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TOPIC HIGHLIGHT

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Role of laparoscopy in rectal cancer: A review

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Abstract

Despite established evidence on the advantages of laparoscopy in colon cancer resection, the use of laparoscopy for rectal cancer resection is still controversial. The initial concern was mainly regarding the feasibility of laparoscopy to achieve an adequate total mesorectal excision specimen. These concerns have been raised following early studies demonstrating higher rates of circumferential margins positivity following laparoscopic resection, as compared to open surgery. Similar to colon resection, patients undergoing laparoscopic rectal cancer resection are expected to benefit from a shorter length of hospital stay, less analgesic requirements, and a faster recovery of bowel function. In the past decade there have been an increasing number of large scale clinical trials investigating the oncological and perioperative outcomes of laparoscopic rectal cancer resection. In this review we summarize the current literature available on laparoscopic rectal cancer surgery.

Key words: Rectal cancer; Laparoscopy; Open resection; Review; Comparison; Outcomes; Laparoscopic resection of gastrointestinal

Core tip: Despite its endorsement for colon cancer resection, laparoscopy for rectal cancer resection is still considered investigational. This is mainly due to initial concerns regarding the feasibility of laparoscopy to achieve an adequate total mesorectal excision specimen. These concerns have been raised following early studies demonstrating higher rates of circumferential margins positivity following laparoscopic resection, as compared to open surgery. In this review, we explore the current relevant literature regarding laparoscopic resection for rectal cancer, with respect to oncologic efficacy and short and long term benefits.

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in males and the second most common in females, with 1.2 million annual new cases worldwide. Over 143000 new cases of CRC are diagnosed annually in the United States, and approximately 52000 Americans die of the disease every year. These deaths account for approximately 9% of all cancer mortality[1].

Since its original implementation as a diagnostic tool, laparoscopy has become widely accepted as the favored approach for many procedures (*e.g.*, appendectomy, cholecystectomy, adrenalectomy, bariatric surgery). Not surprisingly, laparoscopy was also utilized for colon and rectal surgery. Laparoscopic colon resection was first reported in 1991[2,3]. Initial reports raised the concern for port site recurrence in up to 21% of the patients, as well as concerns regarding the adequacy of disease clearance by the laparoscopic approach[4-6]. These reports prompted the initiation of several major comparative studies, and

Table 1 Phase Ⅲ randomized controlled trials showing oncological outcomes

Study and design	Recurrence lap *vs* open		Survival lap *vs* open		Tumor location (cm from AV)	Patient enrollment (*n*)		LN harvested (*n*) lap *vs* open	CRM positivity lap *vs* open
	DR	LR	DFS	OS		Open	Lap		
Liang *et al*[17] Single center	N/A	N/A	N/A	76% *vs* 82.8% *P* = 0.46, (44 mo)	N/A	174	169	7.1 *vs* 7.4 *P* = 0.47	N/A
Kang *et al*[18] "COREAN" Multicenter	N/A	N/A	N/A	N/A	Lap-5.6 Open-5.3	170	170	17 *vs* 18 *P* = 0.08	5% *vs* 7% *P* = 0.77
Jayne *et al*[19] "CLASSIC" update Multicenter	21.9% *vs* 21.9% *P* = 0.86, (5 yr)	9.4% *vs* 7.6% *P* = 0.74, (5 yr)	53.2% *vs* 52.1% *P* = 0.95, (5 yr)	60.3% *vs* 52.9% *P* = 0.13, (5 yr)	N/A	128	253	N/A	N/A
Lujan *et al*[20] Single center	N/A	4.8% *vs* 5.3% *P* = 0.78, (5 yr)	84.8% *vs* 81% *P* = 0.9, (5 yr)	72.1% *vs* 75.3% *P* = 0.98, (5 yr)	Lap-5.5 Open-6.2	103	101	13.6 *vs* 11.6 *P* = 0.02	4% *vs* 3% *P* = 0.4
Ng *et al*[21] Single center	12.3% *vs* 18.1% *P* = 0.37, (10 yr)	7.1% *vs* 4.9% *P* = 0.68, (10 yr)	82.9% *vs* 80.4% *P* = 0.69, (10 yr)	83.5% *vs* 78% *P* = 0.59, (10 yr)	12-15	77	76	11.5 *vs* 12 *P* = 0.7	2.6% *vs* 1.3% *P* = 0.62
Ng *et al*[22] Single center	15% *vs* 25% *P* = 0.6, (5 yr)	5% *vs* 11% *P* = 0.6, (5 yr)	78.1% *vs* 73.6% *P* = 0.55, (5 yr)	75.2% *vs* 76.5% *P* = 0.2, (5 yr)	⩽ 5	48	51	12.4 *vs* 13 *P* = 0.72	5.8% *vs* 4.1% *P* = NS
Pechlivanides *et al*[23] Multicenter	N/A	N/A	N/A	N/A	Lap-6 Open-8	39	34	19.2 *vs* 19.2 *P* = 0.2	N/A
Braga *et al*[24] Single center	N/A	4% *vs* 5.3% *P* = 0.97 (5 yr)	N/A	No difference (5 yr)	Lap-9.1 Open-8.6	85	83	12.7 *vs* 13.6 *P* = NA	1.3% *vs* 2.4% *P* = NA

AV: Anal verge; N/A: Not applicable; OS: Overall survival; DFS: Disease free survival; LR: Local recurrence; DR: Distant recurrence; LN: Lymph nodes; CRM: Circumferential margins; NS: Non-significant; NA: Not available.

randomized controlled trials (RCT) comparing laparoscopic and open colon resection[7-15]. Results from these studies clearly showed no difference in resection margin, number of lymph nodes harvested, tumor recurrence rates, and long term overall survival between the two surgical approaches. Additionally, laparoscopy benefited the patients with earlier recovery of bowel function, reduced blood loss, decreased post-operative pain and analgesic use, and a shortened length of stay[7-11].

Despite its endorsement for colon resection, laparoscopy for rectal cancer resection is still considered investigational. As for laparoscopic colon resection, patients undergoing laparoscopic rectal resection are expected to benefit from a faster recovery. Nevertheless, it is of paramount concern whether laparoscopy can achieve an adequate oncological outcome, with total mesorectal excision (TME) being the gold standard, ever since presented by Heald *et al*[16] in 1982. This concern is further strengthened when considering the technical difficulties in rectal surgery, derived from the narrow confines of the bony pelvis, angling limitations of the stapling devices, high body mass index, and the need for autonomic nerve preservation.

The United Kingdom Medical Research Council Conventional versus Laparoscopic Assisted surgery in Colorectal Cancer (MRC CLASSIC) trial, was the first RCT to include rectal cancer patients. In this RCT, the rate of positive circumferential margins (CRM), was non-significantly higher in patients undergoing laparoscopic anterior resection when compared to open resection (12 % *vs* 6%, respectively, *P* = 0.19)[8]. This observation raised concern about the standards of laparoscopic TME when it is practiced by less experienced surgeons. Interestingly the higher CRM positivity rate did not translate to an increase in the 3 year follow-up local recurrence rate[12]. Many other clinical trials investigating the feasibility and efficacy of laparoscopy for rectal cancer resection have been published since.

In this review, we explore the current relevant literature regarding laparoscopic resection for rectal cancer, with respect to oncologic efficacy and short and long term benefits.

ONCOLOGICAL OUTCOMES

Randomized controlled trials

Following the concern raised by the MRC-CLASSIC trial regarding the relatively higher rate of CRM positivity following laparoscopic rectal surgery, several randomized controlled trials have been conducted in recent years investigating the oncological efficacy of the laparoscopic approach. Naturally, special attention was given to the TME specimen, focusing on proximal, distal, and circumferential margin positivity, as well as, the number of lymph nodes harvested.

Oncological outcomes of major phase Ⅲ randomized controlled trials comparing laparoscopic and open rectal resection are shown in Table 1[17-24]. Parameters investigated were overall (OS) and disease free survival (DFS), ocal recurrence (LR) and distant recurrence (DR) rates, number of lymph nodes (LN) harvested and circumferential margin (CRM) positivity.

Table 2 Meta-analyses showing oncological outcomes

Ref.	Trials (*n*)	Patients (*n*)	OS lap *vs* open	DFS lap *vs* open	LR lap *vs* open	LN harvested lap *vs* open (*n*)	CRM positivity lap *vs* open
Huang *et al*[25]	6	1033	HR = 0.76, P = 0.11, 4 trials (3 yr)	HR = 1.13, *P* = 0.64, 3 trials (3 yr)	RR = 0.55, *P* = 0.21, 4 trials (3 yr)	*P* = 0.43, 5 trials	7.94% *vs* 5.37%, *P* = 0.63, 5 trials (3 yr)
Ohtani *et al*[26]	12	2095	N/A	OR = 1.17, *P* = 0.35 (5 yr)	OR = 0.93, *P* = 0.61 (5 yr)	*P* = NS	*P* = NS
Anderson *et al*[27]	24	3158	72% *vs* 65%, *P* = NS, 13 trials (3 yr)	N/A	7% *vs* 8%, *P* = NS, 16 trials (3 yr)	10 *vs* 11, *P* = 0.001 17 trials	5% *vs* 8%, *P* = NS, 10 trials (3 yr)
Aziz *et al*[28]	20	2071	N/A	N/A	N/A	*P* = NS	9.5% *vs* 10.8%, OR = 0.93, *P* = 0.38

OS: Overall survival; DFS: Disease free survival; LR: Local recurrence; LN: Lymph nodes; CRM: Circumferential margins; HR: Hazard ratio; N/A: Not applicable; NS: Non-significant; OR: Odds ratio.

Six trials presented data comparing OS after laparoscopic and open rectal resection. One trial identified comparable 4 years OS (76% *vs* 82.8%, *P* = 0.46)[17], four trials presented 5 years OS [range: 60.3%-76.0% *vs* 52.5%-82.8%, *P* = non-significant (NS)][19,20,22,24], and one trial demonstrated comparable 10 years OS (83.5% *vs* 78%, *P* = 0.59)[21] for the laparoscopic and open groups, respectively. Data regarding 5 years DFS was presented in three trials (range: 53.2%-84.8% *vs* 52.1%-81%, *P* = NS)[19,20,22], and one trial demonstrated no difference in 10 years DFS (82.9% *vs* 80.4%, *P* = 0.69), for laparoscopic versus open resection[21].

Local recurrence rates after 5 years were presented in four studies (range: 4.0%-9.4% *vs* 5.3%-11.0%, *P* = NS)[19,20,22,24], and after 10 years in one study (7.1% *vs* 4.9%, *P* = 0.68)[21]. Similar distant recurrence rates after 5 years were presented in two studies (range: 15.0%-21.9% *vs* 21.9-25.0%, *P* = NS)[19,22], and after 10 years in one study (12.3% *vs* 18.1%, *P* = 0.37), for the laparoscopic and open groups, respectively[21].

Seven trials showed comparable results regarding the number of lymph nodes harvested after laparoscopic and open resection (range: 7.1-19.2 *vs* 7.4-19.2, *P* = NS)[17,18,20-24]. Circumferential margin positivity was investigated in 5 trials, and no difference was shown between the laparoscopic and open groups (range: 1.3%-5.8% *vs* 1.3%-7.0%, *P* = NS)[18,20-22,24].

To note, only two RCTs[20,21] described the relativity of patients by tumor stage. As expected, a larger number of patients in stage Ⅰ-Ⅲ than in stage Ⅳ, were observed in these studies. Hypothetically, in the other RCTs presented above, the number of patients with a lower stage could have been larger in the laparoscopic group, hence causing selection bias and skewing of results.

It is of extreme importance to acknowledge that surgical outcomes presented by all the RCTs above, except for the CLASSIC trial, are a product of an experienced and dedicated colorectal surgical team with experience in the field of laparoscopic colorectal surgery. In the CLASSIC trial, surgeons needed to have performed more than 20 laparoscopic colon or rectal surgery. This number is truly insufficient when considering the complexity of rectal surgery, and might explain the relatively higher rates of local and distant recurrence, as well as lower rates of OS and DFS.

Meta-analyses

Four, large scale meta-analyses were published in recent years comparing oncological outcomes between laparoscopic and open resection for rectal cancer[25-28]. No difference was found between the groups in regards to OS[25,27], DFS[25,26], LR rates[25-27], number of LN harvested[25-28], or the CRM positivity rate[25-28]. Data is shown Table 2.

Perioperative outcomes

Over the past two decades, the true benefits of laparoscopy, such as, lower postoperative morbidity rates, specifically wound infection rates, shorter time to recovery and discharge, and less pain and analgesic use, have turned it in to the preferred surgical approach in many surgical disciplines. This is true for rectal surgery as well, especially when considering the potential advantage for a faster recovery of the intestinal tract, the ability to surgically dissect deep down in a narrow pelvis, and the magnifying capabilities of the laparoscope, helping in nerve preservation. Although less focused on, laparoscopy has also a clear cosmetic advantage over the open approach. This may become an important issue, as more patients are diagnosed at a younger age[29].

Morbidity and mortality

Morbidity rates were presented by seven large scale clinical trials[8,18,20-22,24,30]. Intraoperative complications analyzed, included injury to the bowel or adjacent organs, hemorrhage, and anesthesia related complications. Postoperative complications included anastomotic leak, wound infection, and various cardiac, renal, pulmonary or vascular complications. Intraoperative complication rates ranged from 6.1%-21.2%, and 12.4%-23.5% for the laparoscopic and open groups, respectively (*P* = 0.01, *P* = 0.60). Postoperative complication rates ranged from 2.4%-45.1% and from 10.6%-52.1%, respectively (*P* = 0.01, *P* = 0.96). A recent meta-analysis published in 2013 by Arezzo *et al*[31] included 23 studies, representing 4539 patients, demonstrated a lower overall complication rate in the laparoscopic group (31.8%) compared to the open

Table 3 Operative time for laparoscopic and open rectal resection data presented as mean ± SD, min

Ref.	Laparoscopy	Open	*P* value
Liang *et al*[17]	138 ± 24	119 ± 22	< 0.001
Kang *et al*[18]	245 ± 75	197 ± 63	< 0.001
Lujan *et al*[20]	194 ± 45	173 ± 59	0.02
Ng *et al*[21]	213 ± 59	154 ± 70	< 0.001
Ng *et al*[22]	214 ± 46	164 ± 43	< 0.001
Braga *et al*[24]	262 ± 72	209 ± 70	< 0.001
Zhou *et al*[30]	120	106	0.05

SD: Standard deviation.

Table 4 Estimated intraoperative blood loss and transfusion rate for laparoscopic and open rectal cancer resection

Ref.	EBL (mL)			Blood transfusion rate		
	Lap	Open	*P* value	Lap	Open	*P* value
Liang *et al*[17]	N/A	N/A	N/A	2.4%	4.6%	0.38
Kang *et al*[18]	200	217.5	0.006	0%	0.005%	*P* > 0.99
Lujan *et al*[20]	127.8	234.2	*P* < 0.001	N/A	N/A	N/A
Ng *et al*[22]	321.7	555.6	*P* = 0.09	N/A	N/A	N/A
Braga *et al*[24]	150	350	*P* < 0.001	7.2%	26.8%	*P* = 0.002
Zhou *et al*[30]	20	92	*P* = 0.05	N/A	N/A	N/A

EBL: Estimated blood loss; N/A: Not applicable.

group (35.4%), RR = 0.83 (95%CI: 0.76-0.91, *P* < 0.001). Importantly, this meta-analysis uniquely showed no difference in the leak rates between the two approaches. A possible explanation may be the advent of new technologies, such as the ultrasonic scalpel, and articulated staplers as well as improved surgical experience. In 2006, Gao *et al*[32] published a meta-analysis demonstrating a lower morbidity rate for patients assigned to laparoscopy than for those assigned to open resection (OR = 0.63, 95%CI: 0.41-0.96, *P* = 0.96).

Short term postoperative mortality was reported by six trials comparing laparoscopic and open resection[8,17,20-22,24]. No significant difference was detected between the groups in either study. The "CLASSIC" trial reported the highest mortality rates (laparoscopy -4% *vs* open -5%, *P* = 0.57)[8]. The meta-analysis by Arezzo *et al*[31] presented above, showed a mortality rate of 1% following laparoscopy and of 2.4 % following open resection, (RR = 0.46, 95%CI: 0.21-0.99, *P* = 0.048).

Conversion rate

Eight randomized controlled trials presented the rate of conversion from a laparoscopic to an open rectal resection. Conversion rates ranged between < 1% to 34%[17-24]. A recent large scale meta-analysis showed that overall, 13% (260 of 2005) of laparoscopic procedures were converted to open surgery, 12.5% in the RCTs and 13.3% in the prospective controlled trials[31]. Conversion was not uniformly defined, but the main reasons for conversion were obesity[33], narrow pelvic anatomy, uncontrollable bleeding, ureteral injury, and advanced disease. To note, that mobilization of the rectum can be performed with a total laparoscopic approach or with a hybrid procedure. In this hybrid approach, inferior mesenteric vessels division, mobilization of splenic flexure, and left-side colon are performed laparoscopically, but TME of the rectum is performed partially by technique of open dissection through a Pfannenstiel wound, which is also used for specimen extraction. In our opinion this approach is not to be considered as a converted procedure, although a mini-laparotomy is considered by some as conversion. Since conversion is associated in several trials with increased morbidity and poorer oncological results[8,34], patients should be routinely pre-operatively evaluated for the potential risk of conversion, using radiological and clinical parameters.

Operative time

Data from seven RCTs[17,18,20-22,24,30] comparing operative time for laparoscopic and open rectal cancer surgery, clearly show a significantly longer operative time for the laparoscopic approach. Data from the RCTs is presented in Table 3. In a meta-analysis published recently, including 11 non-RCTs and 7 RCTs, the mean operative time was 219 *vs* 175 min for laparoscopy and open surgery, respectively, with an overall mean difference of 42.8 min (95%CI: 31.4-54.2, *P* < 0.001). Other trials evaluating the impact of surgeon experience on surgical outcome, showed that operative time decreased significantly with number of operations performed (range: 40-90)[35-37].

Estimated intraoperative blood loss and transfusion rate

Five RCTs compared the estimated intraoperative blood loss (EBL) in laparoscopic and open rectal cancer surgery[18,20,22,24,30]. All trials showed a significantly lower EBL in the laparoscopic group (range: 20.0-321.7 *vs* 92.0-555.6, *P* = 0.05 to *P* < 0.001). The blood transfusion rate was non-significantly higher for the open group in two RCTs[17,18], and significantly higher for the open group in one study[24]. Data is shown in Table 4.

Length of hospital stay

Seven RCTs reported data comparing length of hospital stay (LOS) after laparoscopic and open surgery for rectal cancer[8,18,20-22,24,30]. Three trials showed a significantly shorter LOS following laparoscopy[22,24,30], and the other four RCTs presented a similar trend. This was supported by two meta-analyses showing a shorter LOS by 2.67 d [95%CI: -3.8-(-1.54), *P* = 0.06][28], and by 2.7 d [95%CI: -3.6-(-1.7), *P* < 0.001] after laparoscopic rectal resection[31]. Data is shown in Table 5.

Bowel function recovery

Bowel function recovery after laparoscopic and open surgery for rectal cancer was assessed by six RCTs[8,17,18,21,22,30], and two meta-analyses[28,31]. Variable parameters were assessed such as, time to peristalsis, time to 1st flatus or stool, and time to initiating of oral feeding. Time to peristalsis was significantly shorter after laparoscopy in 3 RCTs[17,22,30], and in one meta-analysis[28]. Time to 1st fla-

Table 5 Length of hospital stay

Ref.	Design	Measure	LOS		
			Lap	Open	*P* value
Guillou *et al*[8] "CLASSIC"	RCT	Median (range)	13 (9-18)	11 (9-15)	N/A
Kang *et al*[18] "COREAN"	RCT	Median (range)	8 (7-12)	9 (8-12)	0.06
Lujan *et al*[20]	RCT	mean ± SD	8.2 ± 7.3	9.9 ± 6.8	0.11
Ng *et al*[21]	RCT	Median (range)	10.8 (5-27)	11.5 (3-38)	0.55
Ng *et al*[22]	RCT	Median (range)	8.4 (2-32)	10 (3-39)	0.013
Braga *et al*[24]	RCT	mean ± SD	10 ± 4.9	13 ± 10	0.004
Zhou *et al*[30]	RCT	mean ± SD	8.1 ± 3.1	13.3 ± 3.4	0.001
Aziz *et al*[28]	MA	MD (d)	-2.67 d, 95%CI: -3.8-(-1.54)		0.06
Arezzo *et al*[31]	MA	MD (d)	-2.7 d, 95%CI: -3.6-(-1.7)		0.001

RCT: Randomized controlled trial; MA: Meta-analysis; LOS: Length of stay; SD: Standard deviation; MD: Mean difference; CI: Confidence intervall; N/A: Not applicable.

Table 6 Bowel function recovery

Ref.	Design	Measurement	Lap	Open	*P* value
Time to peristalsis					
Liang *et al*[17]	RCT	d	3.9	4.2	0.001
Ng *et al*[21]	RCT	d	4.1	4.7	0.06
Ng *et al*[22]	RCT	d	4.3	6.3	0.001
Guillou *et al*[8]	RCT	d	5	6	N/A
Zhou *et al*[30]	RCT	d	1.5	2.7	0.009
Aziz *et al*[28]	MA	d	MD -1.52 d [95%CI: -2.2-(-1.01), *P* = significant]		
Time to 1st flatus					
Ng *et al*[22]	RCT	d	3.1	4.6	0.001
Kang *et al*[18]	RCT	h	38.5	60	0.001
Time to 1st stool					
Kang *et al*[18]	RCT	h	96.5	123	0.001
Liang *et al*[17]	RCT	d	3	3.3	0.001
Arezzo *et al*[31]	MA	d	3.3 *vs* 4.4 MD -0.96 d [95% CI -1.3-(-0.6), *P* < 0.001]		
Time to oral feeding initiation					
Kang *et al*[18]	RCT	h	85	93	0.001
Guillou *et al*[8]	RCT	d	6	6	N/A
Ng *et al*[21]	RCT	d	4.3	4.9	0.001
Ng *et al*[22]	RCT	d	4.3	6.3	0.001
Aziz *et al*[28]	MA	d	MD -0.92 d [95%CI: -1.35-(-0.5), *P* = significant]		
Arezzo *et al*[31]	MA	d	3.8 *vs* 4.8 MD -1 d [95%CI: -1.4-(-0.7), *P* < 0.001]		

RCT: Randomized controlled trial; MA: Meta-analysis; MD: Mean difference; N/A: Not applicable; CI: Confidence interval.

tus was significantly shorter as well in 2 RCTs[18,22]. Arezzo *et al*[31] showed an approximate one day shorter hospital stay after laparoscopic surgery in their meta-analysis [lap 3.3 *vs* open 4.4, median difference -0.96 d, 95%CI: -1.3-(-0.6), $P < 0.001$][31]. Similar results were shown by 2 RCTs[17,18]. Time to initiation of oral feeding was shorter by approximately one day in 2 meta-analyses[28,31]. A Similar trend was observed in three RCTs[18,21,22]. Data is shown in Table 6.

Postoperative pain and analgesic use

In a meta-analysis published in 2006 by Aziz *et al*[28] there was no difference with regards to the analgesic use after laparoscopic or open rectal cancer surgery[28]. However, several RCTs published later showed that patients that underwent laparoscopic resections, required fewer injections of analgesics (6 *vs* 11.4, $P = 0.007$ and 4.9 *vs* 8.3, $P = 0.001$)[21,22], and lower doses of morphine (107.2 mg *vs* 156.9 mg, $P < 0.001$). Through less analgesic use, pulmonary complications maybe reduced and a faster bowel recovery may further benefit the patient. Future studies should make use of monitored patient controlled analgesia, and strict drug documentation, led in specialized centers, to accurately measure and compare the true effect of laparoscopy on postoperative pain.

Bladder and sexual function

Jayne *et al*[38] published data regarding bladder and sexual function from the MRC-CLASSIS trials' patient database[8]. Overall questionnaire response rate was above 50%. No difference was observed in bladder function between the laparoscopic and open groups. Approximately 30% of patients reported moderate to severe urinary symptoms in each group. With regards to sexual function, more than 50% of men and women reported being sexually inactive in the questionnaires. In men, overall sexual function and erectile function tended to be worse after laparoscopic than open rectal surgery [overall function: score difference -11.18, 95%CI: -22.9-0.63, $P = 0.063$; erectile function: score difference -5.84, 95%CI: -10.94-(-0.74), $P = 0.068$]. In women, there was no difference in sexual function. In this trial it was shown that oncological requirement for TME (OR = 6.38; $P = 0.054$) and conversion to open surgery (OR = 2.86; $P = 0.041$) were independent predictors of postoperative sexual dysfunction in men. Kang *et al*[18] demonstrated a higher number of urinary problems after laparoscopy than open surgery ($P < 0.001$), but no difference between the laparoscopic and open groups in regards to sexual function.

Adhesion formation and incisional hernia

Adhesion formation is an increasing problem after colorectal surgery[39-41]. Laparoscopic colorectal surgery may result in fewer adhesions because of reduced tissue handling, and less environmental exposure of the bowel. In a recently published study by Burns *et al*[41], patients undergoing laparoscopic colorectal resection were found to have a lower risk of developing clinically significant adhesions. Interestingly, a retrospective study, supplementary to the CLASICC trial[8], showed that more patients undergoing colonic resection were admitted for adhesive intestinal obstruction (AIO) in the open arm than in the laparoscopic arm (4% *vs* 1.3%); however, this was reversed when considering patients with rectal cancer (2% *vs* 3.9%). Furthermore, more patients with rectal cancer who underwent conversion to open surgery were admitted for AIO than those who had open surgery or completed laparoscopic surgery (8%, 2% and 2% for converted, open

and laparoscopic surgery respectively). Surprisingly, this trend was seen for incisional hernia as well. Although not statistically significant ($P = 0.78$), more patients undergoing colonic resection developed incisional hernia in the open arm than in the laparoscopic arm (10% *vs* 6.6%); however, this was reversed when considering patients with rectal cancer (9% *vs* 10.9%). This may partially be explained by the relatively less experienced surgical team (surgeons were required to perform only 20 laparoscopic colorectal procedures for the trial eligibility), or by the relatively small cohort of the rectal cancer subgroup. In our opinion, laparoscopy has a clear advantage in these aspects, however further randomized trials are needed to clarify the impact of laparoscopy on adhesion formation and incisional hernia in rectal surgery.

Current trials

At present, three large scale randomized controlled trials are being conducted. The European Colon Cancer Laparoscopic or Open Resection (COLOR) Ⅱ trial is a randomized, international, multicenter study comparing the outcomes of laparoscopic and open resection of rectal carcinoma, with primary endpoint being locoregional recurrence at 3 years. Secondary endpoints are recurrence-free and overall survival at 3, 5 and 7 years, rate of distant metastases, port site and wound site recurrences, microscopic evaluation of the resected specimen, 8-wk morbidity and mortality, quality of life, and cost[42]. In the United States, the American College of Surgeons Oncology Group (ACOSOG)-Z6051 trial, opened in 2008, and is a phase Ⅲ randomized controlled trial with a non-inferiority design and a 1:1 randomization of laparoscopic and open rectal resection. Primary endpoints include circumferential and distal resection margins, number of lymph nodes harvested, and integrity of the TME specimen. Secondary endpoints include disease free survival and local recurrence at 2 years[43]. Finally, the Japanese Clinical Oncology Group trial JCOG 0404, is a RCT comparing laparoscopic and open surgery for colorectal cancer, with overall survival and relapse free survival as primary endpoints[44].

CONCLUSION

Current evidence suggests that laparoscopic rectal cancer resection results in similar oncological outcomes when compared with the conventional open approach. Initial concern regarding circumferential margin positivity, has not been demonstrated in other large scale randomized controlled trials or meta-analyses presented in this review. Morbidity and mortality rates are at least comparable, with some meta-analyses even showing reduced morbidity and mortality after the laparoscopic approach. Furthermore, the laparoscopic approach benefits patients with a reduced need for analgesics, faster recovery of bowel function, shorter length of stay, and less blood loss. The impact of laparoscopy on bladder and sexual function as well as clinically significant adhesion formation and incisional hernia rates, is still inconclusive, and needs further investigation.

Undoubtedly, surgeon experience and competence in laparoscopic colorectal surgery have a major impact on oncological and other perioperative outcomes. This has led both the American Society of Colon and Rectal Surgeons and the Society of Gastrointestinal and Endoscopic Surgeons to recommend that laparoscopy for rectal cancer resection should be practiced by expert, trained surgeons in institutions where the outcomes can be meaningfully evaluated.

Current large scale randomized controlled trial are conducted worldwide, further investigating the oncological and clinical efficacy of laparoscopic rectal cancer resection.

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