-center studies have shown the feasibility of laparoscopic-assisted resection of rectal cancer. Many authors have published significant case-series studies establishing the safety of the laparoscopic approach to rectal cancer (13, 14). Cumulatively, >1,200 patients have been included in laparoscopic rectal cancer case-series studies. Feliciotti et al. (13) prospectively studied laparoscopic-assisted and open resections and found both methods to respect surgical oncologic principles, with similar long-term outcomes. Other studies have mimicked these results (14).

Several single-center case-series studies have evaluated morbidity and mortality in laparoscopic rectal resection. Prospective studies have revealed that laparoscopic resection, compared with open surgery, did not worsen survival or disease control in patients with rectosigmoid cancer (15). A review of the literature found that laparoscopic resection for rectal carcinoma is not associated with high morbidity or mortality (16).

Two recent meta-analyses reviewed the current literature on the laparoscopic resection of rectal cancer (17, 18). Gao et al. (18) analyzed 11 studies (1995-2005), which included 285 patients who had undergone laparoscopic resection for rectal cancer. The authors found that laparoscopic surgery was

associated with lower morbidity, but longer operative time; wound infection, anastomotic leakage, and mortality were similar in the open and laparoscopic groups. Aziz et al. (17) analyzed 20 studies (1993-2004), which included 909 patients who had undergone laparoscopic resection and 1,162 who had undergone open resection for rectal cancer. The analysis revealed a reduction in length of hospital stay and time to first bowel movement and stomal function in patients who underwent laparoscopic surgery. Specifically, in the set of patients requiring abdominal perineal resection, laparoscopic patients required fewer parenteral analgesics and had a reduced rate of postoperative wound infection (17). In both meta-analyses, oncologic outcome was similar in the open and laparoscopic surgery groups (17, 18).

Although results from multiple case-series and case-matched studies seem optimistic, solid level 1 evidence to support the practice of laparoscopic resection in rectal cancer is lacking. Only one large, prospective, randomized trial of laparoscopic surgery has reported on both colon and rectal cancer (6), and this trial specifically raised concerns about laparoscopic rectal resection. The conversion rate was 29% (n = 143 conversions; 61 colon and 82 rectal cases) in the entire cohort and 34% (82 of 242) in rectal cases (total rectal cases n = 242). In the rectal surgery subgroup, circumferential radial margin positivity was greater in the laparoscopic than open surgery group, a difference that was not realized in the abdominal perineal laparoscopic procedure group, but that was specific to the laparoscopic low anterior resection procedure. Although this difference did not reach statistical significance, the trend was toward higher margin positivity with laparoscopic low anterior resection than open surgery. These findings raise concerns as to the level of precision that is achievable in laparoscopic surgery and the question of whether laparoscopic-assisted resection is a safe, effective oncologic approach to rectal cancer. A critical level of clinical equipoise has been reached and must be addressed with a prospective, randomized trial of laparoscopic-assisted surgery for rectal cancer.

Future Directions for Laparoscopic Proctectomy in Rectal Cancer

Members of the American College of Surgery Oncology Group have developed a prospective, randomized, phase II trial to test the hypothesis that laparoscopic surgery is a technically and oncologically safe and feasible approach to the resection of rectal cancer. The primary end point of the trial is a composite of oncologic and technical factors that are indicative of a safe and feasible operation. Oncologic variables include adequacy of lymph node harvest and circumferential and distal margin status. Technical factors include anastomotic leak rate and incidence of iatrogenic rectal perforation. These variables are based on surgical guidelines for rectal cancer published in 2001 (19). Disease-free survival and local pelvic recurrence will be evaluated as secondary end points at 2 years. Quality-of-life measures, sexual function outcome, length of stay, and recovery data will be implemented preoperatively, immediately postoperatively, and at established follow-up intervals in the trial. Until our clinical equipoise is resolved regarding this technique, all surgeons and investigators must contribute to the clinical research that addresses laparoscopic rectal surgery.

Through prospective, randomized trials, the appropriate place of laparoscopic surgery will be established in the field of rectal cancer. To establish the equivalency of the laparoscopic approach, all laparoscopic rectal resections should be completed in an environment wherein outcomes can be meaningfully evaluated and the clinical relevance of laparoscopic resection can be determined.

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