

# Early Results of Laparoscopic Surgery for Colorectal Cancer

## Retrospective Analysis of 372 Patients Treated by Clinical Outcomes of Surgical Therapy (Cost) Study Group

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**PURPOSE:** This study was undertaken to determine the early experience of the members of the COST Study Group with colorectal cancer treated by laparoscopic approaches. **METHOD:** A retrospective review was performed of all patients with colorectal cancer treated with laparoscopy by the COST Study Group before August 1994. Tumor site, stage, differentiation, procedure completion, presence of recurrence (local, distant, trocar site), and cause of death were analyzed. **RESULTS:** A total of 372 patients with adenocarcinoma of the colon and rectum were treated by laparoscopic approach between October 1991 and August 1994 (170 men and 192 women): right colectomy, 170; sigmoid colectomy, 55; low anterior resection, 56; abdominoperineal resection, 44; left colectomy, 22; colostomy, 8; total colectomy, 6; transverse colectomy, 7; exploration, 2. Conversion to an open procedure was required in 15.6 percent of cases. Operative mortality was 2 percent. Tumor characteristics were as follows: TNM stage: I, 40 percent; II, 25 percent; III, 18 percent; IV, 17 percent; Differentiation: well-moderate, 88 percent; poor, 12 percent; carcinomatosis, 5 percent. Local (3.6 percent) and distant implantation occurred in four patients (1.1 percent). Only one of these patients died a cancer-related death (Stage III at 36 months). Cancer-related death rates increased with increasing stage of tumor: I, -4 percent; II, 17 percent; III, 31 percent; IV, 70 percent. **CONCLUSION:** A laparoscopic approach to colorectal cancer results in early outcome after treatment that is comparable with conventional therapy for colorectal cancer. A randomized trial is needed to compare long-term outcomes of open and laparoscopic approaches with colorectal cancer. [Key words: Laparoscopic colectomy; Cancer; Recurrence]

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Laparoscopic colectomy has been shown to be feasible, safe, and capable of fulfilling oncologic criteria for cancer surgery.<sup>1-8</sup> All reports on which these statements are based are at best from prospective, noncontrolled, nonrandomized series. As a result, many physicians are unwilling to acknowledge the possibility that laparoscopic techniques may have a role in treatment of colorectal cancer. Much controversy regarding the use of laparoscopic techniques for cancer stems from numerous anecdotal reports in the literature of trocar site implantation of colon cancer after partial colectomy.<sup>9-16</sup> The specific attempts to document adequacy of laparoscopic techniques in treatment of colorectal cancer have answered some of the issues, but questions remain.<sup>17-20</sup> Unfortunately, the true incidence of trocar site implantation and its implication to long-term survival is unknown. Reports from several small series have suggested a rate of 1 to 21 percent.<sup>9</sup>

Laparoscopic techniques may become simply another technique in the surgeon's armamentarium that can be equally well used to treat patients with colorectal cancer. Numerous reports of laparoscopic colectomy suggest that the same operation can be performed laparoscopically as performed open. However, it is unlikely that a small difference in outcome between the two techniques will be readily

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apparent, unless detected in a randomized, controlled trial.<sup>21, 22</sup>

The benefit of laparoscopic colorectal techniques is also the subject of debate. The demanding, advanced techniques require a steep learning curve and a large number of cases to obtain proficiency.<sup>23-25</sup> The number of surgeons routinely performing laparoscopic colorectal procedures, even for benign disease, is small and may limit the usefulness of laparoscopic colectomy. Very few comparative studies have looked closely at the laparoscopic and open techniques, although each group of patients are treated the same in terms of early feeding, ambulation, and discharge. Studies have suggested an advantage for a laparoscopic approach.<sup>26</sup> It is also possible that aggressive treatment and limitation of incision length in patients undergoing open colectomy may yield improved postoperative recovery similar to that reported for laparoscopy. A randomized, prospective, controlled trial is needed to address these less critical (noncancer-related) issues and identify those patients who will truly benefit from a potentially more expensive technique.

A surgical consortium entitled Clinical Outcomes of Surgical Therapies (COST) Study Group has initiated a multi-institutional, prospective, randomized, controlled trial to compare laparoscopic and open colectomy for curable right, left, and sigmoid colon cancer.<sup>27</sup> The trial opened in August 1994 and, funded by the National Cancer Institute, will compare 600 patients in each arm. However, to address some of the questions being raised by reports of trocar site implantation and in an attempt to gauge the early success or adequacy of treatment of colon cancer by trial participants, a retrospective review was undertaken of all patients treated for colorectal cancer by surgeons of the COST group before August 1994.

## METHODS

A survey was taken of all 32 surgeons participating in the National Cancer Institute-sponsored intergroup trial (Int 0146, A Phase III Prospective Randomized Trial Comparing Laparoscopic-Assisted *vs.* Open Colectomy for Colon Cancer) in January 1996. Surgeons were asked to submit data concerning all patients with colorectal cancer treated with laparoscopic colorectal techniques *before* August 1994. This was the date of activation of the national trial and provided at least 15-month follow-up of patients. Only 16 of 32 surgeons had performed laparoscopic procedures for

palliation or cure on patients with colorectal cancer before August 1994. Data supplied for each patient included age, sex, status at most recent follow-up, intent of procedure (curative *vs.* palliative), whether the procedure was completed laparoscopically, tumor TNM stage and differentiation, and presence of carcinomatosis. Follow-up information included presence of local, distant, or trocar site recurrence, death (attributable to disease or unrelated), and particulars of recurrence, if present. Majority of surgeons participating in the Intergroup 0146 Trial maintain their own prospective data collection system, which made data retrieval simple. Procedures were all laparoscopic "assisted" in that a small abdominal incision was made to extract the resected specimen and facilitate colonic or colorectal anastomosis. Only the abdominoperineal resections and colostomy constructions can truly be called totally laparoscopic procedures.

## Statistical Analysis

Kaplan-Meier survival curves were calculated for patients by TNM stage.

## Patient Profile

A total of 372 patients (174 male, 198 female) underwent laparoscopic procedures for colorectal cancer at 16 institutions between November 1991 and August 1994. All but 10 (2.6 percent) of these procedures were colonic or rectal resections (Table 1). Majority of cases were completed laparoscopically (84.4 percent), even though these cases represented the beginning of the learning curve in many of the contributing institutions. Distribution of cases among the 16 contributing surgeons is shown in Table 2. Mean age of patients was 70 (range, 27-95) years, and mean follow-up was 22.6 (range, 15-45) months.

**Table 1.**  
Categories of Procedures

Procedure	No. of Cases Entered
Right colectomy	170
Left colectomy	22
Sigmoid colectomy	58
Abdominoperineal resection	44
Low anterior resection	55
Total colectomy	6
Transverse colectomy	7
Colostomy	8
Exploration	2
	<hr/> 372

Majority of resections were performed for curable lesions (TNM Stage I, II, or III; 82 percent). The ten patients undergoing colostomy (8) or exploration only (2) were operated on for palliative diversion. Carcinomatosis was present in 15 patients on exploration (4 percent). Tumors were found to be well to moderately differentiated (305/372, 82 percent) or poorly differentiated (46/372, 12 percent). The remaining 21 tumors were unspecified.

**RESULTS**

There were 90 deaths in the group of 372 patients (24.2 percent, mean time to death 12.3 (range, 0–37.1) months). Kaplan-Meier survival curves for each TNM stage are seen in Figure 1. Extrapolated three-year survivals for Stages I to IV are 93, 72, 53, and 10 percent, respectively. Operative mortality (30 day) was reported in seven patients (2 percent). Another 21 patients (5.6 percent) died during follow-up from

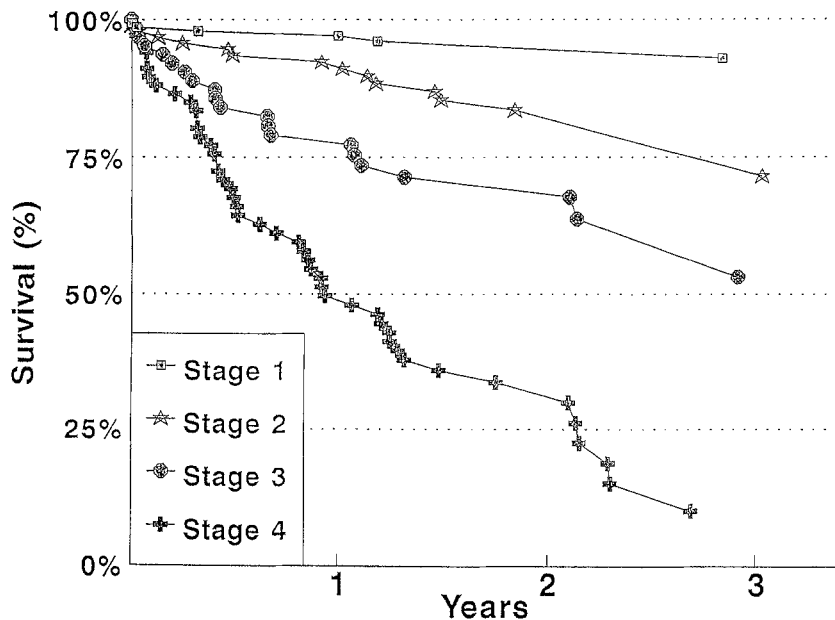
causes unrelated to their cancer or operation. Overall disease-related mortality was 16.7 percent (62/372). During follow-up, 51 of 68 patients treated for palliation died (75 percent). All were TNM Stage IV (Table 3).

Deaths occurred in 11 of 304 patients (3.6 percent) treated for cure (Table 3). The single patient (age 71) with Stage I disease who died did so 14 months postoperatively with liver metastases after a laparoscopic-assisted right colectomy in 1992 for a T2,N0,M0 lesion. Patients with Stage II disease (ages 74, 76, and 84 years) died at 14, 23, and 35 months postoperatively. One patient died with local and distant recurrence (poorly differentiated, metastasis to head of pancreas). The other two died with distant disease only (moderately differentiated). All three patients underwent laparoscopic right colectomy in 1992 for T3,N0,M0 lesions.

Seven patients with Stage III disease (ages 58, 74, 77, 78, 79, 81, and 86 years) died after laparoscopic surgery 5, 5, 5, 13, 25, 26, and 35 months following laparoscopic left colectomy (2), abdominoperineal resection (4), and right colectomy (1). Tumors were staged as T2,N1 (1), T3,N1 (2), T3,N2 (2), T3,N3 (1), and T4,N1 (1) pathologically. Patients died with lung (2) or liver (5) metastases, but only two had evidence of local recurrence. One of these patients (with T4,N1 disease, left colectomy converted to open) was the patient who died after developing a midline wound recurrence in the setting of carcinomatosis (see be-

**Table 2.**  
Surgeon Experience by Cases Entered

No. of Cases Entered	No. of Surgeons
>50	2
31–50	4
10–15	6
5–9	4
<b>Total</b>	<b>16</b>



**Figure 1.** Kaplan-Meier survival curves for patients by tumor TNM stage during three years.

low). All procedures in this group of patients were performed between 1992 and 1994.

Local recurrence of tumor was documented in 13 patients (3.5 percent). Distant recurrence documented by computed tomographic (CT) scan or other noninvasive means was identified in 41 patients (11.02 percent). Trocar site or abdominal wall tumor implantation was demonstrated in four patients (1.08 percent; Table 4). Only one of these four patients suffered a cancer-related death. The patient who died developed recurrent tumor following a left and transverse colectomy that was started laparoscopically and then converted to an open procedure when the tumor was noted to invade into the pancreas (T4,N1); the tumor recurred in the midline wound, and the patient was found to have carcinomatosis. Trocar site recurrences in the other three patients were resected. These three patients remain alive without disease. None of these procedures were considered to have violated cancer principles or to have spilled tumor during the procedure, which could cause tumor implantation. There was no evidence of carcinomatosis at time of initial operation in these four patients. The three patients with tumor recurrence at a trocar site developed implants in an isolated trocar site remote to the wound used for specimen extraction. Recurrence in the patient with a T2,N0,M0 tumor was limited to the subcutaneous fat.

**Table 3.**  
Death by Tumor Stage and Intent to Cure

Disease Related	Death (%)	Stage	% Stage
Treated for cure (n = 304)	11 (36)	I, 1	0.7
		II, 3	3.2
		III, 7	11
Palliative (n = 68)	51 (75)	IV, 51	75
Total	62	90	24

**Table 4.**  
Abdominal Wall Recurrence

Recurrences = 4		
Stage	Site	Outcome
T4N1M0	Midline wound	Died of disease
T3N1M0	Remote site	Resected
T3N0M0	Remote site	Resected
T2N0M0	Remote site	Resected

## DISCUSSION

Laparoscopic procedures in patients with colorectal cancer, in whom cure is possible, should only be performed in the setting of a controlled investigation. The COST Study Group has initiated a randomized, controlled trial (Intergroup 0146) sponsored by the National Cancer Institute and performed through cooperative oncology groups (Cancer and Leukemia Group B, Eastern Cooperative Oncology Group, North Central Cancer Treatment Group, Radiation Therapy Oncology Group, and Southwestern Oncology Group). Principle aim of the study is to compare laparoscopic colectomy and open colectomy in patients with curable right, left, and sigmoid colon cancers. The trial will evaluate not only long-term outcomes of cancer treatment but also quality of life, cost issues, early morbidity, and rapidity of recovery. The only ethical way to proceed with this trial is to assume both treatments are equal. This is not possible if laparoscopy results in a higher rate of trocar and specimen extraction site tumor implantation. Until now, there have been no denominators offered to anecdotally reported cases of trocar site implants. This study reveals four cases of abdominal wall tumor implants of 372 patients (1.08 percent). All four cases occurred in potentially curable patients, making the risk of trocar site or abdominal wall recurrence 4 of 304 (1.3 percent). This is not significantly different from the 1.5 percent rate of abdominal wall recurrence recently reported from the North Central Cancer Treatment Group trials of adjuvant therapy for colorectal cancer.<sup>28</sup> Carcinomatosis or multiple sites of recurrence were present in the majority of patients with abdominal wall recurrence and occurred in patients following resection of B<sub>2</sub> and C lesions. Finally, our rate of laparoscopic wound recurrence is similar to the 1 percent incidence of abdominal incision implantation reported in 1983 by Hughes *et al.*<sup>29</sup> in a group of 1,600 patients following open colectomy for cancer.

Trocar site or abdominal wall implantation of cancer did not seem to influence long-term outcome if recurrence was isolated and could, therefore, be resected. Only one of four patients (25 percent) has died from cancer-related causes after implantation was resected. Long-term follow-up is not available for these patients, even though the three patients remain free of disease. It is, therefore, possible that trocar site implants may not always represent advanced disseminated disease as postulated by Reilly *et al.*<sup>28</sup> and

Hughes *et al.*<sup>29</sup> If the presence of trocar site implants does not affect long-term survival of these patients, the risk of developing trocar site implants may not influence the decision regarding use of laparoscopy for cancer. The final decision should only be made based on long-term survival of patients treated for cure.

Patients undergoing laparoscopic procedures for colorectal cancer had three-year survival rates that were similar to other reports of open colectomy for colorectal cancer.<sup>30</sup> Data taken from the Surveillance, Epidemiology, and End Results Program (SEER) of the National Cancer Institute between 1973 and 1987 reported three-year survival rates for 106,269 patients with colon cancer of approximately 93 percent for Stage I, 82 percent for Stage II, 58 percent for Stage III, and 10 percent for Stage IV.<sup>31</sup> Carcinomatosis did not seem to influence trocar site implantation. Distant metastasis was the major mode of death attributable to cancer in palliative and curable cases alike. However, the issue of long-term survival after curative operation can only be assessed by a randomized trial, which is underway.

Studies using animal models have yielded data that suggest laparoscopy may be beneficial in treatment of cancer because of reduced operative stress and diminished immune suppression.<sup>32</sup> On the other hand, the pneumoperitoneum has been suggested as the cause for an increase in trocar site implantation of tumor at a very high inoculum (approximately  $1.6 \times 10^6$  cells).<sup>33</sup> True number of viable, free intraperitoneal cancer cells present in any given patient with a particular stage of cancer is unknown. The influence of free cancer cells within the abdominal cavity on tumor implantation and the impact of pneumoperitoneum on dissemination of those cells is still unknown. The counteracting positive influence of less operative stress from a laparoscopic procedure has not been quantified.<sup>34</sup> Numerous issues remain unsolved.

## CONCLUSION

Laparoscopic procedures for colorectal cancer performed in the past by members of the COST Study Group, who are currently involved in the National Institutes of Health trial comparing laparoscopic and open colectomy for cancer, have not resulted in a higher incidence of cancer-related complications, recurrences, or deaths. Proceeding with a randomized, controlled trial is, therefore, a reasonable next step for

these surgeons to evaluate the risks and benefits of laparoscopic colectomy for cancer.

## REFERENCES

1. Lord SA, Larach SW, Ferrara A, Williamson PR, Lago CP, Lube MW. Laparoscopic resection for colorectal carcinoma: a three-year experience. *Dis Colon Rectum* 1996; 39:148-54.
2. Lumley JW, Fielding GA, Rhodes M, Nathanson LK, Siu S, Stitz RW. Laparoscopic-assisted colorectal surgery: lessons learned from 240 consecutive patients. *Dis Colon Rectum* 1996;39:155-9.
3. Ortega AE, Beart Jr RW, Steele GD, Winchester DP, Greene FL. Laparoscopic bowel surgery registry: preliminary results. *Dis Colon Rectum* 1995;38:681-6.
4. Zucker KA, Pitcher DE, Martin DT, Ford RS. Laparoscopic-assisted colon resection. *Surg Endosc* 1994;8: 12-8.
5. Hoffman GC, Baker JW, Fitchett CW, Vansant JH. Laparoscopic-assisted colectomy: initial experience. *Ann Surg* 1994;219:732-43.
6. Mathis CR, MacFadyen BV. Laparoscopic colorectal resection: a review of the current experience. *Int Surg* 1994;79:221-225.
7. Falk PM, Beart RW Jr, Wexner SD, *et al.* Laparoscopic colectomy: a critical appraisal. *Dis Colon Rectum* 1993; 36:28-34.
8. Dean PA, Beart RW Jr, Nelson H, Elftmann TD, Schlinkert RT. Laparoscopic-assisted segmental colectomy: early Mayo Clinic experience. *Mayo Clin Proc* 1994;69: 834-40.
9. Wexner SD, Cohen SM. Port site metastases after laparoscopic colorectal surgery for cure of malignancy. *Br J Surg* 1995;82:295-8.
10. Jacquet P, Averbach AM, Jacquet N. Abdominal wall metastasis and peritoneal carcinomatosis after laparoscopic-assisted colectomy for colon cancer. *Eur J Surg Oncol* 1995;21:568-70.
11. Fusco MA, Paluzzi MW. Abdominal wall recurrence after laparoscopic-assisted colectomy for adenocarcinoma of the colon: report of a case. *Dis Colon Rectum* 1993;36:858-61.
12. Walsh DC, Wattoo DA, Wilson TG. Subcutaneous metastases after laparoscopic resection of malignancy. *Aust N Z J Surg* 1993;63:563-5.
13. Montorsi M, Fumagalli U, Rosati R, Bona S, Chella B, Huscher C. Early parietal recurrence of adenocarcinoma of the colon after laparoscopic colectomy. *Br J Surg* 1995;82:1036-7.
14. Ugarte F. Laparoscopic cholecystectomy port seeding from a colon carcinoma. *Am Surg* 1995;61:820-1.
15. Jacquet P, Averbach AM, Stephens AD, Sugarbaker PH. Cancer recurrence following laparoscopic colectomy:

- report of two patients treated with heated intraperitoneal chemotherapy. *Dis Colon Rectum* 1995;38:1110-4.
16. Fodera M, Pello MJ, Atabek U, Spence RK, Alexander JB, Camishion RC. Trocar site tumor recurrence after laparoscopic-assisted colectomy. *J Laparoendosc Surg* 1995;5:259-62.
  17. Lacy AM, Garcia-Valdecasas JC, Pique JM, *et al.* Short-term outcome analysis of randomized study comparing laparoscopic vs open colectomy for colon cancer. *Surg Endosc* 1995;9:1101-5.
  18. Franklin ME Jr, Rosenthal D, Norem RF. Prospective evaluation of laparoscopic colon resection *versus* open colon resection for adenocarcinoma: a multicenter study. *Surg Endosc* 1995;9:811-6.
  19. Gray D, Lee H, Schlinkert R, Beart RW Jr. Adequacy of lymphadenectomy in laparoscopic-assisted colectomy for colorectal cancer: a preliminary report. *J Surg Oncol* 1994;57:8-10.
  20. Milsom JW, Bohm B, Decanini C, Fazio VW. Laparoscopic oncologic proctosigmoidectomy with low colorectal anastomosis in a cadaver model. *Surg Endosc* 1994;8:1117-23.
  21. Ota DM, Nelson H, Weeks JC. Controversies regarding laparoscopic colectomy for malignant diseases. *Curr Opin Gen Surg* 1994:208-213.
  22. Stoker ME. Laparoscopic colon surgery for cancer: controversy, caution and common sense. *Int Surg* 1994;79:240-1.
  23. Senagore AJ, Luchtefeld MA, MacKeigan JM. What is the learning curve for laparoscopic colectomy? *Am Surg* 1995;61:681-5.
  24. Wishner JD, Baker JW Jr, Hoffman GC, *et al.* Laparoscopic-assisted colectomy: the learning curve. *Surg Endosc* 1995;9:1179-83.
  25. Simons AJ, Anthonie GJ, Ortega AE, *et al.* Laparoscopic-assisted colectomy learning curve. *Dis Colon Rectum* 1995;38:600-3.
  26. Fleshman JW, Fry RD, Birnbaum EH. Laparoscopic-assisted minilaparotomy approaches to colorectal diseases are similar in early outcome. *Dis Colon Rectum* 1996;39:15-22.
  27. Nelson H, Weeks JC, Wieand HS. Proposed Phase III trial comparing laparoscopic-assisted colectomy *versus* open colectomy for colon cancer. *J Natl Cancer Inst Monographs* 1995;19:51-6.
  28. Reilly WT, Nelson H, Schroeder G, Wieand HS, Bolton J, O'Connell MJ. Wound recurrence following conventional treatment of colorectal cancer: a rare but perhaps underestimated problem. *Dis Colon Rectum* 1996;39:200-7.
  29. Hughes ES, McDermott FT, Polglase AL, Johnson WR. Tumor recurrence in the abdominal wall scar tissue after large-bowel cancer surgery. *Dis Colon Rectum* 1983;26:571-2.
  30. Corman ML. Colon and rectal surgery. Philadelphia: JB Lippincott, 1993:563.
  31. Beahrs OH, Henson DE, Hutter RV, Kennedy BJ. Manual for staging for cancer. 4th ed. Philadelphia: JB Lippincott, 1992:76-7.
  32. Allendorf JD, Bessler M, Kayton ML, Whelan RL, Treat MR, Nowygrod TR. Tumor growth after laparotomy or laparoscopy: a preliminary study. *Surg Endosc* 1995;9:49-52.
  33. Jones DB, Guo L-W, Reinhard MK, *et al.* Impact of pneumoperitoneum on trocar site implantation of colon cancer in hamster model. *Dis Colon Rectum* 1995;38:1182-8.
  34. Harmon GD, Senagore AJ, Kilbride MJ, Warzynski MJ. Interleukin-6 response to laparoscopic and open colectomy. *Dis Colon Rectum* 1994;37:754-9.