Laparoscopy for Colon Cancer

a report by
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The role of laparoscopy for the treatment of colon and rectal malignancy has been slower to evolve and the subject of much debate over the past decade. From 1991 to 2004, several concerns limited the widespread use of laparoscopy as an approach for the attempted cure of colorectal carcinoma. Firstly, these procedures are technically demanding and time-consuming, presenting prohibitive challenges to the development of laparoscopic approaches in some high-volume centers where operating room (OR) time is at a premium. Secondly, concerns were raised with regard to the effect on the behavior of the tumor and the theoretic compromise of curative oncological techniques. In particular, the adequacy of the lateral and distal margins, the ability to explore the abdomen and the subsequent impact on outcome (recurrence rates and survival) have been sources of controversy, particularly in the hands of novice surgeons. Reports of port-site metastasis rate of up to 21% deterred many surgeons from adopting laparoscopy for colon cancer.[1] Finally, financial constraints posed significant obstacles to widespread adoption, particularly without evidence of dramatic patient benefits.

These concerns and the fear of widespread adoption leading to an explosion of unacceptable cancer outcomes led the American Society of Colon and Rectal Surgeons (ASCRS) to proclaim in a 1994 consensus statement that in the absence of five-year survival data, they did not endorse laparoscopic colon resection for cancer.[2] Subsequently, Chapman published a representative report of growing concerns in a systemic review in 2001 that after a decade of experience via an analysis of 52 studies on laparoscopy for colorectal cancer, little high evidence existed advocating laparoscopy for cancer.[3]

In response, several worldwide prospective randomized trials addressing the long-term recurrence rates and survival were initiated. The recent release of the largest multicenter prospective randomized trial to date marked the beginning of a new, minimally invasive age in colon cancer treatment.[4] Despite incomplete enrollment, this study was the first with sufficient statistical power to be able to conclusively detect any differences between these two procedures. The study revealed that, in experienced hands, laparoscopic colectomy offers the same oncological outcomes as the open procedure with shorter hospital stay and less post-operative pain.

Short-term Benefits

Laparoscopy has traditionally been associated with rapid bowel function recovery due to reduced surgical trauma, compared with laparotomy. Evidence from large retrospective and prospective series has revealed a mean time of bowel recovery of 2.5 days after surgery (see *Table 1*).[5–7] Evidence from non-randomized, case-controlled studies revealed faster bowel function recovery in patients undergoing laparoscopy (mean 2.6 days) when compared with those patients undergoing laparotomy (mean 3.6 days).[8–13] The most definitive evidence comes from randomized trials.[14–17] Lacy et al.[16] published a large randomized controlled trial in which significant benefit was seen. The Clinical Outcomes of Surgical Therapy (COST) trial did not specifically report on the timing of bowel function recovery, although faster perioperative recovery was inferred by the shorter hospital stay and briefer use of parenteral narcotics and oral analgesics.[4]

Evaluation of quality of life has primarily focused on post-operative pain and intravenous analgesic requirements. The few case control and cohort studies that have addressed post-operative pain have reported inconsistent results, possibly due to the small number of patients in these studies (see *Table 2*). In contrast, four randomized trials have shown laparoscopy to be associated with less pain at some point in the post-operative recovery period.[14,17,19,20] In addition, the patients in the COST trial laparoscopic group required two days of intravenous (IV) analgesia and one day of oral analgesia compared with four days and two days, respectively, in the open group.[4] Weeks et al.[18], who performed a broader assessment in quality of life, found that while the laparoscopic group received significantly less analgesics and demonstrated improved global rating scores two weeks after surgery, other aspects of quality of life using validated instruments were no different. In addition, those patients who underwent conversion demonstrated poorer quality-of-life scores than those in whom the open procedure was performed at the outset.

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Table 1: Bowel Function Recovery

Author	Year	N of Patients		Bowel Function (Mean/Median N of Days)	
		Lap	Open	Lap	Open
Retrospective					
Melotti[6]	1999	163	–	2.9	–
Schiedeck[7]	2000	399	–	3	–
Zhou[22]	2003	82	–	1–2	–
Prospective					
Morino[5]	2003	100	–	2.9	–
Tsang[24]	2003	44	–	2	–
Case-control/Cohort Studies					
Seow-Choen[8]	1997	16	11	2	2.5
Ramos[10]	1997	18	18	1.9*	3*
Goh[11]	1997	20	20	3	3
Schwandner[9]	1999	32	32	4.1*	5.1*
Hartley[112]	2001	21	22	3	4
Champault[13]	2002	74	83	1.4*	3.2*
Randomised					
Milsom[14]	1998	54	53	3*	4*
Curet[115]	2000	18	18	2.7*	4.4*
Lacy[16]	2002	111	108	1.5*	2.3*
Hasegawa[17]	2003	29	30	2*	3.3*

* $p<0.05$. Lap = laparoscopy, N = number, Open = open procedure.

Table 2: Post-operative Pain

Author	Year	N of Patients		Less Pain/Analgesic Requirement (Days)	
		Lap	Open	Lap	p value
Case-control/Cohort Studies					
Seow-Choen[8]	1997	16	11	No	–
Ramos[10]	1997	18	18	Yes	<0.005
Goh[11]	1997	20	20	No	–
Psaila[26]	1998	29	25	Yes	0.002
Schwandner[9]	1999	32	32	No	–
Randomised					
Stage[19]	1997	15	14	Yes	<0.05
Schwenk[20]	1998	30	30	Yes	<0.01
Milsom[14]	1998	54	53	Yes	0.02
Weeks[18]	2002	168	221	Yes	0.03
Hasegawa[18]	2003	29	30	Yes	0.0022
Nelson[2]	2004	435	425	Yes	<0.001

Lap = laparoscopy, N = number, Open = open procedure.

Length of hospital stay is a common variable assessed in most laparoscopic studies. It reflects the rapidity of physiological recovery and has economic implications with regard to operative and hospital costs. Results from numerous retrospective and prospective series demonstrate a mean duration of hospitalization of 10.5 days (see *Table 3*). Results from 14 non-randomized controlled studies reveal a mean of 9.6 days in the laparoscopy group and 13.7 days in the laparotomy group.[8,9,12,13,25–31] The COST trial revealed a length of hospital stay of five days in the laparoscopic group and six days in the laparotomy group (<0.001).[4] Similar results were reported in other randomized trials.[15–20]

Several studies evaluating the effect on cost with the laparoscopic approach have suggested that the higher cost is offset by the faster recovery. However, the results are inconsistent, primarily because of differences in perspective and methodology. While Khalili et al.[25] found that the OR costs were higher in the laparoscopic group with no difference in overall hospital cost, Psaila[26] found that the higher OR cost was offset by the overall lower hospitalization costs in the laparoscopic group. The most convincing evidence comes from the recent prospective randomized Swedish Colon Cancer Laparoscopic or Open Resection (COLOR) trial,[32] in which the authors found that the total cost to society were similar for laparoscopic and open procedures, but that the total cost to the healthcare system was significantly higher for the laparoscopic group. The main contributors to this higher cost included higher OR costs and costs resulting from complications and re-operations, which occurred more frequently in the laparoscopic group. In this study, there was no difference in length of hospital stay to offset the higher costs of short-term care. However, early recovery resulted in less loss of productivity such that the two approaches did not differ in economic impact.

Recurrence Rates and Survival

Comparison of long-term outcomes among the various studies must be regarded in light of the lack of homogeneity in patient selection, radiation therapy, site and stage of the tumor, time of follow-up, and violation of the intention-to-treat (ITT) principle in some trials, which can impact recurrence and reported survival rates. However, useful information can be gleaned from initial case studies in which the mean/median follow-up time is 16 to 71 months (see *Table 5*).[7,24,33–35] Recurrence rates varied from 7.2% to 16.1%, including local recurrences from 1.5% to 4.1% and distant recurrences from 6.1% to 10.3%. In contrast to earlier reports, port/extraction site recurrence rates do not seem to surpass 1% after curative resection in the majority of recent studies.[16,36] Comparative studies have found equivalent recurrence rates between laparoscopy and laparotomy, with an overall rate of approximately 4.6% and 20% for both groups.[9,10,12,26–39] Local recurrences have reached 14.8% and 26% and distant recurrences 15% and 18.6% in the laparoscopic and open groups, respectively. In the Lacy and COST randomized trials, no statistical significance was identified with respect to recurrence rates in the laparoscopic or open groups at any stage of cancer.[16,4]

With respect to survival outcome, retrospective and prospective reviews have demonstrated a five-year survival

rate ranging from 72% to 80.9% after curative resection with better outcomes associated with early stage carcinomas (see *Table 6*).[5,21,35,38–40] Comparative case control and cohort studies have not demonstrated any differences in five-year survival between patients who underwent laparoscopy and those who had laparotomy, with rates ranging from 64% to 93% in both groups.[9,12,13,25,31,36,41–45] Lujan[43] published one of the largest non-randomized studies and demonstrated that five-year relative survival rates in the laparoscopic group were 73% for stage I, 61% for stage II, 55% for stage III, and 0% for stage IV disease. These results were comparable with the open group.

The most important information relative to survival and the effects of laparoscopy on disease-specific outcome is provided by prospective randomized trials initiated in several countries. The COLOR group in Europe[46] reported preliminary results demonstrating short-term (less than two years of follow-up) survival rates of 95% for stage I, 98% for stage II, and 93% for stage III carcinomas. The trial by Curet[15] with survival data outcome ranging from 2.5 to 6.3 years (mean 4.9 years) revealed that 67% of cancer related deaths occurred in the open group, while 78% occurred in the laparoscopic group. The randomized trial by Lacy et al.[16] demonstrated no difference in survival rates between patients who underwent laparoscopy and laparotomy (82% compared with 74%). However, the cancer-related survival rate was significantly higher in the laparoscopic group (91% compared with 79%; p=0.02). The effect was the result of the significant benefits seen in those patients with stage III tumors. In summary, there may be no significant differences between laparoscopy and laparotomy for either recurrence or survival rates. However, laparoscopy may indeed be superior for patients with stage III disease.

Conclusion

Laparoscopy for colorectal cancer has shown to be superior to laparotomy with regard to short-term benefits, including pain, length of ileus, length of hospitalization, cosmesis, morbidity, and disability. When performed by appropriately skilled surgeons in properly selected patients, these short-term benefits are usually demonstrated. Since the publication of the COST trial, it appears that laparoscopic colectomy and conventional open colectomy have similar long-term outcomes prompting the ASCRS and the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) to jointly endorse an approval statement on laparoscopic colectomy for curable cancer.[49] That statement claims that as long as surgeons acquire the experience of at least 20 laparoscopic colorectal resections and adhere to oncological principles, the laparoscopic approach is safe to use in curable colon cancer. In addition, a recent meta-analysis performed by Abraham[49] of 12 randomized trials revealed equivalent short- and long-term outcomes.

Table 3: Hospital Stay

Author	Year	N of Patients		Hospital Stay (Days)	
		Lap	Open	Lap	Open
Case Series					
Melotti[6]	1999	163	–	10.9	–
Schiedeck[7]	2000	399	–	14	–
Zhou[22]	2003	82	–	8	–
Prospective Series					
Yamamoto[23]	2002	70	–	8	–
Anderson[21]	2002	100	–	8.3	–
Morino[5]	2003	100	–	16.6	–
Tsang[24]	2003	44	–	8	–
Case-control/Cohort Studies					
Lord[28]	1996	32	32	5.8*	8.2*
Franklin[36]	1996	224	224	5.7*	9.7*
Seow-Choen[8]	1997	16	11	6.5*	8*
Ramos[10]	1997	18	18	7.4*	12.9*
Goh[11]	1997	20	20	5	5.5
Khalili[25]	1998	80	90	6.2*	8.2*
Psaila[26]	1998	29	25	10.7*	17.8*
Schwandner[9]	1999	32	32	15.3	21.9
Fleshman[27]	1999	152	33	7.4*	8.7*
Leung[31]	2000	59	34	16*	25.5*
Hartley[12]	2001	21	22	13.5	15
Baker[29]	2002	28	61	13*	18*
Anthuber[20]	2002	101	334	14.4*	19.9*
Champault[13]	2002	74	83	8.2*	12.3*
Randomised					
Stage[19]	1997	15	14	5*	8*
Schwenk[20]	1998	30	30	10.1*	11.6*
Milsom[14]	1998	54	53	6	7
Curet[15]	2000	18	18	5.2*	7.3*
Lacy[16]	2002	111	108	5.2*	7.9*
Weeks[18]	2002	168	221	5.6*	6.4*
Hasegawa[17]	2003	29	30	7.1*	12.7*
Nelson[2]	2004	435	425	5*	6*

*$p<0.05$. Lap = laparoscopy, N = number, Open = open procedure.

Fortunately, the slow measured growth of laparoscopy for the attempted cure of malignancy has resulted in appropriate evolution of the technique. Surgeons have gained sufficient expertise working with benign conditions. Manufacturers have improved the technology and patients have become more aware of the benefits. Costs have been brought under more effective control and protocols have been adapted to minimize length of hospital stay in all cases. The specter of port-site recurrence that has loomed over the use of a laparoscopic approach has been deemed a technical issue rather than a problem with laparoscopy. Finally, it is clear from randomized studies that laparoscopic oncological surgery now has a role in the management of colorectal cancer patients at all stages of disease. ■

Table 4: Recurrence

Author	Year	N of Patients		Mean/Median Follow-up	Recurrence (%)					
					Overall		Local		Distant	
		Lap	Open		Lap	Open	Lap	Open	Lap	Open
Retrospective										
Huscher[33]	1996	146	–	16 months	11.7	–	4.1	–	6.1	–
Schiedek[17]	2000	399	–	30 months	7.2	–	1.5	–	6.2	–
Prospective										
Lumley[34]	2002	154	–	71 months	13.6	–	1.9	–	10.3	–
Anderson[31]	2002	100	–	43 months	16.1	–	–	–	–	–
Scheidbach[35]	2002	206	–	25.2 months	11.6	–	3.4	–	8.2	–
Case control/Cohort										
Franklin[36]	1996	165	212	60 months	12.2	22	–	–	–	–
Ramos[10]	1997	16	16	20 months	12.5	25	6.2	18.7	6.2	6.2
Khalili[25]	1998	76	82	21/18 months	13.1	18.3	3	6	10	11
Schwandner[9]	1999	32	32	33.1/32.1 months	15.6	15.6	3.1	0	12.5	15.6
Santoro[37]	1999	40	43	24–60 months	20	23	2.5	2.3	15	18.6
Lezoche[38]	2000	99	109	32.2/34.2 months	16	20.2	3	9.2	11	11
Hartley[12]	2001	21	22	38 months	5	4.5	5	4.5	5	0
Feliciotti[39]	2002	74	75	48.9 months	12.7	13.3	1.3	2.7	10.8	10.7
Randomised										
Curet[15]	2000	18	18	59 months	0	6	–	–	–	–
Lacy[14]	2002	106	102	44/43 months	17	27	6.6	6.6	8.8	13.7
Nelson[2]	2004	435	425	53 months	17	20	–	–	–	–

Lap = laparoscopy, N = number, Open = open procedure.

Table 5: Survival

Author	Year	N of patients		Mean/Median Follow-up	Survival	Overall Survival (%)/TNM Stage or Dukes' Classification	
		Lap	Open			Lap	Open
Retrospective							
Fleshman[40]	1996	372	–	22.6 months	3 years	I-93; II-72; III-53	–
COLOR trial[46]	2000	513	–	–	+ 2 years	I-95; II-98; III-93	–
Poulin[41]	2002	70	–	31 months	5 years	72.1	–
Lechaux[42]	2002	166	–	65 months	3 years	79	–
Prospective							
Scheidbach[36]	2002	214	–	25.2 months	5 years	80.9	–
Anderson[21]	2002	100	–	40.3 months	5 years	A-100; B-76; C-51	–
Morino[5]	2003	70	–	45.7 months	5 years	I-92; II-79; III-67	–
Case control/Cohort							
Franklin[36]	1996	165	212	34/4.8 months	5 years	89.7	92.4
Leung[31]	1997	50	50	32.8 months	5 years	67.2	64.1
Khalili[25]	1998	76	82	21 months	5 years	87.5	85
Schwandner[9]	1999	32	32	33.1 months	3 years	93	93
Santoro[37]	1999	40	43	24–60 months	5 years	73.2	70.1
Leung[44]	2000	19	24	30/28 months	4 years	84.2	77.8
Hartley[12]	2001	21	22	38 months	3 years	71	77
Lujan[43]	2002	102	641	64.4 months	5 years	I-73; II-61; III-55	I-75; II-65; III-46
Champault[13]	2002	62	66	60 months	5 years	75.8	74.2
Pantakar[45]	2003	161	174	52 months	5 years	I-76; II-68; III-53	I-80; II-64; III-50
Randomised							
Curet[15]	2000	18	18	59 months	5 years	78	66
Lacy[14]	2002	106	102	44 months	5 years	90*	79*
Nelson[2]	2004	435	425	53 months	4.4 years	79	78

** p<0.05. Lap = laparoscopy, N = number, Open = open procedure.*

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