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LOCAL EXCISION IN EARLY-STAGE RECTAL CANCER

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Summary of Literature Review

Background

Thirty-four percent of patients diagnosed with rectal cancer present with American Joint Commission on Cancer (AJCC) stage I disease [1]. Historically these patients have been treated with low anterior resection (LAR) or abdominoperineal resection (APR) with excellent local control (LC) and survival rates [2-4]. Postulating that early-stage lesions may not warrant such aggressive treatment as well as acknowledging the mortality and morbidity of these procedures, investigators have examined less morbid sphincter-sparing approaches such as local excision (LE). In addition, LE has been presented as an option to patients whose other comorbid conditions would not allow them to tolerate more extensive surgery. Most of the data supporting the use of LE are from single-institution, retrospective reviews [5-9]. Recently, a few prospective multi-institutional trials have investigated the efficacy of LE with or without radiation therapy (RT) in these patients [10-11].

Workup

All patients should receive a full colonoscopy with biopsy, pathology review, proctoscopy, carcinoembryonic antigen (CEA), and computerized tomography of the chest, abdomen, and pelvis. In addition, patients being considered for LE should have an endorectal ultrasound (EUS) to evaluate depth of penetration. EUS is 62%-92% accurate for T staging and 64%-88% accurate for N staging but is highly operator dependent [12-13].

Surgical Techniques

There are three operative approaches for LE of a distal rectal lesion: transanal, posterior trans-sphincteric (York-Mason procedure), or posterior proctotomy (Kraske procedure). Transanal excision (TAE) is the most commonly used approach. Under direct visualization, the lesion is excised with a 1 cm margin including the perirectal fat. The mural defect is then closed. The posterior trans-sphincteric and posterior proctotomy approaches are used less commonly and involve posterior approaches with dissection above or below the levator ani to the rectum [14]. It is important to note that none of these procedures include lymph node evaluation. Transanal endoscopic microsurgery (TEM) allows locally complete excision of rectal neoplasms and has recently been evaluated for curative treatment of invasive cancer. TEM has been shown to be as effective, and possibly better than, conventional TAE and safe to be following chemoradiation [15-21].

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Variant 1: **57-year-old male with preoperative stage uT1N0, freely mobile, moderately differentiated adenocarcinoma. Tumor is 2 cm in diameter, involves <25% of circumference, and is located 6 cm from anal verge. No lymphovascular space invasion is noted.**

Treatment	Rating	Comments
Local Excision, pT1N0 and Negative Margins		
Observation	9	
RT alone	2	
RT + chemotherapy	1	
Local Excision, pT1N0 and Positive Margins		
LAR or APR	9	
RT alone	2	
RT + chemotherapy	2	
Observation	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Patient Selection

In general, the best candidates for LE include small (<4 cm), low-lying tumors confined to the muscularis propria. Patients with adverse pathologic features (signet ring histology, poor differentiation, lymphovascular space invasion) or whose tumors occupy >40% of the rectum are at high risk for local recurrence, and LE is not recommended [22-23]. Patients with positive margins after LE or piecemeal resections are at very high risk of local recurrence and should be offered immediate APR or LAR. Patients with tumors invading through the muscularis propria (T3) are at very high risk (>30%) for local recurrence following LE and should not be treated with LE. Palliative LE may be performed in advanced-stage patients [24].

Variant 2: **65-year-old otherwise healthy female with preoperative stage uT2N0, moderately differentiated adenocarcinoma. Tumor is 3 cm in diameter, freely mobile, and is located 4 cm from anal verge. No lymphovascular space invasion is noted.**

Treatment	Rating	Comments
Surgery		
LAR or APR	9	
Local excision	2	
If Local Excision, then		
RT + chemotherapy	8	
RT alone	2	
Observation	1	
If RT + Chemo: RT Dose to Primary		
45 Gy/1.8 Gy	2	
50.4 Gy/1.8 Gy	8	
54 Gy/1.8 Gy	8	If small bowel can be excluded.
59.4 Gy/1.8 Gy	2	
Simulation		
Patient prone	9	
Small-bowel contrast at simulation	9	
Patient immobilized	9	
Use belly board	9	If patient is prone.
Anal marker	9	
Bladder full at simulation	8	
Patient supine	5	
If RT + Chemo: RT Volume		
L5/S1 pelvis to include perineum	9	In some cases where the lesion is 4 cm above the anal verge, the perineum may be spared as long as 3 cm of inferior margin can be maintained.
RT Technique		
3 field with photons	8	
4 field with photons	8	
AP/PA	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Local Excision with or without Radiation Therapy

Single-institution reviews have reported failure rates of 7%-40% and 25%-62% for LE alone in T1 and T2 tumors, respectively [5-9,17-18,20,25-33]. Postoperative RT may lower these rates to 10%-20% [5,9,11,23,25], however there is little data to suggest the role of prognostic factors to select patients who are at risk for adjuvant treatment. Retrospective studies have investigated the risk of lymph node metastasis according to the depth of tumor invasion in patients with T1 and T2 tumors undergoing resection for rectal cancer, which may have important implications for patients with superficial early rectal cancers in whom LE is being considered. Theses studies indicate that the risk of lymph node metastases cannot be predicted by radiological staging or tumor size; however, multivariate analysis identified the extramural vascular invasion and tumor grade as

independent predictors of lymph node metastasis, but not the depth of submucosal invasion [34-35].

An initial phase II study by the Radiation Oncology Therapy Group® (RTOG®) assigned patients observation (low-grade T1 tumors with negative margins) or chemoradiation (54-65 Gy with 5-fluorouracil (5-FU) 1,000 mg/m^2 IV d1-3, d29-31) based on postexcision pathology [10]. Local recurrence rates were 7%, 8%, and 23% for T1, T2, and T3 tumors, respectively. Cancer and Leukemia Group B study (CALGB 8984) evaluated the role of LE with or without chemotherapy and RT in 177 patients with T1 and T2 adenocarcinomas of the rectum [11]. T1 patients underwent LE followed by observation. T2 patients underwent LE followed by RT (54 Gy/30 fractions) and chemotherapy (5-FU 500 mg/m^2 IV d1-3, d29-31). At 48 months of median follow-up, the 6-year overall survival rate was 85%, and the disease-free survival rate was 78% for all patients. Three of the 59 eligible T1 patients and seven of the 51 eligible T2 patients had experienced local failure. It is important to note, however, that these were highly selected patients and that one-third of patients were excluded after surgery due to large tumor size and/or questionable margin status.

Variant 3: **60-year-old female with uT3Nx adenocarcinoma, located 4 cm from anal verge.**

Treatment	Rating	Comments
Neoadjuvant RT + chemotherapy	9	See the ACR Appropriateness Criteria® topic on "Resectable Rectal Cancer."
LAR or APR	9	
Local excision	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

More recently, LE or TEM following neoadjuvant radiation with or without chemotherapy has been reported. Data from four retrospective studies [17,19,32,36] and one prospective study [18] have demonstrated safety and LC rates ranging from 2.0%-13.2%. No studies to date have prospectively evaluated whether or not the use of neoadjuvant therapy reduces recurrence rates compared to LE or TEM alone.

Future Directions

A multi-institutional phase II trial by the American College of Surgeons Oncology Group (ACSOG Z6041) is investigating neoadjuvant chemoradiation and LE in T2 patients. As of October 2009, accrual to ACSOG Z6041 has been temporarily suspended due to a recent data review that revealed the toxicity threshold written into the toxicity protocol stopping rule has been crossed in the cohort of patients receiving the revised treatment regimen. Nevertheless, the study team has determined that current patients are not at undue risk, and there are continuing plans for the study once all the adverse events have been reviewed.

Supporting Document(s)

- ACR Appropriateness Criteria® Overview
- Evidence Table

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