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BRACHYTHERAPY AND LOCAL EXCISION FOR SPHINCTER PRESERVATION IN T1 AND T2 RECTAL CANCER

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Purpose: To report long-term results of brachytherapy after local excision (LE) in the treatment of T1 and T2 rectal cancer at risk of recurrence due to residual subclinical disease.

Methods and Materials: Between 1989 and 2007, 32 patients undergoing LE and brachytherapy were followed prospectively for a mean of 6.2 years. Estimates of local recurrence (LR), disease-specific survival (DSS), and overall survival (OS) were generated. Treatment-related toxicity and the effect of known prognostic factors were determined.

Results: There were 8 LR (3 T1, 5 T2), of which 5 were salvaged surgically. Median time to the 8 LR was 14 months, and the 5-year rate of local control was 76%. Although there have been 9 deaths to date, only 5 were from disease. Five-year DSS and OS rates were 85% and 78%, respectively. There were 4 cases of Grade 2–3 radionecrosis and 1 case of mild stool incontinence. The sphincter was preserved in 27 of 32 patients.

Conclusion: Local excision and adjuvant brachytherapy for T1 and T2 rectal cancer is an appealing treatment alternative to immediate radical resection, particularly in the frail and elderly who are unable to undergo major surgery, as well as for patients wanting to avoid a permanent colostomy. © 2009 Elsevier Inc.

Brachytherapy, Rectal, Cancer, Recurrence, Survival.

INTRODUCTION

Abdominoperitoneal resection (APR) and low anterior resection are the standard types of radical surgery (RS) used in the management of low rectal carcinoma. Although RS offers good cure rates, there are deleterious sequelae associated with these surgical procedures, including urologic dysfunction and permanent colostomy and a significant perioperative mortality in frail and elderly patients. Local excision (LE), as a treatment alternative, is appealing in the management of rectal cancer because of the low morbidity and mortality associated with this procedure and the potential for sphincter preservation. A trade-off between LE and RS exists, however, with better 5-year rates of local control after RS in T1 (6.9% vs. 12.5%) and T2 (15.1% vs. 22.1%) tumors (1). As such, it is generally accepted that LE be limited to T1 tumors amenable to complete excision (≥2-mm margins) in tumors that are moderately or well differentiated and free of lymphovascular invasion (2, 3). Adjuvant therapy is often recommended in the event of unfavorable T1 and T2 tumors in the frail and elderly or in patients who are medically unable or unwilling to undergo major surgery (4–7).

Treatment options after LE depend on the risk of lymphatic disease and can include radiotherapy, chemotherapy and chemoradiation. In more advanced cases, multimodality adjuvant therapy is required to control cancer spread. Although the ultimate goal of treatment is survival, many patient factors influence the management of rectal cancer, including patient age, comorbid conditions, patient preference for sphincter preservation, and tolerance for the negative side effects of treatment. For patients with early rectal cancer and those unwilling to endure chemotherapy, adjuvant radiotherapy after LE can be an attractive alternative.

Brachytherapy is a highly localized form of radiotherapy, able to effectively target the subclinical disease responsible for most local recurrences of early rectal carcinoma after LE, such as those arising from inadequate surgical margins or contamination of the surgical site (8–10). Although the treatment delivery and toxicity profile of brachytherapy is appealing compared to other forms of adjuvant therapy for rectal cancer, such as external-beam radiotherapy, chemotherapy, and chemoradiation, brachytherapy in the treatment of rectal tumors is not well documented. Brachytherapy after LE can provide additional protection against cancer recurrence with few of the negative side effects of other adjuvant therapies.

This report summarizes our experience with brachytherapy after LE in the treatment of T1 and T2 rectal cancer at risk of

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recurrence due to residual subclinical disease. In a second article we will report our experience using LE combined with brachytherapy as a boost after external-beam radiotherapy (with or without chemotherapy) in patients with more advanced T2 and T3 tumors, for which the causal risk of local or locoregional recurrence is shared between inadequate margins and occult lymphatic dissemination close to the tumor site.

METHODS AND MATERIALS

Patient population

A cohort of 32 patients with T1 ($n = 14$) or T2 ($n = 18$) rectal cancer scheduled to undergo LE and adjuvant brachytherapy in the definitive management of their disease were identified and followed prospectively at The Ottawa Hospital Cancer Centre between 1989 and 2007. All patients consented to having their treatment outcome and follow-up data included in this institutional review board–approved trial. The mean age of patients treated was 66 years (range, 33–88 years). More than 50% of patients in this series were >70 years old (17 of 32), and 15% (5 of 32) were 80 years or older at the time of diagnosis. Patients were selected to receive adjuvant brachytherapy after LE in lieu of RS because of poor medical status ($n = 6$), advanced age ($n = 2$), because they refused APR ($n = 7$), or because of a synchronous primary tumor ($n = 1$). In a further group of medically fit surgical patients with poor pathologic features after LE ($n = 16$), such as positive margins or more advanced (T2) disease, adjuvant brachytherapy was delivered to improve the rate of local control. The clinical characteristics of the patients are presented in Table 1. Staging was carried out using the American Joint Committee on Cancer TNM system based on physical examination, including digital rectal examination, and preoperative imaging. The late introduction of rectal ultrasound at our center, combined with the poor reliability of preoperative rectal ultrasound imaging near the anorectal junction, resulted in staging of patients being based primarily on the results of the physical examination. Similarly, the measurement of carcinoembryonic antigen was inconsistently performed on patients because financial reimbursement for this test was not always provided by the provincial health care plan during the years covered by this series. The mean follow-up of the patients in this series is 74.9 months (range, 12–165 months), with 19 patients (59%) followed for a minimum of 5 years. One patient was lost to follow-up at 29 months.

Table 1. Clinical characteristics.

Characteristic	*n*
Primary site	
Rectum	16
Anorectal junction	16
Stage	
T1N0	13
T1Nx	1
T2N0	18
Gender	
Male	15
Female	17
Differentiation	
Well differentiated	10
Moderately differentiated	20
Poorly differentiated	1
Unknown	1
Depth of invasion	
Muscularis	17
Submucosa	15
Distance from anal verge (cm)	
≤6	25
>6	6
Unknown	1

Surgery

A full-thickness transanal excision was performed in all patients according to techniques already published (11). Although the intent of the surgery was to achieve negative margins (R0), the main goal was to achieve gross excision. Conversion of LE to major resection was not carried out in the event of positive margins (R1) in medically fit surgical patients. The decision to perform LE with adjuvant brachytherapy as opposed to radical surgery was reached on the basis of careful consideration of the risks and benefits of treatment, outcome, and quality of life by the patient and the treating oncologist.

Brachytherapy

Brachytherapy was carried out in the lithotomy position after standard bowel preparation and either spinal or general anesthesia. After Foley catheter insertion, digital examination, and anal canal dilation, a sigmoidoscopy was performed. Using guide needles and template brachytherapy, needles were inserted one by one under finger guidance to a distance of approximately 3 to 4 mm from the surface of the mucosa. Treatment of the tumor bed was carried out using either a single- or double-plane implant with customized templates. The single-plane template is 15 mm thick and has 12-mm spacing between predrilled holes in which 17-gauge needles, 10 or 15 cm in length, are inserted. After closing the tip, the needles were inserted 2.5 cm beyond the volume to be covered by the reference isodose, to take into account the pull-back from patient repositioning (1 cm), the crimped tip (0.5 cm), and the tip of the source to the reference isodose (1 cm) using the Paris system. A rectal tube was inserted and kept in place during treatment to keep the anal canal open and to push the mucosa opposite the implanted needles away from the desired treated volume. The rectal tube also permitted evacuation of some gas and/or feces during treatment. The double-plane template, which has an internal ring with 10-mm spacing between needles and a second outside ring 10 mm beyond, was used in the treatment of anorectal tumors and tumors within 5 cm of the anal verge and in older patients. Insertion of the outer-ring needles for the double-plane template was done all at once after the rectal tube and all inner-ring needles were put in place. After the procedure, patients were on bed rest for the required 2–4 days of therapy. They were given a low residual diet, loperamide (2 mg t.i.d.), i.v. cefazolin (1 g) and i.v. metronidazole (500 mg) every 8 h (three doses), and s.c. heparin (5000 U b.i.d.). The correct position of the implant was verified once daily. Examples of single- and double-plane templates are illustrated in Figs. 1 and 2. The Paris system was chosen for dose specification because of local expertise with this system, ease of use, and published positive results using similar techniques (12–14). In addition, the reproducibility and consistency of dose specification with the well-defined volumes and dose rates (hyperdose sleeve, basal dose rate, reference dose rate) using this technique simplify interpretation of the results by eliminating the subjectivity of isodose selection. The iridium wires used in the treatment of patients were replaced in 2002 by iridium seed ribbons. The methodology for conversion of active length used was that of Marinello *et al*. (15). The implant dosimetry was considered suboptimal when the individual basal dose rate varied by more than 10% from the mean basal dose rate used to define the reference dose rate for the prescription. This inhomogeneity constraint for the