Laparoscopic-Assisted Versus Open Surgery for Colorectal Cancer: Short- and Long-Term Outcomes Comparison

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Abstract

Background: Despite the theoretical advantages of laparoscopic surgery, it is still not considered the standard treatment for colorectal cancer patients because of criticism concerning oncologic stability. This study aimed at examining the short- and long-term follow-up results of laparoscopic surgery versus open surgery for colorectal cancer and at investigating clinical outcomes, oncologic safety, and any potential advantages of laparoscopic colorectal cancer resection.

Subjects and Methods: We retrospectively analyzed a database containing the information about patients who underwent surgery for stage I–III colorectal cancer from January 2004 to January 2012 at our institution.

Results: The patients who underwent the laparoscopic-assisted procedure showed a significantly faster recovery than those who underwent open surgery, namely, less time to first passing flatus ($P = .041$), time of first bowel motion ($P = .04$), time to resume normal diet ($P = .043$), and time to walk independently ($P = .031$). Laparoscopic colorectal surgery caused less pain for patients, leading to lower need of analgesic ($P = .002$) and less hospital recovery time ($P = .034$), compared with patients who underwent open surgery. No differences were found in 3- and 5-year overall and disease-free survival rates.

Conclusions: Our results suggested that the laparoscopic approach was as safe as the open alternative. Laparoscopic-assisted surgery has been shown to be a favorable surgical option with better short-term outcomes and similar long-term oncological control compared with open resection.

Introduction

COLON CANCER REPRESENTS one of the leading cause of death worldwide, and the indications for laparoscopic surgery have expanded gradually.^{1–3} Indeed, laparoscopic colorectal resection has been shown to have more benefits for postoperative recovery, such as postsurgical pain and hospital stay,⁴ and long-term survival,^{5–7} leading to a general acceptance of laparoscopic surgery as an alternative to conventional open surgery for colon cancer.⁸ However, despite the theoretical advantages of laparoscopic surgery, it is still not considered the standard treatment for colorectal cancer patients because of criticism concerning oncologic stability. Potential risks regard

port-site recurrence after curative resection of tumor and incomplete lymph node dissection. In fact, given the technical difficulty of this treatment, laparoscopic colorectal resection is often limited by the need for experienced surgeons. Thus, from a public health perspective, there are controversies regarding the cost-effective value of this treatment, taking into account such issues and the greater economic costs compared with conventional surgery.

This study aimed at examining the short- and long-term follow-up results of laparoscopic surgery versus open surgery for colorectal cancer over a period of 8 years in our center and at investigating clinical outcomes, oncologic safety, and any potential advantages of laparoscopic colorectal cancer resection.

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Subjects and Methods

We retrospectively analyzed a database containing information about patients who underwent surgery for stage I–III colorectal cancer from January 2004 to January 2012 at our institution. Patients were consecutively enrolled and allocated to laparoscopic-assisted or conventional open surgery without any specific indication for one of the two procedures. Patients were assigned to each surgical procedure according to the target dates for treatment and operating theater availability. Patients for whom emergency surgery was needed because of an accompanying complication such as cancer perforation or failure of the self-expanding stent insertion in patients with colorectal cancer obstruction, cases in which colorectal cancer had invaded an adjacent organ or required a multi-organ surgery, and cases in which curative resection could not be performed were excluded from the study.

Preoperative characteristics were obtained regarding age, gender, body mass index, American Society of Anesthesiologists score, and co-morbidities. Pathological and perioperative data analyzed included tumor location, operative time, blood loss, sample length, proximal and distal margin length, number of retrieved lymph nodes, tumor size, pathological differentiation, and clinical stage. Postoperative data analyzed included analgesic usage, peristalsis recovery time, time until flatus, off-bed, first liquid, and semi-liquid intake, and duration of hospital stay. Early and late postoperative complications were also collected.

All patients were followed up after being discharged from the hospital. Survival was calculated in months from the date of diagnosis to the date of death or to the date of the last visit to the outpatient clinic. For patients who did not visit our hospital, telephone interviews were used. The last date for follow-up was December 2011. Data for patients who died or who remained alive at the date of last follow-up were censored.

Surgical technique

All operations were performed or supervised by a stable group of colorectal surgeons within a single surgical team for both laparoscopic-assisted and open surgery procedures. All patients had cefuroxime (1.5 g) and metronidazole (500 mg) administered intravenously at the time of induction of general anesthesia for systemic antibiotic prophylaxis. Other preoperative procedures were standardized, as followed for traditional abdominal surgeries.

For conventional open surgery, the patients were placed in the supine position, and a midline or right paramedian skin incision was performed. Open procedures were performed according to the standard techniques followed by the operating surgeon.

For laparoscopic surgery, the operations were performed with the patient in the modified lithotomy and Trendelenburg position. Pneumoperitoneum was created by the open method. In general, three to five 12-mm ports were used: an umbilical port for the laparoscopic camera and two (or one) ports each in the right and left sides. For extended right colectomy and transverse colectomy, the surgeon and camera operator stood to the left side of the patients, and for extended left colectomy, the surgeon and camera operator stood to the right side of the patients. The first assistant stood on the side opposite the surgeon, and the scrub nurse stood between the patient's legs.

The retroperitoneum and right colon mesocolon were divided, exposing the ventral aspect of the superior mesenteric vein. The ileocolic vessels, right colic vessels, and midcolic vessels were identified in that order. In transverse colectomy, both the transverse colon and the mesocolon were stretched for identification of the midcolic vessels. The terminal ileum, cecum, and ascending colon were mobilized up to the hepatic flexure, while the duodenum and right ureter were being protected. In extended left colectomy, using the medial approach, we identified the left colic artery.

In the laparoscopic group, anastomosis was performed by a small laparotomy.

Postoperative period

All patients enrolled in this study were managed postoperatively by the same group of surgeons. Patients in both groups were supported by infusions in the very first several hours after surgery. After confirmation of the peristalsis recovery, liquid diet was supplied. Semiliquid diet was considered suitable for patients after report of flatus. For pain control, patients were given patient-controlled anesthesia or short-acting drugs according to their own choice. Prophylactic antibiotics were used during the 72-hour period after surgery; however, if there was any indication of infection, this interval was prolonged. The catheter was removed as early as possible except for patients with tumors located in the lower region of the rectum.

One month after surgery and every 3 months thereafter, a physical examination was performed, and laboratory markers such as serum carcinoembryonic antigen and carbohydrate antigen 19.9 levels were assessed. At each patient visit, symptoms were recorded, and wound scars were examined. Either ultrasonography or computed tomography scan of the abdomen, in addition to chest X-ray, was performed every 6 months, and total colonoscopy was performed every year.

Statistical analysis

Categorical data were presented as frequencies and percentage and compared by the chi-squared test. Parametric and nonparametric continuous data were presented as mean and standard deviation and evaluated by Student's *t* test and Mann–Whitney U test, respectively. Comparisons between the two groups were made on an intention-to-treat basis. Thus, patients in the laparoscopic-assisted group who were converted to the open procedure were not excluded from the analysis.

The Kaplan–Meier method was used to calculate the survival data, and their differences were compared by the log-rank test. In estimating disease-free survival, the patients who died without having disease recurrence were censored at the time of death. A *P* value of .05 was considered as significant. All calculations were performed by using the SPSS software package version 17.0 (SPSS Inc., Chicago, IL).

Results

In total, 446 patients were enrolled and analyzed in this study. Of the surgeries performed during the study period, 207 were laparoscopic-assisted colorectal resections, and 239 were conventional open surgeries. No statistically

TABLE 1. DEMOGRAPHIC AND PREOPERATIVE CHARACTERISTICS

	Laparoscopic (n=207)	Open resection (n=239)	P
Gender			.908
Male	121 (58.5)	141 (59)	
Female	86 (41.5)	98 (41)	
Age (years)	65.70 ± 12.89	66.49 ± 12.79	.518
BMI (kg/m ²)	24.16 ± 3.06	24.48 ± 3.35	.308
ASA score			.938
1	25 (12.1)	30 (12.6)	
2	110 (53.1)	130 (54.4)	
3	66 (31.9)	72 (30.1)	
4	6 (2.9)	7 (2.9)	
Preoperative co-morbid diseases	82 (39.6)	99 (41.4)	.698
Cardiovascular	93 (44.9)	102 (42.7)	.633
Respiratory	12 (5.8)	11 (4.6)	.569
Hepatic cirrhosis	1 (0.5)	1 (0.4)	.919
Renal failure	4 (1.9)	6 (2.5)	.681
Cerebral infarction	7 (3.4)	7 (2.9)	.784
Diabetes	29 (14)	26 (10.9)	.316
Autoimmune	2 (1)	0 (0)	.128
Others	12 (5.8)	10 (4.2)	.433

Data are number (%) or mean ± standard deviation values, as indicated.

ASA, American Society of Anesthesiologists; BMI, body mass index.

TABLE 2. PATHOLOGICAL PARAMETERS

	Laparoscopic (n=207)	Open resection (n=239)	P
Tumor location			.450
Right hemicolon	48 (23.2)	69 (28.9)	
Transverse colon	4 (1.9)	2 (0.8)	
Left hemicolon	14 (6.8)	21 (8.8)	
Sigmoid colon	58 (28)	61 (25.5)	
Rectum	83 (40.1)	86 (36)	
Tumor size (cm)	4.42 ± 1.48	4.56 ± 1.41	.293
Proximal margin (cm)	11 ± 2.7	11.1 ± 2.7	.741
Distal margin (cm)	8 ± 3.63	8.19 ± 3.67	.644
Total sample length (cm)	26 ± 5.86	26.29 ± 5.94	.662
Lymph nodes retrieved	12.36 ± 4.36	12.13 ± 4.97	.623
Grade			.772
I	52 (25.1)	58 (24.3)	
II	129 (62.3)	157 (65.7)	
III	17 (8.2)	14 (5.9)	
IV	9 (4.3)	10 (4.2)	
pT			.910
pT1	25 (12.1)	28 (11.7)	
pT2	54 (26.1)	63 (26.4)	
pT3	67 (32.4)	71 (29.7)	
pT4	61 (29.5)	77 (32.2)	
pN			.795
pN0	100 (48.3)	123 (51.5)	
pN1	71 (34.3)	76 (32.8)	
pN3	36 (17.4)	40 (16.7)	
TNM stage			.792
I	38 (18.4)	48 (20.1)	
II	64 (30)	75 (31.4)	
III	107 (51.7)	116 (48.5)	
Chemotherapy	116 (48.5)	96 (46.4)	.649

Data are number (%) or mean ± standard deviation values, as indicated.

TABLE 3. INTRAOPERATIVE DATA AND POSTOPERATIVE OUTCOMES

	Laparoscopic (n=207)	Open resection (n=239)	P
Operative time (minutes)	165.3 ± 37	157 ± 38.7	.022
Blood loss (mL)	108.71 ± 93.91	129.08 ± 118.28	.047
Postoperative analgesic requirement (number of injections)	6.87 ± 3.59	7.95 ± 3.69	.002
Time (days) to			
First passing flatus	2.85 ± 1.79	3.27 ± 2.44	.041
First bowel motion	4.51 ± 2.45	5 ± 2.77	.040
Resume normal diet	4.77 ± 1.93	5.16 ± 2.15	.043
Walk independently	3.68 ± 3.01	4.45 ± 4.29	.031
Hospital stay (days)	8.72 ± 3.2	9.49 ± 4.29	.034

Data are mean ± standard deviation values.

significant difference was found in the majority of the demographic parameters between the two patient populations (Table 1).

Operative and pathological parameters

Most of the cancers (37.9%) were located in the rectum without any difference of allocation in the two groups (Table 2). Resection margins were similar in both groups, and none of them was found to be positive. There were no significant differences in number of lymph nodes retrieved and in pT, pN, and overall TNM staging (Table 2).

A significant difference in the operative time between the two groups was observed (165.3 ± 37 minutes for laparoscopic-assisted versus 157 ± 38.7 minutes for open surgery, $P = .022$) (Table 3). Moreover, significantly lower blood loss during laparoscopic surgery compared with open surgery was found ($P = .047$).

Thirty-three patients (15.9%) were converted from laparoscopic to open surgery.

TABLE 4. EARLY AND LATE COMPLICATIONS FOR COLORECTAL CANCER

	Laparoscopic (n=207)	Open resection (n=239)	P
Intraoperative complications			
Massive hemorrhage (> 1000 mL)	1 (0.5)	1 (0.4)	.919
Organ injury	2 (1)	2 (0.8)	.885
Others	1 (0.5)	0 (0)	.282
Postoperative complications			
Ileus	5 (2.4)	8 (3.3)	.560
Anastomotic hemorrhage	1 (0.5)	0 (0)	.282
Abdominal hemorrhage	1 (0.5)	1 (0.4)	.919
Peritonitis/septic shock	1 (0.5)	1 (0.4)	.919
Pelvic abscess	3 (1.4)	2 (0.8)	.540
Wound infection	4 (1.9)	7 (2.9)	.449
Incisional/port herniation	3 (1.4)	4 (1.7)	.849
Systemic complications			
Cardiovascular	1 (0.5)	3 (1.3)	.388
Renal	1 (0.5)	1 (0.4)	.919
Respiratory	1 (0.5)	2 (0.8)	.649

Data are number (%).

TABLE 5. LOCAL AND DISTANT RECURRENCES ACCORDING TO CANCER LOCATION

	Laparoscopic (n=207)	Open resection (n=239)	P
Recurrence			
Total	60 (29)	68 (28.5)	.901
Colon	29 (14)	31 (13)	.748
Rectum	31 (15)	37 (15.5)	.882
Type of recurrence			
Colon			
Locoregional	16 (7.7)	13 (5.4)	.328
Distant	13 (6.3)	17 (7.1)	.726
Rectum			
Locoregional	16 (7.7)	20 (8.4)	.805
Distant	15 (7.2)	15 (6.3)	.638
Incision	0 (0)	2 (0.8)	.187

Data are number (%).

Perioperative recovery

The patients who underwent the laparoscopic-assisted procedure showed a significantly faster recovery than those who underwent open surgery, namely, less time to first passing flatus ($P=.041$), time of first bowel motion ($P=.04$), time to resume normal diet ($P=.043$), and time to walk independently ($P=.031$) (Table 3). Compared with patients who underwent open surgery, laparoscopic colorectal surgery obviously caused less pain for patients leading to lower need of analgesic ($P=.002$) and less hospital recovery time (8.72 ± 3.2 days for laparoscopic-assisted patients versus 9.49 ± 4.29 days for open surgery, $P=.034$).

Complications and recurrence

No significant difference was found in the number of adverse events during the operation procedures between the laparoscopic-assisted and open surgery groups (Table 4). Most of the late complications were minor in both groups, and almost all were due to wound infection and ileus. No significant difference in the rate of recurrence between the two groups was found (Table 5).

Survival

The mean follow-up times were 51 and 51.3 months in the laparoscopic and open surgically treated groups, respectively.

The 3-year survival rate and disease-free survival rate were examined in 277 patients who could be followed up for longer than 36 months, and the 5-year survival rate and disease-free survival rate were examined in 184 patients who could be followed up for longer than 36 months. Both colon and rectal cancer patients had similar mortality rates at 3-year and 5-year follow-up, although a slightly lower survival was observed for patients with cancer of the rectum (Table 6). The numbers of deaths were thus comparable after 3 and 5 years between the laparoscopic-assisted and open surgery groups. Among colon cancer cases, 3-year survival was 92.3% versus 94.1%, respectively, whereas among rectal cancer cases it was 85.9% versus 77.4%. At 5 years, survival for colon cancer patients was 86.3% and 90.8% in the laparoscopic and open surgery groups, respectively, and for rectal cancer it was 70.4% and 63.5%, respectively.

According to the results of Kaplan-Meier analysis, laparoscopic and open surgery groups did not have significant differences in overall survival trend (Fig. 1) and disease-free survival (Fig. 2).

Discussion

This was a comparative study analyzing data on patients with colon and rectal carcinoma operated on with laparoscopic-assisted or conventional open surgery. At our knowledge, only a few studies conducted in Italy have explored differences between laparoscopic-assisted and conventional open surgery. Our results showed that laparoscopic-assisted surgery was associated with better early postoperative outcomes and comparable rates of complications and survival compared with the conventional open procedure.

In our study we found significant improvements in postoperative recovery among laparoscopic-treated patients, with an earlier resumption of normal diet, shorter hospital stay, and earlier time to ambulation. The postoperative hospital stay for patients who underwent the laparoscopic procedure ranged between about 5 to 8 days in some randomized controlled trials,^{3,5,9} which was a shorter time than the 9 days reported in this study. Several confounding factors could affect the comparison of hospital stay between the two groups as well as between different studies. For example, disparities according to socioeconomic status are well documented in the United States, thus introducing bias in the results if they are not adjusted for this variable. In Italy, the healthcare system provides ensuring equity in the availability of care by

TABLE 6. ONCOLOGIC OUTCOME ACCORDING TO CANCER LOCATION

	3-year			5-year		
	Laparoscopic	Open resection	P	Laparoscopic	Open resection	P
Overall survival						
Total	133 (87.8)	144 (89.3)	.687	82 (78.1)	102 (79.7)	.767
Colon	72 (92.3)	96 (94.1)	.630	44 (86.3)	69 (90.8)	.426
Rectum	61 (85.9)	48 (77.4)	.204	38 (70.4)	33 (63.5)	.450
Disease-free survival						
Total	161 (77.8)	189 (79.1)	.739	153 (73.9)	177 (74.1)	.972
Colon	100 (80.6)	130 (85)	.341	98 (79)	124 (81)	.676
Rectum	61 (73.5)	59 (68.6)	.484	55 (66.3)	53 (61.6)	.530

Data are number (%).

FIG. 1. Overall survival of laparoscopic-assisted versus open resection patient groups. Cum, cumulative; mo, months.

removing financial barriers for all cancer patients. Therefore, in the Italian comparison length of hospital stay should not be influenced by socioeconomic status of patients, and Italian patients tend to leave the hospital slowly because hospital charges are inexpensive and covered by the Italian healthcare system. On the other hand, other variables such as preoperative health status of the patients and chemotherapy undoubtedly extend the length of hospital stay for all patients.

FIG. 2. Disease-free survival of laparoscopic-assisted versus open resection patient groups. Cum, cumulative; mo, months.

As preoperative co-morbidities may affect postoperative patient recovery and patients could not be discharged until the end of the first regimen of postoperative chemotherapy, we examined such covariates to find any substantial differences between the two groups.

We also assessed any significant advantages in the laparoscopic approach over the open surgical method for pain score and analgesic consumption. As the laparoscopic procedure causes less pain, patients who underwent laparoscopic-assisted surgery definitely required smaller doses of analgesic than their counterparts who received open surgery treatment. In the results of most studies reported previously, short-term outcomes after laparoscopic surgery for colorectal cancer were shown to be better than those of open abdominal surgery.⁴

Results about mean operating time of the laparoscopic-assisted procedure versus open surgery vary among studies, with some reporting no differences between the two groups^{4,10} and others reporting a significantly longer time for the laparoscopic-assisted procedure probably because of the higher complexity of technical expertise involved in such technique.¹¹ In our study we also determined a slightly longer operating time for the laparoscopic-assisted procedure than for open surgery, although this difference was not significant. It is possible that as time passed the surgeon's experience with the procedure increased. Therefore, with the stabilization of the learning curve of the surgeon, the operating time was significantly reduced over the time.

The conversion rate of this study was 15.9%, which was far lower than that reported in other studies, which ranged between 15% to 30%.^{3,5,11-13} This variation among studies may be translated into an evolution of operating skills over time, thus reducing conversion rates in the most recent studies. Also, in our study, as the learning curve of the technique is incorporated during the study period and the skills were still evolving during the conduct of the study, it is not surprising that the number of conversions in the latter phase of our study was lower.

In our study, oncological safety was assessed by examining postoperative results, such as the resection margin and the number of resected lymph nodes. Our results showed that laparoscopic-assisted procedure outcomes were comparable to those achieved by open surgery. In this study, none of the resection margins was found to be positive, as reported in most previous articles with data on resection margins.^{5,9,14-17} The average number of resected lymph nodes was 12.36 ± 4.36 in patients who underwent the laparoscopic-assisted procedure and 12.13 ± 4.97 in those who underwent open surgery, thus confirming that there were no differences in lymph nodes harvested between the two groups of patients. This findings demonstrated that the oncologic safety of our laparoscopic surgery was comparable to previous results of other laparoscopic surgery groups.^{18,19}

In this study, the long-term oncological outcomes were assessed over a period of 8 years and a median follow-up of about 51 months for both groups, including early and late complications, local and distant recurrence rate, overall survival, and disease-free survival. Most complications were minor and comparable between the two groups, regarding wound or urinary tract infections (although wound infections were slightly more frequent in patients who underwent the open procedure), as reported in previous studies.^{8,11}

With regard to recurrence rate, patients who underwent laparoscopic surgery were shown to have rates comparable to those who underwent open abdominal surgery. Our study revealed that the recurrence rate for colorectal cancer patients were similar compared with prospective trials, with about 3–7% and 17–19% local and distant recurrence rates, respectively.^{6,7,9,20} It is noteworthy that recurrence rates vary, stratifying patients by cancer location, namely, colon and rectal cancer. Indeed, both local and distant recurrence rates have been shown to be lower in colon (about 2% and 10%, respectively) than in rectal cancer (about 10% and 20%, respectively) patients. This is thought to be related to the different blood flow in the rectum than in the colon. Another possible reason is that the surgery for rectal lesions is difficult because of the location itself. However, even stratifying according to the tumor location, the number of patients who developed a recurrence was similar in laparoscopic-assisted and open surgery patients, and these results were comparable to ours. Similar overall and disease-free survival in the two groups confirmed the long-term oncologic safety of the laparoscopic approach compared with open surgery. Reviewing the results of long-term follow-up conducted in prospective studies, the 3-year survival rates neared about 85% in almost all studies,^{6,9} whereas in other studies they were significantly lower (<70%).⁷ Also, regarding the 5-year survival, a certain degree of controversy has been found among different studies (ranging between 65.3% and 77%).^{6,8} Based on the present findings, our results were in line with those finding slightly higher survival rates, being for patients who underwent laparoscopic-assisted surgery about 87.8% at 3-year and 78.1% at 5-year follow-up, seemingly equivalent to the open method.

The present study was limited in that the patients were partially randomized into the two treatment arms. However, because there were no differences in demographic data, we believe this bias had negligible impact on the results. Furthermore, our study is strengthened by the large sample size and a long follow-up period compared with other Italian studies.

In conclusion, our results suggest that the laparoscopic approach is as safe as the open alternative. Laparoscopic-assisted surgery has been shown to be a favorable surgical option with better short-term outcomes and similar long-term oncological control compared with open resection.

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Disclosure Statement

No competing financial interests exist.

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