

Outcome of laparoscopic colectomy in colorectal cancer at South Egypt Cancer Institute: a randomized controlled study

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Abstract

Background: The short and long-term results of a laparoscopic resection for colorectal cancer have been reported in several studies, but reports on the results of laparoscopic surgery for rectal cancer are limited.

Aim of the study: This study aimed to assess the short term outcomes of laparoscopic assisted colorectal resections in comparison with conventional open resections.

Methods: 20 patients assigned to undergo elective laparoscopic assisted resection of primary colon and rectal cancer matched with 20 cases of colorectal cancer patients with the same epidemiological data (age, site, stage and histological grade) to whom conventional open resections was done in the period from March 2010 to September 2013. The following data were collected and analyzed: preoperative data (individual patient data, indication for surgery), intraoperative data (conversion to open surgery, operative time, complication rate), postoperative data (oncological parameters: length of removed specimen; safety margin; retrieved lymph nodes, post operative pain, recovery of gastrointestinal tract functions, morbidity, mortality and length of hospital stay)

Results: There were significant decrease in postoperative pain, rapid recovery of pulmonary and GIT functions, decreased hospital stay in the laparoscopic group compared to the conventional group.

Conclusion: Laparoscopic surgery for colorectal cancer is a good alternative for open surgery with favorable short term outcomes of surgery and reasonable oncologic results.

{Key words: Colorectal cancer, minimally invasive surgery, laparoscopy}

Introduction

Since its first description in 1991, laparoscopic colectomy has been broadly applied to benign and malignant disease [1]

Four years after the 1st laparoscopic colectomy, *Lacy* published the 1st randomized controlled trial (RCT) comparing the short-term outcomes after laparoscopic and conventional colectomy. Since then, more than 30 publications from randomized controlled trials have investigated different aspects of the postoperative course after laparoscopic or conventional surgery.[2]

Fewer peri-operative complications and faster postoperative recovery resulting in shorter duration of hospital stay appear to be the main advantages [3]

Throughout the past decade, evidence is growing that laparoscopic colorectal surgery (LCS) can be superior to classical open procedures [4].

Initial case reports describing port-site metastasis as a complication of laparoscopic surgery for cancer caused great alarm, with early reports in small case series noting metastasis rates as high as 21% [5].

Multiple studies have now demonstrated that the incidence of port-site metastasis after laparoscopic surgery is low. A prospective evaluation by the Laparoscopic Bowel Surgery Registry, which was initiated in 1992 by the American Society of Colon and Rectal Surgeons, the American College of

Surgeons, and the Society of American Gastrointestinal Endoscopic Surgeons, reported the rate of the complications to be at 1.1% similar to the results for open surgery [6].

The laparoscopic approach for colonic resection is widely accepted but its definitive role in rectal tumors is still controversially debated due to technical difficulties and missing long-term results. Tumor size and volume and pelvic dimensions may influence intra-operative and/or immediate outcome [7].

A prospective analysis of a comparison between laparoscopic and open access surgery in patients with rectal cancer was performed by Strohlein et al. and concluded that minimally invasive surgery (MIS) for rectal cancer shows advantages of shorter hospitalization and faster recovery and obvious beneficial factor, such as pain reduction, limited intestinal atony and reduced trauma. But there have been major concerns regarding the oncologic adequacy of tumor resection, local recurrence rate, and consequentially long-term survival [8].

Laparoscopic resection for rectal cancer has not been yet standardized as a line of treatment. It is feasible but its safety and results remain unknown. *The COLOR II* trial is a randomized, international, multicenter study comparing the outcomes of laparoscopic and conventional resection of rectal carcinoma with loco-regional recurrence rate three years post operatively as a primary end point. Secondary end points cover quality of life, overall and disease free survival, post-operative morbidity and health economy analysis. [9].

Patients and Methods

This randomized prospective study was approved by the local ethics committee of South Egypt Cancer Institute, Assiut University, Assiut, Egypt.

This study was conducted from March 2010 to September 2013.and after written informed consent from 40 patients with colorectal cancer; colonic resection was performed either open or laparoscopic, their data were prospectively collected. Surgical results of laparoscopic resection were compared with conventional resections as regard blood loss, operative time, hospital stay and postoperative outcome including postoperative pain.

Sample size:

Sample size was calculated from population in the study period the total patients 45, Confidence Level 95%, Confidence Interval 5% the sample size calculated for each group 20 patients.

Randomized clinical trial:

The samples numbered from 1 to 40 the odds numbers for laparoscopic colectomy group and even numbers for open colectomy group.

Inclusion Criteria

Patients indicated for curative resection of cancer colon.

Exclusion criteria

- Intestinal obstruction, the small intestine and/or colon are distended.
- Bulky tumors (> 6 cms on CT), cancer invasive into adjacent organs (T4b).
- Pregnancy.
- Coagulopathy.
- Previous major colorectal surgery.
- Distant metastasis

Pre operative work up

- History and clinical examination (including PR examination), ECG,
- Laboratory investigations: CBC, kidney and liver functions, random blood glucose, prothrombin time (PT) and concentration (PC) and Carcinoembryonic antigen (CEA).
- Radiological investigations: abdominal ultrasound, chest X-ray, MDCT abdomen and pelvis.
- Colonoscopic examination and biopsy.
- Written consents were taken from patients explaining the details of surgery, the advantages of minimally invasive surgery and concepts of fast track surgery, clarifying the possible complications of surgery and the possibility of conversion to open surgery.

Post operative Protocol

1st and 2nd postoperative day

- Patients were transferred after the operation to the recovery room and then to the normal unit.
- Analgesia via epidural catheter when required,
- Oral fluids were started 36 hours postoperatively,
- IV fluids (2000 ml ;ringers lactate & glucose 5%)
- Mobilization started 6 hours postoperative,
- Removal of urethral catheter on 2nd postoperative day,
- 1-3 ampoule neostigmine sc per day
- Mobilization for 8 hours per day

3rd postoperative day

- Removal of epidural catheter
- Analgesia with oral NSAIDs twice daily
- Free oral fluids,
- Full mobilization of the patient

If postoperative course was uneventful, nutrition with light diet started on 5^{th} day and patients were discharged on the 5^{th} to 7^{th} postoperative day.

Operative Technique

The following procedures were performed according to the location of the tumor:

- Laparoscopic assisted right colectomy,
- Laparoscopic assisted left colectomy,
- Laparoscopic assisted sigmoidectomy,

Right colectomies were performed while the patient in supine position while other resections were

performed in the modified Lithotomy position.

In right sided resections, we used a diamond shaped configuration of ports. Hasson technique was used to insert 10 mm umbilical port for the telescope and then 3 other ports were inserted under direct vision (one 10 mm and two 5 mm) in the left lower abdomen, suprapubic and right side of abdomen respectively. The operator stood on the left side of the patient. Patients were placed in steep Trendelenburg with the right side elevated. Dissection was done using legasure. A medial to lateral approach was used in all cases. The specimens were exteriorized through minilaparotomy not exceeding 5 cms. The specimens were resected and hand sewen end to end ileotransverse anastomoses were done using modified Gambee technique (single layer interrupted with 3/0 vicrylsuture). Mesentric defects were closed. Minilaparotomy was closed using nylon loop 1. 10 mm ports were closed. One drain was left.

In left sided resections,4 ports were used, 10 mm umbilical port for the telescope which was inserted using Hasson technique, three 5 mm ports in the left upper quadrant, right upper quadrant and right lower quadrant. The operator stood on the right side of the patient. Patients were placed in sleep Trendelenburg with the left side elevated. A medial to lateral approach was used with the aid of legasure.

Follow up

Patients were reviewed every 3 months in outpatient's clinic visits. During such visits, history and physical examination were taken and blood samples were obtained to check CEA. Further imaging (chest, abdominal, and pelvic imaging) and endoscopy were done if CEA level \geq 10 IU per Liter or clinical suspicion of recurrence. Colonoscopy is done 3 years postoperatively unless there is suspicion of recurrence.

Collected Data

The following short term outcomes measures were analyzed:

- Operative time : time from skin incision to skin closure
- Functional date (time of 1st bowel motion, time of 1st passing flatus, post operative mobility)
- Post-operative analgesic requirements.
- Duration of hospital stay: from time of operation till discharge.
- Operative mortality: was defined as deaths that occurred during the same hospital stay or within 30 days following the primary operation.
- Operative morbidity: defined as complications that contribute to prolonged hospital stay or lead to additional interventions or procedures.
- Pathological outcome: length of resection safety margin, number of harvested lymph nodes.

Statistical Analysis

Comparison of the categorical variables was performed using Chi square test. Continuous variables were compared using Student t- test (all variables are normally distributed). *P* values of less than 0.05 were regarded statistically significant. All the calculations were performed with the SPSS 21.0 statistical package.

Results

Of 40 patients with colorectal cancer 20 cases underwent laparoscopic assisted resections; Laparoscopic colectomy (LC) and the other 20 cases underwent conventional open resections; open colectomy (OC).Neither age, gender nor BMI significantly differed between LC and OC groups (Table 1).

There were no significant differences among the two groups in tumor characteristics; site, stage and grade (Table 1).

Although there were no significant differences between both groups in blood transfusion nor extent of resection , operative time significantly differ between OC and LC with longer operation time in LC (P = 0.001; Table 2).

There were no significant differences between OC and LC for any of the pathological outcomes (Table 4).These outcomes included lymph node yield (P=0.274),proximal and distal margin involvement.

Controlling for potential confounders, there was a shorter length of hospital stay in The LC group (P = 0.001; Table 2) with statistically significant reduction of analgesic requirement and faster recovery of GIT function in the LC group (Table 2). Complications included sexual and urological dysfunction, wound infection, anastmotic leakage, fascial burst, prolonged ileus and chest infection. There was no hospital mortality in both groups (Table 3).

Table	1:	Demogr	aphic	data;	pre-operative	patient's
charac	teris	stics and	Tumor	chara	cteristics	

Variable		G(LC)	G (OC)	P. value
Age				
1.	Range	22 - 69Y	26-68Y	0 501Ns
2.	Mean <u>+</u> SD	56 <u>+</u> 11.3Y	58 <u>+</u> 11.4Y	0.381
Sex (N, %	ó)			
1.	Male	12 (60.0%)	14 (70.0%)	0 507Ns
2.	Female	8 (40.0%)	6 (30.0%)	0.307
BMI		23.8 <u>+</u> 1.4	24.1 <u>+</u> 1.3	0.486 ^{Ns}
Site (N, %	(0)			
1.	Right Colon	4 (20.0%)	6 (30.0%)	
2.	Left Colon	2 (10.0%)	3 (15.0%)	
3.	Sigmoid Colon	8 (40.0%)	7 (35.0%)	0.683 ^{Ns}
4.	Rectosigmoid	5 (25.0%)	2 (10.0%)	
5.	Multicenteric	1 (5.0%)	2 (10.0%)	
Staging (N, %)				
1.	Stage 1	3 (15.0%)	2 (10.0%)	
2.	Stage 2	5 (25.0%)	7 (35.0%)	0.749^{Ns}
3.	Stage 3	12 (60.0%)	11 (55.0%)	
Grading	(N, %)			
1.	Well differentiated	5 (25.0%)	3 (15.0%)	
2.	Moderately diff.	9 (45.0%)	7 (35.0%)	0.416^{Ns}
3.	Poorly differentiated	6 (30.0%)	10 (50.0%)	

Ns: Not significant

ruere =: maia operan	e aata affa f	est operation	e aata
Variable	G (LC)	G (OC)	P. value
Surgery duration (minutes) Mean <u>+</u> SD	194.14 <u>+</u> 44.12	164.50 <u>+</u> 35.242	0.001*
Blood transfusion	2(10.0%)	0(0.0%)	0.153 ^{Ns}
Extent of resection			
1. Right Hemicolectomy	4(20.0%)	6(30.0%)	
2. Left Hemicolectomy	2(10.0%)	3(15.0%)	
3. Sigmoid Colectomy	8(40.0%)	7(35.0%)	0.683 ^{Ns}
4. High Anterior Resection	5(25.0%)	2(10.0%)	
5. Total colectomy	1(5.0%)	2(10.0%)	
Variable	G(LC)	G (OC)	D volue
	$(Mean \pm SD)$	$(Mean \pm SD)$	r. value
Analgesia (days)	4.93 <u>+</u> 1.831	7.57 <u>+</u> 2.956	0.001*
Passing Flatus (hours)	61.14 <u>+</u> 26.104	71.33 <u>+</u> 10.880	0.001*
1st bowel motion (hours)	72.55 <u>+</u> 28.146	80.87 <u>+</u> 10.559	0.001*
Hospital stay (days)	6.41 <u>+</u> 2.027	9.43 <u>+</u> 3.202	0.001*
Ns: Not significant		*: Highly sign	nificant

Table 3: Outcome of patients

Variable	G (LC)	G (OC)	P. value
Sexual & urinary complications	1(5.0%)	3(15.0%)	0.307 ^{Ns}
Wound infection	1(5.0%)	3(15.0%)	0.307^{Ns}
Anastomotic leakage	1(5.0%)	2(10.0%)	0.558^{Ns}
Wound Burst	0(0.0%)	1(5.0%)	0.315^{Ns}
Prolonged ileus (>4 days)	2(10.0%)	4(20.0%)	0.400^{Ns}
Chest infection	0(0.0%)	1(5.0%)	0.315^{Ns}
Hospital Mortality	0(0.0%)	0(0.0%)	NA
MA, Matamuliashia			

NA: Not applicable

Table 4: Pathology data in laparoscopic and open resection groups

Variable	G (LC)	G (OC)	P. value
Harvested lymph nodes	14.14 <u>+</u> 3.429	13.6 <u>+</u> 3.362	0.274 ^{Ns}
Safety margins Proximal Distal	Negative (0.0%) Negative (0.0%)	Negative (0.0%) Negative (0.0%)	NA NA
NA: Not applicat	ble	Ns: Not sign	ificant

Discussion

We report our experience of performing laparoscopic assisted colectomy for colorectal cancer in South Egypt Cancer Institute, we found that laparoscopic colectomy is feasible and safe; patients had acceptable rates of complications, less analgesic requirements as well as reasonably short postoperative hospital stay and large number of retrieved lymph nodes.

Numerous randomized controlled trials have demonstrated superior short-term outcomes in favor of laparoscopy with respect to post-operative pain, return of bowel function, length of hospitalization and cosmesis[10-14]. Furthermore, meta-analysis of multiple RCTs have concluded that laparoscopic colectomy for cancer provides superior short term benefits and equivalent oncologic outcomes compared to open colectomy[15]. More recent studies have even shown improved 30-day morbidity [15, 16] and mortality [16-18] with laparoscopic colectomy, with some authors questioning whether it should be standard of care [19].

Despite this evidence, open colectomy remains the most common approach to colonic resection in developing countries [20]. Lohisriwat et al [21] demonstrated equivalent short-term and oncologic outcomes in a retrospective series of patients undergoing open and laparoscopic right hemicolectomy for cancer in Thailand. Those results echo that of the present study where no statistically significant difference was found for positive margins or lymph node yield (p=0.001) between groups [21].

Our results demonstrated a trend towards longer operative time and shorter length of hospital stay in the LC compared to the OC group and these findings are consistent with the literature [12-15].

The equivalence seen between OC and LC groups regarding 30-d morbidity and mortality rates is consistent with previous literature *[12-14]*. Similarly, oncologic outcomes for OC and LC groups, including resection margins and lymph node yield are consistent with previous RCTs *[12-15]*.

This study has several limitations. Firstly, there was small number of cases. This is a limitation of the study, which will impact on the ability to make definitive conclusions.

A recent survey of surgeons in Jamaica suggested that cost and lack of expertise/training were the main barriers of laparoscopy uptake [22]. However, improved short-term outcomes such as shorter hospital stay, faster return to work, and reduced surgical site infection rates, often offset the upfront costs of laparoscopy [23]. In already performing countries laparoscopic cholecystectomy, no additional basic equipment is usually required for colectomy. Institutional investment in reusable bowel graspers and needle drivers would obviate the need for disposables with some cost reduction. Some disposable equipment, however, have no reusable counterpart. As such, the initial cost of these disposables (including energy devices and staplers) to the institution or patient remains a challenge.

Maneuvers to avoid the need for these expensive devices, such as colonic mobilization with extracorporeal anastomoses, and the use of monopolar cautery and clips [24] have been described. Metaanalyses have failed to demonstrate any significant disadvantages to extracorporeal anastomoses for laparoscopic right sided colectomies [25]. Additionally, there is no evidence to suggest that use of energy devices is superior to monopolar cautery for laparoscopic colectomy/26/. The surgical technique employed in the present study utilized reusable instruments and extracorporeal anastomoses in order to reduce costs. Such techniques did not adversely affect outcomes. Future studies should incorporate these contextual factors when describing LC uptake in a resource-restricted setting. Secondly, although this study provides evidence supporting the safe use of LC in resource-restricted settings, contextual factors imperative for LC implementation, such as availability of equipment and cost, were not considered.

Lack of expertise and training as a limiting factor for LC uptake underscores the need to incorporate LC in residency training **[20, 27]**. The recent opening of a skills laboratory and the further addition of minimally invasive surgical staff to our institution have been methods instituted to address this issue. Unfortunately, these factors were not considered in this study and should be discussed in future work.

Conclusion

There remain many challenges to the use of laparoscopic colectomy for colonic carcinoma in developing countries. The equivalent short-term outcomes demonstrated between open and laparoscopic groups in the present study demonstrate that this is an oncologically safe approach in our environment. Continued strategies to reduce costs and increase surgeon training are essential to the further development of laparoscopic colectomy in developing countries. Only through these strategies can caseload increase allowing for progressive high-quality research in the field in these environments.

Disclosures

Authors have no conflicts of interests to be disclosed.

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