

Outcomes in Patients Treated by Laparoscopic Resection of Rectal Carcinoma After Neoadjuvant Therapy for Rectal Cancer

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ABSTRACT

Objective: We analyzed the effect of neoadjuvant chemoradiation on feasibility and outcomes in rectal cancer patients undergoing laparoscopic resection of the rectum.

Methods: This was a retrospective analysis of a consecutive series of laparoscopic resections for rectal cancer from 1998 to 2004 (N=60).

Results: Eight patients received preoperative chemoradiation therapy (neoadjuvant group) for rectal cancer and 52 patients did not (primary surgical group). The conversion rate was higher in the neoadjuvant group, but this did not reach statistical significance (3/8, 37% in the neoadjuvant group vs. 7/52, 13% in the primary surgical group, $P=0.12$). Operative time was longer in the neoadjuvant group (170 ± 60 vs 228 ± 70 min, $P=0.03$). Complication rates (3/52, 5.7% in the primary surgical vs. 0% in the neoadjuvant group, $P=1.0$), and a median number of resected lymph nodes (14.5 in the primary surgical vs. 16.0 in the neoadjuvant group, $P=0.81$) were similar between groups.

Conclusion: Laparoscopic resection of rectal cancer in patients after preoperative chemoradiation treatment seems to be associated with a higher conversion rate and a longer duration of surgery. No change in mortality and morbidity was detected. We encourage further investigation of laparoscopic rectal surgery for treatment of rectal cancer.

Key Words: Rectal cancer, Laparoscopic resection, Neoadjuvant chemoradiation.

INTRODUCTION

Laparoscopic resection of the colon is an accepted option for surgical treatment of colon cancer. Oncologic adequacy is supported by both prospective randomized data^{1,2} and multiple retrospective analyses.³⁻⁵

However, no comparable evidence is available to support laparoscopic resection of rectal cancer at this time. Retrospective studies cautiously report both oncological competence and the technical challenge associated with laparoscopic rectal resections.^{6,7} Initial data from the rectal cancer data set in the CLASSIC trial⁸ also support clinical and oncologic noninferiority. Although laparoscopic rectal resection appears safe, certain concerns remain regarding increased conversion rates and associated complications.⁸

Additionally, the benefits of preoperative radiotherapy in improving local control^{9,10} and overall survival¹⁰ were recognized in the past decade. On the other hand, the addition of preoperative radiation therapy has led to increased perioperative mortality in some patients.^{10,11}

Therefore, we analyzed the effects of neoadjuvant therapy on feasibility and outcomes in patients undergoing laparoscopic rectal resection for rectal cancer.

METHODS

We retrospectively analyzed consecutive patients diagnosed with rectal carcinoma from December 1998 to November 2004 who underwent laparoscopic rectal resection. All patients of the 2 laparoscopic surgeons were offered a laparoscopic approach, and most accepted this option. Patients with tumors of the middle or lower third of the rectum (such as within 8cm of the anal verge) and bulky tumors were offered open resection only during the initial years of this study. All patients had total mesorectal resection. Patients with frank perforation and acute obstruction are not included in this study. Patients with a history of prior abdominal operations and metastasis are included. All patients received a bowel preparation, preoperative antibiotics, subcutaneous heparin, and β -blockers as indicated.

The choice of adjuvant versus neoadjuvant therapy was

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guided by a clinical consensus of the surgeon and medical and radiation oncologists and was not randomized. In cases of neoadjuvant radiation therapy, a dose of 50 Gy radiation was delivered in 2.0 Gy per fraction. All patients receiving neoadjuvant radiation were given concurrent chemotherapy. The medical oncologist determined the choice of chemotherapy. Demographic parameters of both groups are similar.

Categorical data were cross-tabulated and analyzed by the chi-square test or Fischer exact test where appropriate. Continuous data were evaluated by the Mann-Whitney test, and survival was examined by the Kaplan-Meier method. Statistical significance was set at $P < 0.05$.

RESULTS

The study included 60 consecutive patients with a mean age of 70.4 years. Fifty-two patients (86.7%) did not receive neoadjuvant therapy and went directly to surgery (primary surgical group). Eight patients (13.3%) received neoadjuvant therapy in their preoperative course (neoadjuvant group).

During the study period, approximately 250 laparoscopic colorectal cases were completed annually. Patients with rectal cancer were determined to have procedures either attempted laparoscopically or in an open fashion.

Fifty patients (83.3%) had successfully completed laparoscopic procedures. Ten patients (10/60, 16.7%) were converted to open procedures, of which 7 patients were from the primary surgical group (7/52, 13.4%) and 3 were from the neoadjuvant group (3/8, 37.5%; odds ratio 3.8, $P = 0.120$).

Fourteen patients (14/60, 23.3%) underwent abdominoperineal resection (APR), and 46 patients (46/60, 76.6%) had low anterior resection (LAR). Neoadjuvant therapy was more common in those patients who eventually underwent APR (5/14, 35% vs 3/46, 6.5% $P < 0.005$).

The duration of the operation was shorter in the primary surgical group (170 ± 60 min) than in the neoadjuvant group (228 ± 70 minutes, $P = 0.033$). The number of harvested lymph nodes was similar between the 2 groups (median of 14.5 vs 16.0, $P = 0.800$). Median hospital stay for both groups was 4 days. Estimated blood loss of both the primary surgical and neoadjuvant therapy groups was similar (median 150 mL in primary surgical group vs. 200 mL in neoadjuvant therapy group, $P = NS$). Neoadjuvant therapy was not associated with an increase in perioper-

ative death, complications, or a need for reoperation (**Table 1**).

Conversion resulted in a significantly extended length of hospital stay compared with laparoscopically completed procedures (median 5.5 vs 3.0 days, $P = 0.009$). The specific reasons for conversion were anatomic difficulty in 5 patients (3 in primary surgical vs 2 in the neoadjuvant group), bulky tumor (1 in neoadjuvant), intraoperative complications (3 in primary surgical), and an unspecified reason from the operative record (1 in neoadjuvant). Intraoperative complications included 2 instances of bleeding not controllable by the laparoscopic technique and 1 ureteral injury. Conversion was associated with an increase in operative morbidity, but not perioperative mortality (**Table 2**).

Table 1.
Frequency of Perioperative Death, Complications, and Conversion in Patients With (n = 8) and Without (n = 52) Neoadjuvant Therapy*

	Neoadjuvant Therapy	
	-	+
Perioperative death	1 (1.9%)	0 (0%)
Intraoperative complication	3 (5.7%)	0 (0%)
Postoperative complication	4 (7.7%)	0 (0%)
Reoperation	2 (3.8%)	0 (0%)
Conversion	7 (13.4%)	3 (37.5%)

*Data are expressed as frequency (percent). No statistically significant differences detected.

Table 2.
Frequency of Perioperative Death and Complications in Patients With Operative Conversion (n = 10) and Those Laparoscopically Completed (n = 50)*

	Conversion		P	OR
	-	+		
Perioperative death	0 (0%)	1 (10%)	0.167	-
Intraoperative complication†	0 (0%)	3 (30%)	0.004	-
Postoperative complication	3 (6%)	1 (10%)	0.528	1.7
Reoperation	1 (2%)	1 (10%)	0.308	1.6

*Data are expressed as frequency (percent).
†Statistical significance.

DISCUSSION

Since it was first reported approximately 15 years ago,¹² laparoscopic rectal resection has been performed increasingly for benign and malignant rectal diseases.

Current practice depends on extrapolation of data from colon cancer trials. So far, 5 randomized trials reported survival data, all supporting the noninferiority of laparoscopy.^{1,2,8,13,14} In fact, disease-free survival in the Spanish trial² was significantly higher in patients randomized to the laparoscopic arm.

Such evidence is, however, not yet available to support laparoscopic resection of rectal cancer. Retrospective studies cautiously suggest the oncological adequacy of laparoscopic rectal resections.^{6,7} An initial report on rectal cancer data set in the British CLASSIC trial⁸ did not find any significant drawbacks of laparoscopic rectal procedures, but a trend towards a higher positivity of the circumferential resection margin was observed among those receiving laparoscopic low anterior resection. Although laparoscopic rectal resection appears safe, additional concerns regarding increased conversion rates and associated complications in laparoscopic rectal resection remain.⁸

Several other aspects of laparoscopic rectal surgery are attractive for oncologic application. Total mesorectal excision is more commonly achieved in the laparoscopic cohort,⁸ and appears to be technically easier, possibly due to better visualization and magnification. Additionally, an interesting phenomenon of decreased tumor growth after laparoscopic surgery was observed in both animal studies¹⁵ and in vitro studies.¹³

The oncologic effectiveness of rectal cancer therapy is further affected by adjuvant and neoadjuvant therapy. Radiation therapy improves local control, whether given pre-^{9,10} or postoperatively.¹⁶ Furthermore, in the Swedish trial it improved both long-term overall survival and cancer-specific survival.¹⁰ No direct comparison of preoperative versus postoperative radiotherapy for rectal cancer is currently available. The German Rectal Cancer trial¹⁷ accrued a satisfactory number of patients and should address this issue.

Additionally, concurrent fluorouracil chemotherapy with radiation is beneficial. Preoperative or postoperative fluorouracil-based chemotherapy improved local control but has no effect on survival in a recent study of patients receiving neoadjuvant radiotherapy.¹⁸ On the contrary, adjuvant chemoradiation provides both superior local

control and improved survival, as compared with any other combination treatment.¹⁹

Nevertheless, the addition of preoperative radiation therapy led to increased perioperative mortality in some studies.^{10,11} Therefore, we conducted this study to analyze the effects of neoadjuvant therapy on the feasibility and outcomes in patients undergoing laparoscopic rectal resection for rectal cancer.

Our results indicate that patients undergoing operation after neoadjuvant therapy are more frequently converted to open procedures. Even so, this does not appear to be associated with increased morbidity. Our overall conversion rate of 16.7% compares favorably with the 25% to 34% rates reported in the other studies.^{7,8}

We concur with the prior findings suggesting increased complication prevalence among those patients who required conversion.⁸ Yet, the relationship of conversion and complication rate is complex and only partially elucidated.²⁰ In addition, disturbing data from a Canadian retrospective analysis²¹ pointed out significantly decreased survival in converted patients. In our study of 155 patients with colorectal cancer who underwent a laparoscopic procedure, no difference was found in oncologic outcomes between laparoscopic completed and converted procedures.²² More studies are required to investigate the clinical and biological effects of conversion.

We acknowledge several shortcomings of the present study. Selection of neoadjuvant therapy was nonrandomized. If, in fact, patients with less favorable tumors were preferentially selected for neoadjuvant therapy, this alone can dramatically skew the results. The retrospective nature and prolonged time span of the investigation can certainly affect outcomes due to bias and changes in clinical practice over the time period. We believe this small observational study can serve as the basis for future prospective randomized studies.

CONCLUSION

Expected results from the German rectal cancer trial and planned ACOSOG trial hopefully will clarify the role of laparoscopic surgery for rectal cancer. We believe that laparoscopic rectal resection after neoadjuvant therapy for rectal cancer has a higher conversion rate but no increase in the risk of complications. Rectal cancer surgery is a purely technical exercise and extensive experience is required before attempting these cases laparoscopically. Further investigation of laparoscopic rectal surgery for treatment of rectal cancer appears safe and is encouraged.

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