Short-term Quality-of-Life Outcomes Following Laparoscopic-Assisted Colectomy vs Open Colectomy for Colon Cancer

A Randomized Trial

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Context Laparoscopic-assisted colectomy (LAC) has emerged as the preferred minimally invasive surgical strategy for diseases of the colon. The safety and efficacy of LAC for colon cancer are unknown, and the nature and magnitude of any quality-of-life (QOL) benefit resulting from LAC for colon cancer is also unknown.

Objective To compare short-term QOL outcomes after LAC vs open colectomy for colon cancer.

Design, Setting, and Participants Multicenter, randomized controlled trial (Clinical Outcomes of Surgical Therapy [COST]). Between September 1994 and February 1999, 37 of 48 centers provided data for the QOL component of the trial for 449 consecutive patients with clinically resectable colon cancer.

Main Outcome Measures Scores on the Symptoms Distress Scale (SDS), Quality of Life Index, and a single-item global rating scale at 2 days, 2 weeks, and 2 months postoperative; duration of postoperative in-hospital analgesic use; and length of stay.

Results Of 449 patients, 428 provided QOL data. In an intention-to-treat analysis comparing SDS pain intensity, SDS summary, QOL Index summary, and global rating scale scores at each time point, the only statistically significant difference observed between groups was the global rating scale score for 2 weeks postsurgery. The mean (median) global rating scale scores for 2 weeks postsurgery were 76.9 (80) for LAC vs 74.4 (75) for open colectomy ($P=.009$). While in the hospital, patients assigned to LAC required fewer days of both parenteral analgesics compared with patients assigned to open colectomy (mean [median], 3.2 [3] vs 4.0 [4] days; $P<.001$) and oral analgesics (mean [median], 1.9 [1] vs 2.2 [2] days; $P=.03$).

Conclusion Only minimal short-term QOL benefits were found with LAC for colon cancer compared with standard open colectomy. Until ongoing trials establish that LAC is as effective as open colectomy in preventing recurrence and death from colon cancer, this procedure should not be offered to patients with colon cancer.

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Although laparoscopic techniques were first described in 1901,[1] only in the past few years have newer optics and instrumentation allowed for the safe application of laparoscopic resection procedures. The first report of a successful laparoscopic cholecystectomy in 1987 was followed by rapid widespread adoption of the procedure.[2-6] In recent years, laparoscopic procedures for a number of other nonmalignant abdominal diseases, including appendicitis, inguinal hernia, gastroesophageal reflux disease, hiatal hernia, and nonmalignant uterine conditions, have become routine. The interest in laparoscopic approaches for these conditions has been driven by the theoretical benefits, including reduced postoperative pain, shortened length of stay, and earlier return to work, and perhaps by the technological imperative.[5,6]

Improvements in both technology and surgeons' comfort and skill with laparoscopic techniques have led to an interest in extending the indications for laparoscopic surgery to include curative resection of colon cancer. In laparoscopic-assisted colectomy (LAC), mobilization of the bowel is conducted laparoscopically and then the bowel is externalized for resection and anastomosis. Laparoscopic-assisted colectomy has emerged as the preferred minimally invasive strategy for colonic

See also p 377 and Patient Page.

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operations. Several uncontrolled case series have suggested that patients undergoing LAC experience more rapid return of bowel function.[7-11] One small randomized trial comparing laparoscopic with open resections for colorectal tumors found some evidence of decreased postoperative pain among patients undergoing laparoscopic resection.[12] In this trial, follow-up was short and did not include a comprehensive assessment of patients' symptoms. A rigorous evaluation of the nature and magnitude of any quality-of-life (QOL) benefit resulting from LAC is critical. In contrast to procedures performed for nonmalignant conditions, the benefits of laparoscopic resection of colon cancer must be weighed against the potential for poorer long-term cancer outcomes attributable to inadequate resection, port site recurrences, or unusual spread of metastases.[13-17]

To address the risks and benefits of LAC for colon cancer, the National Cancer Institute funded the randomized controlled Clinical Outcomes of Surgical Therapy (COST) study, which was initiated by the North Central Cancer Treatment Group in 1994. The Eastern Cooperative Oncology Group, Cancer and Leukemia Group B, South Western Oncology Group, Radiation Therapy Oncology Group, National Cancer Institute of Canada Clinical Trials Group, and National Surgical Adjuvant Breast Project joined the study, which has been designated as a high-priority trial by the National Cancer Institute.

The primary objective of this COST study was to test the hypothesis that disease-free survival and overall survival following LAC and open colectomy are equivalent. The trial was also designed to test the hypothesis that LAC is associated with superior QOL outcomes.

Enrollment in the QOL component of the study was closed in February 1999 after target accrual for that component was met. To meet the ethical obligation to fully inform patients considering enrollment in this and similar ongoing studies, the North Central Cancer Treatment Group External Data Monitoring Committee and the investigators chose to release the short-term QOL results while the trial was ongoing. The External Data Monitoring Committee also approved the release of several clinical data elements considered essential to the meaningful interpretation of the short-term QOL data (duration of postoperative in-hospital analgesic use, length of stay for the initial hospitalization, and data on conversion from LAC to open colectomy) for patients participating in the QOL component of the study. Overall accrual to the trial was closed on August 21, 2001. The results, with respect to other end points, will not be available for several years.

METHODS

Patients

To be eligible for the clinical study, patients had to be at least 18 years old and have a clinical diagnosis of adenocarcinoma involving a single colon segment. Patients with any concurrent or previous malignant tumor (within the previous 5 years) except superficial nonmelanoma skin cancer or in situ cancer of the cervix were ineligible. Patients were also excluded if they had transverse colon cancer, rectal cancer, an acutely obstructed or perforated colon cancer requiring urgent surgery, evidence of metastatic disease on preoperative studies, scars, adhesions, or advanced local disease that would preclude laparoscopic surgery, or an American Society of Anesthesiologists' physical status classification of IV or V.[18] Additionally, to be eligible for the QOL component, patients had to be able to communicate in English, be free of cognitive impairment, and have a telephone at home or at place of employment. Canadian centers did not participate in the QOL component of the study. The study protocol was approved by the institutional review boards of all participating institutions and all patients provided written informed consent.

Surgery

Laparoscopic-assisted colectomies and open colectomies were performed and monitored according to protocol guidelines. In the LAC procedure, an intracorporeal approach, using multiple small ports, carbon dioxide insufflation of the abdomen, and insertion of a small laparoscope and working instruments, was used to mobilize the colon, explore the abdomen for extent of disease, identify critical structures, and ligate the vascular pedicle. The mobilized, tumor-containing bowel was then exteriorized through a small incision, typically less than 6 cm in length, and standard extracorporeal techniques were used to resect and anastomose the bowel.[19]

Intraoperative conversion to an open colectomy among patients assigned to LAC was allowed at the discretion of the surgeon to overcome technical difficulties, or if more extensive procedures were needed to address conditions arising during surgery. In an effort to maximize cancer control, intraoperative conversion to an open colectomy was required if advanced local disease or positive margins were found. Patients were considered to have been converted if and only if the primary procedure could not be completed using laparoscopic techniques. Anesthesia and postoperative care were provided according to the standard practice of each surgeon investigator. All participating surgeons agreed that these standard practices would not differ between treatment groups. Options for postoperative analgesia included parenteral, intramuscular, intravenous, and epidural narcotics, and ad-lib oral analgesics. Use of parenteral and oral analgesics was recorded daily during the hospital stay.

To become credentialed and eligible to enter patients in the study, surgeons had to demonstrate experience with at least 20 laparoscopic colonic surgical cases and had to submit a video demonstrating proper oncological techniques. For surgical quality assurance, laparoscopic procedures performed on trial patients were videorecorded and members of the COST executive committee audited a randomly selected subset of the first 500 cases.

The 37 centers participating in the trial included tertiary referral academic centers and private practices, lo-

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cated in rural, central areas of the central United States, as well as large urban areas on both coasts.

Randomization was conducted after informed consent but prior to surgery by a telephone call to the North Central Cancer Treatment Group central office after completion of an eligibility checklist. Treatment assignment was balanced for the stratification factors of primary surgeon, site of primary tumor (right, left, or sigmoid), and American Society of Anesthesiologists' classification (I and II vs III), using a minimization procedure.[20]

QOL Assessment

Patients were surveyed with standardized instruments for assessing symptoms and QOL. Each of these instruments had been previously validated in trials of cancer patients. Patient self-reported symptoms were measured using the Symptoms Distress Scale (SDS).[21] This 13-item scale measures symptom frequency and distress in the domains of nausea, appetite, insomnia, pain, fatigue, bowel, concentration, appearance, breathing, outlook, and cough. All items have response categories scaled from 1 through 5 with verbal descriptors for each response category. The response categories for the pain distress item are: (1) When I do have pain it is very mild; (2) When I do have pain it is mildly distressing; (3) The pain I do have is usually fairly intense; (4) The pain I have is usually very intense; and (5) The pain I have is almost unbearable. The SDS summary score is a total for the 13 items, with higher scores indicating poorer QOL.[22]

Quality of life was measured with the QOL Index (QLI) and a global rating scale. The 5-item QLI measures QOL in 5 domains (activity, daily living, health, support, and outlook). Each item has response categories describing normal functioning (scored as 0), moderately impaired functioning (scored as 1), and severely impaired functioning (scored as 2). The QLI summary score is a total of these items, with higher scores indicating poorer QOL. Global QOL was assessed by asking respondents "On a scale of 0 to 100, with 0 being death, and 100 being excellent health, which number would you say best describes your state of health over the past 2 weeks?"[23]

All instruments were administered preoperatively and 2 days, 2 weeks, and 2 months postoperatively. However, the QLI and the global rating scale were omitted from the 2-day postoperative assessment. Surveys were self-administered for patients who were in the clinic or hospital at scheduled assessment time points, and by telephone interviews with sites' data management staff otherwise.

Statistical Analysis

For evaluation of disease-free survival, the primary end point, the study design called for an accrual of 1200 patients. However, it was recognized that the entire cohort might not be required to evaluate the QOL end points. Therefore, the study protocol specified that an interim analysis be conducted on the first 200 patients (100 in each arm) to estimate the variability in the pain distress item and the global rating scale. When this target was met, the SD of each measure at all time points in each group was calculated and used to determine the minimum sample size needed to obtain a 95% confidence interval of ±0.5 for the difference in the pain distress score and ±5 for the difference in the global rating scale. Differences of this magnitude were identified prospectively in the study protocol as the minimum clinically meaningful differences for these 2 measures. More patients were required to achieve the criteria for the global rating scale and the total target accrual of 416 subjects for the QOL analysis was established.

All comparisons between groups were intention-to-treat analyses in which patients were analyzed according to assigned treatment group. Descriptive data on outcomes among patients assigned to LAC who received LAC and patients who ended up receiving open colectomy are reported. However, we did not perform statistical tests comparing outcomes between groups defined by procedure received rather than procedure assigned. Statistical analyses of QOL outcomes evaluated the differences between the open surgery and the LAC groups with respect to the change from preoperative scores for each time point.

Data managers were required to classify the reason for any missing QOL data elements. For most time points there were minimal missing data due to patient illness (1-11 patients per assessment). The exception was the 2-day time point when the SDS item for appetite was missing for 70 patients and the item for bowel was missing for 68 patients. This pattern of missing data would be expected if some patients who did not yet have oral intake or had not had return of bowel function after surgery chose not to respond. In calculating the SDS summary score for the 2-day time point, we imputed values equal to the 25th percentile for all responding patients, arranged from worst to best for these 2 items. A secondary analysis in which a similar imputation was performed for all items classified as missing due to patient illness produced similar results and is not reported. We also conducted analyses in which imputed values were set equal to the best possible score and the worst possible score for all patients, and in which the imputation differed in the 2 treatment groups (the best possible score in one group and the worst possible score in the other). In all but 1 case, these strategies produced results similar to the primary analysis. The exception was the strategy in which values imputed for patients in the LAC group were set at the highest level and for those in the open colectomy group at the lowest level, which resulted in a statistically significant difference in the day 2 SDS summary score in favor of the LAC group.

The change scores for the SDS pain scale, the SDS summary score, the QLI summary score, and the global rating scale values were compared using Wilcoxon rank-sum tests separately for each time point.[24] The SDS score for the item measuring pain distress, the summary score of the QLI, and the global rating scale were selected prospectively in the study protocol as the primary variables of interest to minimize the number of statistical comparisons.

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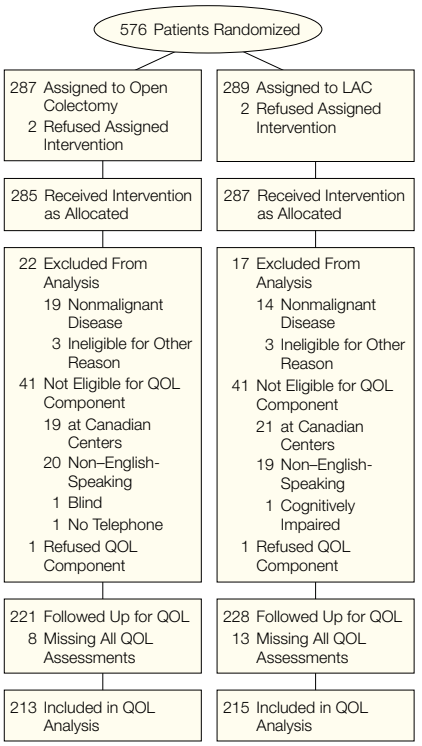
Figure 1. Clinical Outcomes of Surgical Therapy Trial



Patients shown are those accrued to the trial during the period the QOL component was open. LAC indicates laparoscopic-assisted colectomy; QOL, quality of life.

Mixed-effect models of repeated measures with unstructured covariance using SAS software[25] were used to evaluate longitudinal comparisons.

Analyses were conducted to determine if key outcome measures varied by surgeon, and to determine if a learning curve effect was present. These analyses focused on the outcomes of conversion (yes or no), length of stay, and the change in 2 QOL outcomes (the change in pain distress and global rating scale scores from baseline to 2 weeks). Analysis of variance models were used to test the association between surgeon and the length of stay and QOL outcomes. The Fisher exact test was used to test the association of surgeon and the rate of conversion. In these analyses, surgeons who performed 10 or fewer surgeries were combined into a single low-volume group. Linear, logistic, and proportional odds regression models (as appropriate) were used to test for an experience-based improvement in the outcomes of conversion (logistic regression), length of stay (linear regression), the change in global rating scale score from baseline to 2 weeks (proportional odds regression), and the change in the pain distress score from baseline to 2 weeks (linear regression). These models included terms for the trial experience at the time each surgery was performed by the individual surgeon (ie, the surgeon's first, second, etc, patient in the study), the treatment group (open colectomy vs LAC), and the interaction of these 2 terms. All P values reported are 2-sided and $P<.05$ denotes statistical significance.

RESULTS

Patients

Study enrollment began in September 1994. The QOL component of the study was closed to enrollment in February 1999 when the number of patients eligible for this component reached the predetermined target sample size. Of the 576 patients enrolled at that time, 43 were excluded from the study (4 refused treatment assignment; 33 were found to have nonmalignant disease; and 6 were ineligible for other reasons; FIGURE 1). Sixteen patients were found at surgery to have metastatic disease and these patients are included in this analysis. An additional 84 patients were excluded from the QOL analysis (40 were enrolled at Canadian centers, 39 were non–English-speaking, 1 was blind, 1 was cognitively impaired, 1 did not have a telephone, and 2 refused). Therefore, 449 patients were available for this analysis, of whom all but 21 provided some QOL data.

At the 2 month follow-up, 29% of patients in the open colectomy arm and 33% of patients in the LAC arm reported having received chemotherapy ($P=.58$). Five patients underwent repeat surgery during the 2-month follow-up period (2 in the open colectomy arm and 3 in the LAC arm). Four patients died before the 2-month follow-up assessment (2 in each arm). The characteristics of study patients are shown in TABLE 1. There were no statistically significant differences between treatment groups in any of the characteristics examined. Characteristics of patients for whom QOL data were missing were similar to those of patients for whom this information was available, although they were more likely to be nonwhite and to have stage IV disease.

Clinical Outcomes

Perioperative clinical outcomes relevant to the QOL analysis for patients participating in that component of the study are shown in TABLE 2. In an intention-to-treat analysis based on assigned treatment group, patients in the LAC group required somewhat shorter durations of both oral and parenteral analgesic therapy while hospitalized ($P=.03$ and $P<.001$, respectively), and their mean length of stay for the initial hospitalization was shorter by 0.8 days ($P<.001$).

QOL Assessments

Median QOL scores by assessment time point are shown in TABLE 3. In univariate analyses comparing preoperative scores with follow-up QOL scores, the only statistically significant difference between arms was in the global rating scale score at 2 weeks. At that time point, patients assigned to LAC reported slightly better overall QOL. In models examining longitudinal comparisons, only the mean (median) global rating scale scores at 2 weeks postsurgery (76.9 [80] for LAC vs 74.4 [75] for open colectomy) approached statistical significance for the interaction between treatment and assessment time point ($P=.09$).

Of the 226 patients assigned to LAC for whom information was available, 58 (25.7%) required conversion to open colectomy (Table 1). Among patients assigned to LAC, patients who required conversion reported slightly poorer QOL for all measures at baseline and every follow-up assessment than patients who received LAC.

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As demonstrated graphically in FIGURE 2, there was substantial temporal variation in pain distress and total symptom distress. Two-day postoperative scores indicated substantial increases in distress in all groups. By 2 weeks after surgery, scores had declined to below preoperative baseline levels. Further improvement was evident at 2 months.

Determinants of Outcomes

There was no statistically significant association between medical center and the proportion of patients assigned to LAC who received open colectomy ($P=.28$), length of stay ($P=.49$), change in global rating scale score from baseline to 2 weeks ($P=.79$), or change in the pain distress score from baseline to 2 weeks ($P=.64$). We also looked for evidence of a learning curve in multivariate models examining the relationship between surgeon experience at the time of each surgery, and length of stay, and 2 QOL outcomes (the pain distress and global rating scale scores at 2 weeks), controlling for treatment group. No experience-based trends were seen for the outcomes of conversion ($P=.34$), length of stay ($P=.62$), change in global rating scale score from baseline to 2 weeks ($P=.48$), or change in the pain distress score from baseline to 2 weeks ($P=.99$). There was no evidence of an interaction between any of these outcome measures and type of procedure (open colectomy vs LAC).

COMMENT

Our findings demonstrate that compared with open colectomy, LAC for colon cancer results in statistically significant but clinically modest decreases in the duration of postoperative in-hospital analgesia and in length of stay (0.8 days). However, these differences do not translate into statistically significant improvements in symptoms or QOL in the immediate postoperative period or over 2 months of follow-up.

The literature on the QOL benefits associated with minimally invasive surgery for other conditions is dominated by uncontrolled case series. A review of previously published randomized controlled trials reveals some inconsistency in the results of apparently similar studies, perhaps related to

Table 1. Characteristics of the Patients*

Characteristic	No. (%) Assigned to Open Colectomy (n = 221)	No. (%) Assigned to Laparoscopic-Assisted Colectomy (n = 228)†
Age, mean (range), y‡	69.4 (38-95)	68.2 (28-96)
Men	108 (48.9)	118 (51.8)
Race		
Asian	6 (2.7)	1 (0.4)
Black	20 (9.1)	16 (7.0)
Hispanic	5 (2.3)	10 (4.4)
White	190 (86.0)	200 (87.7)
Other	0 (0)	1 (0.4)
Tumor stage§		
I	69 (31.4)	88 (39.1)
II	78 (35.5)	77 (34.2)
III	62 (28.2)	57 (25.3)
IV	11 (5.0)	5 (1.3)
ASA classification		
I or II	189 (85.5)	198 (86.0)
III	32 (14.5)	32 (14.0)
Assigned laparoscopic-assisted colectomy but converted to open colectomy intraoperatively		58 (25.7)
Advanced disease	NA	11 (4.8)
Positive margins	NA	3 (1.3)
Inability to adequately visualize critical structures	NA	10 (4.4)
Inability to mobilize colon	NA	4 (1.8)
Adhesions	NA	12 (5.3)
Intraoperative complications	NA	4 (1.8)
Associated complicating disease	NA	2 (0.9)
Other	NA	12 (5.3)

*ASA indicates American Society of Anesthesiologists.
†Data were missing for 2 patients.
‡Data were missing for 4 patients.
§Data were missing for 4 patients.

Table 2. Clinical Outcomes*

		Assigned to Laparoscopic-Assisted Colectomy (LAC) (n = 228)			
	Assigned to Open Colectomy (n = 221)	All (n = 228)†	Converted to Open Colectomy (n = 58)	Not Converted to Open Colectomy (n = 168)	Open Colectomy vs LAC *P* Value
Oral analgesics, d‡	2.2 (0.15) [2]	1.9 (0.15) [1]	2.3 (0.33) [2]	1.7 (0.16) [1]	.03
Parenteral narcotics/analgesics, d	4.0 (0.16) [4]	3.2 (0.17) [3]	4.4 (0.34) [4]	2.8 (0.18) [2]	<.001
Length of stay, d	6.4 (0.23) [6]	5.6 (0.26) [5]	7.4 (0.58) [6.5]	5.1 (0.28) [4]	<.001

*Values are expressed as mean (SE) [median].
†Conversion data were missing for 2 patients.
‡Information on days with oral analgesics was missing for 3 patients (2 in the open colectomy group and 1 in the LAC group).

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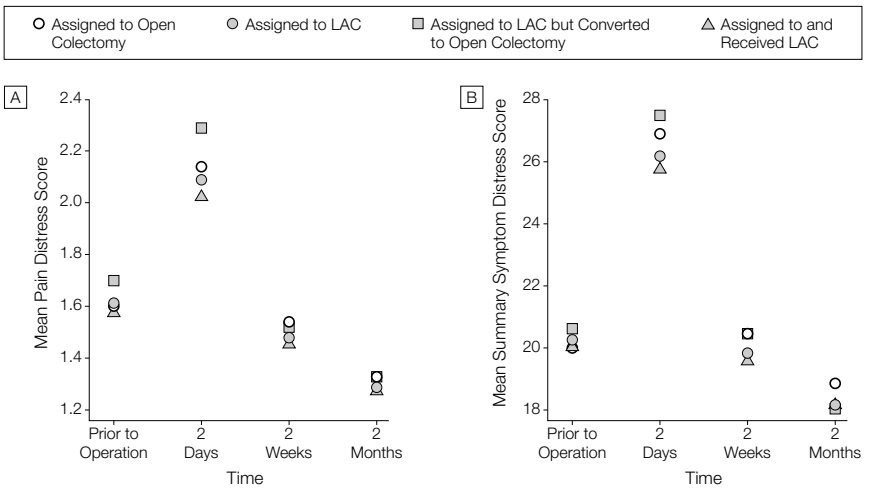
Table 3. Quality-of-Life Scores by Assessment Period and Treatment Arm*

			Assigned to Laparoscopic-Assisted Colectomy (LAC) (n = 228)					
	Assigned to Open Colectomy (n = 221)		All (n = 228)†		Converted to Open Colectomy (n = 58)		Not Converted to Open Colectomy (n = 168)	
Assessment	No. of Patients	Median (Interquartile Range)	No. of Patients	Median (Interquartile Range)	No. of Patients	Median (Interquartile Range)	No. of Patients	Median (Interquartile Range)
Preoperative								
Pain distress‡	207	1 (1-2)	213	1 (1-2)	53	1 (1-2)	160	1 (1-2)
SDS summary	196	19 (16-22)	206	19 (16-23)	51	19 (16-24)	155	19 (16-23)
QLI summary	196	0 (0-1)	204	0 (0-1)	50	0 (0-1)	154	0 (0-1)
Global rating scale	198	90 (75-95)	206	80 (70-90)	52	82.5 (72.5-90)	154	80 (70-95)
2 Days postoperative§								
Pain distress‡	198	2 (1-3)	203	2 (1-3)	49	2 (2-3)	154	2 (1-3)
SDS summary	179	26 (21-32)	183	25 (20-31)	41	26 (22-33)	142	24.5 (20-30)
2 Weeks postoperative								
Pain distress‡	194	1 (1-2)	201	1 (1-2)	50	1 (1-2)	151	1 (1-2)
SDS summary	190	19 (16-23)	190	18 (15-23)	46	20 (16-23)	144	18 (15-23)
QLI summary	189	1 (0-2)	194	1 (0-2)	48	1 (0-3)	146	1 (0-2)
Global rating scale‖	192	75 (60-90)	196	80 (70-90)	48	80 (67.5-87.5)	148	80 (75-90)
2 Months postoperative								
Pain distress‡	180	1 (1-2)	199	1 (1-1)	48	1 (1-1.5)	151	1 (1-1)
SDS summary	175	17 (14-21)	192	17 (15-22.5)	45	16 (14-19)	147	17 (15-21)
QLI summary	172	0 (0-1)	191	0 (0-1)	46	0 (0-2)	145	0 (0-1)
Global rating scale	176	90 (80-95)	195	90 (75-95)	49	90 (80-95)	146	90 (75-97)

*SDS indicates Symptoms Distress Scale; QLI, Quality of Life Index.
†Conversion data were missing for 2 patients.
‡Measured with the single item from the SDS.
§Missing values due to illness were imputed for 2 items in the 13-item questionnaire.
‖P = .009 by Wilcoxon rank-sum test for comparison of change in score from preoperative baseline between groups assigned to open colectomy and to LAC.

Figure 2. Temporal Changes in Distress Scores



LAC indicates laparoscopic-assisted colectomy.

patient selection. Most published studies with a QOL component have found some benefit for minimally invasive surgery, most commonly in surrogate end points, such as analgesic requirements or postoperative pain.[26-30] The magnitude of the differences we observed is not inconsistent with this literature. However, we recognized that any QOL benefit we found would need to be weighed against the effectiveness of LAC in curing cancer. As a result, we demanded more definitive evidence of a meaningful benefit than many prior studies in patients with nonmalignant conditions. Furthermore, we sought evidence that patients themselves appreciated this benefit rather than relying on proxy measures for QOL, such as analgesic requirements or even length of stay. We did not find this evidence.

One possible explanation for our failure to detect differences by treatment group in patients' QOL is that the instruments used to measure QOL were unresponsive to meaningful differences. The striking temporal changes in scores on all instruments, as well as the fact that the small, nonsignificant differences observed between groups were all in the expected direction, argue against this interpretation. These differences did not reach statistical significance partly because of the sample size. However, the sample size was calculated prospec-

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tively to provide adequate power to detect differences regarded as clinically meaningful. Therefore, we cannot conclude that the study was underpowered. The slightly longer duration of in-hospital analgesic use required by patients assigned to open colectomy suggests that effective analgesia may have blunted the difference in postoperative pain between treatment groups. The lack of statistically significant differences in aggregate symptom distress scores suggests that this increased analgesic requirement did not result in any clinically meaningful increases in other bothersome symptoms, however.

The rate of conversion to open colectomy among patients assigned to LAC in this study deserves discussion. Based on earlier, single-institution case series in selected patients undergoing LAC for a variety of conditions, we anticipated a 20% conversion rate for patients assigned to LAC.[31] That the actual conversion rate proved to be 25% among unselected patients in a large multi-institutional study of patients with cancer should not be surprising, especially given that 7% of all patients assigned to LAC required conversion for reasons related to their tumors (advanced disease or positive margins). In addition, the rates of conversion as well as the clinical and QOL outcomes were stable throughout the study period. They did not differ significantly between surgeons, and there was no learning curve within individual surgeons. The heterogeneity of the institutions participating in this study and the stability of intermediate and QOL outcomes over time both support the generalizability of the findings and suggest that if LAC were adopted as standard practice in the community, outcomes similar to those reported here might be expected.

It is interesting that on all measures, and at all assessments, including the preoperative baseline as well as follow-up assessments, patients assigned to LAC who required intraoperative conversion to open colectomy had slightly poorer QOL outcomes than patients who successfully underwent minimally invasive resection. Because our goal was to evaluate LAC as a strategy for managing unselected patients with newly diagnosed colon cancer, data for all patients randomized to LAC were aggregated in an intention-to-treat analysis. Nonetheless, our results suggest that if criteria could be developed to allow the preoperative identification of patients at low risk for intraoperative conversion, the procedure could be used selectively in patients most likely to realize benefits. The fact that several nonrandomized case series of LAC have shown lower rates of intraoperative conversion and shorter lengths of stay than we observed may be explained in part by just such selection by experienced laparoscopic surgeons.[32,33]

Several limitations of this study should be noted. First, only data on the use of inpatient intravenous and oral analgesia were collected. Use of patient-controlled analgesia, regional analgesia, and outpatient analgesics after discharge were not recorded. Second, no data were collected on the site to which patients were discharged (eg, home or nursing home). Therefore, we cannot comment on whether these factors differed by treatment group. However, our data suggest that any effect of treatment assignment on these intermediate outcomes did not translate into a meaningful difference in patients' QOL in the 2 months after surgery.

The American Society of Colon and Rectal Surgeons issued a policy statement in 1994 that LAC for colon cancer should not be performed outside of a randomized controlled clinical trial.[34] Our results confirm this position. The modest benefits in short-term QOL proxy measures we observed are not sufficient to justify the use of this procedure in the routine care setting until the safety and efficacy of the procedure in the treatment of cancer have been definitively established.

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Acquisition of data: Weeks, Nelson, Gelber, Sargent, Schroeder.
Analysis and interpretation of data: Weeks, Nelson, Gelber, Sargent, Schroeder.
Drafting of the manuscript: Weeks, Nelson, Gelber, Sargent, Schroeder.
Critical revision of the manuscript for important intellectual content: Nelson, Gelber, Sargent.
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Language most shows a man: Speak, that I may see thee. It springs out of the most retired and inmost parts of us, and is the image of the parent of it, the mind. No glass renders a man's form or likeness so true as his speech.
—Ben Jonson (c1573-1637)

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