Improving Colon Cancer Survival with Surgical Technique

Lacy AM, Garcia-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.

Study Overview

Objective. To compare the efficacy of laparoscopy-assisted colectomy (LAC) and open colectomy (OC) for treatment of nonmetastatic colon cancer in terms of tumor recurrence and survival.

Design. Prospective randomized study. Analysis was by intention-to-treat.

Setting and participants. From November 1993 to July 1998, all patients admitted to a hospital unit of the University of Barcelona with a diagnosis of adenocarcinoma of the colon, 15 cm above the anal verge, were assessed for eligibility. Patients were excluded if they had cancer in the transverse colon, distant metastases, adjacent organ involvement, intestinal obstruction, or prior colonic surgery. Patients were randomized the day before surgery according to tumor location (right or left with respect to the splenic flexure) and assigned to either LAC or OC. Interim analysis was performed to assess early morbidity, recurrence, and port-site metastases. Preoperative preparations, general anesthesia, and postoperative management were the same for both groups. Both LAC and OC were done by a single surgical team with laparoscopic experience. Tumors were classified according to the TNM staging system. Postoperative adjuvant chemotherapy included standard schedules and doses of fluorouracil and either levamisole (between 1993 and 1995) or calcium folinate (between 1995 and 1998) for patients with stage II and III tumors. Postoperative surveillance included medical history, physical examination, and laboratory studies including carcinoembryonic antigen (CEA) measurements. Imaging, including computed tomography, was done every 6 months and total colonoscopy was done yearly.

Main outcome measure. Cancer-related survival. Secondary outcomes included probability of overall survival and being free of recurrence.

Main results. Of 442 eligible patients, 219 were enrolled after meeting eligibility criteria (111 in the LAC group and 108 in the OC group). The median length of follow-up was 43 months. Baseline characteristics were similar between the 2 groups. Participants were near 70 years of age, and generally had moderately differentiated stage I, II, and III tumors. 61% of the LAC group and 55% of the OC group received adjuvant chemotherapy. Patients in the LAC group recovered sooner, with shorter peristalsis-detection and oral-intake times ($P = 0.001$) as well as shorter hospital stays ($P = 0.005$). Operative time and intraoperative blood loss were lower in the LAC group. The rate and type of recurrence, time to recurrence, and number of patients who had curative reoperation were similar in both groups. Morbidity was lower in the LAC group ($P = 0.001$), although LAC did not influence perioperative mortality. The probability of cancer-related survival was higher in the LAC group ($P = 0.02$). By Cox modeling, LAC was independently associated with a reduced risk of tumor relapse (hazard ratio [HR], 0.39 [95% confidence interval {CI}, 0.19–0.82]), overall survival (HR, 0.48 [95% CI, 0.23–1.01]), and death from a cancer-related cause (HR, 0.38 [95% CI, 0.16–0.91]) compared with OC. This superiority of LAC was specifically seen in patients with stage III tumors ($P = 0.04$, $P = 0.02$, and $P = 0.006$, respectively).

Conclusion. LAC is more effective than OC for treatment of colon cancer in terms of morbidity, hospital length of stay, tumor recurrence, and cancer-related mortality.

Commentary

Colon cancer is the second leading cause of cancer-related mortality in America. After diagnosis, most patients will undergo surgery with curative intent [1]. Depending on stage, the 5-year survival ranges from near 40% to 100%, although data are limited for patients with extensive nodal involvement. Laparoscopic surgery has been a promising alternative to open procedures for curative surgery because of evidence suggesting advantages in reducing operative morbidity and shortening hospital stays [2]. However, laparoscopy is complex, and concerns remain over intra-abdominal complications and port-site or other recurrences. Moreover, early quality of life (QOL) results released by investigators and the monitoring committee for an ongoing large randomized trial comparing LAC with OC in terms of disease-free and overall survival found only minimal gains in 2-week postoperative QOL for laparoscopy [3].

Lacy et al conducted a well-designed study that also sought to compare LAC with OC in terms of disease recurrence and

related survival. The study has several strengths: a randomized prospective design, well-defined primary objectives, balanced perioperative and adjuvant care, and an intention-to-treat analysis. The study clearly showed that patients who underwent LAC had shorter recoveries, fewer complications, shorter stays, and less morbidity than similar patients who underwent open procedures. To the authors' surprise, LAC also was associated with less recurrent disease and related-mortality compared with OC. The Kaplan-Meier curves begin to separate at 24 months.

However, it is important to note that these differences were limited to stage III tumors—representing 73 total patients. Indeed, the differences in cancer-related mortality were based on a comparison of 10 and 21 patients in the LAC and OC groups respectively (albeit statistically significant.) There also were too few patients for fair comparisons of some postoperative complications that occur at low frequencies. One final critique is that the study was conducted at a single institution by one surgical team.

Applications for Clinical Practice

LAC for curative resection of nonmetastatic colon cancer remains somewhat controversial in the United States. Though several studies have shown LAC results in less perioperative morbidity and shorter stays when compared with OC, conclusions regarding recurrence and survival benefits await the results of other well-designed studies, such as the previously mentioned trial sponsored by the National Cancer Institute. Why LAC would result in improved survival for more advanced disease remains unknown but deserves study.

–Review by David R. Spigel, MD

References

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