Journal of the Egyptian Nat. Cancer Inst., Vol. 15, No. 4, December: 342-348, 2003

Surgical Management for Loco-Regional Recurrence in Rectal Cancer

MAHMOUD BASSIOUNY, M.D.; ASHRAF S. ZAGHLOUL, M.D.; ISMAIL MORAD, M.D. and AHMED SHOUKRY, M.D.*

The Departments of Surgical Oncology and Radio-Diagnosis, NCI, Cairo University.*

ABSTRACT

Purpose: The aim of this study was to determine the morbidity, survival and patterns of failure for locally recurrent rectal cancer patients who underwent further surgery with the hope of cure. Evaluation of the accuracy of radiolological imaging in early detection of local recurrence was a second aim.

Methods: Between May 1999 and December 2002, 30 patients with a preoperative diagnosis of recurrent rectal cancer underwent additional surgery at National Cancer Institute, Cairo University. Patients with isolated locoregional recurrence, fit for surgery and with detailed record of the previous treatment of their initial tumor were included in the study. Factors assessed included type of original operation, time interval between operation for primary tumor and recurrence, symptom status, types of reoperations for recurrence and adjuvant therapy.

Results: There were 2 postoperative mortalities. Complications were observed in 17 patients and infection was the most common. Only 4 patients required surgical intervention. Twenty-two patients had no gross/microscopic residual disease at tumor margins after reoperation. Twelve patients developed second tumor recurrence. Our median disease free survival was 23.5 months.

Conclusion: Complete excision of locally recurrent rectal cancer with curative intent was feasible. It provided a significant number of patients with long-term survival. It offered an excellent palliation for the remaining cases. Extended surgery can be accomplished safely in selected patients.

Key Words: *Rectal cancer - Recurrence of rectal cancer.*

INTRODUCTION

Carcinoma of the rectum continues as a significant worldwide problem. Surgical resection remains the mainstay of treatment for operable rectal cancer and provides a good local control in a number of patients. Surgical approach aims at excision of the primary tumor with adequate margin along with the mesorectum, restore the continuity of the bowel whenever possible and to avoid complications. The most important goal in the treatment of rectal cancer next to cure is to limit the rate of local recurrence [1]. Despite adequate surgery, locoregional recurrences of rectal carcinoma have been reported from 7% to 33% with a median of 14% [2]. Without treatment, loco-regional recurrence (LRR) in rectal carcinoma generally heralds a very poor prognosis with a median survival periods ranging from 3.5 to 13 months, and five years survival from 0 to 5% [3]. Because of this poor natural history together with a major disability and impaired performance status that occurs in this situation, eventually most patients receive some kind of therapy. Adjuvant radiation therapy and chemotherapy have decreased the rate of LRR [4], but once LRR has developed these treatment modalities shows short-term relieve of symptoms and no curative potential with few if any long-term survivors [5].

Surgical resection of recurrent rectal tumors is a valid option for certain patients; however, the results of surgical resection differ widely from one series to another [6]. This difference may be explained by differences in operating techniques and selection criteria [7].

The aim of this work is to evaluate accuracy of radiolological imaging in determining the exact extent of loco-regional recurrence and to explain the role of surgical resection in control of local recurrence and its impact on patient's survival and quality of life.

PATIENTS AND METHODS

A total of 80 patients with signs and symptoms of local tumor recurrence after previous surgical resection of rectal cancers were recruited from the outpatient clinic, National Cancer Institute during the period from 1999 to 2002. Only 30 patients with isolated loco-regional tumor recurrence fulfilled the criteria of eligibility to be enrolled in the study as shown in Table (1). These criteria included absence of distant metastasis, fitness for surgery and availability of detailed previous treatment history. The other fifty cases were excluded as two cases refused surgery, 15 cases proved negative for malignant recurrence (8 cases pre-operatively and 7cases after exploration). Twenty cases had L.R.R. in addition to distant metastases and 13 cases proved inoperable after exploration.

The extent of local tumor recurrence was assessed with CT abdomen and pelvis and MRI of the pelvis. Tissue diagnosis of local recurrence was obtained either with colonoscopy in case of anastomotic recurrence or by means of CT guided biopsy in isolated pelvic recurrence. Fine needle aspiration cytology (FNAC) was used in accessible perineal recurrence. Local recurrence is classified as axial (anastomotic, tumor bed, pelvic and perineal), anterior and posterior recurrences.

Surgical resection is defined as limited or conventional if no adjacent organ was excised and extended resection if at least one of the surrounding organs including the sacrum was partly or completely removed. In this work 20 cases underwent extended resection while the remaining 10 cases had conventional procedures. Follow up after surgical resection was carried out periodically every 2 months by means of clinical examination, tumor markers (CEA and CA 19.9), CT scan, MRI and colonoscopy in selected patients. Twelve patients (40%) developed second local tumor recurrences. Salvage surgery was possible in only two patients.

RESULTS

Characteristics of the 30 patients are shown in Table (2). There were 18 women and 12 men. The mean age was 45±11.58 years. The time interval between primary surgery and detection of local recurrence ranged from 8 to 72 months with a mean of 24.5 months. Histo-pathological studies of surgical specimens after initial surgeries are shown in Table (1). Surgical margin were negative in all cases, 87% revealed adenocarcinoma, 90% of the patients were grade 2 and 40% had positive nodes. Tumors were staged according to Modified Astler-Coller staging as illustrated in Table (2). Sixteen patients had both adjuvant chemotherapy and radiation therapy (12 cases were C_1 or $_2$ and 4 cases were B_3); six patients (B_2) had chemotherapy only, while 8 patients received no adjuvant treatment (2 cases were A and 6 cases were B_1).

No significant correlation was found between adjuvant therapy after initial surgery and the frequency, time and pattern of recurrence.

The leading symptoms of local recurrence were bleeding per rectum (47%), pelvic pain (40%), perineal pain (20%), pelvic mass (17%) and both rectal and posterior vaginal wall mass (10%). Tumor markers were elevated in 30% of cases. Only one third of the patients have preoperative histological diagnosis of the tumor recurrence. Radiological imaging helped in exclusion of 27 cases (7 patients had no MRI evidence of LRR and 20 patients had metastatic disease with LRR). However, it showed false +ve results of 14% (7 out of 50 explored cases proved negative for recurrence) and failed to diagnose extensive and metastatic disease in 26% of patients (13 out of 50). The success of radiological imaging in the delineation of the site and extent of local recurrence was only accurate in 57% of the cases (17 out of 30).

The relation of the site of local recurrence to the surgical procedure is outlined in Table (3). Posterior recurrence was the most prevalent type (posterior pelvic excentration "PPE" 7 and abdominosacral resection "ASR" 5) followed by axial recurrence (5 abdominoperineal resection "APR", 3 low anterior resection "LAR" and 2 perineal excision). There were 2 postoperative mortalities. The cause of death in the first patients was due to the occurance of disseminated intravascular coagulopathy (DIC) from massive blood transfusion, while the other patient developed hepato-renal failure from irreversible shock. Infection was the most common complication (perineal 43% and sacral 23%), (Table 4). Four patients developed en-

terocutaneous fistula, two of them occurred after radiation therapy, one through the sacral wound after ASR and the other through the perineum after PPE. Those two patients died from malnutrition, while spontaneous closure of the fistula occurred in the remaining two cases. Urinary leakage occurred in two patients and was managed conservatively with insertion of Foley's catheters. Fourteen out of the 30 resectable patients received both adjuvant radiation and chemotherapy. However, thirteen patients required pain control by means of fentanyl patches and MST (morphin sulphate tablets).

The median disease-free survival was 23.5 months (range 23-38). The 3 years disease free survival (DFS) was 43% and the actuarial 5 years DFS is 23%. Surgical resection was considered curative (Ro) in 22 patients as the histopathology showed negative margins. In those who had close margins (6 patients), surgical resection was considered palliative (R1-2) [8]. The outcome of surgical resection is summarized in Table (5). Twelve patients (40%) developed second local tumor recurrences. Salvage surgery was tried for all patients; however, adequate surgical resection was possible in only two patients. The first case was subjected to excision of nodal recurrence, hepatic focal lesion and stomal recurrence and refashioning of the colostomy. In the other case, excision of stomal recurrence and refashioning of colostomy and atypical excision of hepatic focal lesion were performed.

DISCUSSION

When LRR is diagnosed early, there is a greater probability of being able to proceed with curative re-resection [9]. Surgical resection not only provides the best opportunity for cure, but also results in excellent palliation [10]. On the other hand when recurrence is large and palpable or multiple it is mostly accompanied with systemic disease as proved by the work of Welch and Donaldson [11]. This was the main cause of exclusion in 2/3rds of the studied cases (33/50) in the present study. These cases proved inoperable due to extensive aortic node metastases, lateral or deep pelvic sidewall extension, peritoneal carcinomatosis, extensive liver deposits and bone metastases.

Table (1): Details of the studied cases, (n = 80).

Studied Cases	No.	Cause
1- Cases excluded without surgical exploration, (n=30).	2	Refused surgery.
	8	Negative for malignancy by MRI & histopathology.
	20	Additional distant metastasis to LRR.
2- Cases subjected to surgical exploration, (n=50):		
Subjected to resection for LRR.	30	With isolated LRR.
Excluded after exploration.	7	Negative for malignancy.
	13	Additional distant metastasis with extensive para-aortic, peritoneal and liver metastasis on exploration.

Table 2: Patients' characteristics, (n= 30).

Character	No.
Sex:	
Male	12
Female	18
Initial surgery:	
LAR	13
APR	10
Hartman's operation	3
Abdomino-anal pull through	3
PEE	1
Time of recurrence:	
During 1st year	12 (40.0%)
During 2nd year	10 (33.3%)
During 3rd year	8 (26.7%)
Pathology of initial surgery:	
Grade: I	2 (6.7%)
II	27 (90.0%)
III	1 (3.3%)
Surgical margin:	
+ve	0
-ve	30 (100%)
Lymph nodes:	
+ve	12 (40.0%)
-ve	18 (60.0%)
Pathological type:	
Adenocarcinoma	26 (86.7%)
Mucoid carcinoma	2 (6.7%)
Leiyomyosarcoma	2 (6.7%)
Modified Astler-Coller Stage:	
A	2 (6.6%)
B_1	6 (20.0%)
B_2	6 (20.0%)
B_3	4 (13.4%)
C_1 or C_2	12 (40.0%)

LAR: Low anterior resection.
APR: Abdominoperineal resection.
PPE: Posterior pelvic excentration.

Table (3): Correlation of site of local recurrence and type of surgical procedure, (n = 30).

Site of local recurrence	No.	APR	LAR	PPE	Perineal excision	ASR	ASR+ TPE	APR+ P. cyst.	LAR+ P. cyst.	PPE+ P. cyst.
1- Axial recurrence (anastomotic, tumor bed, pelvic, perineal).	10	5	3		2					
2- Posterior recurrence.	12			7		5				
3- Axial and anterior recurrence.	5							3	2	
4- Posterior and anterior recurrence.	3						2			1

LAR: Low anterior resection. PPE: Posterior pelvic exenteration. TPE : Total pelvic exentration.
APR: Abdominoperineal resection. ASR: Abdominosacral resection. P.Cyst: Partial cystectomy.

Table (4): Postoperative complications, (n= 28).

Complication	No.	%
Perineal wound infection	13	43.3
Sacral wound infection	7	23.3
Perineal fistula	4	13.3
Urinary leak	3	10
Retracted colostomy	2	6.7
Abdominal wound infection	2	6.7
Hemorrhage	2	6.7
Peritonitis	1	3.3
Recto-vaginal fistula	1	3.3
Incisional hernia	1	3.3

Complications had occurred in 17 patients.

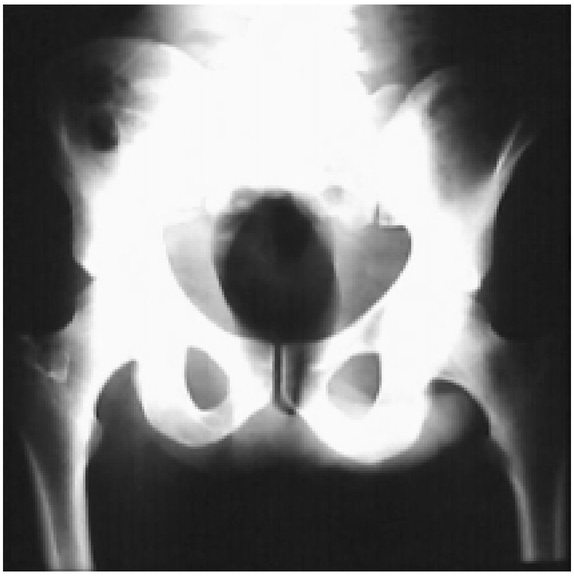

Fig. (1): X-ray pelvis (PA view) after sacrectomy.

Table (5): The outcome of surgical resection, (n = 28).

Status	DOD	LNED	DNED	LWD
No	5	13	5	5
Ro	2	11	4	3
R_{1-2}	3	2	1	2
%	23.3	43.5	16.7	16.7

DOD = Died of disease.
LNED = Living with no evidence of disease.
DNED = Died with no evidence of disease.
LWD = Living with disease.
Ro = Curative resection.
R_{1-2} = Palliative resection.

Fig. (2): Ligation of the sacral dural sac after its dissection in sacrectomy.

In this study, about two thirds of the patients were below the age of fifty. Forty percent of the recurrence developed in the first year, 33% in the second year and 27% of the patients developed the local recurrence between 3 and 5 years follow up. This matched with the results of Abulafi & Williams [12] and Suzuki et al [7]. All patients in the present study presented with symptoms such as bleeding per rectum (47%) and pelvic pain (40%). These results differed from the previously reported findings of the Stockholm rectal cancer trial where pain was the dominant symptoms (62%) followed by disturbances in micturition (26%) [13]. In that trial, 17% of the patients who underwent re-operation were able to have their tumor completely removed. This suggests that existence of pain indicates an advanced local disease.

In spite of having negative margins at the initial surgery they developed LRR, apart from the stage and grade of the tumor. This emphasis the importance of radial margins, which were not examined properly in the pathological studies of the initial surgery. Quirke et al. [14] showed that the radial resection margin was a critical component in local recurrence of rectal cancer. Based on the premise that the extrarectal spread of tumor occurs in a centrifugal pattern and often remains confined to the mesorectum, even in stage three disease, Heald [15] developed the total mesorectal excision (TME). Using TME, without adjuvant radiation, he [16] reported a local recurrence rate of 4% at 10 years and among high-risk cases (stage B2 and C) he reported 5% at 5 years. Heald's impressive results have been reproduced by Enker et al. [17]. All these data, confirm that LRR in rectal cancer can be prevented by an effective primary surgery with TME and adequate radial resection margin, which may include bladder, perineum, sacrum and uterus in female patients.

Advanced radiological imaging has helped in better selection of patients with recurrent rectal cancer amenable for surgery. Consequently 27 patients were saved unnecessary surgery in this study; however, it remains impossible to predict with certainty before operation. Comparing the site of local recurrence by preoperative radiologic imaging and by surgical exploration, CT scan was extremely accurate in determining the need to perform sacrectomy. However, the accuracy of CT scan, MRI and U/S were 57%, which was unsatisfactory in diagnosis of early local recurrence and its location.

Ten patients (33.3%) had axial recurrences, 40% posterior and 26.6% had combined multiple sites recurrence. All the patients having multiple sites recurrence failed to achieve complete recurrence eradication. This distribution was different from that reported by Bagatzounis et al. [18] who found that local recurrence was mostly situated in the presacral space at the level of S4, S5 and the coccyx regardless of operation method and the location of the primary tumor.

In this series, twenty patients required extended resections with either resection of the sacrum, the urinary bladder or the female reproductive system. Of them, seven patients were treated with abdominosacral resection (ASR) with or without total pelvic exentration TPE (5 ASR and 2 ASR with TPE). The mean operative time was 6.35 hours and the mean blood loss was 3.2 liters. There were two postoperative mortalities. These results were better than that of Takagi et al. [19] who performed composite resection for 7 patients with a mean operative time of 8.8 hours and mean blood loss of 6.2 liters. Touran et al. [20] in their series of 20 sacral resections, twelve of them were recurrent recto anal cancer, the median blood loss was 1.4 liters and median operating time was 5 hours.

The morbidity rate varies with the magnitude of surgery; in the present study there were 2 postoperative mortalities among 30 patients (6.7%), all related to massive blood loss in conjunction with sacrectomy. This matched with that reported by Wanebo et al. [21] where postoperative mortality rate reached 9% and that of Temple and Seatler [13] who reported mortality rate of 10%. In an attempt to decrease the post operative mortality, Wanebo et al. [22] adopted staged operation in patients eligible for sacrectomy. Blood loss and morbidity could be minimized by ligation of both internal iliac vessels during the first stage procedure, three days before sacrectomy.

Most of the complications occurred early in the study in 17 patients out of 28 with a rate of 60.7%. Four patients required surgical interference to correct retracted colostomy in two pa-

tients, deal with reactionary hemorrhage in one patient, and manage peritonitis in the last patient. We have found that complications were common with sacral resection specially when performed in one stage. In their series, Temple and Seatler [13] reported serious morbidities in over half of their patients.

Negative margins of resection were achieved in 73.3% in the present series (22 out of 30 cases). Twelve patients developed second tumor recurrences. The cumulative survival for all patients at 12 months was 71.7%, while the cumulative survival for patients who underwent curative resection of recurrences at 12 months was 70.5% and cumulative survival for patients who underwent palliative resections was 62.5%. Three years DFS was 43% and the median disease free survival (DFS) was 23.5 months. This matched with the results of the other investigators. Wanebo et al. [22] reported median DFS of 24 months. On the other hand, Wiggers et al. [23] reported DFS of 8 months and high incidence of second recurrence (59%).

The conclusion of this study is that an adequate surgical resection can offer the patient a good opportunity for local control of the disease and ultimately a cure. If cure cannot be achieved, an excellent palliation is obtained. Refinement in radiological techniques and the use of other investigative modalities as positron emission tomography PET may help better identification and early detection of LRR of rectal cancer.

REFERENCES

1- Ross A., Rusnak C., Weinerman B., Kuechler P., Hayashi A., McLachlan G., et al.: Recurrences and survival after surgical management of rectal cancer. Am. J. Surg. 1999, 177 (5): 392-95.

2- Avradopoulos K.A., Vezeridis M.P. and Wanebo H.J.: Pelvic exentration for recurrent rectal cancer. Adv. Surg. 1996, 29: 215-33.

3- Mc Dermott F.T., Pihl E.S., Johnson W.R. and Price A.B.: Local recurrence after potentially curative resection for rectal cancer in a series of 1008 patients. Br. J. Surg. January, Vol. 1985, 72: 34- 37.

4- Pahlman L. and Glimelius B.: Pre- or postoperative radiotherapy in rectal and rectosigmoid carcinoma: report from a randomized multicenter trial. Ann. Surg. 1990, 211: 187-95.

5- Lybeert M.L., Martijn H., de Neve W., Crommelin M.A. and Ribot J.G.: Radiotherapy for locoregional relapses of rectal carcinoma after initial radical surgery: definite but limited influence on relapses-free survival and survival. Int. J. Radiat. Oncol. Biol. Phys. 1992, 24: 241-6.

6- Huguier M. and Houry S.: Treatment of local recurrence of rectal cancer. Am. J. Surg. 1998, 175: 288-92.

7- Suzuki K., Dozois R.R., Devine R.M., Nelson H., Weaver A.L., Gunderson L.L. and Ilstrup D.M.: Curative reoperations for locally recurrent rectal cancer. Dis. Colon. Rectum. 1996, 39: 730-36.

8- Hermanek P. and Wittekind C.: Residual tumor ® classification and prognosis. Semin.Surg. Oncol. 1994, 10: 12-20.

9- Pietra N., Sarli L., Costi R., Ouchemi C., Grattarola M. and Peracchia A.: Role of follow up in management of local recurrences of colorectal cancer. A prospective randomized study. Dis. Colon. Rectum. 1998, 41: 1127-33.

10- Singh S., Morgan M.B., Broughton M., Caffarey S., Topham C. and Marks C.G.: A 10-years prospective audit of outcome of surgical treatment for colorectal carcinoma. Br. J. Surg. 1995, 82: 1486-90.

11- Welch J.P. and Donaldson G.A.: Detection and treatment of recurrent cancer of the colon and rectum. Am. J. Surg. 1978, 135: 505- 11.

12- Abulafi A.M. and Williams N.S.: Local recurrences of colorectal cancer: The problem, mechanisms, management and adjuvant therapy. Br. J. Surg. 1994, 81: 7-19.

13- Temple W.J. and Saetler E.B.: Locally recurrent rectal cancer: Role of composite resection of extensive pelvic tumors with strategies for minimizing risk of recurrences. J. Surg. Oncolog. 2000, 73: 47-58.

14- Quirke P., Durdey P., Dixon M.F., et al.: Local recurrence of rectal adenocarcinoma due to inadequate surgical resection: Histopathological study of lateral tumour spread and surgical excision. Lancet 1986, 2: 996-999.

15- Heald R.J., Husband E.M. and Ryall R.D.H.: The mesorectum in rectal cancer surgery - the clue to pelvic recurrence? Br. J. Surg. 69: 613-616, 1982.

16- MacFarlane J.K., Ryall R.D.H. and Heald R.J.: Mesorectal excision for rectal cancer. Lancet 1993, 341: 457- 460.

17- Enker W.E., Thaler H.T., Cranor M.L., et al.: Total mesorectal excision in the operative treatment of carcinoma of the rectum. J. Am. Coll. Surg. 1995, 181: 335-346.

18- Bagatzounis A., Kolbl O., Muller G., Oppitz U., Willner J. and Flentje M.: The locoregional recurrence of rectal carcinoma. A computed tomographic analysis and target volume conceptfor adjuvant radiotherapy. Onkol. 1997, 173 (2): 68-75.

19- Takagi H., Morimoto T., Hara S., Suzuki R. and Horio S.: Seven cases of pelvic exentration combined with sacral resection for locally recurrent rectal cancer. J. Surg. Oncolog. 1986, 32: 184-88.

20- Touran T., Frost D.B. and O'Connell T.X.: Sacral resection. Arch. Surg. 1990, 125: 911-13.

21- Wanebo H.J., Gaker D.L., Whiti hill R., Morgan R.F., and Constable W.C.: Pelvic recurrence of rectal cancer options for curative resection. Ann. Surg. 1987, 205 (5): 482-95.

22- Wanebo H.J., Koness R.J., Vezeridis M., Cohen S.I. and Wrobleski D.E.: Pelvic resection of recurrent rectal cancer. Ann. Surg. 1994, 220 (4): 586-97.

23- Wiggers T., De Vries M.R. and Veeze-Kuypers B.: Surgery for local recurrence of rectal carcinoma. Dis. Colon. Rectum. 39: 323- 328.