Immediate *vs.* Salvage Resection After Local Treatment for Early Rectal Cancer

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PURPOSE: There is an increasing awareness of local procedures to treat early stage rectal cancer. Abdominoperineal resection (APR) or low anterior resection (LAR) has been recommended if adverse pathologic findings are encountered in the local excision specimen. No data compare the impact on survival of "immediate" resection for adverse features *vs.* "salvage" resection for clinical recurrence. METHODS: We reviewed retrospectively 155 patients who underwent initial curative treatment of invasive rectal cancer by excision (91), snare-cautery (44), and fulguration (20). RESULTS: Twenty-one patients underwent APR/LAR immediately after initial local treatment, whereas another 21 patients underwent salvage APR/LAR for local recurrence. The disease-free survival after APR/LAR was 94.1 percent for the immediate group and 55.5 percent for the delayed group ($P < 0.05$). CONCLUSION: This decreased survival observed after delayed resection supports the recommendation for immediate APR/LAR when adverse pathologic features are present in the excision specimen. [Key words: Rectum; Carcinoma; Surgery; Transanal excision]

Baron PL, Enker WE, Zakowski MF, Urmacher C. Immediate *vs.* salvage resection after local treatment for early rectal cancer. Dis Colon Rectum 1995;38:177-181.

T raditional curative operations for cancer have often been considered "radical" and sometimes disabling. In recent years, many of these procedures have been replaced by less extensive operations, which seem to result in comparable survival but significantly less morbidity. Examples of these include lumpectomy rather than mastectomy for breast cancer and limb-sparing surgery instead of amputation for soft tissue sarcomas.[1–2]

In a similar effort to reduce morbidity, low anterior resection with stapled anastomosis has supplanted abdominoperineal resection in the curative treatment of cancer of the upper and middle thirds of the rectum. Increasingly, clinically early cancers of the lower third of the rectum are being treated by local and

sphincter-preserving procedures, including fulguration, snare-cautery excision, and operative excision by transanal, transsphincteric, transsacral, or transcoccygeal methods with or without adjuvant radiation therapy.[3–16] Survival following transanal excision (EXC) of early rectal cancers appears to be comparable with that from abdominoperineal resection (APR) or low anterior resection (LAR).[17, 18] Thus, EXC is being used more often to avoid morbidity, *i.e.*, impotence, bladder and sexual dysfunction, and colostomy, associated with resection of the rectum.[19]

Local failure attends all aspects of limited treatment. It is not clear whether survival is affected in patients who have local recurrences following initial EXC of an early rectal cancer. During the past two decades, local excision of rectal cancer has been used as initial therapy for selected cases with clinically early rectal cancers at Memorial Sloan-Kettering Cancer Center. The purpose of this study was to determine whether patients, who undergo APR/LAR immediately after local treatment based on adverse pathologic findings, benefit from early resection when compared with those who require a salvage APR/LAR for clinical recurrence at a later date.

PATIENTS AND METHODS

A retrospective review was performed of all rectal cancer patients treated at Memorial Sloan-Kettering Cancer Center by local means between January 1967 and December 1987. Patients were excluded if the operation was performed for local recurrence of a rectal cancer after initial treatment by APR or LAR, if there was any evidence of distant metastases at presentation, if the procedure was clearly palliative because of advanced, local disease, or if the patient had evidence of a familial polyposis syndrome. All patients were treated by transanal excision, snare-cautery, or fulguration. The few transsphincteric and

transcoccygeal excisions were grouped with the EXC patients.

The available slides from cases with invasive rectal cancers treated by EXC were retrieved and reviewed. Standardized criteria were used to assess depth of invasion, margins, and other pathologic features. Cases treated by snare-cautery or fulguration were not reviewed, because most specimens were fragmented and largely not interpretable. For these samples, the pathology reports served as the sole source of information regarding histology and margins. Follow-up data were retrieved from either the hospital chart or surgeon's current office records. Overall survival and disease-free survival (DFS) were calculated by Kaplan-Meier methods, and statistical significance was determined by log rank. The data were considered statistically different when the P value was less than 0.05.

RESULTS

From 1967 to 1987, 420 patients underwent initial local operations for rectal cancer. One hundred ninety-two patients were excluded for the reasons described in the preceding section. Twelve of the remaining 228 patients were lost to follow-up, and 61 (28 percent) of these 216 tumors were *in situ* only. Thus, 155 (72 percent) patients with invasive rectal cancer were the source for this study. The mean follow-up was 68.3 months, and the median follow-up was 55.3 months. Fifty-four percent of the patients were male (n = 84), 46 percent were female (n = 71), and their mean age was 65.9 years.

A review of the criteria for patient selection demonstrated that most patients (59 percent) underwent local excision because of the early clinical stage of the tumor (Table 1). Comorbid conditions or patient re-

fusal of colostomy were the other reasons why patients were treated locally rather than APR/LAR.

There were 13 major complications of local therapy: significant bleeding requiring readmission or examination under anesthesia (5), urologic complications (3), infections (3), and unrecognized perforations (2). Two operative deaths occurred in patients who sustained unrecognized perforations. One of these was after EXC and the other after fulguration.

Operations used were EXC (91), snare-cautery (44), and fulguration (20). Sixty-eight percent of the tumors were located less than or equal to 6 cm from the anal verge (n = 104), whereas 32 percent were more than 6 cm (n = 50).

The series of 155 invasive cancer patients had a five-year overall survival of 65.1 percent and DFS of 77.6 percent (Fig. 1). Patients who developed a local recurrence had a significantly diminished overall survival and DFS (Table 2). Patients treated by fulguration had a greater incidence of local recurrence and decreased overall survival and disease-free survival when compared with treatment by either EXC or snare-cautery (Table 3). Overall survival was also significantly better in patients treated by EXC compared with those treated by snare-cautery.

It should be noted that 17 of the 20 fulguration patients developed at least one local recurrence and subsequently underwent an average of 4.7 repeat fulgurations for recurrent disease. Five of these patients ultimately required a diverting colostomy, and six other individuals required an APR or LAR. The final analysis showed that only 4 of 20 fulguration patients (20 percent) remained with no evidence of

Table 1.
Indications for Local Therapy

	No. (%)
Limited local extent of tumor	92 (59)
One or more other indications*	63 (41)
Cardiac disease	32
Pulmonary dysfunction	9
"Old age"†	27
Obesity	16
Refused colostomy	13

* Some patients had more than one indication for local therapy.

† "Old age" applied when patient's chart stated this as the reason for local therapy.
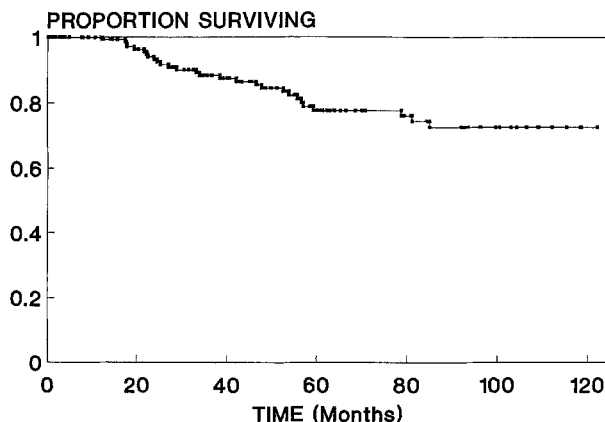
Figure 1. Disease-free survival of patients with early rectal cancers treated locally. Five-year overall survival of 65.1 percent and DFS of 77.6 percent.

Table 2.
Local Recurrence and Survival*

	No.	OS (%)	DFS (%)
All cases			
No recurrence	109	80.1	93.0
Recurrence	46	36.7†	44.0†
EXC only			
No recurrence	72	85.0	96.6
Recurrence	19	54.9†	54.9†

* OS = five-year overall survival; DFS = five-year disease-free survival.
† $P < 0.05$.

Table 3.
Local Recurrence and Survival by Surgical Procedure*

Procedure (No.)	LR No. (%)	OS (%)	DFS (%)
EXC (91)	19 (21)	76.5	86.4
SC (44)	10 (23)	61.8†	78.9
FG (20)	17 (85)	30.0‡	40.5‡

* LR = local recurrence; OS = five-year overall survival; DFS = five-year disease-free survival; SC = snare-cautery excision; FG = fulguration.
† $P < 0.05$ for SC vs. EXC.
‡ $P < 0.05$ for FG vs. EXC or SC.

Table 4.
Local Recurrence and Survival by Tumor Features*

	LR No. (%)	OS (%)	DFS (%)
Size			
All cases (No.)			
≤3 cm (106)	25 (24)	78.3	84.5
>3 cm (42)	17 (41)	35.3†	59.8†
EXC only (No.)			
≤3 cm (68)	14 (21)	83.3	88.6
>3 cm (21)	4 (19)	52.1†	76.0
Surgical margin			
All cases (No.)			
Negative (134)	30 (22)	70.6	81.6
Positive (10)	6 (60)	13.3‡	25.0‡
EXC only (No.)			
Negative (84)	16 (19)	78.6	86.4
Positive (5)	2 (40)	30.0‡	75.0
Tumor depth			
All cases (No.)			
T1 (59)	12 (20)	78.7	84.7
T2 (46)	11 (24)	69.3	87.1
T3 (12)	4 (33)	58.3§‖	77.8
EXC only (No.)			
T1 (42)	8 (19)	83.3	85.6
T2 (34)	7 (21)	71.0	88.9
T3 (11)	3 (27)	63.6§	87.5

* LR = local recurrence; OS = five-year overall survival; DFS = five-year disease-free survival; T1 = tumor confined to submucosa; T2 = tumor invades muscularis propria; T3 = tumor penetrates through muscularis propria.
† $P < 0.01$ for >3 cm vs. ≤3 cm.
‡ $P < 0.01$ for positive vs. negative surgical margins.
§ $P < 0.01$ for T3 vs. T1 tumors.
‖ $P < 0.05$ for T3 vs. T2 tumors.

disease. Ten patients died of disease (50 percent), and six died of other causes (30 percent).

Local recurrence rate, overall survival, and DFS were influenced by size of the tumor at initial assessment. Table 4 shows that positive surgical margins result in greater risk of local recurrence, decreased overall survival, and DFS. Tumor depth altered local recurrence, overall survival, and DFS. Whereas overall survival decreased as depth of invasion increased, DFS failed to show any significant correlation with tumor depth. Lack of DFS association with depth may be attributable to the fact that many patients underwent immediate resection as the depth of invasion increased. All cases were examined for the number of patients who underwent an immediate resection, as it related to tumor depth; 5 of 59 (9 percent) patients with T1 lesions (confined to submucosa), 8 of 46 (17 percent) patients with T2 lesions (invades muscularis propria), and 3 of 12 (25 percent) patients with T3 lesions (penetrates through muscularis propria) were treated by APR/LAR shortly after initial local treatment. Thus, the number of patients at an increased risk for local recurrence decreased as the depth of invasion increased. Degree of tumor differentiation or presence of mucin did not significantly alter local recurrence, overall survival, or DFS.

A total of 48 patients received radiation therapy at some point in their course as an adjunct to their initial local treatment. Preoperative therapy alone was given to 28 patients, postoperative therapy alone was administered to 19 patients, and "sandwich" combined preoperative and postoperative therapy was delivered to 1 individual. Because this retrospective study goes back 25 years, the recorded doses and administration techniques varied widely. The average external beam dose was 2990 cGy and ranged from 1000 to 5580 cGy.

A total of 42 patients underwent APR or LAR after initial local treatment of their rectal cancer. Twenty-one individuals had a resection shortly after the initial local procedure (13 EXC, 7 snare-cautery, 1 fulguration) because of adverse pathologic findings in the operative specimen. An additional 21 patients underwent salvage APR/LAR for a clinically detected local

recurrence, a mean of 38 months after local treatment (12 EXC, 4 snare-cautery, 5 fulguration). Comparison of the features of each primary tumor in these two treatment groups showed that the patient distributions were comparable for depth of invasion but differed slightly in tumor size and margin of excision (Table 5). There was one postoperative death in the immediate resection group and none in the salvage resection group. The DFS of patients treated by immediate resection was significantly greater than DFS for patients requiring salvage resection (Fig. 2) ($P <$ 0.05).

Treatment by fulguration, size > 3 cm, and positive margins had previously shown a negative impact on survival. Analysis following exclusion of these high-risk patients showed diminished DFS for salvage resection patients (Table 6).

DISCUSSION

In 1977, Morson et. al.[5] advocated use of transanal excision as definitive treatment of selected early cases of rectal cancers. He proposed that excision be viewed as a "total biopsy" providing an intact specimen with which to evaluate the margins of excision, the depth of penetration of the bowel wall, and the histologic grade of the cancer. In the event that poor risk factors were present, the policy of treatment provided that the patient be returned to the operating room for a resection. Most initial experience was in patients with clinically early tumors, who were at risk of needing an APR. In some cases, local treatment continued to be reserved only for the very debilitated patients or those with an unusually small cancer or

Table 5.
Distribution by Tumor Features of Patients Treated by Immediate or Salvage Resection*

Feature	Immediate (No.)	Salvage (No.)
Size		
≤3 cm	17	12
>3 cm	4	7
Margin		
Negative	20	14
Positive	1	3
Depth		
T1	5	4
T2	8	8
T3	3	1

* T1 = tumor confined to submucosa; T2 = tumor invades muscularis propria; T3 = tumor penetrates through muscularis propria.
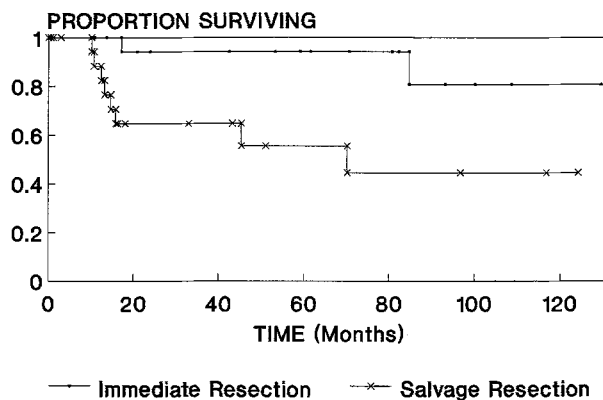
Figure 2. Disease-free survival after APR/LAR of patients treated by local methods, followed by either immediate resection (94.1 percent) or salvage resection for clinical recurrence (55.5 percent) ($P < 0.05$).

Table 6.
Disease-Free Survival in Patients Treated by Immediate or Salvage Resection Following Initial Local Treatment*

	Immediate (%)	Salvage (%)
After date of local treatment	94.7	63.5
After date of APR/LAR	94.1	55.5†
Excluding FG cases	94.4	60.2†
Excluding tumors >3 cm	100	70.0
Excluding positive margin cases	93.8	58.2†

* FG = fulguration.
† $P < 0.05$ for immediate vs. salvage resection.

villous adenoma.[7–9] Several series pointed to successful results attained with local excision in early rectal cancer, broadening interest in this technique.[7–18]

It appears that patients with early, i.e., T1 and T2, rectal cancer, treated by local excision, have a DFS comparable with that reported for the same stages treated by radical surgery.[13] In the event of a local failure following an initial local excision, patients may be retreated by a salvage APR or LAR. Our study confirms Morson et al.'s[5] policy, demonstrating that patients who undergo a salvage APR/LAR for clinical recurrence fair significantly worse than those who undergo an APR/LAR for adverse pathologic features soon after their initial attempt at local excision.

In light of our retrospective study, we examined the two resection groups to determine whether they were indeed comparable (Table 5). The salvage resection group had more cases treated by initial fulguration, a greater number of primary tumors >3 cm, and more instances of positive margins after initial treatment. After accounting for these variables, we still demon-

strated that patients treated by immediate resection have a significantly improved DFS over those requiring salvage resection for local recurrence.

Our study identifies those subgroups of patients who should undergo an immediate APR/LAR based on pathologic findings in the EXC specimen. EXC (of invasive cancers) was associated with a diminished local recurrence rate and improved survival in patients with tumors ≤3 cm, microscopically negative surgical margins, and tumors confined to the submucosa (T1). These data support the policy that if the tumor demonstrates adverse pathologic risk factors, *i.e.*, greater than 3 cm, positive margins, or invasion through the muscularis propria (T3), the patient should, ideally, undergo immediate APR or LAR. Our data do not reflect on the outcome of patients whose tumors are greater than T2, as identified by a preoperative transrectal ultrasound[20–22] or on results of radiation therapy in T2 lesions treated by EXC. Other authors have argued that these patients could benefit from adjuvant radiation therapy rather than further surgery.[13–18] The merits of radiation therapy in T2 lesions can only be decided by a prospective trial.

Retrospective studies confound the analysis of local management of rectal cancer, because the subtle influences of patient selection may have more of an impact on outcome than any one statistically analyzable factor. For example, the healthy patient selected to undergo EXC may be the very same patient to be treated by immediate resection if adverse pathologic findings are noted. Conversely, the less fit patient may be treated by snare-cautery or fulguration, and, when adverse pathologic findings are reported, further surgery may be deferred out of concern for the patient's overall condition. These elements in patient selection and care cannot be gleaned from the data available to a retrospective study, though they may influence outcome.

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