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Total mesorectal excision for the treatment of rectal cancer

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Abstract

Introduction: In the surgical treatment of rectal cancer, a clear circumferential resection margin and distal resection margin should be obtained. The aim of this study was to determine the morbidity, mortality, survival outcome, and local failure after total mesorectal excision (TME) in the surgical treatment of rectal cancer.

Methods: This retrospective study was conducted on 101 patients treated for rectal cancer using low anterior resection (LAR), abdominoperinial resection (APR), or Hartmaan's technique. In all operative procedures, total mesorectal excisions (TMEs) were done. The patients were treated from November 2000 to April 2011 in the South Egypt Cancer Institute (SECI) of Assuit University (Egypt). Neo-adjuvant therapy was given to those patients with serosalin filtration, lymph node involvement, and sexual and urinary function impairment. Data were analyzed using IBM-SPSS version 21, and survival rates were estimated using the Kaplan-Meier method.

Results: One hundred one patients were evaluable (61 males, 40 females). Regarding the operative procedure used, it was: (APR), LAR, Hartmaan's technique in 15.8%, 71.3%, and 12.9% of patients, respectively. Operation-related mortality during the 30 days after surgery was 3%. The operations resulted in morbidity in 25% of the patients, anastomotic site leak in 5.9% of the patients, urinary dysfynction in 9.9% of the patients, and erectile dysfunction in 15.8% of the male patients. Regarding safety margin, the median distances were distal/radial margin, 23/12 mm, distal limit 7 cm. Median lymph nodes harvest 19 nodes. Primary tumor locations were anteriorly 23.8%, laterally 13.9%, posteriorly 38.6%, and circumferential 23.8%. Protective stoma 16.8%. Primary Tumor TNM classification (T1, T2, T3, and T4; 3, 28.7, 55.4, and 12.9%, respectively). Nodes Metastases (N0, N1, and N2; 57.4, 31.7, and 10.9%, respectively). TNM staging (I, II, III, and IV; 15.8, 29.7, 46.5, and 7.9%, respectively). Chemotherapy was administered to 67.3% of the patients. Radiotherapy (short course neoadjuvant, long course neoadjuvant, and adjuvant postoperative used in 33.7, 20.8, and 19.8% of patients, respectively). Survival 5-years CSS was 73% and 5-years RFS 71%. Mean operative time was 213 minutes. The average amount of intraoperative blood loss was 344 mL.

Conclusion: Total mesorectal excision (TME) represents the gold-standard technique in rectal cancer surgery. It is safe with neoadjuvent chemoradiotherapy and provides both maximal oncological efficiency (local control and long-term survival and maintenance of a good quality of life).

Keywords: mesorectal excision, rectal cancer, neoadjuvent chemoradiotherapy

1. Introduction

Rectal cancer is one of the most challenging cancers. It is the second cause of cancer-related deaths, incidence of local recurrence rates of 30% or greater in older series related to surgical technique (1). Surgery for rectal cancer with abdominoperineal resection (APR) or low anterior resection (LAR) has been the mainstay of surgical therapy for rectal cancer since the 1970s, and it is associated with relatively high morbidity and mortality. In 1979, the TME

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technique was introduced by Healed by sharp dissection under direct vision of logically determined planes; dividing the visceral fascia surrounding the mesorectum from the pelvic parietal fascia overlying the pelvic floor (2). Sphincter saving surgery and "nerve sparing surgery" resulted in the decrease of the rate of sexual and urinary dysfunctions with improved local recurrence rate that decreased following conventional surgery compared with 4% to 9% following TME with a 25-30% absolute increase in the overall survival and cancer-specific survival in the TME group (3). Currently, a multi-disciplinary approach is used for the treatment of rectal cancer, and it includes surgery, chemotherapy, and radiotherapy (4, 5, 6). Also, preoperative CRT may result in tumor downstaging, leading to significant reduction in the size of the primary tumor, reduction in the penetration depth, and possible sterilization of the lymph nodes (6). These changes can lead to improved local control and improved down-staging (7). Preoperative radiotherapy is known to be very effective, and it can shrink tumors significantly (9). According to the Swedish concept (25 Gy/5 fx/1 week), short courses of preoperative radiotherapy are used often in patients who have resectable rectal cancer because the treatment time is brief and surgery can be performed immediately (8). Poor tumor characteristics also are associated with a higher incidence of lymph node metastasis, and failure may occur in the mesorectal lymph nodes (9). These poor tumor characteristics can include invasion of the blood vessels and lymphatic system, poor differentiation, and the occurrence of mucinous components. Preoperative magnetic resonance imaging (MRI) can define the mesorectal fascia and its proximity to the tumor (10). The accuracy of endorectal ultrasound (ERUS) in detecting lymph node metastasis ranges from 60 to 80% (1). Metastases to lymph nodes in the mesorectum more than 5 cm distal to the cancer have not been observed in the pathologic examination of mesorectal specimens of upper rectal cancer (11). The relatively common consequences of TME include anastomotic leak, wound infection, urinary and sexual dysfunctions, and frequent defecation (12).

2. Material and Methods

This retrospective study analyzed the data of 101 patients with rectal cancer treated with total mesorectal excision (TME) in the period from January 2000 to January 2011 in the South Egypt Cancer Institute (SECI) of Assuit University (Egypt). Extensive pretreatment evaluations were performed for all patients. These evaluations included a complete history; physical examination; complete blood count, liver, and kidney function profile; serum carcinoembryonic antigen (CEA); colonoscopy, chest X-ray; pelviabdominal sonar; endorectal ultrasound; and computed tomography (CT)/ (MRI) of the pelvis and the abdomen. During the first two years after surgery, the patients were followed at 3-month intervals biannually for five years, and they were followed annually after five years. Every year, serum CEA levels were measured, and physical examinations, chest X-rays, colonoscopies, and abdomino-pelvic CTs were performed.

Based on pelvic anatomy, sharp pelvic dissection was used to remove the rectal cancer and the surrounding mesorectum, including lymph nodes. Also, at the superior rectal vessels overlying the sacral promontory, pelvic autonomic nerve preservation was initiated, and the mobilization was conducted along the aorta. This was done in order to visualize the sympathetic nerve fibers and isolate the inferior mesenteric artery (IMA) at its origin. The cleavage plane between the presacral fascia and the visceral layer that underlines the mesorectumis was identified and divided at the level of the sacral promontory pubo coccygeus muscle. S2-S4 sacral splanchnic nerves should be identified and protected in patients with ultra-low anastomosis and those at high risk, a covering ileostomy sometimes done closed after 12 weeks. Neo-adjuvant therapy was given to those patients with serosal infiltration and/or lymph node involvement. Surgery was performed six weeks after a long, preoperative course of chemoradiation (45-50.4 Gy) and after 1 week of short course radiotherapy (25 Gy/5fx over one week). Sexual function impairment was defined as the impossibility of achieving an erection or ejaculation after surgery. Local recurrence was defined as any recurrence diagnosed or suspected in the pelvis (tumor bed, pelvic nodes, anastomosis, drain site, or perineum) occurring alone or with other sites of recurrence. All analyses were done using IBM-SPSS version 21. Numerical values were expressed as means or medians and standard deviation (SD) or range. Survival rates were estimated using the Kaplan-Meier method.

3. Results

3.1. General findings

Among the 101 patients, 61 were males (60.4%), and 40 were females (39.6%). The median age was 61 (23-89). The median follow-up period was 63 months (range: 14-107 months). Mean operative time was 213 minutes (range 98-453 minutes). Mean blood loss was 344.64 mL (range 100-1200 mL). The mean postoperative stay was 11 days (range 5–23 days) (Table 1).

Table 1. Age distribution and operative time and blood loss

Variables	n	Mean	SD	Median	Minimum	Maximum
Age	101	60.58	14.409	61	23	89
Follow up (month)	101	60.12	23.397	63	14	107
Blood loss (ml)	101	344.64	344.407	200	100	1200
Operation time (min)	101	213.35	75.492	213	98	453

3.2. Tumor characteristics

The mean distal margin, assessed in fresh specimens without traction, was 23.20 mm (range 20-45 mm). Mean radial margin 12.63 mm (range 1-30 mm). The distal limit of rectal neoplasm was, on average, 7 cm (range 2-20 cm) from the anal verge. The surgical specimen was 35.66 cm in length (range 14-45 cm), and the mean tumor size was 4.5 × 3 cm. The mean number of lymph nodes harvested was 19 nodes (range 12-30 nodes). Regarding the tumor's location, the bulk of the tumor was located anteriorly in 14 patients (23.8%), laterally in 14 patients (13.9%), posteriorly in 39 patients (38.6%), and circumferentially in 24 patients (23.8%). Seventeen patients (16.8%) had protective stoma. Regarding the tumor differentiation, they were well (17.8%), moderate (65.3%), and poor grades (16.8%). Regarding the tumor invasion, they were T1 (3%), T2 (28.7%), T3 (55.4%), and T4 (12.9%). Regarding the nodes metastases, they were N0 (57.4%), N1 (31.7%), and N2 (10.9%). Regarding the TNM stage, 15.8%, 29.7%, 46.5%, and 7.9% were in stages I, II, III, and IV, respectively.

3.3. Treatment and outcome

Operation types used were abdominoperineal resections (APR), low anterior resections (LAR), and Hartmaan in 15.8%, 71.3%, and 12.9% of patients, respectively. The 30-day mortality/morbidity rates were 3% and 25%, including anastomotic leaks in six patients (5.9%), wound infections in eight patients (7.9%), adhesive intestinal obstruction (ileus) in six patients (5.95%), DVT in three patients (3%), and cardiopulmonary complication in four patients (4%). Late complications were seen in 30% of the patients, including urinary dysfunction in 10 patients (9.9%), sexual dysfunction in 16 patients (15.8%), hernia in four patients (4%), constipation in six patients (5.9%), and incontinence in two patients (2%). Regarding the chemotherapy and radiotherapy, chemotherapy was used in 68 patients (67.3%) and radiotherapy (short, long, adjuvant) was used in 33.7, 20.8, and 19.8% of patients, respectively. The five-year cumulative local recurrence rate was 6.9%. Nineteen patients had distant metastasis (18.8%), both local and distant failures occurred in three patients (3%). The liver was the most common site of metastasis (40%), followed by the lung (30%), peritoneal seedling (20%), and the brain (10%). The median cancer-specific survival was 65 months (range 18-110 months). The median recurrence-free survival was 63 months (range 3-107 months). Five-year survival CSS was 73% and 5-year survival RFS was 71% (Figure 1).

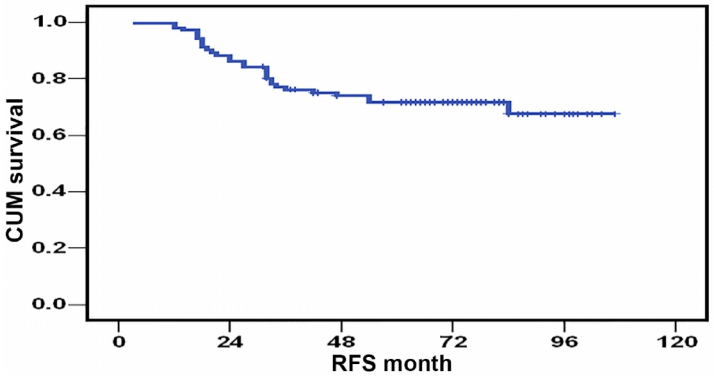

Figure 1. Progression free survival

4. Discussion

Rectal cancer is more common in men (female:male ratio of 1:1.3) (3). Mean length of hospital stay was seven days (range 2 to 25 days) (13). Blood transfusion has been identified previously as the most important factor in post-operative complications. It is very important to avoid administering homologous blood to the patient with rectal cancer who underwent curative surgery, because of the increased risk of post-operative complications (14). Mean operative time was 212 minutes (range 120 to 535 minutes) (15-18). The mean blood-loss volumes during surgery

for rectal cancer patients was 451 mL (range 30 to 1,200 mL) (15, 16, 19). The mean operative time was 213 minutes (range 98-453 minutes). The mean blood loss was 344.64 mL (range 100-1200 mL). The mean post-operative stay was 11days (range 5–23 days). Overall surgical morbidity may range from 22% to 45% sexual and urinary dysfunctions, related to avulsion or direct injury to pelvic autonomic nerves. Despite the autonomic nerve-preserving techniques in TME, bladder and sexual dysfunction, such as retrograde ejaculation, can be up to 12% and 35%, preservation of both hypogastric and pelvic nerves achieved 98% excellent or good urinary function, 68% ejaculation, and 90% erection (20). Total mesorectal excision technique described by RJ Heald support us to preserve the autonomic nerves and therefore to reduce the incidence of urinary (from 10-30% to 0-5%) and sexual dysfunction (from 40-60% to 10-35%) (20). The operative mortality (30-day) was 5% (6). In our study, the 30-day mortality/morbidity were 3%/25%, urinary dysfunction in 9.9%, and sexual dysfunction in 15.8%. Anastomotic leak is the important complication associated with TME. As the risk of anastomotic leakage depends on the level of the anastomosis. Karanjia et al. reported that the leakage rate following TME was 2.7% -17 % (1, 19, 22). Protective ileostomy was performed in cases with anastomoses lower than 4 to 5 cm from the anal verge (14). Morbidity associated with protective stoma and complications of stoma closure were negligible. However, the value of a protective stoma has been the subject of controversy (23). In our study, anastomotic leaks occurred in 5.9%, and protective stoma in 16.8%. A circumferential Resection Margin (CRM) was found in 29.6% of all patients, 44% for anterior, 21% for lateral, 23% for posterior, and 17% for (semi) circular tumor location (P = 0.0001) (22). In our study, tumor location was anteriorly in 23.8%, laterally in 13.9%, posteriorly in 38.6%, and circumferential in 23.8%. With the introduction of the TME technique, a decline in the ratio of abdominoperineal resections (APR) compared with low anterior resections LAR also increased the sphincter saving rate. Heald et al. reported that abdominoperineal resection was only required in a small part of them (19, 24). In our study, abdominoperineal resections (APR), low anterior resections LAR, Hartmaan were 15.8, 71.3, and 12.9%, respectively. Lymph node involvement is an important adverse prognostic factor in patients with rectal cancer (25). The minimum number of the median number of lymph nodes harvested during TME was 17 (range 0 to 63) (18, 21). In our study, the mean number of lymph nodes harvested was 19 nodes (range 12-30 nodes).

The most important predictive factor for local recurrence after rectal cancer excision (26) is the involvement of the radial margin. Local recurrence rates average 30% after conventional surgery, and they vary considerably between institutions from 15 to 45% (27). Since TME surgery was introduced, recurrence rates have decreased to as low as 5 to 8% (28). In the PRT-TME group, the actuarial rate of local recurrence was 4.1%, and it was 11.5% in the TME group. (29). Other significant data included distant metastasis (12.1%), local recurrence (7.8%), and both local and distant failures (3.5%). The most common site of metastasis was the liver (39.1%), followed by the lungs at (30.4%) (31); however, in our study, the local recurrence was 6.9%, whereas distant metastasis was 18.8%, and both local and distant failures were 3%. The most common site of metastasis was the liver (40%), followed by the lungs (30%), peritoneal seedling (20%), and the brain (10%). The volume of tumors can be reduced by preoperative radiochemotherapy, which also induces downstaging, facilitates surgical resection (10, 27), and prevents the distal intramural spread of the tumor, thereby decreasing the surgical distal margin and perirectal lymph node. The technique that allows us to obtain sufficient distal margin in all patients is called transanal intersphincteric resection. This technique also can be used with patients who have lesions on the internal anal sphincter (26, 32), and it has produced 58% five-year survival in the irradiated group as opposed to 48% in the non-irradiated group (32). A short-term regimen of high-dose preoperative radiotherapy (5X5 Gy) resulted in reducing local recurrence rates compared to surgery alone (27% vs. 11%, respectively; p = 0.001). In addition, it also improved the five-year survival rate (58% vs. 48%, respectively (p = 0.004) (15, 28). Paty et al. (20) and Vernava and Moran (21) have indicated that there were no differences in survival or recurrence rates with a distal margin of < 2 cm as opposed to a margin < 2 cm (1). Since the distal intramural spread of cancer rarely is >1 cm (1) in the distal section, a margin of 1-2 cm is now deemed to be adequate for ultra-low rectal cancer in most cases. The mean distal margin was 23.20 mm in our study (range 20-45 mm). How large the radial margin should be is not known, but, generally, it is accepted that a clear radial margin is necessary for curative surgery, which gives TME an advantage over other surgical procedures. In a recent study, it was found that a radial margin of 2 mm was associated with a 16% local recurrence risk, whereas it was only 5.8% in patients with a larger radial margin. There is an increased risk of distant metastasis (37.6 versus 12.7%) and shorter overall survival among patients whose margins were 1 mm (1). The location of the tumors was defined according to the distance from the anal verge, as determined by colonoscopy: lower rectum (0 to 7 cm), middle (7 cm, range 1 to 11 cm), and upper rectum (11 cm, range 1 to 17 cm). Thirty-five percent of tumors occur in the distal rectum, 50 % in midrectum, and 15 % in proximal rectum (33). TME is variably combined with radiation and chemotherapy for locally advanced tumors, and surgery alone is indicated for stage I tumors (2, 34). The cancer-specific survival rate is 74.5% (18). The five-year, tumor-free survival rate was

69.7 - 78% (20, 35) in our study. The five-year cancer-specific survival rate was 73%, and that for five -year RFS was 71%. These results were comparable to those of other researchers.

5. Conclusions

Meticulous sharp pelvic dissection under direct vision should be used to remove the mesorectum an intact unit. This approach, in combination with modality therapy, has been shown to improve local control, and it also increases the overall cancer-related survival rate with an acceptable morbidity.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

Both authors contributed to this project and article equally. All authors read and approved the final manuscript.

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