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Laparoscopic Resection Does Not Adversely Affect Early Survival Curves in Patients Undergoing Surgery for Colorectal Adenocarcinoma

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Objective
To determine the survival curves for laparoscopic resection (LR) of colorectal cancer.

Summary Background Data
Laparoscopic resection for cure of colorectal cancer is controversial, and survival curves have not been determined.

Methods
A prospective database of 177 consecutive LRs of colorectal cancers performed between November 1991 and 1997 was reviewed. The TNM classification (stage 0, I, II, III, and IV) for colorectal cancers and the Kaplan–Meier method were used to determine survival curves.

Results
Of the 177 patients, 5 were excluded for not having adenocarcinomas. Twenty-five patients (14.5%) had conversion to open surgery; most of these patients had rectal cancer or tumor invasion to adjacent organs. Twelve patients were lost to follow-up. All 135 remaining patients had follow-up. Overall, 28 deaths occurred during the follow-up period, 15 of which were cancer-related. The median follow-up was 24 months for patients with stage I, II, and III disease and 9 months for patients with stage IV disease. Observed 2-year survival rates were 100% stage I, 88.7% stage II, 80.6% stage III, and 28.6% stage IV. Survival rates at 4 years were 100% stage I, 79.5% stage II, 53.7% stage III, and 0% stage IV. No trocar site recurrence was observed.

Conclusions
Early survival curves for patients with colorectal cancer who underwent LR do not differ negatively from historical controls for conventional surgery. Further validation is needed.

One of the most controversial areas of laparoscopic surgery has been laparoscopic resection (LR) for cancer, more specifically for colon and rectal cancer.[1,2] This controversy has been fueled by well-publicized anecdotal reports of port-site recurrences in patients undergoing surgery for a variety of neoplastic lesions.[3,4] Further, it has been suggested that cancer cells could be spread at the time of LR through misuse of instruments, detrimental effects of CO_2 pneumoperitoneum, or movement of cell-laden fluid.[5–11] However, there are emerging data showing benefits for patients treated laparoscopically for colon and rectal adenocarcinoma.[12–14] The present survey determines the early survival curves in a cohort of consecutive patients who underwent LR of colorectal adenocarcinoma.

PATIENTS AND METHODS

This study is a review of a longitudinal database established for all consecutive cases of laparoscopic colorectal

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Table 1. COLORECTAL CANCER STAGING: AMERICAN JOINT COMMITTEE ON CANCER (TNM CLASSIFICATION)

Stage	Description	Dukes Stage
Stage 0	Carcinoma *in situ* (Tis, N0, M0)	
Stage I	Tumor invades submucosa (T1, N0, M0)	Dukes A
	Tumor invades muscularis propria (T2, N0, M0)	
Stage II	Tumor invades through muscularis propria into subserosa or into nonperitonealized pericolic or perirectal tissues (T3, N0, M0)	Dukes B
	Tumor perforates the visceral peritoneum or directly invades other organs or structures (T4, N0, M0)	
Stage III	Any degree of bowel wall perforation with regional lymph node metastasis	Dukes C
	N1 1–3 pericolic or perirectal nodes involved	
	N2 4 or more pericolic or perirectal nodes involved	
	N3 Metastasis in any lymph node along a named vascular trunk (Any T, N1, M0) (Any T, N2, N3, M0)	
Stage IV	Any invasion of bowel wall with or without lymph node metastasis, but with evidence of distant metastasis (Any T, Any N, M1)	

resection for cancer (177 cases) performed by three surgeons (ECP, JM, RG) in a university setting between November 1991 and 1997. Preoperative evaluation and follow-up data included physical examination, liver function studies, carcinoembryonic antigen, chest radiographs, computed tomography or ultrasound scan, and endoscopy of the colon with a biopsy when indicated. Informed consent was obtained in all cases. Five patients were excluded because their tumor was not an adenocarcinoma (three carcinoids, one squamous cell carcinoma, one lymphoma). Patients were staged using the American Joint Committee on Cancer classification (TNM) as stage 0, I, II, III, or IV.[15] The TNM classification for cancer of the colon and rectum was modified in 1988 to correspond directly with the Dukes classification, which is often used to estimate the prognosis of colorectal cancers (Table 1).

Tumors involving the right colon were mobilized laparoscopically and extracted using a plastic wound protector through an enlargement of the umbilical incision. The vessels were ligated at the base of the mesentery from the outside, and the anastomosis was performed extracorporeally (Fig. 1). All surgery for left colon, sigmoid colon, and upper rectal lesions was performed intracorporeally, including mobilization, vessel ligation, bowel transection, and anastomosis. Before extraction through a left lower quadrant incision (McBurney type), the specimen was bagged in

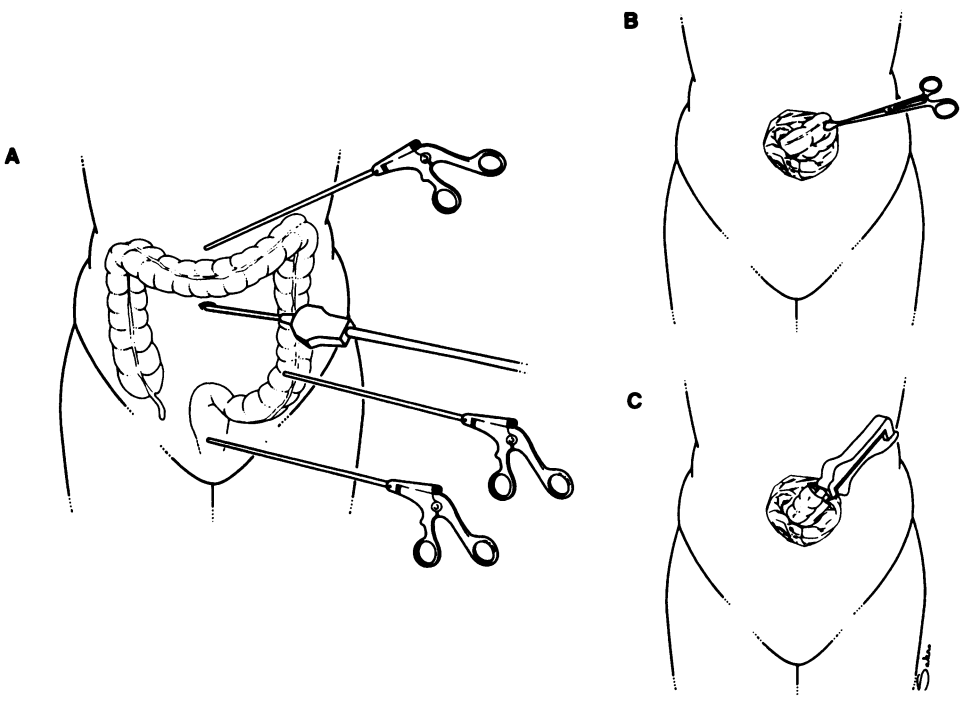

Figure 1. Laparoscopic technique used for right-sided lesions. (A) Usual port sites. (B) Umbilical extraction site, extracorporeal high ligation of vessels and section of bowel, extraction through wound protector. (C) Extracorporeal anastomosis.

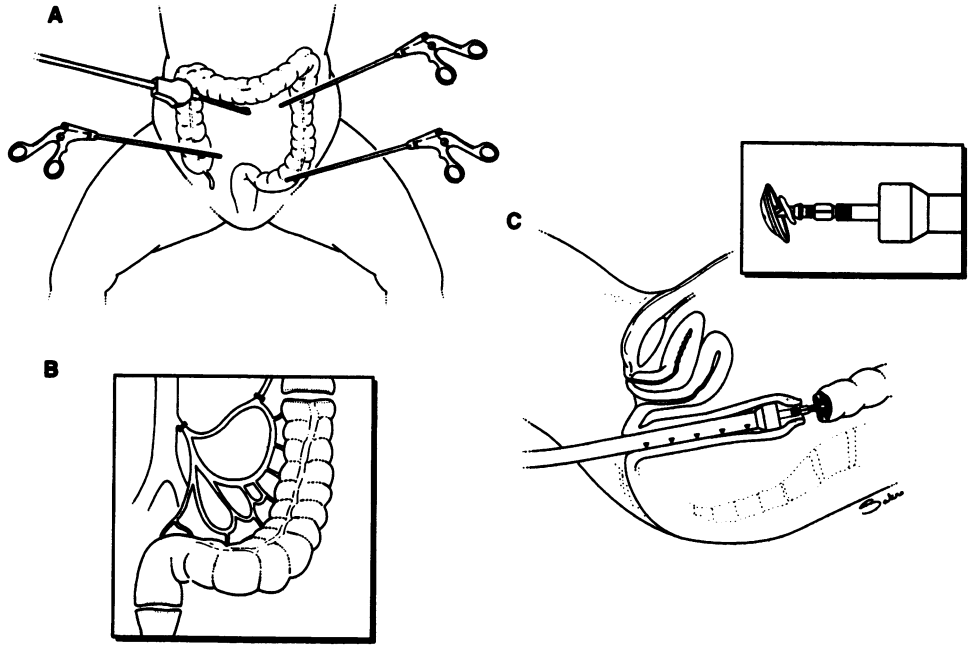

Figure 2. Laparoscopic technique used for left-sided lesions. (A) Usual port sites. (B) Intracorporeal high ligation of vessels and section of bowel, bagged specimen. (C) Intracorporeal anastomosis.

a sterile plastic freezer bag (Ziploc, Dow Brands Canada, Paris, Ontario) (Fig. 2). For abdominoperineal resections, the specimen was extracted through the perineum after laparoscopic dissection and vessel ligation. Occasionally, alternative extraction sites were used (Table 2).

The survival rates for all stages, which account for all deaths regardless of cause, were determined using the Kaplan–Meier method. Estimates for overall, 2-year, and 4-year survival and 95% confidence intervals (CI) were calculated from values used to determine the Kaplan–Meier curves.[16]

RESULTS

Of the 172 patients with adenocarcinomas, in 25 (14.5%) the procedure was converted to an open one, mostly patients with rectal cancer (13/25) or tumor invasion to adjacent organs (6/25). In these 19 cases, the operating surgeon considered that a proper cancer operation could not be performed laparoscopically (Table 3). Therefore, 147 patients had LR. Twelve patients were lost to follow-up. All 135 remaining patients had follow-up (20 stage I, 51 stage II, 43 stage III, and 21 stage IV). The distribution of cases was as follows: cecum and ascending colon, 47 (35%); transverse colon, 3 (2.2%); descending colon, 7 (5.1%); sigmoid colon, 31 (23%); and rectum, 41 (30%). Six patients had a total abdominal colectomy (4.4%). The distribution ratio of left colon to right colon lesions was close to 60:40. The patient cohort comprised 75 men and 61 women whose average age was 67.1 ± 13.1 years (range, 30 to 92). The size of the incision used to extract the specimen was proportional to the size of the tumor and the obesity of the patient (see Table 2). The average operative time was 177 ± 71 minutes (range, 42 to 490). The median time to discharge was 6 days (range, 3 to 72).

Table 2. LAPAROSCOPIC COLORECTAL RESECTION FOR ADENOCARCINOMA: EXTRACTION INCISIONS*

Site	Number	Average size ± SD (cm)	Range (cm)
Umbilical	60	5.9 ± 1.9	3.0–15
LLQ†	35	5.5 ± 1.8	3.5–10
RLQ‡	15	5.8 ± 1.5	3.5–10
Pfannenstiel	2	8	6 and 10

* Information available on 112 patients.
† LLQ, left lower quadrant.
‡ RLQ, right lower quadrant.

The overall operative mortality rate was 4.7% (7/147). Four of the seven deaths resulted from cardiovascular events, and one resulted from sepsis. Only one death occurred in a patient younger than 75 years (Table 4). In all, 28 patients died during the postoperative and follow-up period: there were 7 postoperative deaths, 6 deaths of unrelated causes during follow-up, and 15 deaths related to cancer (0 stage I, 1 stage II, 4 stage III, 10 stage IV).

For patients with stage I, II, and III disease, the median follow-up was 24 months (range, 0 to 65). For patients with stage IV disease, the median follow-up was 9 months (range, 0 to 37).

The overall survival rate for all patients, all stages, and all operations was 81% at 2 years and 68% at 4 years (Fig. 3). The 2-year survival rates were 100% for stage I, 88.7% for stage II (95% CI 79% to 98%), 80.6% for stage III (95% CI

Table 3. REASONS FOR CONVERSION

Reason	Number	RC*	SR†	AR‡	APR§
Fixation to adjacent structures	6	4	2		
Oncologic procedure impossible	8	1		7	
Adhesions	3	3			
Hemorrhage	2	1			1
Technical mishap	1			1	
Small bowel perforation	1			1	
Obesity	1		1		
Unrecorded	3			3	
Total	25	9	3	12	1

* Right colectomy.
† Sigmoid resection.
‡ Anterior resection of rectum.
§ Abdominoperineal resection of rectum.

66% to 95%), and 28.6% for stage IV (95% CI 0% to 58%). The survival rates at 4 years were 100% for stage I, 79.5% for stage II (95% CI 65% to 95%), and 53.7% for stage III (95% CI 20% to 88%). There was no 4-year survivor for patients with stage IV disease. The patient who survived longest who had disseminated disease at surgery lived for 37 months (Fig. 4). No trocar-site recurrence was observed.

DISCUSSION

To be successful, there are a number of prerequisites for laparoscopic colorectal cancer surgery. First, all the accepted principles of surgical resection for colorectal cancer must be followed closely. The goal of surgery is to maximize the chance for cure through *en bloc* removal of the tumor and the lymphatic nodal basin with margins that are adequate to ensure removal of the entire locoregional tumor burden.[17–21] Second, two problems more specific to the laparoscopic technique must be addressed: tumor localization and tumor extraction. With partial loss of tactile feedback during laparoscopy, special precautions must be taken to ensure that tumor localization is made with minimal manipulation before surgery. This is achieved with the liberal use of contrast studies for tumors of the colon, rigid sigmoidoscopy for rectal tumors, and tattooing with India ink through colonoscopy for small lesions. Finally, specimen extraction should always be done through a wound protector or with the specimen isolated in a plastic retrieval bag to avoid seeding the extraction/incision site with tumor cells.

For statistical analysis in this series, tumors were classified using the TNM classification. Of the 15 or so classification systems for colorectal cancer described between 1925 and 1987, the TNM system has the advantage of being accepted and proposed by the American Joint Committee on Cancer Staging for staging colorectal cancer.[15,22] At both 2 and 4 years, the survival data are favorable to laparoscopic treatment (Table 5).

No trocar-site recurrences or unusual locoregional recurrence occurred in this series of patients, and so far survival curves are not affected by any unusual pattern of recurrence.

Table 4. POSTOPERATIVE DEATHS

Stage	Age (yr)	Etiology
II	81	Stroke
II	77	Massive pulmonary embolus
II	87	Cardiac arrest
II	78	Cardiac arrest
II	81	Small bowel infarction
IV	82	Upper GI bleed, respiratory and cardiac arrest
IV	67	Peritoneal sepsis

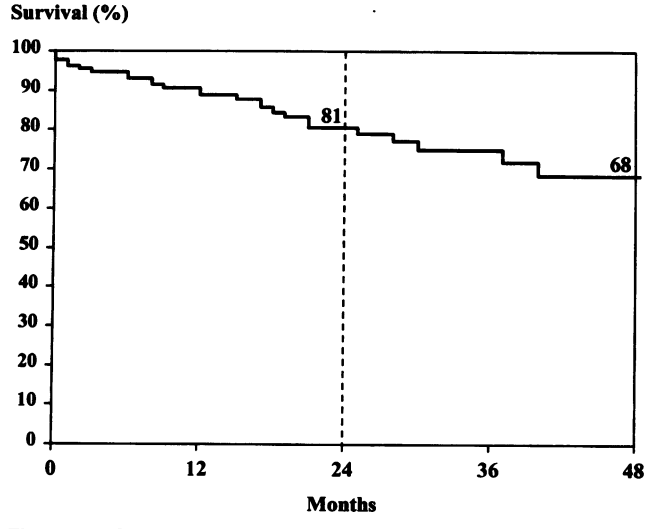

Figure 3. Overall survival rate for patients with colorectal cancer treated laparoscopically, all stages, all operations.

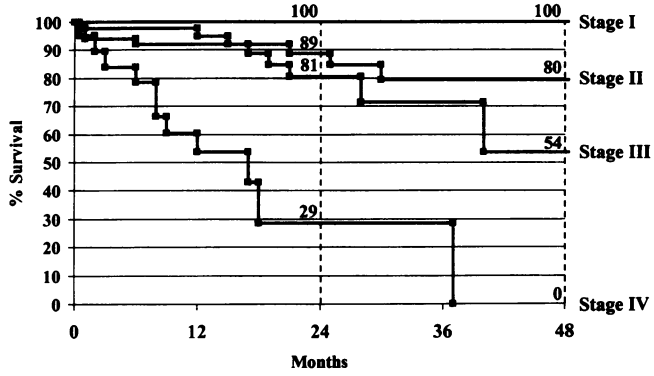

Figure 4. Survival curves by stage for patients with colorectal cancer treated laparoscopically.

If port-site, wound, or other recurrences in laparoscopic surgery are assumed to result from technical causes, breach of proper technique, disrespect of oncologic surgical principles, or the environment of the pneumoperitoneum, they should be apparent even sooner than recurrences because of the severity of the underlying disease. Normally, in conventional surgery, >70% of recurrences are reported to occur within the first 2 years, and most deaths within 3 years, whereas 80% of wound recurrences have been shown to occur within 1 year in patients who had LR.[23–28] It therefore can be assumed that if a breach of technique occurred during LR or if the pneumoperitoneum milieu polluted the treatment, recurrences would become evident early in the follow-up of patients; this was not the case in this series.

Despite these positive outcomes, this study has a number of weaknesses. First, it is not a randomized clinical trial and therefore can have a number of unintentional biases. One of the biases can involve selection. Although the patients reported presented consecutively to the operating surgeons, there was a high conversion rate (52% of the converted cases) for cases involving rectal tumors. At present, for technical reasons mostly having to do with inappropriate instruments, it is impossible to perform a true total mesorectal excision in some patients with rectal tumors, especially in obese men.[25] At present, total mesorectal excision is considered by many to be the standard of an adequate oncologic resection for tumors of the superior and midrectum; therefore, conversion was considered necessary when total mesorectal excision could not be achieved laparoscopically. Some of the procedures in patients with adjacent organ involvement (six cases) were converted because the surgeon believed that a proper oncologic resection could not be guaranteed using laparoscopic technique. It is difficult to determine the impact of these decisions on the final outcome of this patient cohort.

Second, the number of patients is small, and the follow-up, especially in the longer term, is limited. Therefore, the stage subsets that involve the number of positive nodes, especially for stage III (TNM) or Dukes C in the modified Dukes classification, cannot be analyzed at this time. The number of patients available for analysis at 4 or 5 years is also small, and this confers to the tail end of the survival curves a fairly large confidence interval (*i.e.*, wagging tail of the survival curve) (see Fig. 4 and Table 5). Whether the results observed so far will stand up with time and accrual of more cases cannot be determined with precision.

A significant number of publications have reported on how laparoscopic surgery could adversely affect outcomes in patients with colorectal cancer.[1–11] However, little time has been spent on how minimal-access techniques could help improve outcomes. It has been demonstrated that there is less biologic response to trauma and possibly less surgery-related immunosuppression with laparoscopic surgery. The body's response to laparoscopic surgery seems to be one of lesser immune activation as opposed to immunosuppression, and this could translate into better long-term survival[29] (Table 6). Long-term outcomes also could be improved by a reduction of the postoperative mortality rate. Fielding et al[30] in the Large Bowel Cancer Project study in England, which involved 2510 patients undergoing a traditional curative resection, reported an overall postoperative mortality rate of 7%. Patients older than 70 had a mortality rate (12%) more than four times that of younger patients (3%). In that study, 635 patients had palliative resections for metastatic disease, and their overall mortality rate was 14%. The present laparoscopic series had an overall operative mortality rate of 4.8% (7/147); the mortality rate was 8% (6/75) for patients older than 70, 1.4% (1/72) for patients younger than 70, and 9.5% (2/21) for patients with stage IV disease. These mortality rates are inferior by 30% to 50% to the rates in the Fielding study. These preliminary results raise the possibility that laparoscopic surgery could positively influence outcomes by lowering the mortality rate at the front end of the survival curve for all categories of patients.

Although the limitations of this study do not permit any conclusion with high levels of certainty, it cannot be denied

Table 5. OBSERVED SURVIVAL RATES FOR COLORECTAL ADENOCARCINOMA

Stage	Present series (Laparoscopic)	Mayo Clinic* (Open)	Australia† (Open)	Stage
2-year				
I	100	100	85	A
II	88.7 (95%CI79–98)	92 (B1) 88 (B2)	82	B
III	80.6 (95%CI66–95)	65	55	C
IV	28.6 (95%CI0–58)	18	22	D
4-year				
I	100	90	70	A
II	79.5 (95%CI65–95)	90 (B1) 80 (B2)	60	B
III	53.7 (95%CI20–88)	50	35	C
IV	0	2	8	D

* Data from reference 24.
† Data from reference 22.

Table 6. LAPAROSCOPIC COLORECTAL CANCER SURGERY

Potential drawbacks
Related to technique
Inadequate for: Tumor localization, identification of anatomy, mesentery resection, high vessel ligation, resection margins
Tumor cell seeding: Contaminated instruments, tumor manipulation, unprotected or forced tissue retrieval
Related to pneumoperitoneum
Tumor cell seeding: Gas turbulence (chimney effect), movement of cell-laden fluids
Embolization of exfoliated cells
Potential advantages
Overall cost-effectiveness, better short-term outcomes
Lower postoperative mortality rate
Patients older than 70, patients with metastases or significant comorbid factors
Better biologic response to injury and systemic immune response
Decreased acute-phase protein response, better preservation of peripheral and peritoneal leukocyte function; may limit tumor spread if no tumor manipulation; better maintenance of delayed-type hypersensitivity
Better long-term survival

that 135 patients treated laparoscopically for colorectal cancer since 1991 have not shown undesirable results. In the 86 patients with curable disease (stage I, II, and III), only 5 have died from cancer-related causes (1 stage II, 4 stage III). The favorable survival curves for LR observed so far and the absence of port-site recurrence in this series should serve to balance negative opinions concerning LR of colorectal adenocarcinoma.

In conclusion, early survival curves for patients with an adenocarcinoma of the colon and rectum who underwent LR do not differ negatively from the results of conventional surgery. Further validation is needed.

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