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PATTERNS OF LOCOREGIONAL RECURRENCE AFTER SURGERY AND RADIOTHERAPY OR CHEMORADIATION FOR RECTAL CANCER

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Purpose: To identify patterns of locoregional recurrence in patients treated with surgery and preoperative or postoperative radiotherapy or chemoradiation for rectal cancer.

Methods and Materials: Between November 1989 and October 2001, 554 patients with rectal cancer were treated with surgery and preoperative (85%) or postoperative (15%) radiotherapy, with 95% receiving concurrent chemotherapy. Among these patients, 46 had locoregional recurrence as the first site of failure. Computed tomography images showing the site of recurrence and radiotherapy simulation films were available for 36 of the 46 patients. Computed tomography images were used to identify the sites of recurrence and correlate the sites to radiotherapy fields in these 36 patients.

Results: The estimated 5-year locoregional control rate was 91%. The 36 patients in the study had locoregional recurrences at 43 sites. There were 28 (65%) in-field, 7 (16%) marginal, and 8 (19%) out-of-field recurrences. Among the in-field recurrences, 15 (56%) occurred in the low pelvis, 6 (22%) in the presacral region, 4 (15%) in the mid-pelvis, and 2 (7%) in the high pelvis. Clinical T stage, pathologic T stage, and pathologic N stage were significantly associated with the risk of in-field locoregional recurrence. The median survival after locoregional recurrence was 24.6 months.

Conclusions: Patients treated with surgery and radiotherapy or chemoradiation for rectal cancer had a low risk of locoregional recurrence, with the majority of recurrences occurring within the radiation field. Because 78% of in-field recurrences occur in the low pelvic and presacral regions, consideration should be given to including the low pelvic and presacral regions in the radiotherapy boost field, especially in patients at high risk of recurrence.

Rectal cancer, Recurrence, Radiotherapy, Surgery, Patterns of failure.

INTRODUCTION

Preoperative or postoperative radiotherapy with concurrent chemotherapy is a current standard of care for patients with Stage II and III rectal cancer (1–7). Knowledge about patterns of relapse is essential for appropriate radiotherapy field design in rectal cancer patients. More than 3 decades ago, Gunderson and Sosin (8) reported patterns of failure in rectal cancer patients treated with surgery. Subsequently, other studies have characterized patterns of relapse in rectal patients treated with surgery without radiotherapy (9–12). However, there is limited information about patterns of relapse in rectal patients treated with surgery and radiotherapy or chemoradiation. Such information may help determine whether modifications in radiotherapy dose or field design are warranted for rectal cancer patients.

The goal of this study was to identify sites of locoregional recurrence among more than 550 patients treated with surgery and radiotherapy, and to correlate the sites of locoregional recurrence to radiotherapy fields. To our knowledge, this represents the first effort to associate sites of relapse on computed tomography (CT) images with radiotherapy simulation films in rectal cancer patients.

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METHODS AND MATERIALS

Between November 1989 and November 2001, 554 patients with newly diagnosed rectal cancer (located at ≤12 cm from the anal verge) were treated with mesorectal or local excision and either preoperative (85%) or postoperative (15%) radiotherapy, with (95%) or without (5%) concurrent chemotherapy, at M. D. Anderson Cancer Center. Among these patients, 46 patients had a locoregional recurrence as the first site of failure, including those with a simultaneous distant metastasis (n = 9). Patients who had a locoregional recurrence after the development of distant metastasis were excluded from this study. Computed tomography images documenting the site of locoregional recurrence and radiotherapy simulation films were available for 36 of the 46 patients. This study comprised these 36 patients. The clinical characteristics of the 36 patients and the full cohort of 554 patients are shown in Table 1. The M. D. Anderson Institutional Review Board approved this study.

Table 1. Clinical and treatment characteristics

Characteristic	All patients (n = 554)	Study patients (n = 36)
Age (y)	58 (20–88)	55 (24–86)
Sex		
Male	336 (61)	14 (39)
Female	218 (39)	22 (61)
Clinical T stage		
≤T2	61 (11)	4 (11)
T3	414 (75)	21 (58)
T4	41 (7)	7 (19)
Unknown	38 (7)	4 (11)
Clinical N stage		
N0	260 (47)	16 (44)
N1-2	278 (50)	18 (50)
Unknown	16 (3)	2 (6)
Pathologic T stage		
≤T2	311 (56)	14 (39)
T3	213 (38)	15 (42)
T4	22 (4)	4 (11)
Unknown	8 (1)	3 (8)
Pathologic N stage		
N0	331 (60)	14 (39)
N1–2	148 (27)	15 (42)
Unknown	75 (13)	7 (19)
M stage		
M0	522 (94)	34 (94)
M1	32 (6)	2 (6)
Distance from anal verge (cm)	5 (0–12)	5 (0–12)
Radiotherapy type		
Preoperative	473 (85)	28 (78)
Postoperative	81 (15)	8 (22)
Radiotherapy dose (cGy)	4500 (1440–6300)	4500 (4500–5300)
Concurrent chemotherapy	529 (95)	34 (94)
Type of surgery		
Local excision	56 (10)	8 (22)
Low anterior resection	214 (39)	12 (33)
Proctectomy/coloanal anastomosis	103 (19)	4 (11)
Abdominoperineal resection	156 (28)	9 (25)
Pelvic exenteration	17 (3)	2 (6)
Others	8 (1)	1 (3)

Values are number of patients (percentage) or median (range).

Treatment

Of the 36 patients, 28 (78%) had received preoperative radiotherapy and 8 (22%) had received postoperative radiotherapy. The median radiation dose was 45 Gy (range, 45–53 Gy). All 36 patients were treated in the prone position, using an open tabletop (belly board) device for bowel exclusion. Radiotherapy was delivered with a three-field technique (posterior and two lateral fields) in 35 of the 36 patients. Patients were treated with standardized fields, according to departmental guidelines, with the superior border at the L5–S1 interspace, the inferior border at least 3 cm below the inferior extent of the tumor, lateral borders 1.5–2 cm outside the pelvic brim, anterior border 3 cm in front of the sacral promontory, and posterior border 1–1.5 cm behind the sacrum. However, there was some individual variation in field design, based on patient characteristics and physician preference. Radiotherapy was delivered by 18-MV photons with customized blocking. The pelvis was treated to a dose of 45 Gy in 25 fractions in all patients, along with a boost of 7.5–8 Gy in 10 patients. One patient received intraoperative radiotherapy (IORT) with an additional dose of 15 Gy. Thirty-four patients (94%) received concurrent chemotherapy, with 33 receiving concurrent protracted infusional 5-fluorouracil. Local excision was performed in 8 patients (22%), low anterior resection in 12 (33%), proctectomy with coloanal anastomosis in 4 (11%), abdominoperineal resection in 9 (25%), and pelvic exenteration in 2 (6%). The treatment details of the full cohort of 554 patients are shown in Table 1.

Follow-up

Follow-up information was obtained from hospital records, radiotherapy department records, and radiology reports. Follow-up information was also obtained from the M. D. Anderson Tumor Registry, which collects information on patients annually through letters, phone calls, and Bureau of Vital Statistics records. The median follow-up interval was 64 months (range, 2–172 months).

Characterization of locoregional recurrences

Two radiologists (P.R.B. and R.B.I.) reviewed CT images on the 36 patients to identify the precise site of locoregional recurrence for each patient. Some patients had more than one site of locoregional recurrence, and the different sites were considered separately. With the aid of the radiologists, the sites of locoregional recurrence were marked on the radiotherapy simulation films for each patient. Each locoregional recurrence was classified into one of three categories: (*1*) in-field: within the radiation field by more than 1 cm from the field border, (*2*) marginal: within 1 cm inside or outside the field border, and (*3*) out-of-field: more than 1 cm from the field border. Each in-field recurrence was further classified into one of four categories: (*1*) low pelvis: below the top of the acetabulum, (*2*) mid-pelvis: from the top of the acetabulum to the bottom of the sacroiliac joint, (*3*) high pelvis: above the bottom of the sacroiliac joint, and (*4*) presacral: within 2 cm anterior to the sacrum.

Statistical analysis

Fisher's exact test and Pearson's chi-square test were used to evaluate associations between categoric variables. Locoregional control, in-field control, and overall survival were estimated by Kaplan-Meier methods (13). Log–rank tests were performed to identify predictors of in-field recurrence. Cox proportional hazards regression analysis was then performed to identify significant multivariate predictors of recurrence. All univariate significant variables were entered into a multivariate model. In a backward stepwise fashion, the univariate significant variable with the least significance was eliminated from the multivariate model. This was continued until