Anterior Resection for Rectal Cancer with Mesorectal Excision: Institutional Review

Rakesh Kumar Gupta · Chandra Shekhar Agrawal ·
Om Prakash Pathania · Amir Bajracharya ·
Suresh Prasad Sah · Panna Lal Sah

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Abstract This study aims to compare the operative results and oncological outcomes of patients with total mesorectal excision (TME) for mid and distal cancer and partial mesorectal excision (PME) for proximal cancer. Anterior resection has become the preferred treatment option for rectal cancer. TME with sharp dissection has been shown to be associated with a low local recurrence rate. Controversies still exist as to the need for TME in more proximal tumor. Resection of primary rectal and rectosigmoid cancer was performed in 298 patients from January 2003 to November 2010. These 298 patients (163 men and 135 women; median age, 67 years) underwent anterior resection. The curative resection was performed in 269 patients (90.3%). TME was performed in 202 patients (67.8%). Significantly longer median operating time, more blood loss, and a longer

hospital stay were found in patients with TME. The overall operative mortality and morbidity rates were 1.8% and 32.6%, respectively, and there were no significant differences between those of TME and PME. Anastomotic leak occurred in 8.1% and 1.3% of patients with TME and PME, respectively ($P < 0.001$). Independent factors for a higher anastomotic leakage rate were TME, the male gender, the absence of stoma, and increased blood loss. The advanced stage of the disease and the performance of coloanal anastomosis were independent factors for increased local recurrence. By performing TME in patients with mid and distal rectal cancer, the local control and survival of these patients are similar to those of patients with proximal cancers where adequate clearance can be achieved by PME.

Keywords Anterior resection · Total mesorectal excision (TME) · Partial mesorectal excision (PME)

R. K. Gupta (✉) · C. S. Agrawal · A. Bajracharya · S. P. Sah
Department of Surgery, B.P. Koirala Institute of Health Sciences,
Dharan, Nepal
e-mail: rakesh154@yahoo.co.in

C. S. Agrawal
e-mail: Hodsurgery@yahoo.com

A. Bajracharya
e-mail: dr_amirb@hotmail.com

S. P. Sah
e-mail: sureshsah214@yahoo.com

O. P. Pathania
Department of Surgery, Lady Harding Medical College,
New Delhi, India
e-mail: oppathania@yahoo.com

P. L. Sah
Department of Radiology, B.P. Koirala Institute of Health
Sciences,
Dharan, Nepal
e-mail: pannalalsah76@yahoo.com

Introduction

In the recent two decades, improvements have been achieved in the outcomes of rectal cancer surgery with the advances in surgical techniques as well as adjuvant therapy. Abdominoperineal resection, the previous gold standard treatment of rectal cancer, has been regarded as unnecessary in most patients with rectal cancer, and more patients can now be treated with sphincter-saving surgery. The increased understanding of the spread of the disease has contributed significantly to this change. Distal mural spread of the disease was shown to be rarely more than 2 cm [1], and the allowance of a close distal margin has led to an increased incidence of sphincter-saving operations. Moreover, safe anastomosis at the distal rectum or the anal canal has been made possible by the advances of mechanical stapling

devices and the development of the double stapling technique [2, 3].

Local recurrence has always been a formidable problem following rectal cancer surgery. Conventional rectal mobilization by blunt dissection has been associated with a high local recurrence rate [4–6]. The importance of the complete removal of the lymphovascular tissue surrounding the rectum and a free circumferential margin has been recognized in the management of rectal cancer [7]. By sharp meticulous perimesorectal dissection and total mesorectal excision (TME), Heald et al. [8] and Enker et al. [9] have reported low local recurrence rates in patients with rectal cancer. However, routine TME in rectal cancer at all levels has been challenged in view of the increased morbidity associated with it. The anastomotic leakage rates are high in the series of patients with TME [10]. Moreover, the bowel function is also adversely affected with a low colorectal or coloanal anastomosis [11]. Thus, selective TME according to the level of tumor appears to be a reasonable approach. This study examines the mortality, morbidity, local failure rate, and survival following anterior resection with sharp perimesorectal dissection for rectal cancer with selective TME for mid and distal rectal cancers in a high volume center. The risk factors for anastomotic leakage, local recurrence, and survival are analyzed with univariate and multivariate analyses.

Material and Methods

During the 7-year period from January 2003 to November 2010, 298 patients underwent resection of primary rectal and rectosigmoid cancer in the Department of Surgery, B. P.K.I.H.S, Dharan, Nepal. This study included all patients who underwent anterior resection. The patients with abdominoperineal resection ($n=79$), Hartmann's operation ($n=24$), and local excision ($n=21$) were excluded. All the patients had histologically proven adenocarcinoma of the rectum or rectosigmoid. Data on the patients' demographics, comorbidities, operative details, postoperative mortality and morbidity, histological results, and long-term outcomes were collected prospectively. *A proper preoperative staging was done in all patients, with available tools of investigations (transrectal ultrasound, CECT, and MRI, etc.).*

During the study period, the operations were performed by the consultant surgeons. TME, which was defined as the transection of the rectum at the level of the pelvic floor with the entire intact mesorectum, was performed for most patients with mid and distal rectal cancers. For the tumors at the upper rectum or rectosigmoid, transection of the rectum and mesorectum 4–5 cm below the lower border of the tumor was performed following sharp perimesorectal dissection (PME).

Surgical Techniques

The management of rectal cancer and chemoradiation (neoadjuvant and adjuvant) therapy, our department follows the National Cancer Institute Guidelines as standard of care.

Preoperative bowel preparation with polyethylene glycol solution was given the day before surgery except in patients with obstructing cancers. Prophylactic intravenous antibiotics were given at the induction of anesthesia. Most of the patients underwent laparotomy through a lower midline incision.

Rectal mobilization was carried out by sharp dissection under the direct vision. The visceral pelvic fascia together with the mesorectum was kept intact during the course of rectal dissection. Efforts were made to identify and preserve the hypogastric nerves, pelvic nerve plexuses during the dissection. In the anterior dissection, the peritoneum was incised 1–2 cm above the rectouterine or rectovesical pouch. The rectum was mobilized down to the pelvic floor.

In the initial period of the study, selective proximal diversion was performed. Loop transverse colostomy was our preferred mode of proximal diversion. After our analysis on the risk factors for anastomotic leakage, proximal diversion was performed in the majority of the patients with an anastomosis within 5 cm from the anal verge. A hand-sewn interrupted single-layer colorectal/coloanal anastomosis was our preferred mode of restoring bowel continuity.

Adjuvant Therapy

Adjuvant radiation therapy was not routinely given to patients with stage II or stage III disease. Postoperative chemoradiation was offered only when the local clearance was in doubt. Preoperative chemoradiation was given to those with fixed T4 lesions. Chemotherapy based on 5-fluorouracil and leucovorin was offered to patients younger than 75 years with stage II or stage III disease.

Follow-up Protocol

Patients were followed up at intervals of 2–3 months during the first 2 years and 4–6 months from year 3 to year 5. Thereafter, the patients were seen yearly. Follow-up was by clinical history and examination, blood tests, and serum carcinoembryonic antigen. Digital rectal examination was performed at each visit to detect any anastomotic stricture or local recurrence. If recurrences were suspected, endoscopic examination and computed tomography (CT) scan were performed to determine whether salvage surgery could be performed.

Statistics

Comparison of categorical variables was performed with χ^2 test or Fisher Exact test when appropriate. Continuous variables were presented as means (standard deviation) or median values (range). These variables were compared with Mann–Whitney *U* test. Survival was analyzed with the Kaplan Meier method and the factors were compared with the log-rank test. Multivariate analysis was performed with Cox proportional hazard model. *P* values of less than 0.05 were considered statistically significant.

Results

A total of 298 patients underwent anterior resection for primary rectal or rectosigmoid cancer during the study period. There were 163 (54.7%) men and 135 (45.3%) women. The mean age was 52.2 ± 15.7 years (range, 19–80 years). The median level of the tumor from the anal verge was 7 cm (range, 2.5–18 cm). Surgery with curative intent was performed in 272 patients (91.3%). Twenty-six patients (8.7%) had palliative surgery because of unresectable distant metastasis ($n=19$) or residual local disease ($n=7$).

Premorbid medical condition was present in 117 patients (39.2%), and they are shown in Table 1. The majority of the concomitant medical diseases were hypertension, ischemic heart disease, diabetes, and chronic obstructive airway disease. Eleven patients (3.7%) had synchronous cancer in another part of the colon. Seven of the synchronous tumors were distal to the splenic flexure and anterior resection could achieve resection of the synchronous tumors. Four patients had synchronous cancer at the colon proximal to the splenic flexure and synchronous right colectomy was performed. In another three patients, right hemicolectomy was performed for benign lesions of the right colon or appendix.

Table 1 Comorbidities of patients with anterior resection

	Number	%
Cardiac	79	26.5
Hypertension	52	
Ischemic heart disease	19	
Arrhythmia	8	
Diabetes mellitus	21	7.1
Pulmonary disease	12	4.1
Previous tuberculosis	6	
COAD	3	
Bronchiectasis	1	
Asthma	2	
Neurologic diseases	5	1.7
CVA	2	
Epilepsy	3	

Hand-sewn anastomosis was performed in all patients. Twenty-one peranal coloanal anastomosis was performed for ultra-low cancers. The mean operative time was 183 min (± 62 min) and the mean blood loss was 426 mL (± 451 mL). Resection of other organs was required in 21 patients (7.1%). Partial bladder resection was performed in 5 patients.

Three patients with potentially curative surgery had positive margin on histology. One of them underwent abdominoperineal resection and remained well for 6 years following surgery. The other 2 patients refused further operation and died of liver metastasis at 24 months and local recurrence at 41 months, respectively.

Radiation therapy, usually with chemotherapy, was given to 16 patients (preoperative, $n=4$; postoperative, $n=12$). One of the patients showed complete response following neoadjuvant chemoradiation. The TNM system was used for staging, and the final pathologic stages of the tumors were as follows: 1 stage 0 (0.3%), 41 stage I (13.8%), 98 stage II (32%), 132 stage III (44.3%), and 26 stage IV (8.7%).

TME was performed in 202 patients; while in other 96 patients, transection of the rectum and mesorectum (PME) was performed above the pelvic floor either because of high rectal cancer or because of palliative resection. The differences between operations with and without TME are shown in Table 2. Operations with TME were associated with longer operative time, more blood loss, a higher incidence of stoma creation, and a longer hospital stay. The leakage rate was also significantly higher in the TME group. However, the overall postoperative mortality and morbidity did not show any significant differences between patients with TME and PME.

Eleven patients died in the postoperative period from 1 to 38 days after the surgery. The operative mortality was 3.7%. All these patients had premorbid medical diseases. The causes of death included myocardial infarction or ischemia ($n=3$), pneumonia ($n=4$), and sepsis ($n=4$).

A total of 90 patients (30.2%) developed intraoperative or postoperative complications. The types of complications are shown in Table 3. Clinical anastomotic leakage occurred in 18 patients (6.1%). Comparison of risk factors for anastomotic leakage is shown in Table 4. Multivariate analysis showed that the use of TME ($P<0.001$; hazards ratio [HR], 6.3; 95% CI 3.4–46.7), the male sex ($P<0.02$; HR, 2.9; 95% CI 1.2–7.2), the absence of stoma ($P=0.001$; HR, 4.0; 95% CI 1.8–9.0), and blood loss more than 500 mL ($P=0.02$; HR, 2.5; 95% CI 1.2–5.3) were independent factors for a higher incidence of anastomotic leakage.

Local Recurrence

With the median follow-up of the surviving patients of 38.7 months (2–104 months), 32 patients developed local

Table 2 Comparison between patients with and without TME

	TME(N=202)	PME(N=96)	P
Men: women	108:94	55:41	0.61
Median age(range) (years)	56(19–80)	58(21–79)	<0.001
Median level of tumor from anal verge (range) (cm)	6(2.5–11)	14(4–18)	<0.001
Median blood loss (range) (mL)	390(25–4400)	190(50–2400)	<0.001
Median duration of operation (range) (min)	185(65–495)	153(55–340)	<0.001
Diversion stoma (%)	138 (68.3%)	7 (7.3%)	<0.001
Clinical leak (%)	16(7.9%)	2(2.1%)	<0.001
Palliative resection (%)	11 (5.4%)	15 (15.6%)	<0.001
Presence of medial illnesses (%)	68 (33.7%)	49 (51.1%)	0.002
Complications (%)	66 (32.7%)	24 (25%)	0.09
Postoperative mortality (%)	5(2.5%)	6(6.2%)	0.18
Median days of hospital stay (range)	11 (5–92)	9 (5–59)	<0.001

recurrence. The actuarial 2-year and 5-year local recurrence rates were 7.0% and 10.7%, respectively. These included patients with local recurrence alone as well as those with both local and distant diseases. Analysis of the risk factors for local recurrence is shown in Table 5. On univariate analysis, the advanced stage, resection margin of less than 2 cm, the presence of perineural invasion, or lymphovascular permeation were risk factors for local recurrence. In the multivariate analysis, only the stage of the disease ($P=0.001$; HR, 2.9; 95% CI 1.6–5.4) was the independent factor associated with a high incidence of local recurrence.

Table 3 Postoperative complications of patients with anterior resection

	No. of patients	%
Intraoperative complication	6	2
Splenic injury	1	
Ureteric injury	1	
Severe bleeding in pelvis	4	
Cardiac	8	2.6
Pulmonary	12	4
Ileus	13	4.4
Intestinal obstruction	5	1.7
Wound complications	10	3.4
Wound infection	7	
Wound dehiscence	3	
Urinary tract infection	6	2
Urinary retention	4	2.6
Anastomotic leak	18	6.1
Intra-abdominal collection without leak	2	0.7
Postoperative bleeding	3	1
Anastomotic bleeding	2	
Gastrointestinal bleeding	1	
Bowel ischaemia	1	0.3
Others	2	0.7

Survival

The 5-year overall survival and cancer-specific survival rates were 67.5% and 75.5%, respectively. The univariate analysis of the risk factors for the cancer-specific survival is shown in Table 5. Multivariate analysis showed that the stage of disease, the presence of lymphovascular as well as perineural permeation were independent variables associated with poor disease-specific survival.

Discussion

The optimal treatment of rectal cancer should maximize sphincter preservation with low morbidity and mortality.

Table 4 Univariate analysis of risk factors for anastomotic leakage

	No.	No. with leak	P
Male	163	11	0.6
Female	135	7	
TME	202	16	<0.001
PME	96	2	
Anterior resection	71	1	<0.001
Low anterior resection	227	17	
Presence of diversion stoma	145	8	0.8
No diversion stoma	153	10	
Age <70 year	174	14	0.1
Age ≥70 year	124	4	
Medical illness	117	11	0.08
No medical illness	181	7	
Curative resection	272	15	0.2
Palliative resection	26	3	
Level of tumor >10 cm	98	3	0.01
Level of tumor ≤10 cm	200	15	
Blood loss >500 mL	69	10	0.004
Blood loss ≤500 mL	229	8	

Table 5 Univariate analysis of risk factors for local recurrence

	No. of patients (N=272)	5-year actuarial local recurrence(%)	P	5-year cancer- specific survival (%)	P
Male	145	12.2	0.06	73.5	0.5
Female	127	6.8		78.4	
Age ≥ 70 year	116	9	0.6	71.4	0.07
Age < 70 year	156	11.1		78.3	
Level ≤ 10	183	11.4	0.44	75.8	0.53
Level > 10	89	9.3		75.0	
TME	191	11.6	0.2	74.2	0.9
PME	81	8.3		76.3	
Anastomotic leak	15	13	0.19	75.7	0.68
No anastomotic leak	257	8.1		71.6	
No resection of other organs	254	9.8	0.3	63.3	0.09
Resection of other organs	18	20		75.8	
Stage			0.01		< 0.001
0 or I	42	0		95.6	
II	98	7.8		78.3	
III	132	13.9		59.8	
Lymphovascular invasion			0.03		< 0.001
Yes	68	15.8		53	
No	204	9.7		81.4	
Perineural invasion			0.02		< 0.001
Yes	23	18.1		28.6	
No	243	10.4		79.7	
Adjuvant RT			0.36		0.02
Yes	16	10.3		56.6	
No	256	10.5		76.9	
Adjuvant chemotherapy			0.51		0.34
Yes	155	10.6		70.6	
No	117	10.1		78.7	
Distal margin			< 0.001		0.56
> 2 cm	183	6.4		77.4	
< 2 cm	89	18.2		72.3	

Moreover, favorable oncological outcomes in terms of a low local recurrence rate and a high survival rate are also important considerations. The surgical technique plays an important role to achieve these short-term and long-term goals. In the recent two decades, anterior resection with mesorectal excision has become the optimal treatment of rectal cancer.

Sharp meticulous dissection to keep the visceral layer of the pelvic fascia intact is important to avoid breach in the mesorectum, which is now considered an important cause for local recurrence. Heald et al. [8] as well as Enker et al. [9, 13] have reported low local recurrence rates using this technique in a sizable number of patients. The use of sharp perimesorectal dissection and the practice of “close shave” anterior resection have also increased the sphincter saving rate. Heald et al. reported that abdominoperineal resection was only required in 23% of patients with tumors in the

lower rectum [14]. In our institutional series of patients with tumor within 6 cm from the anal verge, abdominoperineal resection was performed in only 29.4% of the patients.

In the original series by Heald et al. [8], TME was performed in the patients with upper rectal cancer. Routine TME in rectal cancer at all levels is now considered unnecessary. Lopez-Kostner et al. [16] demonstrated that the outcomes of the treatment of upper rectal cancer in terms of local recurrence and survival were similar to those of sigmoid cancer and that TME was not necessary in upper rectal lesions.

The present report studied the differences between anterior resection with and without TME, using the approach of selective TME according to the level of the tumor. It revealed that TME was a more complex operation. The blood loss and duration of surgery in patients with TME

compared favorably with the series of Heald et al. [8, 17] and Enker et al. [13] as well as the report from the multi-center randomized trial by the Dutch Colorectal Cancer Group [18]. However, when compared with anterior resection with PME, operations with TME were associated with a longer operation time and more blood loss. There was also a tendency of a higher morbidity rate in patients with TME, although it did not reach statistical significance. Moreover, the median hospital stay was also longer in patients with TME.

Anastomotic leak is the important complication associated with TME. As the risk of anastomotic leakage depends on the level of the anastomosis [19–21], the incidence of leakage following TME is bound to be high because the colorectal or coloanal anastomosis is invariably performed at the level of the pelvic floor. Karanjia et al. [10] reported that the leakage rate following TME was 17%. In our study, we found that the leakage rate following TME with the anastomosis within 5 cm from the anal verge was 7.9%. We also found that the presence of a diversion stoma was an independent factor for a lower anastomotic leakage rate. In the present series, with the more liberal proximal diversion (68.3% in TME), the leakage rate following TME was 7.9%. However, in the patients with anterior resection with PME, the leakage rate was only 2.1% and diversion stomas were only created in 7.3% of patients. Surgery with TME was found to be an independent factor for anastomotic leakage. Thus, in view of the complexity of the operation, the higher incidence anastomotic leakage as well as increased likelihood of a diversion stoma, as shown by Rondelli et al. [12], the operation should be reserved for those who really need complete removal of the mesorectum, namely, those with the tumors at the mid or distal rectum.

Local recurrence is the most important measure of the oncologic outcome following rectal cancer surgery. Conventional rectal surgery, either by abdominoperineal resection or anterior resection, was associated with a high local recurrence rate [4–6]. The management of local recurrence is difficult and salvage surgery for local recurrence is rarely possible, especially in cases following TME.

There has been no uniformity in the reports of local recurrence following rectal cancer surgery. Differences in case selection and the definition of local recurrence as well as the way of calculation are seen in the literature. It is now generally accepted that the recurrence rate should include both local recurrence alone and those with distant metastasis. The local recurrence rate should be calculated with the life table method [22].

In our study, the actuarial 5-year local recurrence rate is 10.7%, and this is comparable to most series with TME [9, 17, 23–25]. This is achieved in a cohort of patients in whom 84% had advanced tumors (either transmural invasion and/or lymph node metastasis). Radiation therapy was only

given to 5.8% of patients with curative resection. The stage of the disease and the performance of peranal coloanal anastomosis were found to be associated with an increased risk of local recurrence in this group of patients. There was no difference in the local recurrence rate of tumor at the upper rectum and rectosigmoid when compared with those in the mid and distal rectum. The local recurrence rates in the patients with and without TME were also similar. Thus, anterior resection without TME is appropriate for those with cancer at the upper rectum and rectosigmoid. In other words, by performing TME in patients with mid and distal rectal cancers, the local recurrence rate approaches that of the rectal cancers situated more proximally.

Those tumors at the very distal rectum that necessitated peranal coloanal anastomosis were associated with a high recurrence rate. Peranal coloanal anastomosis was mostly done in the earlier period of the study with the tumor within 1–2 cm from the dentate line. The margin of resection was very close in these patients. After our analysis showed the poor results in patients with coloanal anastomosis as well as in those treated with abdominoperineal resection, preoperative chemoradiation was offered to these patients with very distal rectal cancer in case of transmural invasion or the presence of lymph node metastasis [15]. In the patients with anastomosis in the pelvis, the local recurrence rate was only 6.9%. Although Kapiteijn et al. [18] showed that preoperative short-course radiation in TME was associated with a lower 2-year local recurrence rate than the group without radiation, the routine administration of radiation to all patients with rectal cancer has not got universal acceptance. Most surgeons would still administer adjuvant therapy according to the results of their institutions [26]. With the low local recurrence rate in patients with anastomosis done in the pelvis, we do not feel routine radiation in this group of patients is justified.

The cancer-specific survival was 75.5%, which is comparable with others results [9, 23, 24]. Survival was related to the histologic characteristics of the tumor such as the stage and the presence of lymphovascular invasion. The level of the tumor and whether TME has been performed were not the determining factors for survival. Thus, tumor at the upper rectum and rectosigmoid can be treated without TME to yield similar survival. With the performance of TME for mid and distal rectal cancers, the local recurrence rate of rectal cancer approaches that of colon cancer. The survival would be dependent on the presence of distant metastasis. Zaheer et al. [27] showed that 30% of the recurrence occurred distantly. Whether survival following rectal cancer surgery could be improved with postoperative chemotherapy alone, as in colonic cancer, is yet to be seen. In this study, we could not demonstrate survival benefit in patients with adjuvant chemotherapy. However, a randomized controlled trial in this aspect is necessary to establish the role of postoperative chemotherapy.

Our series was before 2010. Our revised protocol in 2011; early-stage rectal cancer patients undergo surgery. Intermediate-stage patients undergo short-course preoperative radiotherapy followed by surgery in the next week. Advance-stage patients undergo conventional radiotherapy and chemotherapy followed by surgery.

Whether survival following rectal cancer surgery could be improved with postoperative chemotherapy alone, as in colonic cancer, is yet to be seen. A number of clinical trials are currently ongoing, and are expected to clarify the effectiveness of neoadjuvant treatment for marginally resectable colorectal cancer.

The difficult mountainous terrain of Nepal and poor socioeconomic condition of patients preclude the neoadjuvant and adjuvant therapy in our populations. These conditions affected the recurrence and survival figures in our series. Surgery was the preferred and most feasible modality of the treatment.

Conclusion

Anterior resection is a safe and preferred option for rectal cancer with low mortality and acceptable morbidity. Partial mesorectal excision for the cancer at the upper rectum or rectosigmoid yields similar results when compared with TME for mid and distal rectal cancers in terms of local recurrence and survival. *The recurrence rates can be further reduced by the use of neoadjuvant therapy given to the patients with low tumours, threatened CRM, and T3 or N1 disease.* However, TME is a more complex operation, which is associated with a longer operating time, more blood loss, longer hospital stay, a higher leakage rate, and a higher stoma rate. Thus, selective approach using TME for the mid and distal rectal cancers is a more appropriate and reasonable approach.

All authors approved the final version of the manuscript.

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