Oncological adequacy of laparoscopic rectal cancer resection: An audit in Indian perspective

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INTRODUCTION

Laparoscopic resection of colon cancer has gained wide acceptance,[1,2] however, its role in the treatment of rectal cancer remains controversial. The main controversies are centred on the oncologic adequacy of laparoscopic resection in comparison with open surgery. Two previous large randomised control studies and several meta-analyses had shown similar pathological and oncological outcomes between laparoscopic and open approaches for rectal cancer.[3‑7] However, two recent randomised control trials (Australian Laparoscopic Cancer of the Rectum [ALaCaRT] and the American College of Surgeons Oncology Group [ACOSOG] Z6051) have failed to prove that LRR is non-inferior to open resection.

Background: Laparoscopic resection for rectal cancer (LRR) has gained popularity because of better short-term outcomes and less post-operative morbidity. However, LRR is still not endorsed as a standard of care mainly due to concerns centred on oncological safety in comparison with open approach. Moreover, two recent randomised trials (Australian Laparoscopic Cancer of the Rectum [ALaCaRT] and the American College of Surgeons Oncology Group [ACOSOG] Z6051) have failed to prove that LRR is non-inferior to open resection. Studies on oncological adequacy of LRR in the Indian population in terms of quality of mesorectal excision are scarce. In this article, we aim to audit the oncological adequacy of LRR in our centre and thereby critically analyse the reliability of extrapolation of results of ALaCaRT and ACOSOG trials to the Indian population.

Methods: We retrospectively analysed the oncological adequacy of LRR in terms of completeness of total mesorectal excision (TME), distal and circumferential resection margin (CRM) status and nodal harvest in patients with rectal cancer who underwent LRR between January 2016 and June 2018 at our centre.

Results: Of 157 patients included in this study, a complete TME was achieved in 148 (94.26%) patients and nearly complete in 7 (4.46%) patients. A safe CRM (≥1 mm) was obtained in 151 (96.18%) patients. Distal margin results were negative in 155 (98.73%) patients. Average nodal harvest was 19.86 ± 9.28. Overall surgical success, calculated as a composite measure of negative distal margin and negative CRM and complete TME was 95.54%.

Conclusion: Good quality rectal cancer resection can be achieved by experienced laparoscopic surgeons without compromising oncological safety.

Keywords: Circumferential resection margin, colorectal neoplasms, laparoscopy, minimally invasive surgery, quality of surgery, rectal cancer, total mesorectal excision

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trials (Australian Laparoscopic Cancer of the Rectum [ALaCaRT] trial and the American College of Surgeons Oncology Group [ACOSOG Z6051] trial) have concluded that their findings do not support the routine use of laparoscopic resection in Stage II and III patients.\textsuperscript{[8,9]} They drew this conclusion as their studies failed to prove that the laparoscopic rectal resection is non-inferior to open resection in terms of cancer clearance. Although both studies have been criticised for their non-inferiority design and lack of comparison on long-term outcomes, they have rekindled the debate among surgeons regarding the reliability of laparoscopy for rectal cancer resection.\textsuperscript{[10]} To add to the controversy, a recent meta-analysis by Martínez-Pérez et al. questioned the oncological safety of laparoscopy for the treatment of rectal cancer as they found that the risk for achieving an incomplete mesorectal excision is significantly higher in patients undergoing laparoscopic rectal cancer resection compared with open resection.\textsuperscript{[11]} Essentially, the quality of surgery in terms of completeness of total mesorectal excision (TME) is the factor which is under debate in these recent trials. The quality of TME is considered as a marker for good surgical technique and is an important prognostic factor for the local recurrence independently of other clinicopathologic factors, including circumferential resection margin.\textsuperscript{[12,13]} The skill of the operating surgeon is critical to the success of laparoscopic rectal cancer resection especially when it comes to the deep pelvic dissection.\textsuperscript{[9]}

Studies on the reliability of laparoscopic rectal cancer resection in terms of oncological adequacy in the Indian population are scarce. Moreover, many characteristics of our population such as body mass index (BMI), stage at which the disease is detected are different from that of the Western population. Extrapolation of randomised controlled trial (RCT) measurements depends on the representativeness of the RCT sample, and generalisation of multicentre RCT results to individual surgeons should be done with caution especially when it is related to a procedure in which experience and skills of the surgeon influence the outcome. To date, there is no literature on the quality of laparoscopic rectal cancer resection in the Indian population in terms of completeness of mesorectal excision. In the present study, we aim to audit the oncological adequacy of laparoscopic resection for rectal cancer in our centre in terms of quality of mesorectal excision, distal and circumferential resection margin (CRM) status and lymph nodal harvest.

**METHODS**

The study was designed as a retrospective observational study. Data of patients who underwent laparoscopic resection for adenocarcinoma of the rectum (within 15 cm of the anal verge) from 1\textsuperscript{st} January 2016 to 30\textsuperscript{th} June 2018 at our institution were collected from the prospectively maintained database. Patients with a positive circumferential margin on the pre-operative imaging were excluded from the final analysis.

All patients underwent colonoscopy and biopsy followed by cross-sectional imaging with magnetic resonance imaging and/or computed tomography scan before surgery. Neoadjuvant chemoradiation was given in T3/T4 lesions, those with lymph node involvement and threatened mesorectum. All patients underwent laparoscopic surgery as a primary modality. Inferior mesenteric artery (IMA) ligation is routinely done at the origin of IMA from the aorta (high ligation). The mesorectal mobilisation is performed in the standard way with sharp dissection under direct visualisation. In all patients included in the study, TMEs were done by one of senior surgical faculties (PK or DV) who have experience with more than 200 LRRs.

Standardised routine pathological examination was carried out according to the protocol of Nagtegaal et al.\textsuperscript{[14]} While analysing the quality of the mesorectum for the study purpose, a specimen with smooth mesorectal fascia [complete, Figure 1] or a specimen with minimal irregularity in the mesorectal surface with a defect not involving the muscularis propria (nearly complete) were grouped as complete, and a specimen with mesorectum having a defect into the muscularis propria and very irregular lateral resection margin was considered as incomplete [Table 1]. The circumferential resection margin was evaluated and considered positive if tumour was present within 1 mm of the inked resection margin. The distal margin was regarded to be positive if the line of

![Figure 1: Laparoscopic abdominoperineal excision specimen with smooth intact mesorectal excision and no coning](image-url)
transsection was <5 cm below the tumour for upper rectal lesions, if it was <2 cm below the line of transection for middle rectal lesions, and if the tumour was present within 1 mm for low rectal lesions. Overall surgical success was calculated as a composite measure of negative distal margin, negative CRM and complete TME.

RESULTS

Demographic data
A total of 191 laparoscopic rectal cancer resections were performed from January 2016 to June 2018. Of this, 157 patients were qualified to include in the current study. Mean age of our study population was 61.53 ± 9.86. There were 98 male patients and 59 females patients (M:F = 1.66:1). Mean BMI of the sample was 24.07 ± 4.6. Majority of them were American Society of Anesthesiologists-II (ASA-II) (61%) and around 10% and 29% were ASA I and III, respectively. Nearly 68% of patients received neoadjuvant therapy. Of 157 patients, 18 underwent abdominoperineal resection and rest underwent laparoscopic anterior resection. Mean operative duration was 183.4 ± 61.8 min. There was no conversion to open surgery in the study group [Table 2].

Pathological outcome
A clear negative circumferential margin (≥1 mm) was obtained in 151 (96.18%) patients. With regards to the completeness of TME, a complete TME was achieved in 148 (94.26%) patients and nearly complete in 7 (4.5%) patients. Distal margin results were negative in 155 (98.73%) patients. Average nodal harvest was 19.86 ± 9.28 [Table 3]. Overall surgical success measured by a negative distal and circumferential radial margin results and complete TME was 95.54% (150/157).

DISCUSSION
The introduction of TME with radial clearance has considerably improved local recurrence and long-term survival after surgical management of carcinoma of the rectum.\textsuperscript{15,16} TME is the precise surgical dissection technique which encompasses the complete removal of the rectum together with its draining lymph nodes within an intact mesorectum.\textsuperscript{15,17} It has been demonstrated that macroscopic pathologic assessment of the completeness of the mesorectum of the specimen, scored as complete, partially complete, or incomplete, accurately predicts both local recurrence and distant metastasis. Minimally invasive surgeons argue that the magnified views obtained deep in the pelvis at laparoscopy may facilitate precise mesorectal dissection and nerve preservation. With advances in technology, standardisation of the technique and experience of surgeons, the utilisation of laparoscopic TME for rectal cancer has recently become more widespread. For the laparoscopic approach to be widely accepted in rectal cancer surgery, demonstration of oncological equivalence to open resection is of paramount importance. Short-term pathological outcomes measured in terms of the completeness of the mesorectal excision, involvement of the circumferential resection margin and distal margin positivity may have key implications on long-term outcomes.\textsuperscript{15,17} However, there are only few studies which have assessed the quality of surgery based on the pathologic evaluation

| Table 1: Grading of the quality of mesorectum |
|---|---|---|
| Complete | Nearly complete | Incomplete |
| Smooth intact bulky mesorectum | Moderate bulk to the mesorectum | Little bulk to the mesorectum |
| Mesorectal defects not deeper than 5 mm | Defects >5 mm, but none extending to the muscularis propria | Exposed muscularis propria |
| No coning | Moderate coning | Moderate to marked coning |
| Smooth regular CRM\textsuperscript{*} | Irregular CRM\textsuperscript{*} | Irregular CRM\textsuperscript{*} |

\textsuperscript{*}Circumferential margin

| Table 2: Patient characteristics in our study (n=157) |
|---|---|
| Age\textsuperscript{#} | 61.53±9.86 (24-86) |
| Sex | |
| Males | 87 |
| Females | 47 |
| BMI\textsuperscript{#} | 24.07±4.6 (14.97-47.09) |
| ASA\textsuperscript{#} | |
| I | 16 (10.19%) |
| II | 96 (61.15%) |
| III | 45 (28.66%) |
| Tumor location (%) | |
| Upper rectum | 36 (22.93%) |
| Middle rectum | 50 (31.85%) |
| Lower rectum | 71 (45.22%) |
| Neoadjuvant therapy | 107 (68.15%) |
| Laparoscopic anterior resection | 139 (88.54%) |
| Abdominoperineal resection | 18 (11.46%) |
| Operative duration (minutes)* | 183.4±61.8 (128-230) |

\textsuperscript{*}Mean±Standard deviation (range), \textsuperscript{#}BMI: Body mass index, \textsuperscript{*}ASA: American Society of Anesthesiologists

| Table 3: Pathological analysis of patients in our study (n=157) |
|---|---|---|
| Pathological T Stage (%) | |
| T\textsubscript{1} | 11 (7.01%) |
| T\textsubscript{2} | 18 (11.5%) |
| T\textsubscript{3} | 41 (26.11%) |
| T\textsubscript{4} | 77 (49.04%) |
| Pathological outcome | 10 (6.37%) |
| Negative CRM\textsuperscript{*} (%) | 151 (96.18%) |
| Completeness of TME\textsuperscript{*} (%) | |
| Complete | 148 (94.26%) |
| Nearly complete | 7 (4.46%) |
| Incomplete | 2 (1.27%) |
| Negative distal margin (%) | 155 (98.73%) |
| Average nodal harvest* | 19.86±9.28 (8-60) |

\textsuperscript{*}CRM: Circumferential margin, \textsuperscript{*}TME: Total mesorectal excision, \textsuperscript{*}Mean±Standard deviation (range)
of the resection specimen which has been shown to be a sensitive means of assessing the quality of rectal surgery.

ALaCaRT trial was conducted in Australia and New Zealand and enrolled patients with T1-T3 rectal adenocarcinoma <15 cm from the anal verge. Similarly, ACOSOG Z6051 trial was conducted across the United States and Canada and enrolled patients with clinical stage II or III rectal cancer within 12 cm of the anal verge who received neoadjuvant treatment. There were 238 patients in ALaCaRT trial and 240 patients in ACOSOG trial available for analysis in the laparoscopic arm. Both ALaCaRT and ACOSOG Z6051 trials used a composite endpoint assessed by histopathology consisting of a complete mesorectal excision, a negative circumferential resection margin (CRM), and a negative distal margin. All three parameters needed to be satisfied for the resection to be deemed complete (surgical success). This well-intentioned composite score was devised to minimise the number of patients to accrue and therefore the time needed to complete the study. However, the relevance of this composite score as a prognostic marker is not yet evaluated in any trial. In our study, we were able to achieve a complete TME in 98.7% of patients while it was 92.1% in ACOSOG trial and 97% (complete + nearly complete) in ALaCaRT laparoscopic surgery groups. Negative circumferential resection margin rate in our study was 96.2% while it was 87.9% and 93% in laparoscopic arms of ACOSOG and ALaCaRT trials, respectively. Distal margin negativity rate in our study group (98.7%) was comparable to laparoscopic surgery groups of ACOSOG and ALaCaRT trials (98.3% and 99%, respectively). In the ACOSOG trial, complete resection was achieved in 81.7% of laparoscopic cases and 86.9% of open cases ($P = 0.41$ for non-inferiority). Similarly, in the ALaCaRT trial, the primary outcome of a complete resection was achieved in 82% compared to 89% in the open surgery group ($P = 0.38$ for non-inferiority). We could achieve successful resection in 95.54% of our patients. Average nodal harvest was found to be slightly higher in the present study (19.86 ± 9.28) compared to ACOSOG (17.9 ± 10.1). Conversion of laparoscopic surgery to an open procedure was required for 11% of patients in ACOSOG trial and 9% of patients in ALaCaRT trial. There was no conversion to open surgery in our study group. Mean operative duration in minutes was shorter in our study group (183.4 ± 61.8) compared to ACOSOG (266.2 ± 101.9) and ALaCaRT – (median 210). These results could be attributed to the population characteristics, standardisation of the technique and the experience of surgeons. The relationship between individual surgeons’ technique and quality of the surgery were not assessed in most multi-institutional trials.

Indian perspective
Although acceptance of laparoscopy in colorectal surgery in India had faced considerable resistance in the initial period mainly due to concerns which related to the steep learning curve and the oncological adequacy, minimally invasive approaches have slowly started gaining the momentum over the last two decades. We had shown that as the experience of surgical team improved, there was a trend towards selecting difficult cases and performing complex laparoscopic colorectal resections. In a study comprising 170 laparoscopic anterior resections Palanivelu C et al. concluded that laparoscopic anterior resections could be done for rectal tumours at all levels, which would allow sphincter preservation and maintain oncological safety. Ayloor Seshadri et al. in a matched case–control study compared the short-term outcomes and oncologic adequacy of laparoscopic ($n = 72$) and conventional open surgery ($n = 72$) for rectal cancer after neoadjuvant chemotherapy. Short-term outcomes were significantly better with laparoscopy in terms of blood loss, duration of surgery, time to passing of first flatus, time to start of normal diet and hospital stay. Although the number of lymph nodes harvested was comparable between the two groups, more patients in the open group had a positive circumferential resection margin than in the laparoscopy group (10% vs. 1%; $P = 0.03$). Our study is the first attempt which analysed the adequacy of laparoscopic rectal cancer resection in terms of quality of mesorectal excision along with resection margin status in Indian population.

CONCLUSION
Good quality rectal cancer resection can be achieved laparoscopically by well-experienced surgeons without compromising oncological safety. Well-designed RCTs with long-term survival data are needed to further explore the oncological adequacy of laparoscopic rectal cancer resection in our population.

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Conflicts of interest
There are no conflicts of interest.

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