

Laparoscopic Colectomy for Colorectal Cancer*

Nir Wasserberg MD

Department of Surgery, Rabin Medical Center (Beilinson Campus), Petah Tikva, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

ABSTRACT: The laparoscopic approach to the treatment of colon and rectal cancer remains controversial long after it was accepted for benign conditions. Laparoscopic cancer resection should meet appropriate oncologic standards and achieve a long-term oncologic outcome at least equivalent to that of open resection. Several international randomized controlled trials have provided adequate data to ascertain the oncologic quality of laparoscopic colon resection, showing a benefit in short-term outcome over open resection. The use of laparoscopic resection for rectal cancer is awaiting further investigation.

IMAJ 2010; 12: 572–576

KEY WORDS: laparoscopy, colectomy, colon cancer, rectal cancer, anterior resection

Colorectal cancer is one of the most common cancers in the developed world [1]. Surgical removal of the primary tumor with adequate margins and lymphadenectomy provide the best chance of long-term disease-free and overall survival. Conventional open colectomy is considered the gold standard for both benign and malignant diseases.

Laparoscopy-assisted colectomy was first described in the early 1990s [2] and, although technically challenging, has become a feasible option for colon resection. Its advantages over open colectomy include better cosmetic results, less postoperative pain, more rapid return of bowel function and, consequently, shorter hospital stay and expedited return to work [3]. Moreover, a recent population-based study from the United Kingdom including 3709 LACs among 192,620 elective colon and rectal resections performed in 1996–2006 demonstrated a significantly reduced 30 day and 365 day mortality rate compared with open colectomy [4]. However, although LAC has been accepted for the treatment of benign diseases, because of concerns regarding its safety and efficacy and short- and long-term oncologic outcomes, its use in patients with laparoscopic

colorectal cancer has been limited to major clinical trials. Several international randomized controlled trials in addition to abundant articles and a few meta-analyses have addressed these concerns. Although some of these studies were criticized for selection bias and poor methodology [5], in general, LAC was found to be safe and oncologically equivalent to open colectomy for colon cancer. For data on laparoscopic rectal resection, we are still awaiting the long-term results of ongoing studies.

This review summarizes the current information on LAC for colorectal cancer.

LAPAROSCOPIC RESECTION FOR COLON CANCER

Standard oncologic surgery consists of en bloc bowel resection with appropriate proximal and distal resection margins and more than 12 harvested lymph nodes [6]. Measures of the oncologic outcome of colectomy for colon cancer include cancer recurrence and cancer-related mortality.

The first meaningful study of LAC for the treatment of colon cancer was the single-center Barcelona trial [7], published in 2002. A total of 219 patients with right and left colon cancer were randomized to undergo open colectomy or LAC. The LAC group showed comparable oncologic results to the open colectomy group and even better survival rates in the patients with stage III disease. These results were later confirmed on long-term follow-up (mean 95 months, range 77–133 months) [8].

The landmark Clinical Outcome of Surgical Therapy (COST) study [9] was published in the *New England Journal of Medicine* in 2004. This trial included 872 patients with colon cancer from 48 centers in the United States and Canada operated on by a

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total of 66 surgeons. The patients were randomized to undergo LAC or open colectomy, and the results were analyzed on an intent-to-treat basis. The median duration of this study (4.4 years) together with a subsequent long-term study [10] was 7 years (range 5–10 years). There were no differences between the LAC and open colectomy groups regardless of disease stage, in disease-free 5 year survival (open colectomy 68.4%, LAC 69.2%, $P = 0.94$), overall 5 year survival (open colectomy

*Presented at the World Congress for the Advancement of Surgery, November 2009, Israel

LAC = laparoscopy-assisted colectomy

74.6%, LAC 76.4%, $P = 0.93$), and overall recurrence rate (open colectomy 21.8%, LAC 19.4%, $P = 0.25$). These findings confirmed the oncologic soundness of laparoscopic resection for colon cancer.

Three subsequent multicenter randomized controlled trials yielded similar results. The Colon Cancer Laparoscopic or Open Resection (COLOR) trial [11] included 1248 patients with colon cancer and similar characteristics from 29 centers in Western Europe. The median duration of follow-up was 53 months (range 0.03–60 months) [12]. The Medical Research Council Conventional vs. Laparoscopic Assisted Surgery in Colorectal Cancer (CLASICC) trial included 794 patients: 413 with colon cancer and 381 with rectal cancer [13,14], and the short-term Australasian randomized clinical study comparing laparoscopic and conventional open surgery for colon cancer (ALCCaS) [15] compared 294 LAC with 298 open colectomy procedures performed in 31 centers in Australia and New Zealand [Table 1].

Finally, in a report by the transatlantic laparoscopically assisted versus open colectomy trials study group [16], authors from the Barcelona, COST, COLOR, and CLASICC trials collaborated in an analysis of their pooled data. Three year disease-free survival was 75.8% in the LAC arm and 75.3% in the open colectomy arm; the respective rates of overall survival were 82.2% and 83.5%. These findings remained consistent when the data were analyzed by cancer stage.

Taken together, these studies [Table 2], along with several meta-analyses and systematic reviews [17-19], confirmed the oncologic adequacy of the laparoscopically resected colon and the similar long-term oncologic results of LAC and open colectomy.

Another oncologic issue related specifically to laparoscopic surgery is the reported high rate (up to 21%) of port-site recurrence [20,21]. The mechanisms suggested to account for this finding were pneumoperitoneum – the "chimney effect," CO₂-enhanced tumor growth, and mechanical factors during bowel extraction [22]. In further studies, however, the American multicenter COST group [9] found only a 0.5% port-site metastasis rate, and the Barcelona trial [7] a 0.9% rate. This suggested that port-site recurrence was related to surgical technique and the long learning curve of laparoscopic colectomy for cancer. Thus, with proper tissue handling and wound protection, tumor recurrence at the surgical wound appears to be reassuringly rare, with no significant difference between the open and laparoscopic techniques.

In summary, considering the available data, LAC may offer some short-term postoperative benefit over open colectomy. From an oncologic perspective, there is no apparent reason not to offer LAC to patients with colon cancer of any stage.

Although laparoscopic colon resection does not compromise oncologic outcome, there are no data to support its superiority over open resection

Table 1. Laparoscopic colectomy: operative and short term results

Study [ref] year	Group	No. of patients	Intraoperative parameters			Postoperative parameters		
			Conversion rate (%)	OR time (min)	Mean EBL (ml)	Time to BM (days)	LOS (days)	Leak rate (%)
Barcelona [7,8] 2002, 2008	LAC	111		142*	105	1.5	5.2	0
	OC	108	11	118	193*	2.3*	7.9*	1
COST [9,10] 2004, 2007	LAC	435		150*	–	–	5	–
	OC	428	21	95	–	–	6*	–
CLASICC [13,14] 2005, 2007	LAC	273		–	–	5	9	3
	OC	253	29	–	–	6	11	2
COLOR [11,12] 2005, 2009	LAC	621		150*	100	3.6	8.2	2
	OC	627	17	95	175*	4.6*	9.3*	1
ALCCaS [15] 2008	LAC	298		145*	100	4	7	1.4
	OC	294	14.6	115	100	5*	8*	3.4

*Statistically significant difference
LAC = laparoscopic assisted colectomy, OC = open colectomy, OR = operating room, EBL = estimated blood loss, BM = bowel movement, LOS = length of stay.

Table 2. Laparoscopic colectomy: oncologic results

Study [ref]	Follow-up (mos)	Group	Port/incision recurrence (%)	Positive margins (%)	Lymph nodes retrieved (mean)	Recurrence (%)	Disease-free survival (%)	Overall survival (%)
Barcelona [7,8]	95	LAC	0.9	–	–	18	–	66
		OC	0	–	–	28	–	51
COST [9,10]	84	LAC	0.5	0(6)	12	19.4	69.2	76.4
		OC	0.2	0(5)	12	21.8	68.4	74.6
CLASICC [13,14]	50	LAC	2.1	0.5	12	–	66.3	68.4
		OC	0.5	0	13.5	–	67.7	66.7
COLOR [11,12]	53	LAC	–	0.4	10	–	74.2	81.8
		OC	–	0.2	10	–	76.2	84.2
ALCCaS [15]	–	LAC	–	22*	13	–	–	–
		OC	–	13	13	–	–	–

*Statistically significance difference for margin < 5 cm
LAC = laparoscopic assisted colectomy, OC = open colectomy

LAPAROSCOPIC RESECTION FOR RECTAL CANCER

Surgical resection is the most important modality for the treatment of rectal cancer. The procedure of choice is total mesorectal excision [23], which includes removal of the rectum along with complete excision of its lymphatic drainage system. Total mesorectal excision TME has consistently been shown to reduce local failure and to increase survival [24,25], compared to traditional standard blunt rectal dissection. Some researchers suggested that laparoscopic TME may offer potential benefits over an open procedure; specifically, reduced blood loss, less postoperative pain, faster recovery, and lower mor-

TME = total mesorectal excision

bility [26]. Moreover, the magnified laparoscopic view could supplement the pelvic dissection regarding sphincters and nerve preservation, thereby improving functional outcome and, perhaps, even oncologic outcome.

However, since rectal cancer surgery is technically demanding and any deviation from oncologic principles could compromise patient outcome, it has been excluded from most of the randomized control studies that compared laparoscopic and open resection for cancer. The bulk of available data comes from relatively small randomized control studies and larger non-randomized case series, and the interpretation of the findings is sometimes difficult because of the heterogeneity of the protocols and lack of consistent evidence. Some of the studies included patients with sigmoid and upper rectal cancer [27], whereas others included patients after open/laparoscopic low anterior resec-

tion [28] or abdominoperineal resection [29], or both [26]. Additionally, oncologic results may vary in accordance with the neoadjuvant and adjuvant treatment policy. So far, these studies [Tables 3 and 4], together with several meta-analyses [30-32] suggest that laparoscopic TME is feasible and is not associated with increased morbidity and mortality. Conversely,

Faiz et al. [4], in a large population-based series, reported a higher readmission rate after laparoscopic rectal resection for malignancy.

Erectile and urinary bladder dysfunction are common complications of TME for rectal cancer, with reported rates ranging from 10% to 35% and 0 to 10%, respectively [33,34]. Although laparoscopic TME may have an advantage over open TME in terms of genitourinary dysfunction, this factor has been addressed in only a few studies. A report based on the CLASICC trial [34] including 247 patients after open or laparoscopic rectal resection, total mesorectal or conventional, found no difference in bladder function between the groups, but overall, sexual and erectile function tended to be worse in men after laparoscopic resection ($P = 0.063$ and $P = 0.068$, respectively). The authors attributed this finding to the higher rate of TME in the laparoscopy group. However, the data thus far on functional outcome are insufficient to reach a conclusion.

As for colon cancer, to meet the standards of proper oncologic resection, TME rectal specimens should have specific macroscopic characteristics [35]. The best measures of total mesorectal excision quality are the number of harvested lymph nodes and clear distal and circumferential margins. In the published series [Table 4] and a recent report from the Cochrane database [38], the number of removed lymph nodes and rates of involved margins were equal after laparoscopic and open rectal resection. Noteworthy is the CLASICC trial [13,14], which reported a worrisomely high rate of involved radial margins after laparoscopic low anterior resection (12% vs. 6% for open surgery, $P = 0.19$). Although this difference was not statistically significant and did not translate to a clinical difference between the groups, it raised concerns regarding the adequacy of laparoscopic LAR if widely performed by non-dedicated surgeons.

Further data were derived from the CLASSICC trial, where 48% of the patients underwent rectal cancer resection (128 open vs. 253 laparoscopic). After 3 years follow-up, there was no difference in overall survival, disease-free survival, or tumor recurrence rate between the laparoscopy and open surgery group [14]. There was also no statistically significant between-group difference when the rectal cancer cases were analyzed by type of surgery (LAR versus abdominoperineal resection). Overall survival was 74.6% in the patients after

Currently there is no solid level 1 evidence to support the use of laparoscopic resection in rectal cancer outside of clinical trials

Table 3. Laparoscopic rectal resection: operative and short term results

Study [ref] year	Group procedure	No. of patients	Intraoperative parameters			Postoperative parameters		
			Conversion (%)	OR time (min)	EBL (ml)	Anastomotic leak (%)	Bowel movement	Hospital stay (days)
Braga et al. [26] 2007	LAC OC (AR+APR)	83 85	7.2	262 209*	213 296*	9.6 10.6		10 13.6*
CLASICC [13,14] 2005, 2007	LAC OC (AR)	230 113	34	180 165		10 7	5 6	11 13
Ng et al. [29] 2008	LAC OC (APR)	51 48	9.8	213.5 163.7*	20 92*	–	4.3 6.3	10.8 11.5
Zhou et al. [28] 2004	LAC OC (AR)	83 89	–	120 106	–	1 3	1.5 2.7*	8.1 13.3*

*Statistically significant difference

LAC = laparoscopic assisted colectomy, OC= open colectomy, AR = anterior resection, APR = abdominoperineal resection, OR = operating room, EBL = estimated blood loss

Table 4. Laparoscopic rectal resection: oncologic results

Study [ref] year	Follow-up (mos)	Group procedure	Positive radial margins (%)	Lymph nodes retrieved (mean)	Local recurrence (%)	Overall survival (%)
Braga et al. [26] 2007	53.6	LAC OC (AR+APR)	1.2	12.7 13.6	4 5.2	–
CLASICC [13,14] 2005, 2007	36.8	LAC OC (AR)	12 6	7.8 7	7.8 7	74.6 66.7
Ng et al. [29] 2008	87.2	LAC OC (APR)	–	12.4 13	5 11	75.2 76.5

*Statistically significant difference

LAC = laparoscopic assisted colectomy, OC = open colectomy, AR = anterior resection, APR = abdominoperineal resection

LAR = low anterior resection

laparoscopic LAR and 66.7% in those after open LAR; for patients treated with APR, the corresponding rates were 65.2% and 57.7%. The local recurrence rate was 7.8% after laparoscopic LAR and 7% after open LAR; the corresponding rates for APR were 15.1% and 21%.

The Cochrane systematic review of laparoscopic versus open TME for rectal cancer [30], published in 2006, reported respective local recurrence rates of 7.2% and 7.7%, distant metastasis rates of 13.5% and 9.1%, and cancer-related mortality rates of 9.2% and 10%; none of these between-group differences was statistically significant.

In conclusion, although the results from several small randomized control trials and other studies showed a short-term postoperative benefit for laparoscopic TME compared to open TME, with equivalent oncologic outcomes, currently there is no solid level 1 evidence to support the use of laparoscopic resection in rectal cancer outside of clinical trials. Two major multicenter randomized control studies are currently ongoing: the European COLOR II trial and the American ACOSOG-Z6051, which compare laparoscopic and open resection for the treatment of curable rectal cancer. Results from these studies will hopefully provide adequate information on the role of laparoscopic resection for rectal cancer.

CONCLUSION

There is sufficient solid evidence indicating that laparoscopic colon resection is a feasible and safe alternative to the open approach, with some short-term advantages. The laparoscopic technique when performed by an experienced surgeon with proper patient selection can achieve results that meet accepted oncologic standards, including proper resection margins and adequate lymph node removal. Although laparoscopic colon resection does not compromise oncologic outcome, there are no data to support its superiority over open resection. In patients with primary resectable rectal cancer, laparoscopic resection may have limited short-term advantages over open surgery. The existing data indicate no significant differences between open and laparoscopic TME in terms of resection margins and recovered lymph nodes, and in disease-free survival and local recurrence rates. However, the evidence base is still insufficient, and use of this technique in clinical practice awaits further information from ongoing large randomized control trials.

Corresponding author:

Dr. N. Wasserberg

Dept. of Surgery B, Rabin Medical Center (Beilinson Campus), Petah Tikva 49100, Israel

Phone: (972-3) 937-6200

Fax: (972-3) 937-6251

email: nirw@clalit.org.il

APR = abdominoperineal resection

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