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TOPIC HIGHLIGHT

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Laparoscopic rectal cancer surgery: Where do we stand?

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Abstract

Large comparative studies and multiple prospective randomized control trials (RCTs) have reported equivalence in short and long-term outcomes between the open and laparoscopic approaches for the surgical treatment of colon cancer which has heralded widespread acceptance for laparoscopic resection of colon cancer. In contrast, laparoscopic total mesorectal excision (TME) for the treatment of rectal cancer has been welcomed with significantly less enthusiasm. While it is likely that patients with rectal cancer will experience the same benefits of early recovery and decreased postoperative pain from the laparoscopic approach, whether the same oncologic clearance, specifically an adequate TME can be obtained is of concern. The aim of the current study is to review the current level of evidence in the literature on laparoscopic rectal cancer surgery with regard to short-term and long-term oncologic outcomes. The data from 8 RCTs, 3 meta-analyses, and 2 Cochrane Database of Systematic Reviews was reviewed. Current data suggests that laparoscopic rectal cancer resection may benefit patients with reduced blood loss, earlier return of bowel function, and shorter hospital length of stay. Concerns that laparoscopic rectal cancer surgery compromises short-term oncologic outcomes including number of lymph nodes retrieved and circumferential resection margin and jeopardizes long-term oncologic outcomes has not conclusively been refuted by the available literature. Laparoscopic rectal cancer resection is feasible but whether or not it compromises short-term or long-term results still needs to be further studied.

Key words: Rectal cancer; Laparoscopy; Total mesorectal excision; Anterior resection; Abdominoperineal resection

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INTRODUCTION

Laparoscopic colon resection was introduced in 1991[1,2]. Concern for port site metastasis and inadequate oncologic clearance initially hampered its adoption in the treatment of colon and rectal malignancy[3-6]. However, recently large comparative studies and multiple prospective randomized control trials (RCTs) have reported equivalence in resection margin, lymph node collection, tumor recurrence, postoperative complications, and long-term outcomes between open and laparoscopic

resection for colon cancer[7-12]. In addition, these studies demonstrated earlier recovery of bowel function, less postoperative pain, and decreased hospital stay with the laparoscopic approach which has heralded widespread acceptance for laparoscopic resection of colon cancer[8,9,13-16]. In contrast, laparoscopic total mesorectal excision (TME) for the treatment of rectal cancer has been welcomed with significantly less enthusiasm.

While it is likely that patients with rectal cancer will experience the same benefits of early recovery and decreased postoperative pain from the laparoscopic approach, whether the same oncologic clearance, specifically an adequate TME can be obtained is of concern[17-23]. Involvement of the circumferential resection margin (CRM) after TME is a prognostic factor for local recurrence[24-28]. Marijnen *et al*[29] found that in the Dutch Rectal Cancer Trial, 13.1% of patients with a positive CRM developed a local recurrence within 2 years of follow-up, whereas patients with a margin > 2 mm had a local recurrence rate of 3.3% at 2 years ($P < 0.0001$). Postoperative radiation did not lead to a reduction in the local recurrence rate (17.3% *vs* 15.7% local recurrence in patients with CRM < 1 mm with and without adjuvant radiotherapy respectively, $P = 0.98$)[29]. In addition, preoperative radiotherapy had no significant effect on the prevention of local recurrence in patients with positive CRM (9.3% in the irradiated group *vs* 16.4% in the surgery alone group, $P = 0.08$) highlighting the importance of adequate surgery. In conventional open resection of rectal cancer, considerable variation between surgeons in oncologic outcomes has been demonstrated[30]. Differences in local recurrence and disease-free survival may be amplified by the technical challenges of laparoscopic proctectomy. While, the laparoscopic approach provides a magnified view compared to open surgery, TME and autonomic nerve preservation which are prerequisites for satisfactory oncologic and functional results require significant laparoscopic expertise[31]. A number of studies have reported on the safety and feasibility of laparoscopic low anterior resection (LAR) and abdominoperineal resection (APR) with TME but there is no level one evidence supporting laparoscopic TME in terms of oncologic outcomes[19,20,32-36]. The aim of this study is to provide a systematic review of the short-term and long-term oncologic outcomes of laparoscopic rectal cancer resection.

DATA SOURCE

Peer-reviewed papers published on laparoscopic rectal cancer resection were found by searching the following terms in the Ovid Medline, PubMed, and Cochrane Database of Systematic Reviews from 1993 to 2010: "laparoscopy", "laparoscopic surgery", and "rectal cancer". Review articles found using the search terms "colon cancer" or "rectal cancer" and "laparoscopy" were also reviewed to find pertinent articles. All relevant articles were assessed and inclusion and exclusion criteria applied.

Study designs included prospective RCTs, meta-analyses, and Cochrane Database of Systematic Reviews. Studies were included if short-term outcomes, morbidity and mortality, or oncologic data specifically, recurrence rates, number of lymph nodes retrieved, margin status, and overall survival for patients undergoing curative laparoscopic rectal cancer resection were reported. When more than one trial containing overlapping patient inclusion periods and data was reported from the same institution, the most recent publication was included. Studies were excluded if they (1) reported both colonic and rectal outcomes, but did not analyze rectal cancer outcomes individually; (2) were non-randomized comparative trials, descriptive trials, or case reports; (3) were not published in the English language; and (4) reported on patients undergoing palliative treatment (non-curative surgical intent).

The majority of data on laparoscopic resection for rectal cancer come from non-randomized comparative and descriptive studies. The literature review yielded a total of 79 studies published in the English language from 1993 to 2010. Sixty-five studies were excluded because they were non-randomized comparative trials or descriptive trials. One meta-analysis was excluded because individual studies were not analyzed according to the site of disease or the type of resection. The remaining 2 Cochrane reviews, 3 meta-analyses, and 8 RCTs comparing laparoscopic *vs* open TME for rectal cancer form the basis of this review. When assessing the data on laparoscopic resection of rectal cancer it is important to remember that results may vary greatly based on level of the tumor, APR *vs* LAR, use of neoadjuvant chemoradiation, and completeness of TME.

OUTCOMES OF INTEREST

Intraoperative outcomes include: duration of operation, blood loss, length of incision, and conversion rate. Short-terms parameters of interest include: early postoperative complications (hemorrhage, anastomotic leak, wound complications, chest infection, prolonged ileus, incidence of pulmonary embolism or deep vein thrombosis, and urinary infection/retention), and mortality. Oncologic outcomes reviewed include: number of lymph nodes retrieved, margin status, completeness of TME, local recurrence, and overall survival.

Intraoperative results

The proven benefits of laparoscopy noted in colon cancer surgery including decreased intraoperative blood loss, smaller length of incision, less postoperative pain, faster recovery of intestinal function, and shorter length of hospital stay likely also apply to rectal cancer surgery[37]. In RCTs (Table 1) the mean operative time for open surgical resection of rectal cancer ranged from 106 to 284 min compared to 120 to 245 min for laparoscopic resection (Table 2). As expected, duration of operation was significantly longer in the laparoscopic group com-

Table 1 Patient characteristics from randomized control trials

Ref.	Patients			M/F		BMI		Age (yr)		% Pre-op ChemoRT	
	Total	Open	Lap	Open	Lap	Open	Lap	Open	Lap	Open	Lap
Kang *et al*[40]	340	170	170	110/60	110/60	24.1 (3.2)	24.1 (3.2)	59.1 (9.9)	57.8 (11.1)	100	100
Ng *et al*[45]	153	77	76	48/29	37/39	NA	NA	65.7 (12)	66.5 (11.9)	NA	NA
Lujan *et al*[31]	204	103	101	64/39	62/39	NA	NA	66.0 (9.9)	67.8 (12.9)	74.8	72.3
Ng *et al*[39]	99	48	51	30/18	31/20	NA	NA	63.5 (12.6)	63.7 (11.8)	0	0
Guillou *et al*[7]/Jayne *et al*[12]	343	113	230	NA	NA	26 (4)	25 (4)	69 (12)	69 (11)	NA	NA
Braga *et al*[38]	168	85	83	64/21	55/28	NA	NA	65.3 (10.3)	62.8 (12.6)	14.1	16.9
Zhou *et al*[35]	171	89	82	43/46	46/36	NA	NA	45 (30-81)	44 (26-85)	NA	NA
Araujo *et al*[34]	28	15	13	10/5	9/4	25.6 (17.1-38.5)	23.5 (21.7-24.6)	56.4 (24-78)	59.1 (31-75)	15 (100%)	13 (100%)

BMI: Body mass index; ChemoRT: Chemoradiation.

Table 2 Intraoperative characteristics of patients from randomized control trials

Ref.	Number of patients (%)							Conv %	Op time (min)		Blood loss (mL)		Length of incision (cm)	
	Total	Open			Lap				Open	Lap	Open	Lap	Open	Lap
		Total	LAR	APR	Total	LAR	APR							
Kang *et al*[40]	340	170	146 (75.9)	24 (14.1)	170	151 (88.8)	19 (11.2)	1.2	197.0 (62.9)	244.9 (75.4)[a]	217.5 (150.0-400.0)	200.0 (100.0-300.0)[a]	20.0 (18.0-23.0)	5.0 (4.5-6.0)
Ng e*et al*[45]	153	77	77 (100)	0 (0)	76	76 (100)	0 (0)	30.3	154.0 (70.3)	213.1 (59.3)[a]	337.3 (0-2542)	280.0 (0-3000)	NA	NS
Lujan *et al*[31]	204	103	81 (78.6)	22 (21.4)	101	77 (76.2)	24 (23.8)	7.9	172.9 (59.4)	193.7 (45.1)[a]	234.2 (± 174.3)	127.8 (± 113.3)[a]	NA	NA
Ng *et al*[39]	99	48	0 (0)	48 (100)	51	0 (0)	51 (100)	9.8	163.7 (43.4)	213.5 (46.2)[a]	555.6 (0-4720)	321.7 (0-3000)		
Guillou *et al*[7]/ Jayne *et al*[12]	343	113	79 (69.9)	34 (30.1)	230	167 (72.6)	63 (27.4)	34	180 (135-220)	135 (100-180)	NA	NA	22 (18-29)	10 (6-17)
Braga *et al*[38]	168	85	74 (87.1)	11 (12.9)	83	76 (92)	7 (84)	7.2	209 (72)	262 (72)[a]	396 (50-1600)	213 (50-1600)[a]	19.1 (± 3.1)	5.8 (± 0.8)[a]
Zhou *et al*[35]	171	89	89 (100)	0 (0)	82	82 (100)	0 (0)	NA	106 (80-230)	120 (110-220)[a]	92 (50-200)	20 (5-120)[a]	NA	NA
Araujo *et al*[34]	28	15	0 (0)	15 (100)	13	0 (0)	13 (100)	0	284	228[a]	NA	NA	NA	NA

Conv: Conversion rate; LAR: Low anterior resection; APR: Abdominoperineal resection; NA: Not available. [a]$P < 0.05$ *vs* Open.

pared to the open group in 6 of the 8 RCTs[7,22,31,38-40]. Similar results were reported in RCTs of open *vs* laparoscopic resection for colon cancer. Zhou *et al*[35] reported both shorter open and laparoscopic operative times compared to other trials with no significant difference between the two operative approaches (120 min *vs* 106 min for laparoscopic *vs* open resection respectively, $P = 0.051$). However, no details were provided on tumor stage, conversion rate, or whether the analysis was performed on an intent-to-treat basis. Araujo *et al*[34] was the only RCT to demonstrate significantly shorter operative times with laparoscopic compared to open resection (228 min *vs* 284 min respectively, $P = 0.04$). However, they attributed these results to fact that the surgical team performing laparoscopic APR was the same whereas open APR was often performed by different surgical teams. In addition, extraction of the specimen from the perineum likely decreased operative time because there was not an abdominal incision to close.

Two meta-analyses included operative time as an outcome of interest. Aziz *et al*[41] included 22 studies comparing laparoscopic *vs* open rectal cancer resection in 2071 patients and found that operative time was significantly increased with the laparoscopic group as compared to the open group with a weighted mean difference (WMD) of 40.18 (95% CI, 26.46-56.13). Gao *et al*[42] performed a meta-analysis of short-term outcomes after laparoscopic resection for rectal cancer based on 11 studies and included 643 patients which reported no difference in operating time between open and laparoscopic approaches with a WMD of 1.59 (1.2-1.98).

Intraoperative blood loss was significantly less for the laparoscopic group compared to the open group in 4 of 6 RCTs and ranged from 20 mL to 321.7 mL and from 92 mL to 555.6 mL in the laparoscopic and open groups respectively (Table 2)[31,35,38,40]. Araujo *et al*[34] did not specifically report on the amount of intraoperative blood loss but there was no statistically significant difference in the need for blood transfusions between the two groups which was attributed to the fact that in an APR the majority of blood loss occurs during the perineal portion of the case which is the same regardless of surgical access.

Table 3 Short-term oncologic outcomes of patients from randomized control trials

Ref.	LN		Positive margin (CRM/distal) (%)	
	Open	Lap	Open	Lap
Kang *et al*[40]	18 (13-24)	17 (12-22)	7 (4.1)/NA	5 (2.9)/NA
Ng e*et al*[45]	12 (7)	11.5 (7.9)	1 (1.3)/NA	2 (2.6)/NA
Lujan *et al*[31]	11.57 (5.10)	13.63 (6.26)[a]	3 (2.9)/0	4 (4.0)/0
Ng *et al*[39]	13.0 (7)	12.4 (6.7)	2 (4.2)/NA	3 (5.9)/NA
Guillou *et al*[7]/ Jayne *et al*[12]	NA	NA	(14)/NA	(16)/NA
Braga *et al*[38]	13.6 (6.9)	12.7 (7.3)	2 (2.4)/0	1 (1.2)/0
Zhou *et al*[35]	NA	NA	NA	NA
Araujo *et al*[34]	11.9	5.5[a]	NA	NA

LN: Lymph nodes; CRM: Circumferential resection margin; NA: Not available. [a]$P < 0.05$ *vs* Open.

A recent Cochrane review by Breukink *et al*[43] evaluating the safety and efficacy of elective laparoscopic TME for the resection of rectal cancer found that in the majority of studies blood loss was reduced with the laparoscopic approach although this did not translate to fewer blood transfusions. Length of incision was measured in 3 of 8 RCTs and ranged from an average of 5 cm to 10 cm with the laparoscopic approach compared to an average of 19.1 cm to 22 cm with the open approach (Table 2)[7,38,40].

Seven of the 8 trials reported a conversion rate which ranged from 0%-34% (Table 2)[7,12,22,31,34,38-40]. Conversion to the open approach was commonly defined as length of incision greater than the size needed for tumor extraction or premature abdominal incision to allow improved mobilization. In the majority of studies conversion to open surgery was required because of local tumor invasion or difficult dissection in a narrow pelvis although bulky tumor, dilated small bowel, dense adhesions, bleeding, rectal perforation, difficulty mobilizing the splenic flexure, failure to identify or injury to the ureter, ischemia of the descending colon, and anastomotic failure were also cited. Breukink *et al*[44] reported that 36 of 48 studies assessed conversion and showed a highly variable rate ranging from 0% to 33%. However, they report that the lack of consensus in the definition made results difficult to interpret. In addition, surgeon experience and patient selection criteria were often not mentioned.

Two trials reported particularly high rates of conversion. Ng *et al*[45] had a conversion rate of 30.3% but they did not routinely perform preoperative staging with computed tomography scans and therefore frequently converted after diagnostic laparoscopy. Twelve of the 23 patients randomized to laparoscopic surgery were converted to open due to local tumor invasion, bulky tumor, or dilated small bowel which may have been recognized by preoperative imaging. In the CLASICC trial the conversion rate for laparoscopic resection of rectal cancer was reported at 34% and attributed to excessive tumor fixation and uncertainty of tumor clearance[7]. Surgeon learning curve may account for this high rate of conversion as evidenced by the fact that the overall rate of conversion dropped by year of study from 38% in year one to 16% in year six. However, consistent with several non-randomized reports, in the CLASICC trial patients converted to open resection had a higher operative mortality compared to patients in the laparoscopic or open groups (9% *vs* 1% *vs* 5% respectively)[7]. Conversion was also associated with worse oncologic outcomes in non-randomized comparative and descriptive studies[46].

Short-term oncologic outcomes

While the number of lymph nodes retrieved can vary based on age, gender, tumor site, use of pre-operative radiation, and tumor grade, the extent and quality of surgical resection can also have an impact on the number of nodes collected and is therefore often considered a surrogate marker of the oncologic completeness of the resection[47-53]. The American Joint Committee on Cancer recommends that at least 12 lymph nodes be examined in patients with rectal cancer to confirm the absence of nodal involvement by the tumor[54]. In addition, a number of studies have reported that the number of lymph nodes examined may be associated with patient outcome[55,56]. Six of the 8 RCTs reported the mean number of lymph nodes retrieved with a range of 5.5 to 17 nodes in the laparoscopic group compared to 11.6 to 18 nodes in the open group (Table 3)[22,31,34,38-40]. In 4 of the 6 trials the number of lymph nodes isolated was not significantly different based on surgical approach. Araujo *et al*[34] reported a significantly lower yield of lymph nodes with laparoscopic rectal resection compared to open resection (5.5 *vs* 11.9 respectively, $P = 0.04$). However, the number of lymph nodes obtained in the study by Lujan *et al*[31] was higher in the laparoscopic group (13.63 *vs* 11.57 in the laparoscopic *vs* open approach respectively, $P = 0.026$). They suggested that laparoscopy offered better dissection and accuracy due to better visualization and exposure of structures with less manipulation of the mesorectum especially in a narrow pelvis. Four of the 8 RCTs reported the use of pre-operative chemoradiation. In these trials, the mean number of lymph nodes retrieved ranged from 5.5 to 17 nodes in the laparoscopic group and from 11.6 to 18 nodes in the open group[31,34,38,40]. Anderson *et al*[57] found that in the 17 trials that reported the number of lymph nodes retrieved, the mean number of nodes was 10 for the laparoscopic group and 12 for the open group ($P = 0.001$) with the majority of trials reporting a median of 11 or fewer nodes obtained. In 9 of these 17 trials, both groups were treated with preoperative radiation therapy and reported a mean of 10 lymph nodes harvested in the laparoscopic group and 11 in the open group.

One of the greatest concerns of laparoscopic TME is that obtaining a complete oncologic resection will be more difficult. Involvement of the circumferential or distal margin is one of the most important prognostic factors in rectal resection with TME and can lead to an increase in local recurrence and a reduction in survival. Radial margins of less than 2 mm are associated with

Table 4 Short-term outcomes of patients in randomized control trial

Ref.	Length of stay (d)		Anastomotic leak (%)		Wound infection (%)		Ileus (%)		Pain/PCA use (mg) or (number of shots)		Mortality	
	Open	Lap	Open	Lap	Open	Lap	Open	Lap	Open	Lap	Open	Lap
Kang *et al*[40]	9 (8-12)	8 (7-12)	0	2 (1.2)	11 (6.5)	2 (1.2)[a]	22 (12.9)	17 (10)	156.9 (117.0-185.2)	107.2 (80.0-150.0)	0	0
Ng e*et al*[45]	10.0 (3-39)	8.4 (2-32)[a]	4 (5.2)	1 (1.3)	9 (11.7)	5 (6.6)	2 (2.6)	1 (1.3)	8.3 (0-49)	4.9 (0-23)[a]	3 (3.9)	2 (2.6)
Lujan *et al*[31]	9.9 (6.8)	8.2 (7.3)	10 (12)	5 (6)	2 (1.9)	0 (0)	8 (7.8)	6 (5.9)	NA	NA	3 (2.9)	2 (1.9)
Ng *et al*[39]	11.5 (5-38)	10.8 (5-27)	NA	NA	4 (8.3)	0 (0)	2 (4.2)	1 (2.0)	11.4 (0-49)	6.0 (0-47)[a]	1 (2.8)	1 (2.5)
Guillou *et al*[7]/ Jayne *et al*[12]	13 (9-18)	11 (9-15)	9 (7)	26 (10)	15 (12)	33 (13)	NA	NA	NA	NA	NA	NA
Braga *et al*[38]	13.6 (6-80)	10 (6-27)[a]	9 (10.6)	8 (9.6)	13 (15.3)	6 (7.2)	2 (2.3)	2 (2.4)	NA	NA	1 (1.2)	1 (1.2)
Zhou *et al*[35]	13.3 (3.4)	8.1 (3.1)[a]	3 (3.4)	1 (1.2)	NA	NA	NA	NA	NA	NA	0 (0)	0 (0)
Araujo *et al*[34]	< 10.5	10.5	NA	NA	NA	NA	NA	NA	NA	NA		

PCA: Patient controlled analgesia; NA: Not available. [a]$P < 0.05$ *vs* Open.

a local recurrence rate of 16% compared to a significantly reduced local recurrence rate of 6% with margins greater than 2 mm[27]. Six of the 8 RCTs reported the involvement of the CRM and no difference was found by surgical approach (Table 3)[7,31,38-40,45]. In the majority of trials the rate of CRM involvement was less than 5%. Patients with positive radial margins often had tumor invading the pelvic side wall or adjacent structure and were frequently converted from a laparoscopic to an open procedure[39]. In the CLASICC study, the only multicenter trial, a positive CRM was identified in 14 of 97 (14%) patients with open surgery and in 30 of 193 (16%) patients with laparoscopic rectal resection ($P = 0.8$)[7]. Of patients undergoing anterior resection, the CRM was positive in 16 of 129 (12%) individuals in the laparoscopic group and in 4 of 64 (6%) individuals in the open group ($P = 0.19$). While there is a non-significant higher positivity of the CRM in the laparoscopic anterior resection group, this is once again likely due to the fact that the learning curve was not completed before the start of this study. Two RCTs reported on distal margin status and the incidence of distal margin positivity was not significantly different between the two surgical approaches and in fact was 0%[31,38]. All 3 meta-analyses and the Cochrane review by Breukink *et al*[44] found no difference in positive margins based on surgical access.

Postoperative course: Less postoperative pain, faster recovery of intestinal function, and shorter length of stay are important benefits of laparoscopic colorectal surgery. Only 3 of 8 RCTs compared the exact amount of post-operative pain medication and 2 of these studies reported a significant reduction in analgesic use in the laparoscopic group (Table 4)[39,40,45]. Zhou *et al*[35] did not quantify the exact usage of pain medication, but found no significant difference in the number of days parental analgesics were necessary (4.1 *vs* 3.9 in the open and laparoscopic groups respectively, $P = 0.225$).

Resumption of bowel function was usually reported on post-operative days 3 to 5 and ability to tolerate a solid food diet was reported on post-operative days 3 to 6[7,31,35,39,40,45]. In the majority of RCTs earlier bowel movements and diet advancement was reported with the laparoscopic approach. The return of bowel function and reduction in wound pain was thought to contribute to earlier discharge after laparoscopic surgery. While in a majority of trials, the length of stay was not significantly different between surgical approaches, there was a trend toward decreased length of stay with laparoscopic rectal surgery. Breukink *et al*[58] found that laparoscopic TME resulted in earlier return of normal diet, less pain, less narcotic use and a shorter hospital stay.

Complications: Rectal cancer surgery is associated with a high rate of morbidity and mortality. Post-operative mortality in RCTs ranged from 1%-4% and demonstrated no statistically significant difference based on surgical approach (Table 4). The rate of post-operative complications ranged from 6% to 69% and with the exception of Zhou *et al*[35] did not differ significantly between laparoscopic and open groups. Wound infection and urinary tract infection accounted for the majority of perioperative complications in both groups. There was a higher incidence of wound infection with the open approach however this did not reach statistical significance. Breukink *et al*[58] found no difference in morbidity between the laparoscopic and open groups although there was a trend toward lower morbidity with laparoscopic TME. Aziz *et al*[41] found no difference in perioperative morbidity between the 2 groups while Gao *et al*[42] found that the overall morbidity rate of the laparoscopic group was significantly lower than that of the open group.

Anastomotic leak is the most serious complication after sphincter sparing rectal cancer resection especially with neoadjuvant chemoradiation. In addition, development of an anastomotic leak is reported to be associated with decreased long-term survival and higher rates of local recurrence after curative resection for colorectal cancer[59-63]. Operative expertise and selective diversion in high risk patients has resulted in a anastomotic leak rate of 1%-17% in most published series studying laparoscopic resection for rectal cancer[46,64,65]. Consistent with reports from non-randomized comparative trials, RCTs demonstrated no significant difference in the incidence

Table 5 Long-term oncologic outcomes of patients in randomized control trials

Ref.	Mean F/U (mo)		LR (%)		DFS (%)		OS (%)	
	Open	Lap	Open	Lap	Open	Lap	Open	Lap
Kang *et al*[40]	NA	NA	NA	NA	NA	NA	NA	NA
Ng e*et al*[45]	108.8 (69.8-168.7)	112.5 (71.1-168.3)	7.1	4.9	80.4 (5.1)	82.9 (4.9)	55.1 (6.5)	63.9 (6.6)
Lujan *et al*[31]	34.1 (20)	32.8 (18.9)	5.3	4.8	81	84.8	75.3	42.1
Ng *et al*[39]	90.1 (27.0-145.5)	87.2 (22.8-150.0)	11.1	5	73.6 (8.1)	78.1 (6.9)	76.5 (7.3)	75.2 (7.2)
Guillou *et al*[7]/Jayne *et al*[12]	36.8 (20.0-61.5)	36.8 (20.0-61.5)	10.1	9.7	70.4/46.9	70.9/49.8	66.7/57.7	74.6/65.2
Braga *et al*[38]	53.6	53.6	5.2	4	NA	NA	NA	NA
Zhou *et al*[35]	1.0-16.0	1.0-16.0	NA	NA	NA	NA	NA	NA
Araujo *et al*[34]	47.2	47.2	13.3	0	NA	NA	NA	NA

F/U: Follow-up; LR: Local recurrence; DFS: Disease-free survival; OS: Overall survival; NA: Not available.

of anastomotic leak between the laparoscopic and open technique for the resection of rectal cancer (Table 4).

While the incidence of perioperative morbidity was not different based on surgical access, fewer patients had long-term complications with laparoscopic rectal cancer resection compared to the open approach. Adhesion related bowel obstruction was the most common long-term morbidity. With a median follow-up of greater than 9 years, Ng *et al*[45] found that adhesion-related obstruction requiring hospitalization (18.9% *vs* 2.7%) and re-operation (6.8% *vs* 0%) was higher in the open group. They report a cumulative probability of adhesion-related bowel obstruction at 10 years of 20.5% in the open group and 3.9% in the laparoscopic group ($P = 0.001$)[45]. Kuhry *et al*[66] performed a systematic review including 12 trials (3346 patients) to evaluate the long-term outcomes of laparoscopically assisted *vs* open surgery for resectable colorectal cancer. Data on long-term complications was not separated by site of disease but the overall occurrence of incisional hernia (7.9% *vs* 10.9%, $P = 0.32$) and reoperation for adhesions (1.1% *vs* 2.5%, $P = 0.30$) was not statistically difference between laparoscopic and open resection. Long-term studies need to be done to determine if laparoscopy decreases the incidence of intra-abdominal adhesion formation by reduced surgical trauma, less tissue handling, and smaller incisions.

Long-term oncologic outcomes

A number of the clinical trials were performed to determine the safety and feasibility of the laparoscopic approach for rectal adenocarcinoma and therefore the data we have for long-term outcomes is limited (Table 5). Braga *et al*[38] found no difference in local recurrence (4.0% in the laparoscopic group *vs* 5.2% in the open group, $P = 0.97$), overall five-year survival, or disease-free five-year survival based on surgical approach. With a median follow-up of 87.2 mo in the laparoscopic group and 90.1 mo in the open group, Ng *et al*[39] demonstrated that after curative resection, the probability of five-year survival was 75.2% *vs* 76.5% for laparoscopic *vs* open APR respectively ($P = 0.20$). In addition, stage-by-stage comparison for the two groups showed no statistical difference. There were no port site recurrences and overall recurrence rates were not significantly different between the two groups (laparoscopic 20% *vs* open 25%, $P = 0.60$). Despite the higher rate of circumferential margin positivity in patients undergoing laparoscopic anterior resection in the CLASICC trial, there was no difference in local recurrence, three- year overall or three-year disease free survival between the two approaches (open OS 66.7% and laparoscopic OS 74.6%, $P = 0.17$; open DFS 70.4% and laparoscopic DFS 70.9%, $P = 0.72$; open LR 7.0% and laparoscopic LR 7.98%, $P = 0.70$)[12]. In addition, there was no significant difference in the rates of local recurrence, three-year overall survival, or three-year disease-free survival in patients undergoing laparoscopic *vs* open APR[12]. However, the sample size is small and therefore larger studies are needed for conclusive results. Ng *et al*[45] published results of a randomized trial of laparoscopic *vs* open anterior resection for upper rectal cancer with a median follow-up of 9 years. No difference in local recurrence, overall survival, or disease-free survival was reported. Although these studies suggest comparative oncologic outcomes between laparoscopic and open rectal cancer resection, they include small sample sizes and are almost all are single institution studies, highlighting the need for large, multi-center RCTs to provide confirmatory data.

In a meta-analysis by Anderson *et al*[57] 18 of 24 studies reported recurrence rates. With a mean follow-up of 35 mo for both groups, overall local recurrence was not statistically different between the 2 groups (laparoscopic 7% *vs* open 8%, P = NS). Eleven studies provided sufficient data to compare overall survival. Overall survival was 72% for patients undergoing laparoscopic rectal cancer resection and 65% for open resection at an average of 4.4 years ($P = 0.5$). Subset analysis by Kuhry *et al*[66] demonstrated no significant difference between laparoscopic and open rectal cancer resection in terms of local recurrence (laparoscopic 7.2% *vs* open 7.8%, $P = 0.46$), development of distant metastases (laparoscopic 13.5% *vs* open 9.1%, $P = 0.60$), or cancer-related mortality (laparoscopic 9% *vs* open 10%, $P = 0.16$). While, this data is encouraging, it is no conclusive.

CONCLUSION

The primary goal of this study was to outline and review

the short-term and long-term oncologic outcomes and complications of laparoscopic rectal cancer resection compared to the gold standard of conventional open resection currently available in the literature. Due to the heterogeneity in tumor stage, surgeon experience, and surgical technique, descriptive and non-randomized trials were not included in this review. However, because of the relatively few RCTs, information on the long-term outcomes is sparse and our conclusions are thus based on a small number of patients. A second limitation is that in a number of these trials data accrual started before the effectiveness of neoadjuvant therapy had been proven and thus the majority of patients did not receive pre-operative chemoradiation which is the current standard of care. Given these limitations, we found no difference in adequacy of oncologic resection, perioperative morbidity, recurrence rates, overall survival, or disease-free survival between open and laparoscopic rectal cancer resection.

In conclusion, RCTs have demonstrated that laparoscopy does not adversely affect cancer related survival in patients with adenocarcinoma of the colon. Concerns about the technical difficulty of TME may have contributed to the exclusion of rectal cancer patients from most of these large multicenter RCTs resulting in little data on oncologic outcomes with laparoscopic rectal cancer resection.

Laparoscopic rectal dissection is technically more demanding than open and constraints of a narrow pelvis may result in difficulty assessing and obtaining adequate surgical margins. However, there are several proposed benefits of laparoscopic rectal resection. A clear and magnified view of the pelvis provided by the improved optics of laparoscopy may aid sharp dissection for TME and assist in identification of vital pelvic structures including the ureters and autonomic nerves. In addition, pneumoperitoneum may separate the parietal and visceral fascia of the mesorectum facilitating dissection in this plane. Laparoscopic rectal cancer resection has a steep learning curve but increased experience with both open and laparoscopic TME will lead to shorter operating times and decreased morbidity[67].

Current data suggests that laparoscopic rectal cancer resection may benefit patients because of reduced blood loss, earlier return of bowel function, and shorter hospital length of stay[68,69]. Concerns that laparoscopic rectal cancer surgery may compromise short-term oncologic outcomes including number of lymph nodes harvested and CRM positivity do not appear to be supported by the available literature. However, there is a paucity of data concerning long-term oncologic outcomes and complications with laparoscopic rectal cancer surgery. There are two large, multicenter RCTs that are currently being conducted: the COLOR Ⅱ trial in Europe and the ACOSOG-Z6051 trial in the United States[70]. Both of these studies are comparing the laparoscopic and open approach for treatment of resectable rectal cancer. Results from these trials will provide information on the long-term outcomes of laparoscopic rectal cancer resection and are eagerly awaited. In view of the lack of level one data on oncologic outcomes, laparoscopic TME for locally advanced, curable rectal cancer should only be performed within the confines of a RCT.

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