Long-Term Functional and Oncological Outcomes Following Intersphincteric Resection for Low Rectal Cancers

Sivakumar Mahalingam¹ · Ramakrishnan Ayloor Seshadri¹ · Surendran Veeraiah²

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Abstract Surgery for low rectal cancer often involves a permanent stoma. Intersphincteric resection (ISR) with colo-anal anastomosis is a valuable sphincter sparing surgical procedure that avoids the need for permanent stoma in patients with low rectal cancer. The aim of this study was to analyze the long-term functional and oncological outcomes following ISR. This was a retrospective analysis of patients with low rectal cancer who underwent ISR with colo-anal anastomosis in our institution between 2007 and 2015. All patients had a diversion stoma. Bowel function outcomes were assessed prospectively using Wexner incontinence score, low anterior resection syndrome score (LARS), and the Cancer Institute Quality of Life (QoL) questionnaire. The histological reports were reviewed to assess the oncological adequacy of the surgery. Patterns of recurrence and survival were analyzed in this group of patients. Thirty-three patients who underwent an ISR were eligible for this study. Laparoscopic resection was performed in five patients. All the patients received neoadjuvant chemoradiation except the two who received short course radiation and one who did not receive any neoadjuvant treatment. The median distance from the anal verge to the distal edge of the tumor was 3 cm (range 1.5–5 cm). Distal resection margins and circumferential resection margins were negative in all the patients. The 30-day post-operative mortality rate was 3.03%. In 20 patients with a median follow-up of

48 months, the 3-year overall survival was 95%. One patient had recurrence in the para-aortic nodes. No patient had a local recurrence. Bowel function was assessed in 18 patients who had a minimum stoma free period of 1 year. After a median of 43 months following stoma closure, the median Wexner score was 3.56 (range 0–19), median LARS score was 4.78 (range 0–33), and the mean Cancer Institute QoL score was 151.56 ± 15.741 . The QoL was average to very high with an overall acceptable quality of life. In this study, ISR was associated with acceptable long-term functional and oncological outcomes. It can be considered as a safe alternative to a permanent stoma in selected patients with low rectal cancer.

Keywords Low rectal cancer · Intersphincteric resection · Sphincter sparing surgery · Outcome · Neoadjuvant chemoradiation

Introduction

The incidence of rectal cancer is less in India compared to the western countries. The age standardized incidence rate among men and women in Chennai is 3.8 and 2.3/100,000 population [1]. There is an increasing incidence of low rectal cancers in the younger population [2]. In India, patients are reluctant to have a permanent stoma since it has a major impact on their psychosocial life [3]. Intersphincteric resection (ISR) with colo-anal anastomosis is a type of sphincter sparing surgery for low rectal cancers that avoids the need for a permanent stoma. There has been no published report of the long-term outcomes of this procedure from India. This study aims to analyze the long-term oncological and functional outcomes of ISR for low rectal cancer.

✉ Ramakrishnan Ayloor Seshadri
ram_a_s@yahoo.com

¹ Department of Surgical Oncology, Cancer Institute (WIA), Dr. S. Krishnamurthy Campus, No.18, Sardar Patel Road, Guindy, Chennai 600036, India

² Department of Psycho-Oncology, Cancer Institute (WIA), Chennai, India

Materials and Methods

This was a retrospective analysis of all consecutive patients who underwent ISR in our institution between 2007 and 2015. The records of the patients were reviewed and data pertaining to the demographic details, surgical details, and post-operative histopathology were retrieved. The pre-operative imaging of the rectal tumor was done using an MRI (or by a computerized tomography (CT) scan prior to 2012). Neoadjuvant chemoradiation was offered to patients with T3/T4 tumor or node positive tumor on imaging. Patients were reassessed 4 weeks after completion of chemoradiation. The option of intersphincteric resection was offered to patients in whom the lower border of the residual tumor was clinically at or within 1 cm above the anorectal ring and radiologically if the intersphincteric groove was preserved and the levator muscle was not involved. The patients were also counseled extensively about the possibility of adverse functional outcomes. In general, elderly patients, obese patients, and those with a poor anal sphincter tone were not considered for ISR. In some patients undergoing an ultra-low anterior resection, a decision to perform ISR was taken if it was felt intra-operatively that a stapled anastomosis was not feasible.

ISR Technique The abdominal part of the surgery consisted of high ligation of the inferior mesenteric artery in all cases, mobilization of the splenic flexure, ligation of the inferior mesenteric vein at the lower border of pancreas, and then a total mesorectal excision. Beyond the inferior margin of the mesorectal envelope, the puborectalis muscle was separated from the rectal tube and the intersphincteric groove was entered wherever possible from above. The perineal phase began with anal dilation followed by exposure of the anal canal using either multiple sutures or a Lone Star Retractor. A 1:200,000 solution of adrenaline saline was injected in the intersphincteric groove. A circumferential incision was made on the anal mucosa at the level of dentate line (for partial ISR) or distal to it (for total ISR) depending on the lower border of the tumor so as to give a 1-cm clearance distally. This was deepened to incise the internal sphincter. The intersphincteric plane was developed circumferentially towards the cranial end to meet the plane from the abdominal dissection. In laparoscopic cases, the rectum was delivered through the anus and the sigmoid colon was transected at the appropriate level. An end-to-side or an end-to-end colo-anal hand-sewn anastomosis was performed using 3-0 absorbable sutures. A diverting colostomy or ileostomy was performed for all patients. The same was closed after completion of adjuvant chemotherapy. The patients were encouraged to do pelvic floor exercises to strengthen the sphincter.

Follow-up Patients were followed up every 3 months with a physical examination and serum carcino-embryonic antigen

(CEA) estimation for the first 3 years, every 6 months for the next 2 years, and annually thereafter. A CT scan of the abdomen and a chest skiagram were done annually for the first 3 years.

Function Assessment Only those patients who underwent closure of the diversion stoma were eligible for functional outcome assessment. The general quality of life was assessed by the validated Cancer Institute Quality of Life (CI-QoL) questionnaire [4], and the bowel function was assessed using the low anterior resection syndrome (LARS) score and the Wexner incontinence scoring system for anal continence [5, 6].

Statistical Analysis The statistical analysis was performed using SPSS software v.10. Overall survival was calculated using Kaplan–Meier curves.

Results

Between 2007 and 2015, a total of 455 patients underwent radical surgery for cancer involving the lower third rectum in our institution. A sphincter sparing surgery was performed in 219 of these patients while the remaining had a permanent stoma. An intersphincteric resection was performed in 35 patients. However, two procedures were converted to an abdominoperineal resection since the frozen section of the distal margin showed dysplastic changes. Although the paraffin sections showed no evidence of malignancy in the distal margin, these two patients were excluded from this study. All patients received pre-operative chemoradiation except the two who received short course radiation and one who underwent straight surgery. The demographic and treatment related details are listed in Table 1. Twenty-five patients completed adjuvant chemotherapy while eight patients are receiving adjuvant chemotherapy.

Complications The 30-day post-operative mortality was 3.03% (1/33). This patient had a myocardial infarction on the fourth post-operative day. The overall morbidity was 39.3% (13/33), whereas the major morbidity (Clavien–Dindo grade III–IV) was 12.1%. None of the patients developed an anastomotic leak. Late complications included subacute obstruction due to adhesions in two patients and a stricture of the anastomotic site in one patient which was easily dilated with the finger.

Pathology All patients had a grade 1 TME specimen (mesorectal fascial plane) and none of the patients had a positive circumferential resection margin. The pathological details are listed in Table 2.

Table 1 Demographic and treatment details

Median age	50 years (range 28 to 69)
Gender	Males—21, females—12
Median distance from anal verge	3cm (range 1.5 to 5 cm)
Median BMI	23 (range 14 to 31)
No. of patients who received neoadjuvant chemoradiation	30 (90.9%)
Median interval between chemoradiation and surgery	9 weeks (range 6 to 39 weeks)
Median blood loss	300 ml (range 200 to 850 ml)
Median duration of surgery	265 min (range 210 to 410 min)
Morbidity (Clavien–Dindo grade)	
Grade II	9 (27.2%)
Grade IIIa	4 (12.1%)
Late complications	
Adhesions	2 (6%)
Anastomotic stricture	1(3%)
Median hospital stay	11 days (range 4 to 39 days)

Oncological Outcomes The oncological outcomes were assessed for 20 of the 33 patients who had more than 1 year follow-up. The median follow-up in these patients was 48 months (range 18 to 83 months). The overall recurrence rate was 5% (1/20). No patients experienced a local recurrence. One patient had a para-aortic nodal recurrence 18 months after completion of treatment and received palliative chemotherapy but died of progressive disease. The 3-year overall survival rate was 95%.

Bowel Function Eighteen patients who had a stoma closure were assessed for long-term bowel function outcomes. The remaining 15 patients were not eligible for bowel function assessment for the following reasons: eight were receiving adjuvant chemotherapy, four had stoma closed only very recently (<3 months), one patient expired post-operatively, and two patients were not willing for stoma closure. After a median time of 43 months following colostomy closure in these 18

patients, the median Wexner score was 0.50 (range 0–19) and the median LARS was 2.00 (range 0–33). The number of bowel movements in 24 h was <3, 3 to 7, and >7 in 40, 50, and 11% of patients, respectively. Anti-diarrhoeal medication was advised for patients who have >10 bowel movements per day. Due to the small sample size, analysis of various factors influencing bowel function was not considered worthwhile.

Quality of Life The Cancer Institute Quality of Life (CI-QoL) questionnaire was utilized to assess the QoL for the eligible 18 patients. The QoL was acceptable in all our patients and correlated with the bowel function outcomes. Patients with a good continence had very high QoL. The mean CI-QoL was 151.56 ± 15.741 after a median follow-up of 43 months. The CI-QoL was average in 27.8% (5/18), high in 50% (9/18), and very high in 22.2% (4/18) of patients. No patient had a low or very low QoL.

Table 2 Pathology distribution

Pathological stage	No. of patients
yp T0	5
yp Tis	2
ypT1	3
ypT2	10
ypT3	11
ypT4	2
ypN0	21
ypN1	6
ypN2	6
Median nodal yield	9 (range 2 to 40)
Median distal margin	2 cm (range 0.4 to 4 cm)
No. of positive circumferential resection margins	NIL ^a
R0 resection	100%

^a One patient with a complete pathological response had only mucin pools in the CRM

In 11 patients, it was possible to compare bowel function and QoL within a year of colostomy closure and beyond 1 year of colostomy closure. The mean Wexner score and mean CI-QoL in these patients were 6.09 and 142.91, respectively after a median of 7 months following stoma closure. This improved to a mean Wexner score of 1.03 and mean CI-QoL 154.09 after a median of 45 months from stoma closure.

Discussion

To the best of our knowledge, this is the first study to report the long-term outcomes after ISR in Indian patients. An earlier study from Mumbai had analyzed 33 patients who underwent ISR for low rectal cancer and reported a morbidity and 30-day mortality of 6 and 0%, respectively [7]. However, long-term oncological and functional outcomes were not reported in this study.

Sphincter preserving surgery for rectal cancer should follow oncological principles and must have good long-term oncological outcomes. Local recurrence after ISR varies from 2 to 10.6% and the 5-year survival rates range from 80 to 92% (Table 3). The long-term survival and recurrence rates after ISR are comparable to patients undergoing (APR) abdominoperineal resection [12, 14]. Saito et al. reported a local recurrence rate of 11 and 16% and a 5-year overall survival of 80 and 60% in patients undergoing ISR and APR, respectively [12]. The long-term oncological outcomes of ISR have been analyzed in two systematic reviews. Tilney et al. reviewed 21 studies that included 612 patients and reported a local recurrence rate of 9.5% and a 5-year overall survival of 81.5% [15]. In a subsequent systematic review of 14 studies that included 1289 patients, Martin et al. reported a mean local recurrence of 6.7% and a 5-year overall and disease-free survival of 86.3 and 78.6%, respectively [16]. The long-term oncological outcomes in our study are comparable to the published literature.

The functional outcome after ISR has been reported in a few earlier studies [17–19]. Kuo et al. reported that 90.8% of patients who underwent ISR were satisfied with the functional outcome even though a third of them had to use anti-diarrhoeal medications [18]. In his systematic review, Martin

et al. reported a mean bowel movement of 2.7 ± 0.6 per 24 h with 51% of the patients having perfect continence. In our series, only two patient had >7 bowel movements in a 24-h period. Although the initial 1 year after ISR is often associated with a major low anterior resection syndrome and a higher Wexner incontinence score, it usually improves after 1 year [19]. In our study, the mean Wexner score improved from 6.09 to 1.03 after 1 year of stoma closure.

Few studies had reported about the QoL after an ISR [19–21]. Barisic et al. reported that most of the patients after ISR had a good QoL based on functional and symptoms scores of the European Organization for Research and Treatment of Cancer (EORTC) QoL C-30 questionnaire [19]. Bretagno et al. reported that after ISR, the symptom-related QoL was poor, but the global QoL was good when compared to the patients who underwent a low anterior resection [21]. We used the validated CI-QoL and found that most patients had a satisfactory QoL after ISR. We found that bowel function has a strong impact on the QoL of the patients since those who had a good bowel function had a good QoL. Further, we demonstrated that an improvement of bowel function with passage of time correlated with an improved QoL.

In our study, five patients had a laparoscopic ISR. Minimally invasive ISR, by either laparoscopic or robotic approaches has been reported to have comparable oncological outcomes with the benefit of early post-operative recovery [22–25]. Complications after ISR can include wound infection, anastomotic leak, pelvic abscess, stricture, fistula, bleeding, bowel obstruction, etc. A large study of 228 patients reported an operative mortality of 0.8% and an anastomotic leak rate of 10.1% [10]. A systematic review of the published studies reported an overall morbidity of 25.8% and mortality rate 0.8% [16]. We did not encounter anastomotic leak in our series. The late complications reported in this study like anastomotic stricture and adhesive obstruction has also been reported by others [8].

A unique feature of this study is the high proportion of patients who have undergone ISR after chemoradiation. In our study, 90.9% received neoadjuvant long course. In a systematic review, only 38% of the patients undergoing ISR received pre-operative chemoradiation [16]. This assumes significance since the use of pre-operative radiation has been

Table 3 Long-term oncological outcomes after intersphincteric resection

Author	No. of patients	Local recurrence	5-year overall survival
Schiessel et al. [8]	121	5.3%	88%
Rullier et al. [9]	92	2%	81%
Saito et al. [10]	228	3.6%	92%
Chamlou et al. [11]	90	7%	82%
Saito et al. [12]	132	10.6%	80%
Yamada et al. [13]	107	2.5%	92%

found to be associated with poor functional outcomes after an ISR. Canda et al. reported a worsening of the Wexner score who received pre-operative chemoradiation [26]. We were unable to assess the influence of pre-operative radiation on the bowel function since only one patient did not receive the same. However, in spite of radiation, our patients had a reasonably good bowel function.

The strength of this study is the long follow-up of patients. No patient was lost to follow-up. The success of any new surgical technique in oncology depends not only on good short-term results but also more importantly on the long-term oncological outcomes. On the other hand, the small number of patients and the retrospective nature of this study with its inherent bias are the limitations of this study. Nevertheless, this study assumes significance in a country like India where social taboos associated with a permanent stoma often lead many patients to refuse curative surgery for rectal cancer. Moreover, an increasing number of young rectal cancer patients will further increase the demand for sphincter preservation in the years to come.

Conclusion

In carefully selected patients with low rectal cancer, ISR is an oncologically safe alternative to a permanent stoma with an acceptable bowel function and quality of life even after pre-operative radiation. Patient selection, accurate staging, adequate counseling, and meticulous surgical techniques are vital for achieving good results.

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