Comparison between laparoscopic and open surgery of rectal cancer in terms of pathological findings and early outcome: a randomized controlled trial

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Background
Laparoscopic surgery has progressively replaced open colonic surgery in recent decades owing to favorable short-term outcomes, such as less pain, reduced blood loss, and improved recovery time. The current study was designed to compare laparoscopic surgery with open surgery in patients with rectal cancer by incorporating clinical endpoints and detailed pathological analysis of all resected samples.
Methods
A prospective randomized controlled trial was conducted to compare laparoscopic surgery with open surgery for rectal cancer patients. The primary endpoint was postoperative clinical outcome in terms of morbidity and mortality. Secondary endpoints were adequacy of surgical margins and number of lymph nodes harvested for rectal cancer cases.
Results
Sixty patients underwent 40 laparoscopic and 20 open rectal resections between January 2014 and January 2016. There was no mortality, and there were significantly improved short-term surgical outcomes (less blood loss, less use of epidural analgesia, earlier restoration of bowel function, and reduction of the hospital stay) in the laparoscopic group. There were similar rates of intraoperative complications as open surgery, and the incidence of anastomotic leakage was similar between the two techniques. The conversion rate in the laparoscopic group was 12.5%. The short-term outcomes of the current study showed that the radicality of laparoscopic resection (as assessed by pathology report) in patients with rectal cancer is no different from that of open surgery; the median number of lymph nodes harvested for malignancies was 14 in the laparoscopic group and 13 in the open surgery group.
Conclusion
Laparoscopic surgery in patients with rectal cancer may confer clinical benefits in terms of faster recovery, smaller incisions, and a shorter hospital stay. The procedure can be technically difficult and time consuming. Laparoscopic resection of rectal cancer provided oncological radicality, using the pathology report as a proxy, similar to open surgery. Long-term follow-up to assess local recurrence and survival is necessary to ascertain oncological safety of laparoscopic resection in patients with rectal cancer.

Keywords:
cancer, laparoscopic, rectum

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Introduction

Colorectal cancer including rectal cancer is the third most common cause of cancer deaths in the Western world. The incidence of rectal cancer in the Western world is 28–35% of the total colorectal cancer incidence, with 15–25/100 000 new patients per year; the associated mortality is between 4 and 10/100 000/year [1,2].

Laparoscopic surgery has progressively replaced open colonic surgery in recent decades owing to favorable short-term outcomes, such as less pain, reduced blood loss, and improved recovery time [3,4]. Laparoscopic surgical techniques have been performed to treat colorectal cancer for more than two decades, as the first publications of laparoscopic application to the treatment of colon cancer date from 1991 [5].

Laparoscopy techniques in rectal cancer are more challenging than the ones performed for colon cancer. There are specific questions related to rectal anatomy, such as difficult exposure in a narrow pelvis,

proximity to nerve structures, and difficult intestinal resection [6]. Problems with anastomosis and difficulties in rectal resection, narrow pelvis, bulky tumors, adhesions, and obesity are among the most commonly reported reasons for conversion and can represent relative contraindications to laparoscopy. Studies suggest that the open approach may be more suitable for these patients [6–8].

Since the introduction of laparoscopy in the treatment for colorectal cancer, one of the main concerns was whether it provides rectal excision equivalent to the open procedure, with adequate lymphadenectomy and radial and circumferential clearance to avoid recurrence of cancer. Negative surgical margins are crucial to avoid local recurrence. Circumferential margin positivity is considered an independent factor in local recurrence [9,10]. Radial margins less than 2 cm are related to a 16% local recurrence rate, contrasting with a 6% rate if the radial margin is more than 2 cm [10,11]. With regard to distal resection margin, most surgeons consider a 2 cm distal margin acceptable [12].

The number of lymph nodes (LN) harvested during surgery varies widely. For a correct pathological staging, removal of 12 LN is advised, but most series report a lower number of harvested LN. This could be because of the chemoradiotherapy regimens that are applied. However, high ligation of the inferior mesenteric vessels, which is now performed in laparoscopic total mesorectal excision (TME), can help improve node harvest, allowing more accurate tumor staging [10,12].The current study was designed to compare laparoscopic surgery with open surgery in patients with rectal cancer by incorporating clinical endpoints and detailed pathological analysis of all resected samples [13]. Short-term endpoints were used as surrogates to predict long-term clinical outcomes and also to assess the quality of surgery in cancer of the rectum.

Methods

Data collection

All demographic and surgical data were prospectively recorded using an electronic database. The data included all relevant perioperative information such as the use of neoadjuvant chemoradiation, as well as events in the postoperative course. Follow-up data were obtained from surgery clinic visits, the oncology files, and telephone interviews.

Patients

Patients with a solitary adenocarcinoma of the rectum within 15 cm from the anal verge without distant metastases, who were candidates for elective surgery, were eligible for inclusion. The localization of the tumor was categorized as the upper rectum (distal border of the tumor, 10–15 cm from the anal verge), middle rectum (5–10 cm from the anal verge), or lower rectum (<5 cm from the anal verge). Patients with T4 or T3 tumors within 2 mm of the endopelvic fascia, as determined on computed tomography or MRI, were excluded. Other exclusion criteria have been reported previously [14]. The study was approved by the Alexandria Ethical Committee. All patients provided written informed consent.

Randomization

Randomization was performed at the patient level. Eligible patients were randomly assigned in a 2 : 1 ratio to undergo either laparoscopy or open surgery according to a list of randomization numbers with treatment assignments. This list was computer generated, with stratification according to tumor location, and the presence or absence of preoperative radiotherapy.

Surgical technique

For high rectal tumors, more than 10 cm from the anal verge, we performed anterior resection of the rectum with partial mesorectal excision, aiming for a distal margin of 5 cm below the tumor. Tumors located less than or equal to 10 cm from the anal verge were treated according to accepted TME principles.

Low rectal resection was performed using laparoscopic-assisted approach: a short Pfannenstiel incision was made after the laparoscopic dissection, and the resection was completed using a mechanical stapler. An end-to-end anastomosis stapler was used to restore the continuity. A diverting ileostomy was commonly created after performing a low colorectal anastomosis, or for higher anastomoses if technical difficulties or other factors suggested a high risk for anastomotic breakdown. Bowel preparation before surgery was performed routinely in all cases.

Follow-up

Follow-up visits were 1 and 3 months after the surgery, and then every 3 months for the first year and every 4 months for the second year. Primary short-term endpoints were positivity rates of circumferential and longitudinal resection margins, proportion of Dukes' C2 tumors, and in-hospital mortality.

Secondary short-term endpoints were complication rates measured during surgery and 30 days and 3 months after surgery, as well as transfusion requirements. We will report long-term endpoints

(survival, recurrence, and quality of life) at 3 and 5 years.

Statistical analyses

Data were expressed as mean±SD or number (%). Continuous variables were compared using the Student's *t*-test (normal distribution) or the Mann–Whitney *U*-test (non-normal distribution); categorical variables were compared by the χ^2-test. All statistical analyses were performed using SPSS statistical software, version 13.0 for Windows (SPSS Inc., Chicago, Illinois, USA). A *P* value less than 0.05 was considered to be statistically significant.

Results

Between January 2014 and January 2016, 65 patients with rectal cancer were randomly assigned to either laparoscopic or open surgery of patients admitted to Colorectal Unit, Surgical Department, Alexandria Main University Hospitals; five patients were excluded after randomization, and the reasons for exclusion included distant metastases and a T4 tumor. Forty patients were assigned to laparoscopic surgery and 20 to open surgery at a ratio of 2 : 1.

The proportions of patients given preoperative radiotherapy and preoperative chemotherapy were similar in the laparoscopic and open surgery groups (Table 1). Twenty-five patients in the laparoscopy group and 12 patients in the open surgery group received long-course radiotherapy.

The distributions of the different operative procedures were similar in both groups. A diverting ileostomy was created in about a third of all patients (Table 2). Of 20 patients with a tumor located in the upper rectum, 14 (70%) had a TME (nine in the laparoscopic surgery group vs. five in the open surgery group) and six (30%) had a partial mesorectal excision (four vs. two, respectively). Of 26 patients with cancer of the middle rectum, 20 (76.92%) had a sphincter-saving TME (13 in the laparoscopic surgery group vs. seven in the open surgery group) and six (23.08%) underwent an abdominoperineal resection (four vs. two, respectively). Of 14 patients with a tumor located within 5 cm from the anal verge, 10 (71.44%) had an abdominoperineal resection (seven in the laparoscopic surgery group vs. three in the open surgery group) and four (28.76%) had sphincter-saving TME (three vs. one, respectively).

Of 20 patients with cancer of the upper rectum, 18 (90%) had a stapled anastomosis (12 in the laparoscopic surgery group vs. six in the open surgery group) and two (10%) had a hand-sewn anastomosis (one vs. one, respectively). Of 26 patients with cancer of the middle rectum, 18 (69.23%) had a stapled anastomosis (12 in the laparoscopic surgery group vs. six in the open surgery group), two (7.69%) had a hand-sewn anastomosis (one

Table 1 Clinical characteristics of patients

	Laparoscopic surgery (*n*=40)	Open surgery (*n*=20)
Sex		
Male	24 (60)	11 (55)
Female	16 (40)	9 (45)
Age (years)	54.6±10.4	53.7±10.6
American Society of Anesthesiologists category		
I	12 (30)	6 (30)
II	22 (55)	12 (60)
III	6(15)	4 (10)
IV	0	0
BMI (kg/m^2)	26.4±4.2	26.2±4.1
Location of tumor (distance from anal verge) (cm)		
Upper rectum (10–15)	13 (32.5)	7 (35)
Middle rectum (5–10)	17 (42.5)	9 (45)
Lower rectum (<5)	10 (25)	4 (20)
Clinical stage[a]		
I	12 (30)	6 (30)
II	13 (32.5)	7 (35)
III	15 (37.5)	7 (35)
Preoperative radiotherapy	25 (62.5)	12 (60)
Preoperative chemotherapy	13 (32.5)	7 (35)

Data presented as mean±SD or n (%) of patients. [a]International Union Against Cancer staging system: stage I, localized cancer; stage II, early locally advanced cancer; stage III, late locally advanced cancer [15]. No statistically significant between-group differences (P≥0.05); Student's t-test (continuous variables) or χ^2-test (categorical variables).

Table 2 Operative findings

	Laparoscopic surgery (*n*=40)	Open surgery (*n*=20)	*P* value
Intervention			
Resection with partial mesorectal excision	4/40 (10)	2/20 (10)	1.000
Resection with total mesorectal excision	25/40 (62.5)	13/20 (65)	0.928
Abdominoperineal resection	11/40 (27.5)	5/20 (25)	0.874
Diverting ileostomy			
Total group[a]	14/40 (35)	7/20 (35)	1.000
Upper rectum[b]	2/13 (15.38)	1/7 (14.29)	0.954
Middle rectum[b]	10/17 (58.82)	5/9 (55.55)	0.933
Lower rectum[b]	2/10 (20)	1/4 (25)	0.869
Duration of intervention (min)[c]	260 (184–350)	177 (150–230)	<0.0001
Blood loss (ml)			
Total group	180 (100–400)	450 (250–650)	<0.0001
Conversion	5/40 (12.5)		
Intraoperative complications	5/40 (12.5)	3/20 (15)	0.815
Hemorrhage	3/40 (7.5)	2/20 (10)	0.762
Anastomosis related	1/40 (2.5)	1/20 (5)	0.624
Ureter injury	1/40 (2.5)	0/20	0.481

Data are represented as n/N (%) or median (interquartile range). [a]Number of patients who had an anastomosis. [b]Denominator was the number of patients who had ileostomies. [c]Time between first incision and closure of the surgical incision.

vs. one, respectively), and six (23.08%) had a colostomy (four vs. two, respectively). Of 14 patients with cancer of the lower rectum, three (21.43%) had a stapled anastomosis (two in the laparoscopic group vs. one in the open group), one (7.14%) had a hand-sewn anastomosis in the open group, and 10 (71.44%) had a colostomy (seven vs. three, respectively).

The median duration of laparoscopic surgery was 260 min (interquartile range 184–350) compared with 177 min (150–230; $P<0.0001$) for open surgery. Median blood loss was 180 ml (100–400) during laparoscopic surgery and 450 ml (250–650; $P<0.0001$) during open surgery (Table 2).

Laparoscopic procedures were converted to open surgery in five (12.5%) of 40 patients; conversions were done in three cases for bleeding, in one case of ureter injury, and in another case of extensive adhesions. Intraoperative complications occurred in five patients (Table 2).

First bowel movement occurred on the second day after laparoscopic surgery, which was 1 day earlier than after open surgery. Oral intake of more than 1 l of fluid was tolerated significantly earlier after laparoscopic surgery. Median hospital stay after laparoscopic surgery was 8.9 ±6.8 days, which was shorter than after open surgery: 14.1±10.6 days (Table 3).

The postoperative use of opiates or nonopiates did not differ significantly between groups. Epidural analgesics on the first, second, and third days after surgery were used by a greater proportion of patients in the open surgery group than in the laparoscopic surgery group (Table 3).

There was no reported mortality, whereas morbidity was reported in 10 (25%) of 40 patients in the laparoscopic surgery group and in six (30%) of 20 patients in the open surgery group (Table 3). Anastomotic leaks were noted in one (3.45%) of 29 patients after laparoscopic surgery and in one (6.67%) of 15 patients in the open surgery group (Table 3).

The median distal resection margin was 3.2 cm in laparoscopic surgery compared with 3.5 cm after open surgery; the proximal resection margin was 16.5 cm after laparoscopic surgery and 17 cm after open surgery. There was no difference in the proportion of patients, with a positive circumferential resection margin, between the two groups (Table 4).

The median number of LN harvested after surgery was 14.0 (12.0–19.0) in the laparoscopic surgery group compared with 13.0 (11.0–18.0) in open surgery group, which was not significantly different (Table 4). The proportion of patients in whom no evidence of tumor was found after preoperative (neoadjuvant) radiation or preoperative chemoradiatherapy did not differ significantly between the two groups (Table 4).

Discussion

Laparoscopic surgery is a less invasive approach to use for tumor resection compared with open surgery, and the operation can be performed through a few small

Table 3 Postoperative recovery, morbidity, and mortality within 28 days

	Laparoscopic surgery (*n*=40)	Open surgery (*n*=20)	*P* value
Days until first bowel movement (mean±SD) (days)	2.1±2.3	3.8±3.5	0.042**
Days until intake of more than 1 l of fluid (mean±SD) (days)	2.1±3.1	3.9±2.7	0.031**
Use of analgesic drugs			
Day 1			
Opiates	14/40 (35)	8/20 (40)	0.797
Nonopiates	36/40 (90)	19/20 (95)	0.890
Epidural	11/40 (27.5)	16/20 (80)	0.041**
Day 2			
Opiates	14/40 (35)	8/20 (40)	0.452
Nonopiates	36/40 (90)	19/20 (95)	0.890
Epidural	9/40 (22.5)	14/20 (70)	0.042**
Day 3			
Opiates	12/40 (30)	10/20 (50)	0.085
Nonopiates	36/40 (90)	19/20 (95)	0.890
Epidural	7/40 (17.5)	8/20 (40)	0.042**
Morbidity (patients with at least one postoperative complication)	10/40 (25)	6/20 (30)	0.987
Cardiac	1/40 (2.5)	1/20 (5)	0.624
Anastomotic leak[a]	1/29 (3.45)	1/15 (6.67)	0.644
Respiratory	2/40 (5)	1/20 (5)	1.000
Abscess	2/40 (5)	1/20 (5)	1.000
Wound infection	2/40 (5)	1/20 (5)	1.000
Ileus	2/40 (5)	1/20 (5)	1.000
Reintervention	4/40 (10)	2/20 (10)	1.000
Hospital stay (mean±SD) (days)	8.9±6.8	14.1±10.6	0.024**

Data are represented as n/N (%). [a]The numerator was the number of leaks and the denominator was the total number of patients after excluding those without an anastomosis – i.e. abdominoperineal resection. **Statistically significant difference.

Table 4 Pathology

	Laparoscopic surgery (*n*=40)	Open surgery (*n*=20)	*P* value
Distance to proximal resection margin (cm)	16.5±4.8	17.0±5.1	0.710
Distance to distal resection margin (cm)	3.2±1.1	3.5±1.4	0.231
Positive CRM[a]	4/40 (10)	2/20 (10)	0.436
Median CRM (cm)	1.1±0.6	1.0±0.7	0.567
Number of harvested lymph nodes	14.0 (12.0–19.0)	13.0 (11.0–18.0)	0.494
Pathology stage			0.457
I	14/40 (35)	7/20 (35)	1.000
II	12/40 (30)	7/20 (35)	0.787
III	14/40 (35)	6/20 (30)	0.782
IV	0	0	

Data are represented as n/N (%) or mean±SD. CRM, circumferential resection margin. [a]Circumferential margins were judged positive when tumor cells were present within 2 mm from the lateral edge of the mesorectum.

incisions. This results in improved short-term surgical outcomes (less blood loss, less use of epidural analgesia, earlier restoration of bowel function, and reduction of the hospital stay) [16–18], which is consistent with the findings of the present study.

Laparoscopic rectal resection is, however, generally more complicated than traditional open surgery, and the duration of surgery was longer in the laparoscopic group than in the open surgery group. Laparoscopic surgery, in the current study, was associated with similar rates of intraoperative complications and morbidity as open surgery, and the incidence of anastomotic leakage was similar between the two techniques. These findings are similar to other trials [8,19–21].

Complete removal of the primary tumor and tumor deposits in the mesorectum is the goal of surgery in patients with rectal cancer. A resection is judged as radical when the circumferential, distal, and proximal edges of the specimen are devoid of tumor cells. Clear circumferential margins are of great importance because the risk of local recurrence increases three to four times when these margins are invaded with tumor cells [22,23]. The short-term outcomes of the current

study showed that the radicality of laparoscopic resection (as assessed by pathology report) in patients with rectal cancer is no different from that of open surgery.

In the current study, there was no difference between groups in the proportion of patients with a positive circumferential resection margin, which was judged as positive when tumor cells were present within 2 mm from the lateral edge of the mesorectum. Similar results were observed in many studies [22,24,25].

There has been much debate in the literature and no real consensus about the minimum number of LN necessary to adequately stage colorectal cancers. General recommendation today is to harvest at least 12–15 LN to accurately predict regional node negativity [26]. In the current study, the median number of LN harvested for malignancies was 14 in the laparoscopic group and 13 in the open surgery group, which is similar to previously published studies [27].

The present study was limited by small sample size and short period of follow-up, but the between-group similarities in demographic and clinicopathological characteristics suggest that the results were consistent. Furthermore, the results of the current study confirm those of several other published studies [22,27–31]. Long-term follow-up to assess local recurrence and survival is necessary to ascertain oncological safety of laparoscopic resection in patients with rectal cancer.

Conclusion

In conclusion, laparoscopic surgery in patients with rectal cancer may confer clinical benefits in terms of faster recovery, smaller incisions, and a shorter hospital stay. Laparoscopic resection of rectal cancer provided oncological radicality, using the pathology report as a proxy, similar to open surgery. Long-term follow-up to assess local recurrence and survival is necessary to ascertain oncological safety of laparoscopic resection in patients with rectal cancer.

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Conflicts of interest

There are no conflicts of interest.

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