Determining the Need for Radical Surgery in Patients With T1 Rectal Cancer

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Hypothesis: In the era of modern preoperative staging of patients with rectal cancer, lymph node metastases can be reliably predicted by the histological features of the tumor and preoperative imaging. Local resection can then be safely offered to the patients who are at low risk of having malignant lymph nodes.

Design: We reviewed the records of 109 consecutive patients with preoperative imaging results suggestive of T1N0 or T2N0 disease who underwent total mesorectal excision. All patients underwent preoperative endorectal ultrasonography or magnetic resonance imaging and computed tomography, with or without positron emission tomography. Final pathologic investigation identified T3 disease in 27 patients. History, physical examination results, and radiologic and pathologic data were evaluated for predictors of positive nodes in the remaining 82 patients.

Setting: Tertiary care referral center.

Patients: Patients with preoperative imaging suggestive of T1N0 or T2N0 rectal cancer.

Main Outcome Measures: To evaluate different clinical and pathologic tumor features as predictors of positive lymph nodes in T1 and T2 rectal cancers with negative radiographic nodes.

Background: Local resection of T1 and T2 rectal cancer results in lower morbidity compared with radical resection. However, recurrence rates after local resection are higher, likely owing to unresented nodal metastasis. Reports on predictors of lymph node metastasis remain inconsistent in the literature. Although local resection may be appropriate for some rectal cancers, selection criteria remain unclear.

Results: Despite indications of negative nodes on radiographic examination, 4 of 35 patients with T1 disease (11%) and 13 of 47 with T2 disease (28%) had positive nodes. On univariate analysis, the only significant predictor was depth of invasion: 24 of 65 patients with negative nodes (37%) vs 13 of 17 patients with positive nodes (76%) had tumors invading the lower third of the submucosa and beyond ($P = .02$). On logistic regression analysis accounting for depth of invasion (lower third of the submucosa and beyond), size, distance from anal verge, differentiation, and lymphovascular and small-vessel invasion, only depth of invasion remained a significant predictor.

Conclusions: In all, 89% of patients with T1 disease (31 of 35) and 72% of those with T2 disease (34 of 47) underwent unnecessary radical resection. Endorectal ultrasonography or magnetic resonance imaging and computed tomography, with or without positron emission tomography, for preoperative staging could not identify these patients reliably. In addition, histologic markers of aggressive disease were not helpful. Thus, local resection for T2 rectal cancer is not justified. Local resection should be offered only to patients with superficial T1 tumors who will adhere to aggressive postoperative surveillance.

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RADICAL RESECTION OF EARLY rectal cancer results in excellent oncologic outcomes. However, radical resection does not guarantee cure, as recurrence rates of unselected T1 tumors are 3% to 6% for cohorts that include patients with positive nodes.1 Furthermore, radical resections continue to be associated with significant morbidity and mortality. A recent report2 on 1304 patients undergoing abdominoperineal resection or low anterior resection reported overall morbidity and mortality of 13.6% and 2.7%, respectively. Radical resection is also associated with a 50% rate of sphincter loss in the United States.3 Patients whose

See Invited Critique at end of article

sphincters have been preserved are at high risk for developing functional sequelae such as symptoms of low anterior syndrome (fragmentation, urgency, and fe-
cal incontinence), urinary incontinence, and sexual dysfunction.\(^4,5\)

Given these data, many patients choose to undergo local resection. A review of the National Cancer Database performed by You et al\(^6\) revealed that, of 35 179 patients undergoing treatment for stage I rectal cancer, local resection was performed for 37.9% of T1 tumors and 12% of T2 tumors. Furthermore, the rate of local resection for T1 tumors increased from 26.6% in 1989 to 43.7% in 2003. This rising trend is of concern given the vast literature showing much higher rates of recurrence after local resection vs radical resection.

Local resection leaves lymphatic drainage of the rectum intact. Nevertheless, even T1 rectal cancers carry a 10% to 20% risk of lymph node metastases.\(^1,7,8\) Nascimento et al\(^7\) analyzed a cohort of 353 patients who underwent radical resection for sessile T1 adenocarcinomas to address the question of frequency of and risk factors for lymph node metastasis. Thirteen percent of the patients were found to have metastatic disease in their lymph nodes. Lymphovascular invasion, depth of submucosal invasion, and location in the lower third of the rectum were statistically significant predictors. Many other studies\(^1,8-13\) have found similar rates of lymph node involvement with a variety of statistically significant risk factors. To date, there are no reliable criteria for selecting patients who have no lymph node metastasis for local resection. Possibly for this reason, local resection carries a higher risk of recurrence compared with radical resection.\(^1,16-20\)

Bentrem et al\(^1\) published the Memorial Sloan-Kettering experience comparing recurrence rates in patients undergoing local resection vs total mesorectal excision. The overall recurrence rate was 17% in the local resection group (9% local, 5% distant, and 3% local + distant recurrence) and 5% in the total mesorectal excision group (half local and half distant). With the development of transanal endoscopic microsurgery, better results have been achieved. Tsi et al\(^21\) reported on a large series of patients treated with transanal endoscopic microsurgery for benign and early malignant rectal tumors. They found local recurrence rates of 9.8% and 23.5% for T1 and T2 adenocarcinomas, respectively.

Studies looking for predictors of positive lymph nodes in early rectal cancer have selected patients on the basis of postoperative histologic stage, regardless of preoperative imaging. We hypothesized that, with modern imaging, we could predict which patients with early rectal cancers harbor positive lymph nodes by combining information from preoperative imaging and tumor histologic findings. We reviewed the records of 109 consecutive patients with preoperative imaging suggestive of T1N0 or T2N0 rectal cancer who underwent total mesorectal excision.

### METHODS

#### PATIENTS

After approval from the institutional review board of Massachusetts General Hospital, we reviewed the records of 390 consecutive patients who underwent surgical procedures for rectal cancer between January 1, 1998, and December 31, 2008. Medical data were gathered from electronic and paper medical records. Two hundred eighty-one patients treated with neoadjuvant chemotherapy and radiotherapy for T3 and/or N1 disease were excluded; this left 109 patients who were thought to have T1N0 or T2N0 disease based on preoperative imaging with either endorectal ultrasonography or magnetic resonance imaging and computed tomography, with or without positron emission tomography. History, physical examination results, and radiologic and pathologic data were reviewed. For each patient, the preoperative presence or absence of bleeding, obstruction, and perforation, as well as personal or family history of colorectal neoplasms, was recorded. Twenty-seven patients within this cohort were eventually found to have T3 disease and were excluded from our statistical analysis. The remaining 82 patients with histologically confirmed T1 and T2 rectal cancer constituted our study population.

### PATHOLOGIC ANALYSIS

All tissue samples were examined by the same group of gastrointestinal pathologists at our institution. Pathologic analysis was performed using a standard protocol, and reports included histologic type, description of resection margins, vascular and lymphovascular invasion, depth of invasion, tumor size, and lymph node positivity. In patients with T1 tumors, special mention was made as to whether the tumor abutted muscularis propria or was superficial, which allowed for retrospective reclassification of these tumors, based on their depth of invasion into the submucosa (upper third, SM1; middle third, SM2; and lower third, SM3, as described by Nascimento et al\(^7\)).

### STATISTICAL ANALYSIS

Categorical variables are reported as frequencies and percentages, and continuous variables are reported as mean (SD). Patients with and without positive lymph nodes were compared in regard to age, sex, clinical presentation, and pathologic tumor characteristics with Fisher exact test, \(\chi^2\) test, or paired \(t\) test, as appropriate. We then fitted a logistic regression analysis model accounting for the following a priori chosen variables to determine predictors of positive lymph nodes: depth of invasion, tumor size, distance from the anal verge, degree of differentiation, and lymphovascular invasion. \(P<.05\) was considered statistically significant.

### RESULTS

We identified 82 patients (48 men and 34 women) with histologically confirmed T1 or T2 rectal cancer (mean age, 66; range, 39–91 years). All patients underwent total mesorectal excision (low anterior resection in 63 patients and abdominoperineal resection in 19). Three patients had a tumor involving the distal margin that was recognized intraoperatively, and resection was extended to a clear distal margin.

Despite negative nodes shown on preoperative imaging, 4 of 35 patients with T1 tumors (11%) and 13 of 47 patients with T2 tumors (28%) had positive lymph nodes identified on final pathologic examination. Patients with and without positive lymph nodes were similar in sex, age, preoperative symptoms, and the distance of the tumor from the anal verge (Table 1).

On univariate analysis of pathologic features, patients with and those without positive lymph nodes had similar rates of lymphovascular invasion, small-vessel inva-
sion, or moderately or well-differentiated tumors (Table 2). However, patients with positive lymph nodes were more likely to have tumors invading the SM3 level of the submucosa or beyond. Interestingly, the SM3 cutoff appeared more likely to discriminate positive lymph nodes than the cutoff at the level of T1 vs T2 (Table 2).

On logistic regression analysis incorporating depth of invasion (into and beyond SM3), size, distance from the anal verge, degree of differentiation, and lymphovascular and small-vessel invasion, only depth of invasion remained a statistically significant predictor (Table 3).

When treating early rectal cancer, the decision must be made between local resection and radical resection. Radical resection provides an excellent oncologic outcome but with appreciable morbidity, whereas local resection is associated with a higher risk of local recurrence but with preserved function. The risk of local recurrence is probably the result of occult lymph node metastases.

Previous reports on predictors of positive lymph nodes have been inconsistent. These have included (1) lymphovascular invasion, death of submucosal invasion, and location in the lower third of the rectum; (2) lymphovascular invasion and poor differentiation; (3) sex, lymphovascular invasion, and poor differentiation; (4) lymphovascular invasion, poor differentiation, and close or positive margins; (5) lymphovascular invasion and positive margins; (6) extensive budding, microacinar structures, lymphovascular invasion, and poor differentiation; (7) depth of submucosal invasion; and (8) flat or depressed lesions, depth of submucosal invasion, lymphovascular invasion, and poor differentiation. In our series, among patients with lymph nodes appearing to be negative on radiologic examination, the only positive predictor was depth of invasion. Perhaps with a larger number of patients, lymphovascular invasion and distance from the anal verge would also have been statistically significant predictors.

The studies discussed herein selected patients on the basis of histologic T category, regardless of preoperative radiographically determined TNM stage. They have shown that up to 18% of T1 rectal cancers harbor lymph node metastases. Our series included only patients with negative nodes shown on preoperative imaging. Despite this, 11% of patients with T1 disease and 28% of those with T2 disease had positive nodes, demonstrating that negative results of imaging can be falsely reassuring. Furthermore, 27 patients who were thought to have T2 disease had T3 disease identified on final pathologic examination.

### Table 1. Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>39 (60)</td>
<td>.60</td>
</tr>
<tr>
<td>Age, mean, y</td>
<td>66 65</td>
<td>70.10</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative continence</td>
<td>57 (88)</td>
<td>.68</td>
</tr>
<tr>
<td>Rectal pain</td>
<td>2 (3)</td>
<td>.37</td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td>37 (57)</td>
<td>.79</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>1 (2)</td>
<td>.37</td>
</tr>
<tr>
<td>Distance from anal verge, cm</td>
<td>7.0 4.9</td>
<td>17</td>
</tr>
</tbody>
</table>

### Table 2. Histologic Data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2 category</td>
<td>34 (52)</td>
<td>.10</td>
</tr>
<tr>
<td>Sessile lesion</td>
<td>3 (5)</td>
<td>.00</td>
</tr>
<tr>
<td>Average No. of lymph nodes</td>
<td>14</td>
<td>.72</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>9 (14)</td>
<td>.15</td>
</tr>
<tr>
<td>Small-vessel invasion</td>
<td>5 (8)</td>
<td>.99</td>
</tr>
<tr>
<td>Moderately or well-differentiated tumor</td>
<td>48 (74)</td>
<td>.36</td>
</tr>
<tr>
<td>Depth of invasion to SM3 and beyond</td>
<td>24 (37)</td>
<td>.02</td>
</tr>
<tr>
<td>Size, mean, cm</td>
<td>3.05 2.75</td>
<td>.53</td>
</tr>
</tbody>
</table>

### Table 3. Logistic Regression Analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
<th>P Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depth of invasion to SM3 and beyond</td>
<td>24 (37)</td>
<td>.03</td>
<td>8.18 (1.21-55.20)</td>
</tr>
<tr>
<td>Size, mean, cm</td>
<td>3.05 2.75</td>
<td>.11</td>
<td>0.58 (0.30-1.14)</td>
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<tr>
<td>Distance from anal verge, cm</td>
<td>7 4.9</td>
<td>.09</td>
<td>0.89 (0.78-1.02)</td>
</tr>
<tr>
<td>Well-differentiated tumor</td>
<td>6 (9)</td>
<td>.92</td>
<td>1.15 (0.08-16.24)</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>9 (14)</td>
<td>.55</td>
<td>1.69 (0.30-9.57)</td>
</tr>
<tr>
<td>Small-vessel invasion</td>
<td>5 (8)</td>
<td>.84</td>
<td>0.76 (0.05-11.09)</td>
</tr>
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</table>

Abbreviations: CI, confidence interval; OR, odds ratio; SM3, lower third of the submucosa. 

a Sessile lesions were defined as having no discernable stalk.
The rate of positive lymph nodes probably directly correlates with the rates of local recurrence, which in recent reports, has been shown to be up to 18% for T1 cancers. For T2 tumors, the local recurrence rate is an even greater concern—up to 47% without adjuvant therapy. Despite this evidence, the rate of local resection in the United States has nearly doubled during a 15-year period, with almost half of T1 tumors being treated by local resection. Transanal endoscopic microsurgery is associated with slightly better results but is still far from perfect: 9.8% and 23.5% local recurrence rates for T1 and T2, respectively.

Our series shows that 89% of patients with T1 disease (31 of 35) and 72% of patients with T2 disease (34 of 47) may have undergone unnecessary radical resection. Endorectal ultrasonography or magnetic resonance imaging and computed tomography, with or without positron emission tomography, for preoperative staging could not identify these patients reliably, and histologic markers of aggressive disease were not helpful. Because patients with local recurrence have survival rates of 43% to 58% after salvage operations, we believe that local resection should be performed only for superficial T1 tumors, preferably using transanal endoscopic microsurgery, in patients who will adhere to aggressive postoperative surveillance. Local resection for T2 tumors should be reserved for palliation or for patients unable to tolerate radical resection.

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Author Contributions: Dr Salinas had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Salinas and Bordeianou. Acquisition of data: Salinas and Bordeianou. Analysis and interpretation of data: Salinas, Dursun, Klos, Shellito, Sylla, Berger, and Bordeianou. Drafting of the manuscript: Salinas and Bordeianou. Critical revision of the manuscript for important intellectual content: Salinas, Dursun, Klos, Shellito, Berger, and Bordeianou. Administrative, technical, and material support: Salinas. Study supervision: Shellito, Sylla, Berger, and Bordeianou.
Financial Disclosure: None reported.
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REFERENCES