



## Comparison of Clinical Outcomes of Laparoscopic Assisted Vs Open Surgery for Rectal Cancers- A Retrospective Study

Authors

Dr Akshay H Nerlekar, Dr N J Gadekar, Dr J M Gadekar

### Abstract

**Introduction:** Rapidly developed technique in rectal surgery is the laparoscopic procedure. In this investigation aim is to assess the distinctiveness of short-term and medium-term clinical outcomes of laparoscopic-assisted versus open surgery for rectal cancer.

**Methods:** Patients with non-metastatic rectal cancer were enrolled for this study. They were 51 in number. The patients underwent either laparoscopic-assisted surgery (LAP) ( $n = 25$ ) or open surgery (OP) ( $n = 26$ ). Surgical techniques, perioperative managements and clinical follow-ups were standardized. Short-term perioperative data, medium-term clinical outcomes & survival were compared and analysed between the two groups.

**Results:** No differences were found in perioperative parameters between the two groups except that there was a trend of faster recovery in laparoscopic procedures. Statistically there was no significant difference in postoperative complications, re operation rate, or perioperative mortality. There was statistically significant difference in a faster return of gastrointestinal function and shorter hospital stay which were identified in favour of laparoscopic-assisted resection. In all rectal cancer cases, the overall survival, cancer-free survival and recurrence rate were same in two groups. No tendency of significant differences in overall survival, cancer-free survival and recurrence in stage I-II and stage III patients in two cancer categories between the two groups, respectively.

**Conclusions:** In the treatment of non-metastatic rectal cancer, Laparoscopic-assisted procedure has more benefits on postoperative recovery, medium-term clinical outcomes & survival as compared with open surgery.

### Introduction

Worldwide rectal cancer has gradually become one of the most significant leading causes of death from malignancies, especially in India. Surgical management is still the mainstay of the treatment [1,2]. Significant morbidity and a long recovery period is reported with conventional open surgery. With the laparoscopic techniques applied to the surgical field for rectal diseases, laparoscopic colorectal surgery was first per-formed in Japan in

1992, very soon after its initial description by Jacobs et al [3,4]. The first laparoscopic colectomy was successfully performed in China, in 1993. Since then, laparoscopic surgeries have been widely performed for various benign colorectal diseases [5-8], and furthermore, colorectal cancer. Laparoscopic colorectal surgery is complicated technically as it involves almost all advanced laparoscopic techniques, such as mobilization, intracorporeal division, dissection of major

vessels, and anastomosis. Steep learning curve is there to achieve advanced laparoscopic skills. But when the learning phase has been surmounted, the benefits of laparoscopic surgery have been suggested with respect to reduced morbidity, decreased pain, faster recovery, shorter hospital stay and possibly reduced immunosuppression, comparing with open surgery <sup>[9-12]</sup>.

However, even after the great success of laparoscopic colorectal surgery, there are still many questions that remain unanswered, including whether laparoscopic colorectal cancer surgery is radical or not, seldom reported superior short-term outcomes. Still laparoscopic surgery is not considered standard treatment <sup>[13]</sup>. There are also controversies regarding potential port site recurrence even after curative resection of tumour, and also to add is the higher economical costs.

In this study, we investigated the short-term and medium-term clinical outcomes of laparoscopic surgery versus open surgery for rectal cancer over a period of 3 years in our institute, aiming whether the laparoscopic surgery has any advantages for the patients with rectal cancer or not.

## Methods

### Patient selection

Between July 2014 and January 2017, patients who underwent rectal surgery for rectal cancer in DVVPS Medical College & Hospital, Ahmednagar were consecutively enrolled in this study. Both open surgeries (OP) and laparoscopic-assisted surgeries (LAP) were performed. No selection criteria was used to allocate patients to either a laparoscopic or an open surgery. Patients were assigned to same surgical team (open or laparoscopic) according to their target dates for treatment and operating theatre availability. A minority of patients who wished to be operated laparoscopically were accommodated whenever possible. Written informed consent was obtained from all patients before the investigation.

All patients enrolled were subjected to preoperative laboratory examination including

tumour markers screening, coagulation test, chest x-ray, abdominal ultrasound, colonoscopy and if necessary, computed tomography scan of the abdomen and pelvis. All patients were confirmed to have a malignant tumour after post-operative pathologic examination. None of the patients had accepted preoperative radiotherapy or chemotherapy; out of the patients who were pathologically diagnosed as stage III, all accepted adjuvant chemotherapy with oxaliplatin and 5-fluorouracil for 6 months postoperatively. Exclusion criteria were: in situ or metastatic disease, emergency presentation, morbid obesity (defined as body mass index, i.e. BMI > 35 kg/m<sup>2</sup>), associated gastrointestinal disease that required extensive operative evaluation or intervention, pregnancy or malignant disease in the past 5 years.

### Preoperative preparations and operative procedures

All patients had oral administration of gentamicin and metronidazole, 3 times a day for 3 days before surgery. For bowel preparation polyethylene glycol-electrolyte solution or magnesium sulphate was given one day before the surgery. Other preoperative preparations were standardized, as followed for traditional abdominal surgeries.

Laparoscopic-assisted resection involved mobilization of the colon, visualization of critical structures, and intracorporeal vascular ligation. A standard total mesorectal excision (TME) procedure was essential for rectal cancer resection. A small abdominal incision was essential to remove the specimen. Anastomosis was performed either through the small incision or laparoscopically with a double-stapling technique, for rectal cancer. If the tumour was located close to the dentation line that anal-saving could not guarantee the radical standards and operation safety, the APR procedure was performed. In majority of cases, the operation was performed utilizing a lateral to medial approach. In this study, an incision longer or different to that planned was used to determine a conversion. Conversion to

open colectomy was at the discretion of the surgeon based on concerns regarding patient safety, technical difficulties, or associated unexpected conditions requiring treatment by laparotomy. Conversions were recorded and analysed as part of the laparoscopic arm of the study, but were excluded for further analysis. Open procedures were performed according to the standard techniques followed by the operating surgeon. All surgeries achieved a standard D2 lymph node dissection.

### **Perioperative surveillance, postoperative managements and follow-up evaluation**

Demographic and operative data was obtained regarding age, gender, BMI, co-morbidities, history of previous abdominal surgery, tumour location, surgical intervention, maximum incision length, blood loss, operative time, number of retrieved lymph nodes. Postoperative data included analgesic usage, Visual Analogue Scales (VAS) score, peristalsis recovery time, time until passage of flatus, time required to ambulate, time until first liquid and semi-liquid intake, postoperative duration of hospital stay and total time of hospital stay, were recorded.

Patients enrolled in the present study were managed postoperatively by the same surgeons. Patients in both groups were given infusions in the first several hours after surgery. After confirmation of the recovery of peristalsis, liquid diet was supplied. Semi-solid diet was considered suitable for patients after report of flatus. For pain control, patients were given patient-controlled anaesthesia (PCA) or short-acting drugs according to their own aspirations. Prophylactic antibiotics were used 72 hours before surgery; however, if there was any indication of infection, this time was prolonged. The catheter was removed as early as possible except for patients with tumour located in the lower region of the rectum. The peritoneal drain was removed on post operative day 7, only if no leakage or haemorrhage was confirmed, as well as the patient had taken semi-solid food and had reported passage of stool. In patients with

postoperative complications, the management was almost the same in both the treatments groups, respectively. All patients were followed-up after being discharged from the hospital, according to a pre established protocol. This included recording of medical history, physical examination, and laboratory studies such as, serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) levels, which were assessed 1 month after surgery and every 3 months thereafter. At each patient visit, symptoms were recorded and wound scars examined for subcutaneous metastasis. Either ultrasonography or computed tomography scan of the abdomen, in addition to chest X-ray was performed every 6 months.

### **Statistical Analysis**

Data was collected retrospectively. Quantitative data was given as a mean  $\pm$  standard deviation, and was analysed using Student's t-test. Comparisons between the two groups were made on an intention-to-treat basis; thus, patients in the LAP group converted to the open procedure were not excluded from the analysis. Time to: (1) last follow-up evaluation, (2) treatment failure or (3) death was measured from the date of operation.

Recurrence and overall survivals were evaluated. Analysis of predictive factors of survival was performed. Variables analysed univariately were, age, gender, BMI, preoperative co morbidities, tumour location, intervention, surgical procedures, tumour size, lymph nodes metastasis, clinical stage, and postoperative complications. Statistical significance was defined as  $P < 0.05$ .

**Results****Demographic Data:**

Sr.no.			LAP (25)	OP(26)
1	Age (yr)	Mean± deviation	62±5	65±3
2	Gender	M : F :	13 12	12 14
3	BMI (kg/m <sup>2</sup> )	Mean ± deviation	23.3±3.9	23.6±4.1
4	Abdominal operation history	NO : YES :	18 7	20 6
5	Preoperative co morbid disease	NO : YES :	16 9	14 12
		CVS	6	9
		RS	1	2
		Liver cirrhosis	-	-
		Renal failure	1	-
		Diabetes	1	1
		CNS	-	-
		Autoimmune	-	-
		Others	-	-

Out of total 51 patient enrolled in the study LAP was performed in patients and OP was performed in 26 patients. Mean age group (yrs) in LAP patients was 62±5 & OP was 65±3. M:F in LAP (25) 13:12 & OP(26) 12:14. BMI of patient who underwent LAP 23.3±3.9 & OP 23.6±4.1. Negative abdominal operation history was found in 18 patients who underwent LAP & 20 who underwent OP, while positive abdominal

operation history was noted in 7 cases who underwent LAP & 6 who underwent OP. 9 patients who underwent LAP had preoperative co morbid diseases CVS(6), RS(1), RF(1), Diabetes(1) while 16 had no co morbid diseases. 12 patients who underwent OP had pre operative co morbid diseases CVS(9), RS(2), Diabetes(1) while 14 had no co morbid diseases.

**Intra Operative**

Sr.no.		Lap (25)	Op (26)
1	Intervention		
	1. AR	8	7
	2. LAR	9	10
	3. Ultra low resection	3	3
	4. APR	5	6
2	Conversion to open	2	-
3	Operative time (min) Mean± deviation	140±35	135±42
4	Blood loss (ml) Mean±deviation	98±60	112±85
5	Incision (cm) Mean±deviation	4.2±1.2	12.5±2.5
6	Lymph node retrieval (no) Mean±deviation	10±4	8±5

Out of 25 LAP cases 8 underwent AR, 9 LAR, 3 ultra low resection, 5 APR. Out of 26 OP cases 7 AR, 10 LAR, 3 ultra low resection, 6 APR. Among the 25 LAP cases conversion to open was required in 2 cases. Operative time (min) in LAP 140±35, OP 135±42. Blood loss (ml) in LAP

98±60, OP 112±85. Incision( cm) in LAP 4.2±1.2 , OP 12.5±2.5 . LN retrieval no. was 10±4 in LAP, 8±5 in OP.

**Perioperative complications:****Intraoperative**

Sr.no.	Complication	LAP (25)	OP(26)
1	Massive haemorrhage	-	-
2	Organ injury	1	1
3	Equipment disorder	-	1
4	Subcutaneous emphysema	1	-
5	Stapler leakage	1	-
	Total	3	2

Out of 25 LAP cases organ injury (1), subcutaneous emphysema (1) & stapler leakage (1) were intraoperative complication. In 26 OP

cases, organ injury (1) and equipment disorder(1) were intraoperative complication.

**Post Operative**

Sr.no.	Complication	LAP	OP
1	Ileus	4	5
2	Anastomotic haemorrhage	-	1
3	Abdominal haemorrhage	-	-
4	Peritonitis / septic shock	1	1
5	Anastomotic leakage	2	2
6	Pelvic abscess	1	-
7	Wound infection	1	2
8	Incisional /port hernia	-	1
9	Rectovaginal fistula	-	1
	Total	9	13

Post operative complication in LAP cases ileus complication (4), peritonitis/septic shock(1), anastomotic leakage (2), pelvis abscess(1), wound infection(1). In OP cases ileus complication (5), anastomotic haemorrhage (1), peritonitis/ septic

shock(1), anastomotic leakage (2), wound infection (2), incisional/ port hernia (1), rectovaginal fistula (1).

**Post Operative Recovery**

Sr.no.	Parameters	LAP	OP
1	Analgesics		
	No	16	5
	Short acting drugs	3	2
	3. I.V. Analgesia	6	19
2	VAS Mean $\pm$ deviation	2.6 $\pm$ 1.5	3.4 $\pm$ 2.1
3	Off bed (d) Mean $\pm$ deviation	2.8 $\pm$ 1.2	4.5 $\pm$ 3.2
4	Peristalsis recovery (d) Mean $\pm$ deviation	1.8 $\pm$ 1.0	2.5 $\pm$ 1.4
5	Flatus (d) Mean $\pm$ deviation	3.0 $\pm$ 1.5	4.5 $\pm$ 2.0
6	Liq intake (d) Mean $\pm$ deviation	4.6 $\pm$ 2.2	5.2 $\pm$ 2.8
7	Semi solid intake (d) Mean $\pm$ deviation	6.2 $\pm$ 2.1	8.4 $\pm$ 3.5
8	Post op hospital stay (d) Mean $\pm$ deviation	9.8 $\pm$ 4.2	13.2 $\pm$ 6.8

Out 25 LAP cases 16 required no analgesia, 3 required short acting drugs & 6 required i.v. analgesia while in 26 OP cases 5 required no

analgesia, 2 required short acting drugs and 19 required i.v analgesia.VAS was 2.6 $\pm$ 1.5 in LAP cases& 3.4 $\pm$ 2.1 in OP cases. Days required to get



off bed were  $2.8 \pm 1.2$  in LAP cases and  $4.5 \pm 3.2$  in OP cases. Peristaltic recovery (d) was  $1.8 \pm 1.0$  in LAP cases &  $2.5 \pm 1.4$  in OP cases. In LAP cases flatus was passed in  $3.0 \pm 1.5$  days &  $4.5 \pm 2.0$  in OP cases. In LAP cases liquid intake was started after  $4.6 \pm 2.2$  days &  $5.2 \pm 2.8$  in OP cases. Semisolid intake was started in  $6.2 \pm 2.1$  days in LAP cases,  $8.4 \pm 3.5$  in OP cases. Post operative hospital stay was  $9.8 \pm 4.2$  in LAP cases while  $13.2 \pm 6.8$  in OP cases.

## Discussion

We found that LAP for rectal cancer is safe and feasible; patients had acceptable rates of complications and conversion to open laparotomy, as well as reasonably short postoperative durations of stay, a large number of lymph node retrieval, and finally, similar survival rates.

With the development of laparoscopic techniques, along with the improvement of laparoscopic instruments, a standard laparoscopic procedure for rectal cancer surgery has gradually become widely accepted, and a radical cure resection seems feasible for laparoscopic surgeries. The present study showed that there were no differences in the outcomes between the two treatment groups. Apart from acquirement of a new skill the laparoscopic surgeon being a factor, which cannot be totally ignored, this was a straightforward comparison. Furthermore, there was no apparent deterioration in the quality of surgery associated with the introduction of laparoscopic resection, as stoma formation and APR rates in rectal cancer remained unchanged over time. The intraoperative comparison between the two groups in our study indicated almost similar operative time and complications, which was not in keeping with other randomized controlled studies <sup>[14-20]</sup>. The mean operating time for the laparoscopic-assisted procedure was shorter in this study than in the Multi centre Randomized Controlled trial – Conventional versus Laparoscopic-Assisted Surgery In patients with rectal cancer (MRC CLASICC) <sup>[14]</sup> trial but similar to the Colon Carcinoma Laparoscopic or Open Resection (COLOR) <sup>[15,17]</sup> trial.

The number of lymph nodes retrieved during the surgical procedure influences clinical staging of the tumour and is not only influenced by the operative technique or the extent of lymphadenectomy, but to an even greater extent by pathological techniques involved in processing the specimens. Examining fewer than 12 lymph nodes in a specimen can result in under-staging <sup>[21]</sup>. Since the specimens retrieved by either laparoscopic-assisted or open resection were processed in different ways, it has been difficult to compare the harvested lymph nodes in different studies. Nevertheless, since the standard D2 lymph node dissection was consistently followed for all operations, and the lymph node was always collected by a permanent surgeon and a permanent pathologist, a diminished bias during lymph node collection was assured. Our final analysis confirmed that there were no differences in lymph nodes harvested between the LAP and OP groups in this study, with the majority of patients having sufficient lymph nodes to be collected for accurate staging.

In previous reports with data on resection margins, none of the margins was found to be positive. Although this is a remarkable finding, it can be explained by the fact that most of these studies <sup>[22-27]</sup> only reported distal and proximal margins. No data on circumferential margins were available from these studies. Results of the primary analysis indicated that laparoscopic procedure might have the ability to reach a better dissect field than the open procedure, assuring the radical cure resection.

Among our patients, those who underwent laparoscopic procedure had significantly faster recovery than those who underwent open surgery. LAP group patients definitely need a smaller dose of analgesic than their counterparts who received open surgery treatment. In fact, most laparoscopic procedures seem to cause less pain, so that analgesics are rarely necessary. It is reported that some centres are in favour of the epidural combined with general anaesthesia during the operation. Thus, usually the PCEA (patient

controlled epidural analgesia) and PCIA are both usual options of post-operative pain-control procedures. Some reports revealed that PCEA has greater advantages over PCIA <sup>[28,29]</sup>. In our centre, general anaesthesia is used routinely for laparoscopic surgery; PCIA is the choice only for patient controlled pain-control procedures. However, since the majority of LAP group patients did not require analgesia, the paincontrol method did not seem to be an important parameter for laparoscopic rectal surgery.

Total hospital stay and postoperative hospital stay are two important evaluation criteria for fast recovery surgery. The postoperative hospital stay for LAP and OP group in the Multi centre Randomized Controlled trial - MRC-CLASICC Trial was 9 days and 11 days, respectively <sup>[14]</sup>; however, the Clinical Outcomes of Surgical Therapy Study group (COST) Trial was 5.1 days and 5.6 days, respectively <sup>[22,23]</sup>. Length of hospital stay is an indicator which can be easily affected by different con-founding factors, such as geographic locations, reflecting cultural and possibly financial reimbursement differences <sup>[30]</sup>. In our group, all stage III patients accepted postoperative adjuvant chemotherapy. There were a set of patients in both groups who could not be discharged until the end of the first regimen of chemotherapy. This undoubtedly extended the length of hospital stay for these patients, thus introducing bias in the comparison of hospital stay between the two groups. Thus, we calculated the actual hospital stay after eliminating any such excess periods of stay during the investigation.

The anastomotic leakage rate in LAR patients is significantly higher in laparoscopically treated cases than in the OP group. However, after revisiting the data in the LAP group we discovered that all the leakage occurred in early cases; this may be explained as effect of learning curve. The investigation enrolled these patients when our laparoscopic surgeon was in the early stages of learning curve, which led to a higher rate of complications. However, for the open surgery, all enrolled patients were operated by a surgeon

with experience of more than 500 cases of open rectal cancer surgeries.

The conversion done in this study was only in 2 cases, which was far lower than that reported in other trials. The conversion rate from laparoscopic to open surgery was 17% in the COLOR trial <sup>[15,17]</sup>, 25.4% in the COST <sup>[22]</sup> and 29% in the MRC-CLASICC <sup>[14]</sup> trial.

It is also worth noting that in the MRC-CLASICC trial the rate of intraoperative conversions fell by the year of study from 38% in the first year to 16% in the sixth year <sup>[14]</sup>. In our study, the laparoscopic procedures were all performed by a single surgeon and the conversion cases all reported in the early period. However, as time passed the experience in the procedure increased. With stabilization of the learning curve of the operating surgeon, the conversion rate significantly reduced. Furthermore, in our study stage IV patients were not included, and all patients were found in preoperative evaluation to be suitable for laparoscopic procedure, thus the conversion rate was lower than other trials. It was reported that there was no difference when comparing conversions to those completed in operative time, morbidity, length of stay, costs, and readmission <sup>[32]</sup>. There was greater blood loss, longer time to first bowel movement, longer length of stay when converted cases were compared with the cases completed with the laparoscopic-assisted approach but no difference when compared with open surgery <sup>[33]</sup>.

Since there were no differences in demographic data, and all observed biases have negligible impact on the results we believe our results are accurate. This study has confirmed the feasibility of laparoscopic procedures for rectal cancer, advocating the fast recovery times, and demonstrating similar medium-term recurrence and survival between LAP and OP groups. Thus, in a dedicated laparoscopic centre, laparoscopic procedures may result in a potential perioperative and follow-up survival benefit compared with open procedures, particularly in advanced cases.

## Conclusions

In this clinical research, we conclude that laparoscopic-assisted procedures have more benefits on postoperative recovery, and also the effectiveness on survival as compared with open surgery in the treatment of non-metastatic rectal cancer. Thus, in the future laparoscopic procedures may become the most effective treatments for rectal cancer.

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