Rectal Carcinoid Tumors

Review of Results After Endoscopic and Surgical Therapy

Mary R. Kwaan, MD, MPH; Joel E. Goldberg, MD; Ronald Bleday, MD

Objective: To assess whether endoscopic treatment can clear local disease in patients with carcinoid tumor.

Design: Retrospective cohort study.

Setting: Tertiary care academic medical center.

Patients: All patients diagnosed as having a neuroendocrine tumor or carcinoid tumor of the rectum who were evaluated at our institution between January 1, 1990, and December 31, 2006.

Main Outcome Measure: Margin status of tumor resection.

Results: Eighty-five patients were identified (median age at diagnosis, 55 years). Thirty-three tumors (39%) were asymptomatic and diagnosed during screening colonoscopy. Eleven tumors (13%) were metastatic at presentation. Of the 85 tumors, 48 (56%) were smaller than 1.0 cm. Endoscopic therapy was performed in 46 patients (54%). Of these, 38 patients (83%) had tumors with positive or indeterminate margins on histologic examination; of whom 6 (16%) had residual tumor on subsequent endoscopy and 1 (3%) had recurrence as metastatic disease. One patient who had a negative margin had residual tumor on follow-up. Thirty-one patients (36%) underwent surgical resection; of these, 23 (74%) underwent transanal excision or transanal endoscopic microsurgery, 6 (19%) underwent low anterior resection, and 2 (6%) underwent abdominoperineal resection. Eight patients who did not receive local clearance of tumor had metastases on presentation, had another active malignant neoplasm, or refused further surgical treatment. Among the 85 patients, 4 metastases occurred during follow-up, including 2 from tumors smaller than 1.0 cm at presentation.

Conclusions: Endoscopic treatment is sufficient for tumors that are small, for tumors limited to the mucosa, and when a margin is negative for tumor. Transanal excision should be considered when margins of endoscopic resection are positive. We recommend rectal resection for tumors that are 1.0 to 1.9 cm and have high-risk features.


Rectal carcinoids are uncommon tumors, representing 1.8% of malignant anorectal neoplasms. They are discovered either incidentally during screening colonoscopy or during an evaluation for symptoms such as rectal bleeding (18%-40%) or diarrhea. Previous reports suggest that these rectal tumors are usually smaller than 1.0 cm at the time of diagnosis (60%-90%). Treatment approaches are still controversial because long-term outcomes for patients without metastasis are poorly described in the literature. In most case series, rectal carcinoid tumors smaller than 1.0 cm do not metastasize. A case series and review of the literature from Japan showed a 5.5% rate of metastasis among 710 carcinoid tumors smaller than 1.0 cm, with most metastases occurring in tumors 0.6 to 1.0 cm. Because small tumors rarely metastasize, local excision via endoscopic polypectomy or endoscopic submucosal resection is thought to be sufficient. Rectal carcinoids that are 1.0 to 1.9 cm do not have predictable behavior and have a metastatic rate of 4% to 30%. There is no consensus in the literature concerning the appropriate therapy for this size tumor, with some recommending rectal resection and others recommending transanal excision in selected patients. Rectal carcinoid tumors that are 2.0 cm or larger have a 70% to 80% chance of presenting with metastasis or developing metastasis in follow-up. These are the tumors that should be resected via abdominoperineal resection or low anterior resection. Because patients often die of disease, some centers have argued that extended resection with intent to cure offers no benefit over local excision. Other centers have argued that, as the most effective treatment...
option for this type of tumor, resection offers local control of tumor even if hepatic metastases, which can remain indolent for years, develop soon after resection.2

Depth of invasion is another consideration when treating patients with rectal carcinoids smaller than 2.0 cm. Tumors invading the muscularis propria are at higher risk of metastasis. Atypical histologic features such as lymphovascular invasion, perineural invasion, anaplastic appearance, or frequent mitoses are also a consideration when deciding on a treatment approach for a carcinoid tumor smaller than 2.0 cm.8

With the advent of intensified efforts to screen for colon cancer, rectal carcinoid tumors will become a more frequent management issue. Although endoscopic resection has been considered adequate for small tumors that do not invade the muscularis propria,7,9,10 the literature provides limited information on the quality of margins after polypectomy and on tumor recurrence after such procedures. This concern is highlighted by the fact that many such specimens are obtained without advance knowledge that the endoscopic finding represents a neoplasm. We sought to determine the quality of margins after polypectomy and to elucidate which patients would likely benefit from local excision, ie, transanal excision or transanal endoscopic microsurgery (TEM). We further sought to describe our experience with surgical resection of carcinoid tumors, including local excision, low anterior resection, and abdominoperineal resection.

Eighty-five patients with rectal carcinoid tumors were included in the study. Eighteen patients were excluded because of insufficient clinical information. The mean patient age at diagnosis was 55 years (range, 21-82 years). Forty-eight patients (56%) were men, and 37 (44%) were women. Thirty-two patients (22%) presented with rectal bleeding, 15 (18%) with a change in bowel habits, 7 (8%) with abdominal or rectal pain, and 11 (13%) with metastatic disease. Some patients had multiple symptoms. Thirty-three carcinoid tumors (39%) were asymptomatic and found on screening colonoscopy. Three patients (4%) had a history of colorectal adenocarcinoma, and 11 (13%) had a history of another malignant neoplasm. No patient had a history of inflammatory bowel disease.

TUMOR CHARACTERISTICS

Tumor size, as assessed on endoscopy or pathologic examination, was smaller than 1.0 cm in 48 cases (56%). The tumor features are provided in the Table. Where described, tumors were located within 5 cm of the anal verge in 16 of 41 patients (39%), 6 to 10 cm from the anal verge in 17 of 41 (41%), and 11 cm or further from the anal verge in 8 of 41 (20%).

### METHODS

Using a surgical pathology database at the Brigham and Women’s Hospital, we identified patients who carried a diagnosis of rectal carcinoid tumor or neuroendocrine tumor on a pathology report between January 1, 1990, and December 31, 2006. Patients were excluded if they had not been seen by a clinician in the Partners HealthCare System or if review of the clinical data indicated that the tumor was not located in the rectum. Only patients older than 18 years were included in the study. Data were extracted from clinic and hospital medical records and from the Partners HealthCare System’s longitudinal medical record. If the patient had initially been evaluated and treated at an outside institution, we obtained the patient’s data from the note written by the clinician at the Partners HealthCare System in which the patient’s course was summarized.

Data elements, retrospectively collected, included patient age, medical history, modality of diagnosis, symptoms at presentation, clinical size and location of tumor indicated at endoscopy or examination under anesthesia, pathologic features, treatment, margin status of excisions, complications of treatment, clinical and endoscopic follow-up, chemotherapy and/or radiotherapy, and details surrounding mortality. A palliative operation was defined by metastatic disease or no clear attempt to obtain a complete local excision.

Pathologic features of the tumor were determined using pathology reports. Margins were indeterminate if a comment in the pathology report indicated that the margins could not be assessed, or if the specimen was histologically described as being “in fragments.” Margins were considered positive if tumor extended to the cauterized edges or base. For the purpose of analysis, margins smaller than 0.1 cm were considered positive.

Comparisons between groups were made using the Fisher exact test. The study was approved by the Partners HealthCare System Human Research Committee.

### RESULTS

Eighty-five patients with rectal carcinoid tumors were included in the study. Eighteen patients were excluded because of insufficient clinical information. The mean patient age at diagnosis was 55 years (range, 21-82 years). Forty-eight patients (56%) were men, and 37 (44%) were women. Thirty-two patients (22%) presented with rectal bleeding, 15 (18%) with a change in bowel habits, 7 (8%) with abdominal or rectal pain, and 11 (13%) with metastatic disease. Some patients had multiple symptoms. Thirty-three carcinoid tumors (39%) were asymptomatic and found on screening colonoscopy. Three patients (4%) had a history of colorectal adenocarcinoma, and 11 (13%) had a history of another malignant neoplasm. No patient had a history of inflammatory bowel disease.

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### Table. Characteristics of Tumors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Tumors (n=85)</th>
<th>Tumors Treated Endoscopically (n=46)</th>
<th>Tumors Treated With Transanal Excision/TEM (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor size, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-0.4</td>
<td>21 (25)</td>
<td>18 (39)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>0.5-0.9</td>
<td>27 (32)</td>
<td>19 (41)</td>
<td>8 (35)</td>
</tr>
<tr>
<td>1.0-1.9</td>
<td>12 (14)</td>
<td>4 (9)</td>
<td>5 (22)</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>12 (14)</td>
<td>1 (2)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Not described</td>
<td>13 (15)</td>
<td>4 (9)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Tumor morphologic features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyp</td>
<td>34 (40)</td>
<td>24 (52)</td>
<td>8 (35)</td>
</tr>
<tr>
<td>Nodule</td>
<td>34 (40)</td>
<td>10 (22)</td>
<td>13 (57)</td>
</tr>
<tr>
<td>Depth of invasion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited to mucosa</td>
<td>18 (21)</td>
<td>15 (33)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Into submucosa</td>
<td>32 (38)</td>
<td>18 (39)</td>
<td>11 (48)</td>
</tr>
<tr>
<td>Into muscularis propria</td>
<td>11 (13)</td>
<td>3 (7)</td>
<td>6 (26)</td>
</tr>
<tr>
<td>Through muscularis propria</td>
<td>3 (4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Not described</td>
<td>21 (25)</td>
<td>10 (22)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>8 (9)</td>
<td>0</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>5 (6)</td>
<td>0</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Poorly differentiated histologic features</td>
<td>2 (2)</td>
<td>0</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Positive margins</td>
<td>. . .</td>
<td>38 (83)</td>
<td>. . .</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; TEM, transanal endoscopic microsurgery; ellipses, not calculated.

*Percentages do not add to 100 because of missing data or percentage rounding.

Explained in the “Transanal Excision/TEM” portion of the “Surgical Resection” subsection of the “Results.”
Patients were treated with endoscopic resection (46 of the 85 patients [54%]) or surgical resection (31 patients [36%]). Eight patients (9%) who did not receive an attempt at local clearance of the tumor had metastases on presentation, refused surgical treatment, or had another active malignant neoplasm, which obviated a decision to treat the rectal carcinoid tumor. One patient died of acute myelogenous leukemia and another died of complications from a bone marrow transplant for chronic lymphocytic leukemia 3½ years and 8 years, respectively, after diagnosis of rectal carcinoid tumor.

**ENDOSCOPIC THERAPY**

Forty-six patients had carcinoid tumors treated with endoscopic excision alone. Features of these tumors are described in the Table. The margins of excision were positive in 38 of the 46 patients (83%). Among these 38 patients, 6 (16%) had residual tumor on a subsequent endoscopy. One patient with a negative margin (3%) had residual tumor on follow-up. Complications of endoscopic therapy included 1 patient (2%) in whom bleeding occurred 8 days after endoscopic submucosal resection, requiring a second proctoscopy.

**Endoscopic Submucosal Resection**

Of all 85 patients, 12 (14%) underwent an endoscopic submucosal resection after diagnosis of rectal carcinoid tumor. Five of these 12 resections (42%) showed positive cauterized margins.

**Tumors Larger Than 1.0 cm**

Four of 46 patients had 1.0-cm tumors and 1 patient had a 2.0-cm tumor treated with endoscopic excision. Of these 5 tumors, 3 were limited to the mucosa, 1 invaded the submucosa, and the depth of invasion was not specified for 1 tumor that had been described as “polypoid.” Margins were negative in 1 patient, indeterminate in 1, and within 0.1 cm of the tumor in 3. These 5 patients were followed-up with 2 to 4 endoscopies each over the next 3½ to 8 years, with no recurrence. One patient underwent sigmoid resection for colon cancer and had no further endoscopic follow-up examinations but was clinically well 12 years after his diagnosis of rectal carcinoid tumor.

**Follow-up**

The median follow-up for endoscopically treated patients was 2.0 years (range, 0.16 years; mean [SD], 3.6 [4.1] years). The median number of follow-up endoscopies was 2 (range, 0–7). One patient was found to have hepatic metastases 5 years after diagnosis. She had a positive margin after endoscopic excision of a 0.7-cm tumor invading the muscularis propria. There was 1 death in the endoscopic treatment group; that patient died of metastatic colon adenocarcinoma.

**SURGICAL RESECTION**

Thirty-one of the 85 patients (36%) underwent surgical resection. Of these, there were 19 transanal excisions (61%), 4 TEM procedures (13%), 6 low anterior resections (19%), and 2 abdominoperineal resections (6%). Median follow-up for patients after resection was 1.7 years (range, 0–15 years).

**Transanal Excision/TEM**

Tumor characteristics for the 23 patients who underwent transanal excision or TEM are given in the Table. The tumors were larger than 1.0 cm in 9 patients (39%) and invaded into the submucosa or muscularis propria in 17 (74%).

Almost all of the patients (22 of 23 [96%]) had undergone endoscopy prior to transanal excision or TEM. In 13 of these 23 patients (65%), endoscopy yielded only biopsy specimens or showed positive margins on excision. Three patients (13%) underwent transanal excision or TEM after a follow-up endoscopic biopsy specimen showed residual carcinoid tumor. One patient underwent TEM because endoscopic ultrasonography showed invasion of tumor into the muscularis propria. One patient had 2 carcinoid tumors; both tumors were treated with transanal excision. One local excision was palliative and performed concurrently with an end colostomy. One patient had unclear indications for transanal excision. Transanal excision or TEM was performed a median of 2.4 months after the initial diagnosis (range, 19 days to 6 months).

No residual tumor was noted in 10 of the 23 patients (43%). Residual tumor with negative margins was seen in 10 patients (43%). Residual tumor with positive margins was seen in 2 patients (9%), including 1 who underwent a palliative procedure and 1 who underwent a diagnostic procedure in the setting of a metastatic workup. One patient with positive margins underwent transanal excision as the initial diagnostic procedure; thrombosed hemorrhoid was included in the differential diagnosis. All of the 20 patients who underwent curative resection had negative margins. Among the 20 patients who did not have metastases at presentation, recurrence was noted in 1 (5%) who developed liver metastases 13 years after a transanal excision that had shown no residual tumor. (The tumor was 0.6 cm invasive into submucosa and was endoscopically removed.) One patient who presented with 2 rectal carcinoid tumors developed another small primary tumor 5 months after transanal excision.

Postoperative complications occurred in 2 patients (9%). One woman whose tumor invaded the submucosa had a rectovaginal fistula, which was repaired 1 year later with an endorectal advancement flap that healed. One patient with multiple comorbidities experienced acute renal failure and required an 8-day hospitalization.

**Rectal Resection**

Most of the 8 patients undergoing rectal resection had either high rectal tumors or bulky tumors. Three pa-
Patients had large tumors (>3.0 cm), 1 had a near-obstructing tumor, 1 had evidence of growth through the rectal wall on preoperative computed tomography of the pelvis, and 1 tumor was at the rectosigmoid junction. Three patients undergoing rectal resection (38%) had metastases on presentation, 2 (25%) had no residual tumor, and 5 (62%) had nodal disease.

The outcome after rectal resection resulted in cure in 4 patients (50%), of whom 2 patients had more than 10 years of follow-up. One patient died of disease after local recurrence less than 1 year after resection, and liver metastases developed 1 year postoperatively in 1 patient who underwent curative resection. Postoperative complications occurred in patients: an anastomotic stricture occurred 1.5 months postoperatively in one patient, and a partial small-bowel obstruction occurred 2 months postoperatively in the other.

Among the 31 patients who underwent surgical resection, 2 died of advanced medical disease unrelated to carcinoid tumor and 1 died of advanced pelvic disease 1 year after low anterior resection.

**ENDOSCOPIC VS SURGICAL RESECTION**

Patients undergoing endoscopic resection were more likely than patients undergoing surgical resection to have tumors smaller than 0.5 cm (18 tumors [39%] vs 2 [6%]; \(P = .001\)), polyoid as opposed to nodular tumors (24 polyoid tumors [52%] vs 8 [22%]; \(P = .03\)), and tumor limited to the mucosa (15 tumors [33%] vs 1 [3%]; \(P = .002\)). Local excision or TEM was significantly less likely to result in positive margins (no tumors [0%] vs 38 [83%]; \(P < .001\)). Despite this, patients undergoing curative surgical resection were more likely than those treated with endoscopic resection to have a recurrence (risk ratio, 2.3; \(P = .06\)).

**LABORATORY TESTS AND IMAGING**

Urinary 5-hydroxyindoleacetic acid or serum chromogranin A levels were measured in 23 of the 85 patients (27%). Ten of the 15 patients with metastatic disease (67%) underwent testing of serum chromogranin A or urinary 5-hydroxyindoleacetic acid levels; of these, 2 patients had chromogranin A levels measured at the upper range of normal and the others showed levels that were not elevated. No patient with hepatic metastases showed signs of carcinoid syndrome. Endoscopic ultrasonography was performed as part of the evaluation in 28 of 77 patients (36%) who underwent treatment. Half were performed prior to excision and half were used in short-term follow-up. Four patients underwent rectal magnetic resonance imaging (MRI). Periprocedural somatostatin receptor scintigraphy was performed in 22 of the 77 patients (29%) who underwent treatment.

**METASTATIC DISEASE**

Eleven patients presented with distant metastases and 4 patients were found to have metastases on follow-up. Metastases occurred from 2 tumors smaller than 1.0 cm at 5 and 13 years: one as a pelvic nodule and multiple liver metastases and the other as multiple liver metastases. Metastatic disease occurred mostly in the liver (12 of 15 patients [80%]) but also in the lungs (3 of 15 [20%]), periaortic nodes (2 of 15 [13%]), pancreas (2 of 15 [13%]), groin nodes (1 of 15 [7%]), and subcutaneous tissue (1 of 15 [7%]). No patient had carcinoid syndrome.

Herein we review our institutional experience with all rectal carcinoid tumors. Although smaller tumors typically have a benign course, our finding of metastases from 2 of the 48 tumors smaller than 1.0 cm (4%) many years after excision reminds us that the behavior of these tumors is not easily predicted.

We found that endoscopic excision alone had a poor success rate in achieving negative margins (8 of 46 tumors [17%]). Local excision or TEM was more likely to achieve disease clearance. Endoscopic submucosal resection achieved a better rate of negative margins (7 of 12 patients [58%]) than did endoscopic excision. Patients who are treated endoscopically require close endoscopic follow-up because 16% of our patients with positive margins (6 of 38 patients) showed residual tumor on subsequent biopsy. We found that, compared with surgical resection, endoscopic excision was not associated with disease recurrence. However, the small number of patients in our study precludes risk adjustment when making this comparison. Local excision in the operating room provided the best rate of success in achieving negative margins. Nearly all patients with positive margins in the endoscopic resection group were free of local recurrence, nodal disease, and distant metastases on follow-up, raising the question of whether complete local clearance of tumor is required to prevent disease progression. Despite this finding, we believe that therapy should attempt to achieve negative margins for the following reasons. First, distinguishing features between benign and malignant tumors are not yet clearly defined. Second, recurrence of rectal carcinoid tumors can evolve over a prolonged period, making it difficult for these events to be captured in the literature. Finally, chemotherapy and radiotherapy have little to offer patients who have advanced disease. Until such therapies evolve, complete resection of local disease offers the only chance for cure.

In our series, the complication rate after local excision was 9%, which is in the same range as reports in the literature for transanal excision and TEM for all rectal neoplasms (0%-12%). We recommend consideration of local excision for rectal carcinoid tumors with positive margins on endoscopy in patients who can tolerate surgery. We recommend low anterior resection or abdominoperineal resection for tumors 1.0 to 1.9 cm with high-risk features such as muscular, lymphovascular, or perineural invasion. A rectal resection should be considered for tumors in this size range without high-risk features if the margins are positive on endoscopic or local excision. Somatostatin receptor scintigraphy and cross-sectional imaging can be used to assess for nodal disease in these patients. For patients with localized tumors larger than 2.0 cm, we recommend rectal resection in light of...
the high rate of metastases (74% to 77%) described in the literature, and of the 50% cure rate (4 of 8 patients) in our series. It is unclear whether resecting local disease is of benefit in patients who have metastatic disease at presentation.

After rectal carcinoid tumors have been resected, appropriate follow-up includes endoscopy and, in some cases, imaging. Imaging methods include endoscopic ultrasonography, abdominopelvic computed tomography, rectal MRI, and octreotide imaging (somatostatin receptor scintigraphy). Clear patterns in the use of imaging were not evident, likely because our study included patients treated during a 16-year period. In patients with higher risk tumors who have been treated with local or endoscopic excision, we recommend that endoscopic ultrasonography or rectal MRI be performed in conjunction with octreotide imaging. We follow-up patients every 6 months with proctoscopy for 2 years and then annually for 5 years. For higher risk tumors, we recommend imaging on an annual basis for 3 years, which is similar to the National Comprehensive Cancer Network’s recommendations for rectal adenocarcinoma follow-up. Because metastases can occur years after diagnosis, patients should be made aware of the need for imaging if there are even minor abdominal symptoms.

The major limitation of our study is that it used retrospective methods of data collection. In addition, patients were seen in referral from other institutions, which skewed the patient sample toward those with advanced disease and limited complete data. Although follow-up was extensive for some patients, others returned to the referring institutions after evaluation at ours, making it possible that disease recurrence was diagnosed elsewhere.

To our knowledge, this study is one of the largest US series of rectal carcinoid tumors and the first to assess the adequacy of endoscopic resection in a substantial number of patients. We found that surgical transanal excision was more reliable than endoscopic resection in the local clearance of small tumors.

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Author Contributions: Study concept and design: Kwaan and Bleday. Acquisition of data: Kwaan. Analysis and interpretation of data: Kwaan, Goldberg, and Bleday. Drafting of the manuscript: Kwaan and Bleday. Critical revision of the manuscript for important intellectual content: Kwaan, Goldberg, and Bleday. Statistical analysis: Kwaan. Administrative, technical, and material support: Kwaan and Bleday. Study supervision: Goldberg and Bleday.

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Additional Contributions: Jason F. Schmidt, MD (Department of Pathology, Brigham and Women’s Hospital), assisted with identifying patients for the study.

REFERENCES