Evaluation of the short-term outcomes of minimally invasive surgery in colon cancer: an initial experience in a Middle Eastern oncology center using a randomized comparative design

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Background
The surgical approach to treat colon cancer has remained a matter of debate for many years. The assessment of short-term outcomes of the most common available modalities for surgical resection of colon cancer, which are the laparoscopic and open techniques, is considered a tool by which the best approach for colon cancer resection can be judged and documented. The aim of this work was to report on the initial experience in laparoscopic resection of colon cancer in a Middle Eastern oncology center.

Patients and methods
A total of 88 patients were involved in the current study who were proved to have colon cancer by a confirmed biopsy. They were subjected randomly to open or laparoscopic colectomy (LAC) and followed up for short-term outcomes (operative time, blood loss, and postoperative sequelae) to determine the most beneficial strategy based on its advantages. Data were collected and analyzed using Statistical Package for the Social Sciences version 20.

Results
The results showed that LAC was significantly different compared with open colectomy (OC) regarding the postoperative pain score, which was 3.14 and 6.85 for LAC and OC, respectively (P=0.02). Time to bowel sounds return was faster in LAC at 3.48 vs 7.5 h in OC ($P<0.05$). Postoperative ileus and surgical site infection were less frequent in LAC (P=0.03 and 0.05, respectively). The most impressive statistically significant differences were in hospital stay (4.75 days after LAC vs 8.11 days after OC; P=0.02) and the reported overall morbidity, which was recorded in 6.6% of LAC cases compared with 21% of OC cases; this difference was significant ($P<0.01$).

Conclusion
LAC showed multiple advantages over OC in many aspects related to short-term outcomes. The results of this study support the view that minimally invasive LAC is an effective and safe procedure for resection of colon cancer.

Keywords:
colon cancer, laparoscopic colectomy, laparoscopy, minimally invasive, outcomes

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Introduction

Colon cancer remains one of the primary causes of cancer-related deaths worldwide, as the incidence and mortality of colon cancer rank third (10.2%) among all cancers worldwide [1]. Moreover, according to the latest global cancer report issued by the International Agency for Research on Cancer, in 2018 alone, more than 1.8 million individuals were newly diagnosed with colon cancer, of whom 881 000 died owing to the disease [1].

Colon cancer is considered the seventh most common cancer in Egypt, as it accounts for 3.47 and 3% of all cancers in males and females, respectively. The actual assumed figure of those with colon cancer (excluding rectal cancer) in 2015 exceeded 3000. The epidemiology of colon cancer varies in each individual nation [2].

The fundamental point of disease management is sufficient resection of the primary tumor. Since its establishment, minimally invasive laparoscopic surgery has become the most preferred surgery for diseases of the gastrointestinal tract for a multitude of reasons such as reduced postoperative pain, hospital stay, time to return to daily activities, decreased morbidity rates, and aesthetics [3].

Regarding therapeutic approaches, in the late 1980s, the successes of laparoscopic surgery for gallbladder disease laid the foundations for the modern use of this surgical technique in a variety of diseases. Among the most frequent benign and malignant diseases that require surgical therapy, the best results have been achieved using a laparoscopic approach in colon cancer in terms of safety, reduced postoperative recovery, and improved long-term survival [4,5].

Laparoscopic resection for colon malignancies is now regarded as a valid alternative to traditional laparotomy. Compared with the open technique, this approach allows the same oncological radicality in terms of length of specimen, extent of regional lymphadenectomy, and recurrence rate [6].

In terms of oncological safety, laparoscopic colon surgery for colon cancer has been demonstrated to have reasonable short-term as well as long-term oncological outcomes in multiple randomized controlled studies [7].

Study aim

The aim of this study was to report on the initial experience in laparoscopic resection of colon cancer in a Middle Eastern oncology center.

Patients and methods

Study design

A prospective randomized comparative study was performed on 88 patients diagnosed with colon cancer from January 2017 to January 2020 who met our selection criteria, after exclusion of those patients who ended up with stoma formation (n=2) and others who were converted to open colectomy (OC) (n=3) owing to extensive adhesions and locally advanced disease. The patients were enrolled randomly into two study groups: OC (n=43) was performed in one group and laparoscopic colectomy (LAC) (n=45) in the other group, with a standardized approach for patient positioning and port placement for all laparoscopic colon cancer procedures. This study was reviewed and approved by the Institutional Ethics Committee, and a written and verbal informed consent was obtained from the selected patients.

Inclusion criteria

The following were the inclusion criteria:

(1) Both sexes and age above 18 years.
(2) Patients diagnosed with colon cancer confirmed by colonoscopy and biopsy.

Exclusion criteria

The following were the inclusion criteria:

(1) Patients with distant metastasis.
(2) Patients converted to open.
(3) Patients with rectal and rectosigmoid cancer.
(4) Malignant intestinal obstruction owing to colon cancer.
(5) Procedure ended up with stoma.

All patients who met the inclusion criteria (Fig. 1) were subjected to the following:

(1) History taking and physical examination.
(2) Laboratory investigation: complete blood count test and tumor marker detection together with preoperative investigations, including coagulation profile, serum electrolytes, and liver and renal profile.
(3) Radiological investigation:
    (a) Contrast-enhanced abdominal computed tomography.
    (b) Metastatic workup including computed tomography chest and bone scans if necessary.
(4) Colonoscopy with tissue biopsy.

Preoperative preparation

Mechanical bowel preparation and nonresidue diet for 48 h in addition to nutritional support when needed and prophylactic antibiotics were initiated.

Operative preparation

The patients were divided into two groups:

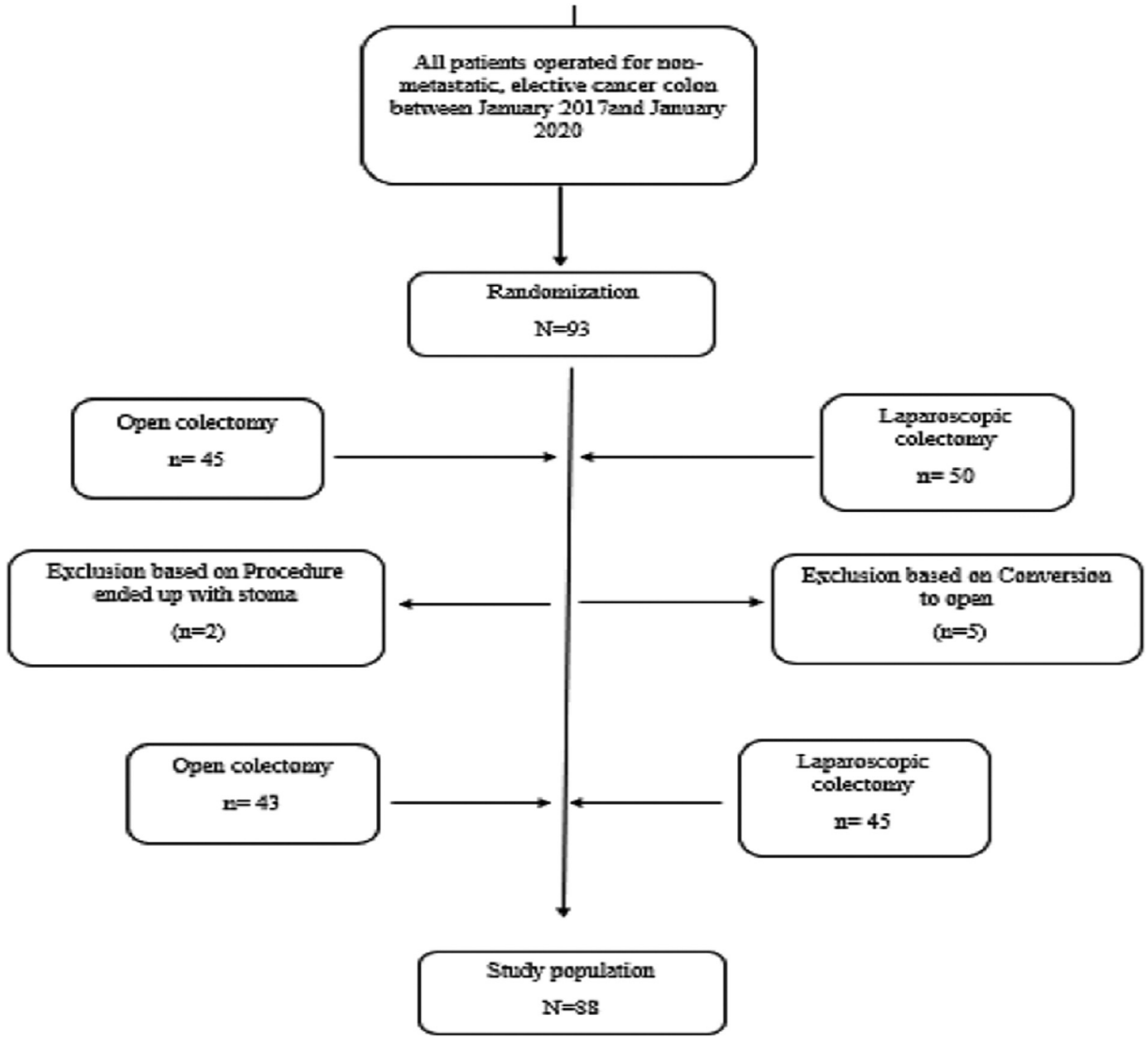
The first group included patients who underwent conventional OC.

The second group included patients who underwent LAC. A standardized technique for patient positioning, port placement, and specimen extraction was followed.

After general anesthesia had been given to all patients, insertions of the nasogastric tube and Foley catheter were commenced. An initial exploration to assess the feasibility of resection was conducted in both groups.

Most procedures were performed with the patient in the Trendelenburg position, whereas the Lloyd-Davis position was used for left-sided colectomies.

Figure 1



Flow chart of participant.

Right colon

The patient was placed in a supine position. A Trendelenburg position was required at the initial stage of the operation with some left rotation. The ports were then placed: a 10-mm port was placed in the supraumbilical region, a 12-mm port in the left subcostal, and two 5-mm ports were each placed in the suprapubic and left iliac fossa.

Next, mobilization of the colon using the lateral to medial approach was performed, and ligation of the main vessels and division of the mesentery were performed using a Harmonic scalpel combined with intracorporeal clipping.

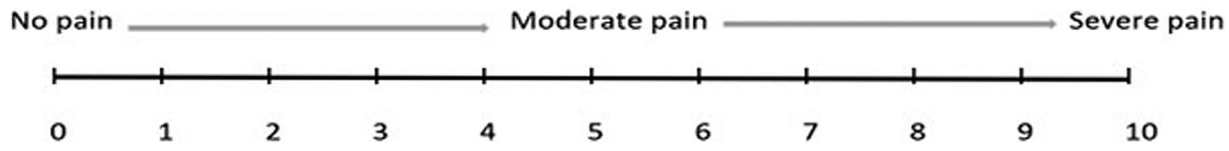
Mini-laparotomy was performed using a 5-cm skin incision to extract the pathological specimen with hand-sewn extracorporeal interrupted anastomosis.

Left colon

The patient in a supine position with ready anal access and the legs slightly flexed, but not severely so, aided by Lloyd-Davis or Allen stirrups and the buttocks near the edge of the table is extremely helpful. The ports were then placed: a 10-mm port was placed in the supraumbilical region, two 5-mm ports were each placed in the right subcostal and suprapubic fossa, and a 12-mm port was placed in the right iliac fossa.

A medial to lateral approach was used with ligation of the inferior mesenteric artery and vein. Distal margins were achieved by cutting the colon with a 60-mm Endo GIA stapler (MEDTRONIC, USA). Extraction of the specimen occurred through a Pfannenstiel incision, whereas restoration of bowel continuity was performed using circular stapler anastomosis whenever possible throughout the transanal route. However, in case of

Figure 2



Visual analog scale (VAS) for pain assessment.

higher resection and inability to fully mobilize the splenic flexure, we do the anastomosis under vision together with specimen extraction through a mini-laparotomy incision.

Evaluation of short-term outcomes

The short-term outcomes evaluated were as follows:

(1) Operative time and intraoperative blood loss.
(2) Multiple postoperative variables, including hospital stay; postoperative pain, which was assessed using the visual analog scale (Fig. 2) [8]; postoperative complications; ileus; adhesive intestinal obstruction; and wound infection.
(3) Hospital stay was recorded from day 1 postoperatively till the day of the patients' discharge after they tolerated a normal diet and achieved full mobility. They were followed up to assess postoperative sequelae (wound infection, incisional hernia, and adhesive intestinal obstruction).

Statistical analysis of the data

Data were input into the computer and analyzed using IBM Statistical Package for the Social Sciences software package version 20.0 (IBM Corp., Armonk, New York, USA). Qualitative data were described using numbers and percentages. The Kolmogorov–Smirnov test was used to verify the normality of distribution. Quantitative data were described using means and SD. Significance of the obtained results was judged at the 5% level.

Results

A total of 88 patients were enrolled in the study after being subjected to inclusion criteria (Fig. 1). They were divided into two groups. Group A included those patients who underwent OC, whereas group B was limited to those who underwent a laparoscopic approach. The mean age of the included patients was 50 and 54 years for groups A and B, respectively.

Table 1 shows that most affected patients had stage II disease (67.6% of patients who underwent an open approach and 60% of patients who underwent a laparoscopic approach) based on the preoperative investigations, which also found that the tumors were mainly localized in the sigmoid colon in 60% of group B, whereas it was nearly equally distributed in the right, sigmoid, and left sides in the other group. Other demographic data do not demonstrate any sex or BMI differences between the two groups.

Intraoperative outcomes

The main concern for the assessment of intraoperative outcomes in this study involves both the operative time and intraoperative complications. However, no statistically significant differences were recorded (P=0.06 and 0.73, respectively, for operative time and intraoperative complications). The intraoperative data showed that blood loss was statistically significantly lower in the laparoscopic approach (70.5 vs 157.2 ml), whereas the operative time was shorter in the open technique (155 vs 171 min). The only intraoperative complication recorded was bleeding in three cases, which was controlled adequately.

In this study, exclusion of cases in the first arm was based on conversion from laparoscopic to open in two cases of left sided and one case in the right sided lesion owing to locally advanced disease T4b, another case owing to advanced nodal disease related to inferior mesenteric pedicle, and the last one owing to extensive adhesion following repair of midline incisional hernia in the first arm, whereas the second arm excluded cases owing to higher rate of infection and postoperative morbidity, which included two covering ileostomy cases owing to inadequately prepared distal sigmoid colon.

Postoperative outcomes

In this study, the short-term outcome was assessed using several criteria, which are summarized in Table 2. A comparison between the two groups illustrated a statistically significant difference in hospital stay, which was shorter in the laparoscopic group (4.75 vs 8.11 days; P=0.02). During hospitalization of those patients, favorable short-term outcomes were registered for patients in the laparoscopic series. Postoperative pain, ileus, and time to the restoration

of normal bowel sound were assessed in the ward by the resident on duty during the clinical examination and auscultation of the patients' abdomen. These variables showed a significant difference with less postoperative pain, rapid return of bowel sounds, and less bowel atonia in the laparoscopic cases (P=0.02, 0.03, and 0.05, respectively).

The overall morbidity recorded over a mean follow-up time of 14±23 months was significantly different (P=0.03) between the two groups. Most of the included patients in both groups experienced no general serious complications (80 and 93.4% in groups A and B, respectively). Overall, the rate of general complications was equally distributed between the two groups, which included 10 cases of lung atelectasis without any other significant complications. The local postoperative complications included adhesive intestinal obstruction, which was recorded in 4.7% of patients in group A, whereas no patients in group B developed adhesive intestinal obstruction. Moreover, 14% of patients in group A had wound infection, whereas only 4.4% in group B developed wound infection (P<0.05). The recorded rate of incisional hernia in group A was 7%, whereas only a single patient developed port site hernia in group B. The pathological analysis revealed no statistically significant difference between the groups, as most of the patients in both groups had moderately differentiated tumors: 21 (48.9%) in group A and 28 (62.3%) in group B. All retrieved lymph nodes numbered more than 12, which matches the oncological criteria for colonic tumor resection.

Discussion

Oncological safety in laparoscopic procedures for diseases of the colon has been demonstrated to be successful for many years. A systematic review in the Cochrane Library published in 2012 by Kuhry *et al.* [9]

Table 1 Demographic data of the studied groups

Variables	Open colectomy (n=43) [n (%)]	Laparoscopic colectomy (n=45) [n (%)]	P value
Age (mean±SD) (years)	52.65±7.89	48.58±10.70	0.912
Sex (male/female)	26 (60.5)/17 (39.5)	19 (42.2)/26 (57.8)	0.785
BMI (mean±SD)	27.2±6.12	29.6±4.65	0.832
Site of tumor			
Right side	15 (34.9)	16 (35.6)	
Sigmoid	15 (34.9)	19 (42.2)	0.643
Left side	13 (30.2)	10 (22.2)	
Stage of tumor			
I	17 (39.5)	6 (13.3)	
II	21 (48.9)	27 (60)	0.411
III	5 (11.6)	12 (26.7)	

Table 2 Perioperative data and postoperative local complications

Variables	Open colectomy (n=43) (mean±SD)	Laparoscopic colectomy (n=45) (mean±SD)	P value
Duration of operation (min)	155.58±12.34	171.65±13.88	0.065
Blood loss (ml)	157.2±17.65	70.5±28.12	0.0128*
Intraoperative complications (yes/no)	3 (7%)/40 (93%)	2 (4.4%)/43 (95.6%)	0.732
Postoperative pain (VAS score)	6.85±3.26	3.14±2.54	0.023*
Time to bowel sounds (h)	7.5±2.15	3.48±9.3	0.052*
Postoperative ileus (yes/no)	8 (18.6)/35 (81.4%)	3 (6.6%)/42 (93.4%)	0.039*
Surgical site infection (yes/no)	6 (14%)/37 (86%)	2 (4.4%)/43 (95.6%)	0.051*
Anastomotic leak (yes/no)	3 (7%)/40 (93%)	1 (2.2%)/44 (97.8%)	0.523
Adhesive intestinal obstruction (yes/no)	2 (4.7%)/41 (95.3%)	0	0.267
Incisional hernia	3 (7%)/40 (93%)	1 (2.2%)/44 (97.8%)	0.442
Morbidity (yes/no)	9 (21%)/34 (79%)	3 (6.6%)/42 (93.4%)	0.010*
Hospital stay (days)	8.11±2.44	4.75±5.17	0.022*
Tumor differentiation [n (%)]			
Well	16 (35.6)	14 (31.1)	
Moderate	24 (53.3)	28 (62.3)	0.34
Poor	5 (11.1)	3 (6.6)	
Lymph node retrieval	13.8±9.6	12.1±2.7	0.65

VAS, visual analog scale.

Table 3 Comparison of short-term variables in colon cancer surgery

	Tomimaru *et al*. [10]	Fujii *et al*. [11]	Shigeta *et al*. [12]	This study
		Laparoscopic approach (LAC)/open approach (OC)		
Type of study	Comparative retrospective	RCT	Comparative retrospective	Comparative prospective
Year	2011	2014	2015	2020
Patients	36/15	100/100	52/55	45/45
Age	82.0±4.6 81.9±5.7	79.8±3.6 80.1±4.2	82 (81–84) 83 (81–87)	48.58±10.70 52.65±7.89
Operative time	202±47 170±49	172±56 150±49	N/A	171.65±13.88 155.5±12.34
Blood loss	68±168 118±130	63±154 157±157	N/A	70.5±28.12 157±17.65
Wound infection	3 of 33 and 1 of 14	5 of 95 and 10 of 90	N/A	2 of 45 and 6 of 43
Anastomotic leak	N/A	5 of 95 and 8 of 92	1 of 51 and 2 of 53	3 of 45 and 1 of 43
Bowel ileus	N/A	4 of 96 and 12 of 88	3 of 49 and 8 of 47	8 of 45 and 3 of 43
Morbidity	5 of 31 and 3 of 12	23 of 77 and 36 of 64	4 of 48 and 19 of 36	3 of 45 and 9 of 43

stated that laparoscopic resection of colon carcinoma is associated with a long-term outcome no different from that of OC.

Comparison of the short-term outcomes between LAC and OC demonstrates remarkable benefits in short-term outcomes after LAC. Reduced hospital stay, intraoperative blood loss, time to regain normal bowel sound, paralytic ileus, wound infection, and overall morbidity have been found to be favorable after the LAC approach in this study. Tomimaru *et al.* [10], Fujii *et al.* [11], and Shigeta *et al.* [12] reported similar results to those registered in this study and are summarized in Table 3.

In analyses of the amount of estimated blood loss, 7% of patients in the OC group experienced intraoperative bleeding with a mean volume of 157.2±17.65 ml, whereas only 4.4% of patients in the LAC group experienced bleeding with a mean volume of 70.5 ±28.12 ml ($P<0.01$). This shows that the incidence of bleeding is lower in LAC, which is consistent with other studies. For example, Zhou *et al.* [13] found that the mean±SD amount of bleeding in patients who underwent OC was 108.1±78.5 ml, whereas it was 50.9±44.9 ml in those who underwent LAC, and this difference was statistically significant.

It has been suggested that decreases in postoperative pain reduce the stress of surgery and therefore allow the patient to recover more quickly with a reduction in overall morbidity. According to the visual pain score, the mean±SD pain score of those who underwent OC was 6.85±3.26, whereas it was 3.14±2.54 in those who underwent LAC. This shows that postoperative pain was much lower in LAC, and this difference was statistically significant ($P=0.02$).

Return to normal bowel sound and decreases in the incidence of ileus were noted in LAC. This is attributed to limitations in the exposure of the intestines and decreased trauma to the abdominal wall, which might explain the decreased incidence of bowel paralysis and adhesion in LAC [14].

The operative time for OC was shorter than that for LAC. This result was consistent with the findings reported by Tomimaru *et al.* [10] and Fujii *et al.* [11] (Table 3). The increased operative time that was associated with the LAC approach was not considered an influencing factor in postoperative morbidity.

In this study, the overall anastomotic leak rate was four (4.5%) cases of the studied patients, which represented 2.2% of those who underwent laparoscopic resection, and was 7% in the open surgery group. Only one case was related to LAC, and was a leaking ileotransverse anastomosis that was performed extracorporeally. The other two cases were related to leaking right-sided and left-sided anastomoses in OC. Only one case required reoperation for revision of the anastomosis, whereas the others were managed conservatively. A consistent study performed by Zhou *et al.* [13] also reported similar results, where 4.3% of patients who underwent OC developed anastomotic leakage, whereas only 2.2% of those who underwent LAC developed anastomotic leakage.

In a mean follow-up of 14 months, only one case in the LAC group developed port site hernia. Additionally, 7% of those who underwent OC developed an incisional hernia, but the difference between groups was not statistically significant. A controversial study by Mishra *et al.* [15], whose results were inconsistent with ours, found that the incidence of incisional hernia was 14.4% in those who underwent OC but was 15.9% in those who underwent LAC. Although this difference was not statistically significant, this result shows that the incidence of incisional hernia was slightly higher in the LAC group.

A statistically significant difference was reported here when surgical site infection was assessed between the two groups: 14% in the OC group vs 4.4% in the LAC group ($P<0.05$). Zhou *et al.* [13] found a similar result, where the incidence of wound infection was higher in those who underwent OC, as 9.7% of patients who underwent OC developed wound infection and only 1.1% of those who underwent LAC developed wound infection.

The incidence of postoperative adhesive intestinal obstruction was 4.7% in those who underwent OC, whereas none of those who underwent LAC developed adhesive intestinal obstruction; this difference was statistically significant. Another two studies concluded a similar result regarding this aspect, as Rosin *et al.* [16] and Ha *et al.* [17] found that the incidence of adhesive intestinal obstruction after LAC was very low compared with the incidence after OC.

Obviously, several studies have been published that discussed the superiority of a certain technique in colon cancer resection. However, the main focus of the current study was to address the short-term outcomes, which demonstrated the validity of LAC for colon cancer, whereas the long-term follow-up was limited to a few studies. Völkel *et al.* [7] reported the 10-year follow-up and stated that LAC for nonmetastatic colon cancer is associated with similar rates of disease-free survival, overall survival, and recurrence as open surgery.

Additionally, certain parts of our objectives were not properly fulfilled owing to lack of feasibility. This is why, our study should be repeated on a wider scale and with a larger sample size to obtain statistically significant results and to generalize our findings in larger populations.

Conclusion

LAC showed multiple advantages over OC in terms of incidence and amount of bleeding and length of hospital stay, in addition to postoperative pain, wound infection, and overall morbidity. Despite the clinical significance of these results, the only factor where LAC did not show a benefit over OC was in operative time. These results support the view that LAC is an effective and safe procedure for colon cancer resection.

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Conflicts of interest

There are no conflicts of interest.

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