

ORIGINAL ARTICLE

SAFETY AND EFFICACY OF LOW ANTERIOR RESECTION WITH MESORECTAL EXCISION FOR RECTAL CANCER: A PROSPECTIVE STUDY

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Aim: This prospective study aimed to assess the operative results and oncological outcomes of total mesorectal excision (TME) and partial mesorectal excision (PME).

Methods: Resection of primary rectal and rectosigmoid cancer was performed in 34 patients from March 2005 to February 2007. There were 22 (65%) men and 12 (35%) women. The median age was 61 years (range, 30–81 years). Risk factors for anastomotic leakage, local recurrence, and survival of the patients were analyzed.

Results: The median level of the tumor from the anal verge was 9 cm (range, 6–20 cm). Curative resection was performed in 29 patients (85%). Five patients (15%) had palliative surgery because of unresectable distant metastasis ($n = 4$) or residual local disease ($n = 1$). Significantly longer median operating time, and a longer hospital stay were found in patients with TME. The overall operative mortality and morbidity rates were 12% and 32%, respectively. Anastomotic leak occurred in 6% and 3% of patients with TME and PME, respectively. The 2 year actuarial local recurrence rate was 9%. The 2-year cancer-specific survival was 82%.

Conclusions: Anterior resection is the safe and preferred option for rectal cancer with low mortality and acceptable morbidity.

Keywords: Colorectal carcinoma, surgical treatment, local recurrence.

INTRODUCTION

Total mesorectal excision has become accepted as the standard surgical technique in rectal cancer resection.⁽¹⁾ In patients with rectal cancer, the development of surgical technique led to the improvement of local control of the disease and patient survival.⁽²⁾ In the recent 2 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, and the allowance of a close distal margin has led to an increased incidence of sphincter-saving operations.⁽³⁾ Currently the gold standard surgical procedure combines proctectomy with mesorectal excision in a sphincter-saving operation.⁽⁴⁾ Sphincter-saving operations were introduced in the 1950s for the rectosigmoid tumors,⁽⁵⁾ then for the midrectal tumors,⁽⁶⁾ and more recently for some low rectal cancers.⁽⁷⁾ Moreover, safe anastomoses at the distal rectum or the anal canal have been made possible by the advances of

mechanical stapling devices and the development of the double stapling technique.^(8,9) 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.⁽¹⁰⁻¹²⁾ The importance of the complete removal of the lymphovascular tissue surrounding the rectum and a free circumferential margin have been recognized in the management of rectal cancer.⁽⁴⁾ By sharp meticulous perimesorectal dissection and total mesorectal excision (TME), Heald et al^(2,13) 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 TME. The anastomotic leakage rates are high in series of patients with TME.⁽¹⁴⁾ Moreover, the bowel function will also be adversely affected with a low colorectal or coloanal anastomosis.⁽¹⁵⁾ Thus, selective TME according to the level of tumor appears to be a reasonable approach. Risk factors for anastomotic leakage, local recurrence, and survival are analyzed with univariate and multivariate analysis.⁽¹⁶⁾

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 cancer in a high volume center.

PATIENTS AND METHODS

During the two year period from March 2005 to February 2007, 34 patients underwent resection of primary rectal and rectosigmoid cancer in the Department of Surgery, El-Minia University Hospital. An informed consent was taken from all patients. This study included all patients who underwent anterior resection with restoration of the bowel continuity. Patients with abdominoperineal resection, Hartmann's operation, and local excision 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, histologic results, and long-term outcomes were collected prospectively.

During the study period, the operations were performed by the staff of colorectal surgeons or under their supervision.

Definitions⁽¹⁶⁾: TME was defined as the excision of the rectum with the surrounding mesorectum enclosed by the visceral pelvic fascia at the level of the pelvic floor. Transection of the mesorectum at a higher level was considered PME.

Rectosigmoid was defined as the zone overlying the sacral promontory that begins with the divergence of the teniae

coli proximally and ends when they coalesce to form the longitudinal muscle of the rectum. Cancers within 12 cm from the anal verge were considered as mid and distal rectal cancer.

Resection was defined as curative if all the macroscopic disease could be removed at the end of surgery with negative histologic margin. In the presence of distant disease, surgery was still considered curative if the synchronous metastases were completely removed in the same setting or in subsequent operations.

Clinical anastomotic leak was considered to be present if any of the following features was observed: the presence of peritonitis caused by anastomotic dehiscence; the presence of feculent substances and gas from the pelvic drain; the presence of pelvic abscess with demonstration of anastomotic leak by rectal examination, sigmoidoscopy, or contrast study.

Operative mortality was defined as death that occurred during the hospital stay or within 30 days following the primary operation. Operative morbidities were defined as complications that contributed to prolonged hospital stay or led to additional procedures.

Local recurrence was defined as the presence of radiologically confirmed or histologically proven tumor in the pelvis within the field of surgery. Isolated local recurrences as well as the presence of both locoregional diseases and distant metastases were included. The time to local recurrence was the duration between time of surgical resection and the time of documentation of the recurrence.

The endpoints of the study were survival and the presence of recurrence during the last follow-up.

Surgical Techniques: Preoperative bowel preparation with polyethylene glycol electrolyte solution was given the day before surgery. Prophylactic intravenous antibiotics (ceftriaxone 2 gram with metranidazole 500 mg. I.V.E very 8 hours) were given at the induction of anesthesia. The patient was put in the Lloyd Davis position and a urethral catheter was inserted after anesthesia had been induced. The patients underwent laparotomy through a lower midline incision. The mobilization of the rectum was performed with sharp dissection under direct vision so that the visceral pelvic fascia, which enclosed the mesorectum, was kept intact. 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 cancer. For those tumors at upper rectum or rectosigmoid, transection of the rectum and mesorectum 4 to 5 cm below the lower border of the tumor was performed following sharp perimesorectal dissection.

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 pelvic nerve plexuses during the dissection. The hypogastric nerves were identified at the level of the sacral promontory and the main trunks would be preserved. By using nerve stimulator the lateral ligaments were divided with diathermy, with the retraction of the rectum to the contralateral side. In the anterior dissection, the peritoneum was incised 1 to 2 cm above the rectovaginal or rectovesical pouch. In a male patient, the seminal vesicles were separated from the anterior rectal wall, which was covered with fascia propria and the Denovillier's fascia. The Denovillier's fascia was incised close to the level of rectal transection. In a female patient, the anterior dissection separated the vagina from the anterior rectal wall. The rectum was mobilized down to the pelvic floor, and stapling anastomosis was constructed.

The rectal stump was irrigated with water when there was enough space distal to the tumor to allow the application of a pair of bowel clamps. A circular E.E.A stapler of the appropriate size was introduced transanally to perform the stapling anastomosis with the guidance of the abdominal surgeon.

For those patients with cancer of the upper rectum or rectosigmoid, rectal mobilization was also performed by sharp perimesorectal dissection. The rectum would be transected 4 to 5 cm distal to the lower border of the tumor. The mesorectum also would also be divided at that level perpendicular to the rectum. The operation was regarded as partial mesorectal excision (PME).

Adjuvant Therapy: Postoperative chemoradiation was offered only to those when the local clearance was in doubt. Preoperative chemoradiation was given to those with fixed T4 lesions.⁽¹⁶⁾

Follow-up Protocol: Patients were followed up at intervals of 2 to 3 months during the study period and one year thereafter. Follow-up was by history, physical 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 CT scan would be performed to determine whether salvage surgery could be performed.

Statistics: Categorical variables were compared with the X² or Fisher's exact test when appropriate. Continuous variable were presented as median values and were compared with the Mann-Whitney U test. Survival data were analyzed using Kaplan-Meier method, and factors

were compared with the log rank test. Multivariate analysis was performed with Cox proportional hazard model. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 34 patients underwent anterior resection for primary rectal or rectosigmoid cancer during the study period. There were 22 (65%) men and 12 (35%) women. The median age was 61 years (range, 30–81 years). The median level of the tumor from the anal verge was 9 cm (range, 6–20 cm). Dukes staging was B in 11 patients (32.3%), C in 18 patients (52.9%) and D in 5 patients (14.7%). Surgery with curative intent was performed in 29 patients (85%). Five patients (15%) had palliative surgery because of unresectable distant metastasis (n=4) or residual local disease (n=1).

Premorbid medical condition was present in 16 patients (47%) 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. Stapled anastomosis was performed in all patients. The mean operative time was 152 minutes (\pm 43 minutes). Bladder resection was performed in 1 patient.

Table 1. Comorbidities of patients with anterior resection.

Type of Comorbidity	No.	%
Cardiac	9	26
- Hypertension	6	
- Ischemic heart disease	2	
- Arrhythmia	1	
Diabetes Mellitus	5	15
Pulmonary disease	2	6

Two patients had positive margin on histology. One of them underwent abdominoperineal resection and the other patient lost during follow up.

TME was performed in 21 patients; while in other 13 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, 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.

Table 2. Comparison between patients with and without TME.

Demographic Data	TME (N=)	PME (N=)	P
Men: women	14: 7	8: 5	0.30
Median age (range)	59 (30-79)	66 (31-81)	<0.001
Median level of tumor from anal verge (range) (cm)	7 (6-12) *	15 (14-20)	<0.001
Median duration of operation (range) (min)	162 (62-420)*	134(50-320)	<0.001
Clinical leak (%)	3 (9%) *	1 (3%)	<0.001
Palliative resection (%)	0 (0%) *	4 (12%)	<0.001
Presence of medical illness (%)	7 (21%)	9 (26%)	0.002
Complications (%)	7 (21%)	4 (12%)	0.08
Postoperative mortality (%)	2 (6%)	2 (6%)	
Median days of hospital stay (range)	10 (4-32) *	8 (3-35)	<0.001

* p < 0.05 is significant when compared with PME.

The operative mortality was 12% (n=4). All these patients had pre-morbid medical diseases. The causes of death included pulmonary embolism (n=2), and pneumonia (n=2).

A total of 11 patients (32%) developed intraoperative or postoperative complications. The types of complications are shown in Table 3. Clinical anastomotic leakage occurred in 3 patients (9%). Comparison of risk factors for anastomotic leakage is shown in Table 4 showed that the use of T.M.E was associated with higher incidence of anastomotic leakage (3 patients with significant P. < 0.001) and the other factors were independent factors for a higher incidence of anastomotic leakage with the median follow-up of the surviving patients of 14.6 months (9-24 months), one patient (3%) developed local recurrence and two (6%) developed distant metastasis. The 2-year overall survival was 82% (n=28).

Table 3. Postoperative complications of patients with anterior resection.

Type of complications	No. of patients	%
Intraoperative complications	2	6%
- Twisting of colon	1	3%
- Severe bleeding in pelvis	1	3%
Cardiac	4	12%
DVT & pulmonary embolism	1	3%
Wound infection	1	3%
Anastomotic leak	3	9%

Table 4. Analysis of risk factors for anastomotic leak.

Variables	No.	No. with leak	P
Male	22	2	0.10 †
Female	12	1	
TME	21	3 *	<0.001
PME	13	0	
Age<60 yr	19	2	0.05 †
Age>60yr	15	1	
Medical illness	16	1	0.85 †
No medical illness	18	2	
Curative resection	29	1	0.07†
Palliative resection	5	2	

* P < 0.05 is significant when compared with PME.

† The male gender (p=0.1), medical illness (p=0.85) and the age of patients were independent factors for a higher incidence of anastomotic leakage.

DISCUSSION

The optimal treatment of rectal cancer should maximize sphincter preservation with low morbidity and mortality. 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 2 decades, anterior resection with mesorectal excision has become the optimal treatment of rectal cancer.⁽¹⁷⁾

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.⁽²⁾ as well as⁽¹³⁾ have reported low local recurrence rates using this technique in a sizable number of patients. The use of sharp perimesorectal dissection has also increased the sphincter saving rate and due to the lack of experience and lack of expertise in laparoscopic surgery and assisted laparoscopic colorectal resection respectively, the open technique was done in spite of the advantages of laparoscopy (less postoperative pain, ileus and hospitalization) faster return to normal activity and less wound infection but laparoscopic technique has a higher incidence of the positivity of circumferential resection margins (12%) than the open surgery (6%).⁽¹⁸⁾ Heald et al reported that abdominoperineal resection was only required in 23% of patients with tumors in the lower rectum.⁽¹⁹⁾ In our review, it is required only in one patient with positive margin on histology.

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 duration of surgery in patients with TME compared favorably with the series of⁽²⁾ and⁽²⁰⁾ as well as the report from the multicenter randomized trial by the Dutch Colorectal Cancer Group.⁽²¹⁾ However, when compared with anterior resection with PME, operations with TME were associated with a longer operation time. 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,^(22,23) the incidence of leakage following TME is bound to be high because the colorectal anastomosis is invariably performed at the level of the pelvic floor. Karanjia et al reported that the leakage rate following TME was 17%.⁽¹⁵⁾ In our study, we found that the leakage rate following TME was 9%. However, our patients with anterior resection and PME, there was no leakage reported.

Because of the local recurrence is the most important measure of the oncologic outcome following rectal cancer surgery. 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.⁽²⁴⁾

In our study, recurrence rate is 9% and this is comparable

to most series with TME.^(13,17,25-27) This is achieved in a cohort of patients in whom 84% had advanced tumors (either transmural invasion and/or lymph node metastasis).

The cancer-specific survival was 82%, which is comparable with others' results.^(13,25,26) 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 as well as whether TME has been performed were not determining factors for survival. Thus, tumor at upper rectum and rectosigmoid can be treated without TME to yield similar survival. The survival would be dependent on the presence of distant metastasis.

In conclusion anterior resection is the safe and preferred option for rectal cancer with low mortality and acceptable morbidity. Partial mesorectal excision for cancer at the upper rectum or rectosigmoid yields nearly has a similar results when compared with total mesorectal excision for mid and distal rectal cancer. However, total mesorectal excision is a more complex operation, which is associated with a longer operating time, longer hospital stay and a higher leakage rate. Thus, selective approach using total mesorectal excision for mid and distal rectal cancer is more appropriate and reasonable approach.

REFERENCES

1. Wolpin BM, Meyerhardt JA, Mamon HJ, Mayer RJ. Adjuvant treatment of colorectal cancer. *Cancer J clin.* 2007;57:168-85.
2. Heald RJ, Moran BJ, Ryall RD. Rectal cancer: the Basingstoke experience of total mesorectal excision. 1978-1997. *Arch Surg.* 1998;133:894-9.
3. Williams NS, Dixon MF, Johnston D. Reappraisal of the 5 centimetre rule of distal excision for carcinoma of the rectum: a study of distal intramural spread and of patients' survival. *Br J Surg.* 1983;70:150-4.
4. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery-the clue to pelvic recurrence? *Br J Surg.* 1982;69:613-6.
5. Goligher JC, Dukes CE, Bussey HJR. Local recurrence after sphincter saving excisions for carcinoma of the rectum and rectosigmoid. *Br J Surg.* 1951;39:199.
6. Localio SA, Eng K. Sphincter-saving operations for cancer of the rectum. *N Engl J Med.* 1979;300:1028-30.
7. Tytherleigh MG, Mortensen NJMcC. Options for sphincter preservation in surgery for low rectal cancer. *Br J Surg.* 2003;90:922-33.
8. Griffen FD, Knight CD Sr, Whitaker JM. The double stapling technique for low anterior resection: results, modifications, and observations. *Ann Surg.* 1990;211:745-51.

9. Knight CD, Griffen FD. An improved technique for low anterior resection of the rectum using the EEA stapler. *Surgery*. 1980;88:710-14.
10. Nymann T, Jess P, Christiansen J. Rate and treatment of pelvic recurrence after abdominoperineal resection and low anterior resection for rectal cancer. *Dis Colon Rectum*. 1995;38:799-802.
11. Pilipshen SJ, Heilweil M, Quan SH. Patterns of pelvic recurrence following definitive resections of rectal cancer. *Cancer*. 1984;53:1354-62.
12. Pahlman L, Glimelius B. Local recurrences after surgical treatment for rectal carcinoma. *Acta Chir Scand*. 1984;150:331-5.
13. Enker WE, Thaler HT, Cranor ML. Total mesorectal excision in the operative treatment of carcinoma of the rectum. *J Am Coll Surg*. 1995;181:335-46.
14. Karanjia ND, Corder AP, Bearn P. Leakage from stapled low anastomosis after total mesorectal excision for carcinoma of the rectum. *Br J Surg*. 1994;81:1224-6.
15. Karanjia ND, Schache DJ, Heald RJ. Function of the distal rectum after low anterior resection for carcinoma [see comments]. *Br J Surg*. 1992;79:114-16.
16. Law WL and Chu KW. Anterior Resection for Rectal Cancer With Mesorectal Excision. *Ann Surg*. 2004;240:260-8.
17. MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. *Lancet*. 1993;341:457-60.
18. Kumar M P S. Review of recent randomised clinical trials in surgery . *Recent advances in surgery*. 2007;30:183-95.
19. Heald RJ, Smedh RK, Kald A. Abdominoperineal excision of the rectum: an endangered operation [Norman Nigro Lectureship]. *Dis Colon Rectum*. 1997;40:747-51.
20. Enker WE, Merchant N, Cohen AM. Safety and efficacy of low anterior resection for rectal cancer: 681 consecutive cases from a specialty service. *Ann Surg*. 1999;230:544-52.
21. Kapiteijn E, Marijnen CA, Nagtegaal ID. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med*. 2001;345:638-46.
22. Vignali A, Fazio VW, Lavery IC. Factors associated with the occurrence of leaks in stapled rectal anastomoses: a review of 1,014 patients. *J Am Coll Surg*. 1997;185:105-13.
23. Pakkaste TE, Luukkonen PE, Jarvinen HJ. Anastomotic leakage after anterior resection of the rectum. *Eur J Surg*. 1994;160:293-7.
24. Dent OF, Chapuis PH, Bokey EL. Methodology and reporting in studies of local recurrence after curative excision of the rectum for cancer. *Br J Surg*. 2001;88:1476-80.
25. Martling AL, Holm T, Rutqvist LE. Effect of a surgical training programme on outcome of rectal cancer in the County of Stockholm. Stockholm Colorectal Cancer Study Group, Basingstoke Bowel Cancer Research Project. *Lancet*. 2000;356:93-6.
26. Arenas RB, Fichera A, Mhoon D. Total mesenteric excision in the surgical treatment of rectal cancer: a prospective study. *Arch Surg*. 1998;133:608-11.
27. Tocchi A, Mazzoni G, Lepre L. Total mesorectal excision and low rectal anastomosis for the treatment of rectal cancer and prevention of pelvic recurrences. *Arch Surg*. 2001;136:216-20.