Treatment Strategies and Outcomes for Rectal Villous Adenoma From a Single-Center Experience

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Objectives: To analyze a 13-year, single-surgeon experience with villous adenoma of the rectum with respect to procedure, complications, recurrence, and cancer incidence.

Design: Retrospective review of patient and tumor characteristics, procedure, recurrence, and complications.

Setting: University hospital.

Patients: Patients who underwent excision of rectal villous adenoma.

Main Outcome Measures: Complication, recurrence, and malignancy rates.

Results: Thirty-six patients underwent 30 transanal and 10 transabdominal excisions. Mean age was 66 years (range, 41-86 years) and mean follow-up was 25 months (range, 0.5-132 months). Mean tumor size was 3.0 cm (range, 0.5-11 cm) and the mean distance of the tumor from the anal verge was 4.9 cm (range, 0-10 cm). Preoperatively, 18 (45%) lesions harbored low-grade dysplasia while 17 (43%) had high-grade dysplasia. Postoperative pathology was discordant in 50% of patients, including 5 of 40 lesions (13%) that were recategorized as invasive cancer. Tumor size did not correlate with malignancy. The complication rate was significantly lower in transanal compared with transabdominal excisions (3.6% vs 50%, \( P = .005 \)). There were 4 (12.5%) benign recurrences, all after transanal excisions.

Conclusions: Complete excision is warranted for rectal villous adenomas, as biopsies were accurate only 50% of the time, and 1 in 8 patients had unsuspected cancer found after excision. Transanal excision with negative margins is associated with low recurrence and complication rates and is the preferred approach, even with large lesions.

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Villous adenoma is a premalignant polyp of the gastrointestinal tract. Up to two-thirds of these lesions occur in the rectum. They have an equal distribution between sexes and a peak incidence in the sixth and seventh decades of life. They can be difficult to palpate on rectal examination and difficult to detect by colonoscopy owing to their flat, soft nature and indistinct borders. These lesions have been reported to harbor malignancy in 4% to 40% of cases. Biopsy is inaccurate in this setting, missing invasive cancer about 40% of the time. Appropriate treatment consists of complete excision, either endoscopically or by removal of the entire rectum, and pathologic analysis of the entire specimen.

Surgical options for resection of villous adenoma of the rectum include local treatments, such as transanal excision (TAE), transanal endoscopic microsurgery, and mucosal resections, or radical resections, such as proctectomy. The most commonly performed procedures are TAEs and proctectomies. Whenever possible, local excision and sphincter preservation is the procedure of choice for accessible lesions with favorable characteristics. Despite complete excision, recurrence is seen in up to 40% of cases.

Ongoing challenges in managing these lesions continue to be identifying risk factors for failure of local therapy and identifying diagnostic techniques that may aid in deciding appropriate surgical therapy. The broad range of reported recurrence rates for treatment of villous adenoma of the rectum indicates a need for additional data. Therefore, we analyzed the 13-year experience of a single surgeon in the management of these tumors with respect to the oncologic outcome of different surgical techniques, complication rates, and concordance of preoperative and postoperative diagnoses. We hypothesized that TAE of rectal villous adenoma would provide good oncologic outcome with acceptable complication and recurrence rates.
The operative log of a single surgeon (K.E.D.) was reviewed for patients who underwent a surgical procedure for villous adenoma of the rectum between January 1995 and June 2007. Institutional review board approval was obtained before medical record review. All procedures were performed at Oregon Health & Science University, Portland, a tertiary care university hospital. Variables collected included patient and tumor characteristics, history of rectal polyps and treatment, preoperative pathology, use of endoscopic ultrasonography (EUS), type of procedure, complications, recurrence status, and time and results of follow-up. Patients who had a preoperative diagnosis of malignancy using biopsy were excluded. All patients were preferentially considered for TAE unless the extent of the tumor precluded this procedure (eg, nearly or totally circumferential or carpeting of the entire rectum).

Continuous data were compared using the t test, while categorical data were compared via χ² analysis, the Fisher exact test, or the Mann-Whitney U test as appropriate. Significance was set at P < .05. Statistical analyses were performed using SPSS, version 15.0 (SPSS Inc, Chicago, Illinois).

RESULTS

PATIENT CHARACTERISTICS

Forty procedures were performed in 36 patients during this period. Mean age was 66 years, and the male to female ratio was 1:2.6. An attempt at excision, either endoscopically or surgically, was made in 20 (55.6%) patients before they were referred to us. Two patients died during the study period: one received a subsequent diagnosis of cholangiocarcinoma; the other, breast cancer during the study period: one received a subsequent diagnosis of cholangiocarcinoma; the other, breast cancer during the study period: one received a subsequent diagnosis of cholangiocarcinoma; the other, breast cancer (see Table 1).

Table 1. Characteristics of Patients Who Underwent Excision of a Rectal Villous Adenoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, N. M/F</td>
<td>9/23</td>
</tr>
<tr>
<td>Age, mean (range), y</td>
<td>66 (41-86)</td>
</tr>
<tr>
<td>Follow-up, mean (range), mo a</td>
<td>25 (0.5-132)</td>
</tr>
<tr>
<td>Survival rate, No. (%) a</td>
<td>30/32 (93.8)</td>
</tr>
<tr>
<td>Attempts at excision before initial referral, No. (%), mean (range)</td>
<td>20/36 (55.6), 1.1 (0-5)</td>
</tr>
<tr>
<td>Endoscopic, No. (%)</td>
<td>15 (41.7)</td>
</tr>
<tr>
<td>Transanal, No. (%)</td>
<td>5 (13.9)</td>
</tr>
</tbody>
</table>

aFour patients were lost to follow-up.

DISEASE/TUMOR CHARACTERISTICS

Preoperative pathology reports were available in all 40 cases and were divided into 3 categories: no or low-grade dysplasia; high-grade dysplasia; or no comment on dysplasia made. No tumor was found to harbor invasive adenocarcinoma preoperatively. We examined the proportion of tumors that were either upgraded or downgraded by definitive excision. Postoperatively, there were 5 cases (13%) of invasive carcinoma diagnosed. All 5 cases were preoperatively assessed as high-grade dysplasia. In total, 50% of patients had an incorrect preoperative diagnosis based on biopsy, with 13% of cases upstaged to invasive cancer. Table 2 presents the distribution of preoperative pathologic diagnoses and the concordance between preoperative and postoperative pathology.

We also analyzed the association of tumor size (defined as the greatest dimension in centimeters), distance from the anal verge (defined as the distance, in centimeters, to the lower or distal edge of the tumor), and patient age and sex with the presence of malignancy or high-grade dysplasia. The mean distance from the anal verge was 4.9 cm (range, 0-10 cm) and mean size was 3.0 cm (range, 0.5-11 cm). Tumors that were classified as having either no or low-grade dysplasia were compared with tumors classified as having high-grade dysplasia or invasive adenocarcinoma. There were no significant differences between the distance from the anal verge, greatest dimension of tumor, age, or sex (Table 3). However, patients who underwent prior attempts at excision, either colonoscopically or by previous TAE, were more likely to present with a lesion categorized as having no or low-grade dysplasia, while those with high-grade dysplasia or invasive adenocarcinoma were more likely to present with their index lesions.

Table 2. Concordance Between Preoperative and Postoperative Pathology of Rectal Villous Adenomas

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases, No. (%) (N=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative diagnosis</td>
<td></td>
</tr>
<tr>
<td>No or low-grade dysplasia</td>
<td>18 (45)</td>
</tr>
<tr>
<td>High-grade dysplasia</td>
<td>17 (43)</td>
</tr>
<tr>
<td>No comment on dysplasia</td>
<td>5 (13)</td>
</tr>
<tr>
<td>Preoperative and postoperative concordance</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>20 (50)</td>
</tr>
<tr>
<td>Higher grade</td>
<td>7 (18)</td>
</tr>
<tr>
<td>Lower grade</td>
<td>7 (18)</td>
</tr>
<tr>
<td>Upstage to cancer</td>
<td>5 (13)</td>
</tr>
</tbody>
</table>

Table 3. Comparison of Patient and Tumor Characteristics With Regard to Pathologic Status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Dysplasia or LGD</th>
<th>HG or CA</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greatest dimension of tumor, mean, cm</td>
<td>3.0</td>
<td>3.0</td>
<td>.95</td>
</tr>
<tr>
<td>Distance of tumor from anal verge, cm</td>
<td>4.4</td>
<td>5.6</td>
<td>.23</td>
</tr>
<tr>
<td>Age, mean, y</td>
<td>65</td>
<td>68</td>
<td>.47</td>
</tr>
<tr>
<td>Sex, N. M/F</td>
<td>10/19</td>
<td>4/7</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Attempts at excision before initial referral, median</td>
<td>1</td>
<td>0</td>
<td>.04</td>
</tr>
</tbody>
</table>

Abbreviations: CA, invasive adenocarcinoma; HG, high-grade dysplasia; LGD, low-grade dysplasia.
Table 4. Factors Potentially Associated With Recurrence of Villous Adenoma

<table>
<thead>
<tr>
<th>Factor</th>
<th>Cases, No. (%)</th>
<th>Recurrence</th>
<th>No Recurrence</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attempts at excision before initial referral, median (IQR)</td>
<td></td>
<td>2 (1-4)</td>
<td>1 (0-2)</td>
<td>.08^</td>
</tr>
<tr>
<td>Age, mean, y</td>
<td></td>
<td>68</td>
<td>66</td>
<td>.69</td>
</tr>
<tr>
<td>Sex, No., M/F</td>
<td></td>
<td>1/3</td>
<td>9/23</td>
<td>.72</td>
</tr>
<tr>
<td>Distance from anal verge, mean cm</td>
<td></td>
<td>5.5</td>
<td>4.7</td>
<td>.63</td>
</tr>
<tr>
<td>Mean greatest dimension of tumor, cm</td>
<td></td>
<td>5.0</td>
<td>2.8</td>
<td>.10</td>
</tr>
<tr>
<td>Transanal excision</td>
<td></td>
<td>4/4</td>
<td>26/36 (72)</td>
<td>.56</td>
</tr>
<tr>
<td>Transabdominal excision</td>
<td></td>
<td>0/10/40 (25)</td>
<td></td>
<td>.56</td>
</tr>
<tr>
<td>Final pathology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
<td>0/4</td>
<td>5/36 (14)</td>
<td>.68</td>
</tr>
<tr>
<td>HGD/CA</td>
<td></td>
<td>1/4 (25)</td>
<td>13/36 (36)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Postoperative complication</td>
<td></td>
<td>1/4 (25)</td>
<td>5/36 (14)</td>
<td>.42</td>
</tr>
<tr>
<td>Positive marginb</td>
<td></td>
<td>1/2 (50)</td>
<td>1/29 (3.4)</td>
<td>.35</td>
</tr>
</tbody>
</table>

Abbreviations: CA, invasive adenocarcinoma; HGD, high-grade dysplasia; IQR, interquartile range.
^Comparison made by Mann-Whitney U test.
bComment on margin status was made in 29 of 36 cases in the group without recurrence and in 2 of 4 cases in the group with recurrence.

OPERATIVE CHARACTERISTICS

Thirty of 40 tumors were excised via the transanal route (75%) and 10 were removed transabdominally by proctectomy (25%). The mean size of lesions removed by transabdominal methods was 5.6 cm compared with 2.2 cm for lesions removed via TAE (P < .001). Mean distance from the anal verge did not differ (3.9 cm for transabdominal vs 5.1 cm for transanal, P = .37). Six complications were noted (16%). The complication rate for TAE was significantly lower than for transabdominal procedures (3.6% vs 50%, P = .005). Mean length of stay was 12 days for the transabdominal group and 1.7 days for the transanal group (P = .005).

DISEASE RECURRENCE

We defined recurrence as a villous adenoma diagnosed by any means on postoperative follow-up after the index procedure and as occurring after initial referral to the operating surgeon (Table 4). Four patients fit this definition, and no patient recurred more than once during the study period. All recurrences were benign, occurred after TAE, and were all in patients who had had prior attempts at excision before referral. No patient who presented with their first lesion had a recurrence. Tumor size, distance from the anal verge, and positive margins were not associated with recurrence. No patient who had an invasive cancer had a recurrence during a mean follow-up of 17.4 months (range, 5-33 months). Three of the 5 recurrent cancers were pT1, 2 of which were in the TAE group (no further resection was recommended). The other 2 recurrent cancers were pT2 and were removed transanally; no additional treatment was recommended owing to the patients’ age and comorbid conditions.

ENDOSCOPIC ULTRASONOGRAPHY

Endoscopic ultrasonography was used in 10 patients (25%) to assess 11 lesions. This was an emerging technology at Oregon Health & Science University during the study period. All EUSs at our institution were performed by 1 of 2 endoscopists. Ten of 11 tumors assessed by EUS were characterized as at least stage T1. Five of these lesions ultimately harbored invasive cancer based on postoperative surgical pathology. One of 11 lesions was characterized correctly as a benign villous adenoma by EUS.

Overstaging by EUS was seen in 2 uT1 lesions resected transanally, which later proved to be pT0. These lesions were 4.5 and 11 cm in their greatest dimension. Overstaging by EUS was seen in 3 uT1 lesions resected transanally, which were later identified to be stage pT0. These lesions had a mean size of 1.1 cm. Endoscopic ultrasonography correctly staged 54% and overstaged 45.5% of lesions. No tumors were understaged.

Endoscopic ultrasonography had a sensitivity of 100%, a specificity of 16.7%, a positive predictive value of 50%, and a negative predictive value of 100% for the presence of malignancy. Preoperative biopsy had a sensitivity of 80%, a specificity of 94.3%, a positive predictive value of 66.7%, and a negative predictive value of 97.1% for the presence of malignancy.

COMMENT

This article provides new perspective on the management of villous adenoma of the rectum. Our patient population was similar in age to populations in published articles, but ours had a slightly higher female to male ratio of 2.6:1. In contrast to prior reports, more than 60% of this patient group had been referred after a previous attempt at excision.

The 13% rate of invasive cancer is consistent with previous articles, which describe rates between 1% and 40%, 1-4,10,11 In our analysis, we grouped high-grade dysplasia and carcinoma in situ together in concordance with the Vienna criteria12 (Vienna grade 4). All cases of invasive cancer arose from lesions classified as high-grade dysplasia, which is consistent with the natural history of villous tumors. Interestingly, patients with high-grade dysplasia or invasive adenocarcinoma were more likely to have undergone their initial excision at our institution, rather than being referred for a re-excision, perhaps because of earlier referral of more advanced appearing lesions. There were no other significant predictors of malignancy, such as tumor size or ultrasonographic findings. That 50% of biopsy results were incorrect, nearly 1 in 5 lesions were upgraded postoperatively, and 1 in 8 lesions harbored invasive adenocarcinoma supports complete excision as the only means of definitive diagnosis.

The inaccuracy of preoperative diagnosis did not appear to affect outcomes in our series, possibly because the treatment was determined with the supposition that the preoperative diagnosis is often inaccurate. This finding may be proven to be incorrect with longer follow-up, though most recurrences are expected in the first 2
years. In addition, while many cases were upstaged, 18% of our cases were downstaged. Our findings about the inaccuracy of the preoperative diagnosis are consistent with the experiences of other authors who have reported low accuracy of preoperative biopsy.5,13

While size of the tumor was not predictive of invasive cancer, it did influence the procedure performed. In our series, transanal methods were attempted unless the tumor was large, circumferential, or associated with multiple adenomas on preoperative assessment, either endoscopically or by clinical examination. A limitation of this retrospective review is the lack of a standard process for determining which operation was offered.

The overall complication rate in our series was 16%. In a series of 50 patients, Featherstone et al14 reported no morbidity or mortality for TAE during a 24-month follow-up period. This compares with 1 complication in 28 (3.6%) TAEs in our patient group. Winburn3 reported a 24% (12% major and 12% minor) complication rate and no mortality in a series of 16 patients, 14 of whom underwent TAEs and 2 of whom underwent low anterior resections. They note that all patients had follow-up to at least 2 years, though details about the distribution of complications among the different operations is lacking. In a series of 207 patients, Pigot et al5 report a 10% complication rate, 4% early and 6% late, with 1 death (0.5%).

In articles published within the last 10 years,2,3,14 no direct comparison is made between TAE and transabdominal procedures. Our 50% rate of overall complications for transabdominal resections is comparable with rates reported in the literature15 and represents a 13.9-fold higher complication rate for transabdominal procedures (50% vs 3.6%, P = .005), corresponding to a number needed to treat of 2.2. Thus, just over 2 TAEs have to be performed to avoid 1 complication from a transabdominal procedure. Counterbalancing this, the number needed to treat for benign recurrence is 7 (14% in the TAE group vs 0% in the transabdominal group). Therefore, 7 transabdominal procedures need to be performed to avoid 1 recurrence by TAE. However, we and others have demonstrated a complication rate of 50% to 56% with transabdominal procedures for rectal lesions. Our data show that 4 complications would occur in attempting to prevent 1 recurrence. Therefore, despite a higher recurrence with TAE, routine use of transabdominal excision would result in an unacceptably high complication rate and far outweighs the cost of benign, easily managed recurrences. This supports our methodological strategy of preferentially performing TAE (unless tumor characteristics did not allow a TAE).

Similarly, although all 5 invasive cancers were in the high-grade dysplasia group, transabdominal excision of all 17 tumors with a preoperative diagnosis of high-grade dysplasia would lead to 8 to 9 potential complications. Of 4 cases in the TAE group, 2 cancers were curatively resected and 2 patients would not have tolerated a more aggressive operation. Thus, the prognosis would not have changed at the expense of a dramatic increase in potential morbidity and mortality.

A trend toward increased benign recurrence was noted for patients who underwent prior attempts at excision before being referred to us (P = .08). One possible explanation is that this group may have had incomplete initial excisions. The failure rate of endoscopic therapy before initial referral was 41.7% (15 of 36 patients), which suggests a high rate of recurrence with limited resection. Statistical analysis failed to show any association between benign recurrence and tumor size, distance from the anal verge, presence of malignancy, positive resection margins, or transanal procedure (Table 4). Other authors have found that size, the presence of severe dysplasia or malignancy, positive surgical margins, and treatment by local excision are predictors of benign recurrence.2,4 However, Adams and Wong10 described a series of 62 patients with rectal villous adenoma (57 of whom were treated by TAE), in which depth of excision and presence of malignant focus did not predict recurrence.

Other possible reasons for the increased benign recurrence rate in patients with previous excisions could be that prior excision methods were inadequate or the entire mucosal area had a propensity to develop villous adenomas (field effect) and the recurrence represents adenoma developing in an adjacent site. This may be a potential area of study with regard to identifying possible differences in cytokine expression, genetic alterations, or changes in immunohistochemical markers. Early work in this field is promising. Hao and coworkers41 examined 15 genes shown to have altered expression in colon cancer. Using a single rectosigmoid biopsy, they were able to show differences in gene profiles in 169 biopsies of 24 patients with adenomatous polyps anywhere in the colon. This effect persisted both in patients with and without a personal or family history of colon cancer.

Given the high rate of occult malignancy reported in villous tumors of the rectum in our series (13%), the use of EUS holds promise as an adjunct to clinical examination and preoperative biopsy. This technique was emerging at our institution during the study period. Our data showed that EUS had high sensitivity and negative predictive value but poor specificity and positive predictive value. In our series, EUS tended to erroneously upstage tumors but did not appear to influence the choice of procedure performed. The rate of TAE was similar whether or not EUS was performed (79% vs 70%, respectively), despite 10 of 11 EUS results that were reportedly positive for malignancy. Worrell and colleagues11 performed a systematic review of the literature assessing the use of EUS for detecting foci of malignancy within rectal adenomas. They identified only 5 articles that met their inclusion criteria of adequate preoperative and postoperative reporting. These authors found, in a pooled analysis, that EUS diagnosed 81% of focal cancers missed by biopsy and that the false-negative rate would be decreased from 24% to 5% with combined use of biopsy and EUS. Thus, 5 adenomas negative on biopsy would need to be assessed by EUS to prevent 1 missed cancer, while 1 case of overstaging would occur per 11 correct diagnoses by EUS (9%). Adams and Wong10 reported a sensitivity of 50%, a specificity of 94%, a positive predictive value of 66.7%, and a negative predictive value of 88.7% for the detection of malignant foci within rectal villous lesions using EUS in 62 patients. They also note that a technically imperfect examination produced a 37.1% rate
Management of villous adenoma of the rectum remains a diagnostic and treatment challenge. No specific factor, including tumor size and EUS findings, predicted malignancy. Because 50% of lesions were incorrectly diagnosed using preoperative biopsy, 18% were upstaged postoperatively and 13% were upstaged to carcinoma, complete excision is required for accurate diagnosis. When feasible, this should be done with TAE to avoid the higher complication rate of transabdominal excision.

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Author Contributions: The authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

CONCLUSIONS

Management of villous adenoma of the rectum remains a diagnostic and treatment challenge. No specific factor, including tumor size and EUS findings, predicted malignancy. Because 50% of lesions were incorrectly diagnosed using preoperative biopsy, 18% were upstaged postoperatively and 13% were upstaged to carcinoma, complete excision is required for accurate diagnosis. When feasible, this should be done with TAE to avoid the higher complication rate of transabdominal excision.

Study concept and design: Cho, Herzig, Douthit, and Deveney. Acquisition of data: Cho, Herzig, Douthit, and Deveney. Analysis and interpretation of data: Cho, Herzig, Douthit, and Deveney. Drafting of the manuscript: Cho, Herzig, Douthit, and Deveney. Critical revision of the manuscript for important intellectual content: Cho, Herzig, Douthit, and Deveney. Statistical analysis: Cho. Administrative, technical, and material support: Herzig. Study supervision: Herzig and Deveney.

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REFERENCES

DISCUSSION

Theodore X. O’Connell, MD, Los Angeles, California: This paper emphasizes the necessity of complete resection of villous adenomas of the rectum. Villous adenomas are considered premalignant and should be removed to prevent the development of invasive carcinoma. However, the second reason to remove them is that in spite of random biopsies of the lesions that are reportedly benign, the lesion may still harbor cancer. Random preoperative biopsies have a high degree of sampling errors, and complete excision is the only accurate diagnostic and adequate therapeutic approach to villous adenomas of the rectum.

Villous adenomas are usually sessile and are not easily removed by endoscopic snare polypectomy. Therefore, the complete resection of a villous adenoma often requires a complete operative colonic resection and/or excision.

Villous adenomas are most often found in the right colon and rectum. Obviously, in the right colon and cecum a formal colectomy is done. However, in the rectum, except for high rectal lesions, an effort should be made to remove these transanally to prevent the morbidity of the abdominal operation and loss of sphincter control and to maintain proper bowel movements. While this paper emphasizes all these points quite well, I have several questions for the authors.

1. Extent of resection. In the paper it is stressed, rightly so, that villous adenoma is a benign though premalignant lesion and that simple excision is adequate therapy even when they harbor a superficial cancer; therefore, preservation of the sphincter is of paramount importance; however, in your original manuscript, 7 of the 36 patients, approximately 20%, had abdomino-perineal resection. In the revised manuscript it states that 25% of the patients had transabdominal proctectomy. How many of these were LAR [low anterior resection] vs APR [abdomino-perineal resection]? If the patients had APR what is the explanation for this? Were some of these cases in which the villous adenoma’s distal edge was at or just above the dentate line but its proximal extent was high, eg, 10 cm or above, so that the entire lesion could not be removed completely by transabdominal approach or by a low anterior resection? In this circumstance, I have combined the procedures doing TAE for the lower portion and LAR for the upper portion with reanastomosis to the mucosally resected distal rectum. Have you ever used this approach?

2. Transabdominal vs TAE. It was proven quite well that transabdominal resection has a significantly higher complication rate than TAE, but isn’t this an apples and oranges comparison? Isn’t the characteristics of the tumor, ie, distance from the anal verge, size, etc, that [which] drives the selection rather than surgeon’s choice?

3. Selection of patients. What are your criteria for distance from the anal verge for attempting a TAE? Do you have a definite cut-off point? Also would you attempt TAE at a higher level in older patients, especially females, who have more laxity permitting the rectum to be pulled down and more easily accessed through the transanal approach? Also do you avoid TAEs in midrectal lesions in the anterior positions in the female for fear of perforating into the peritoneal cavity?

4. Recurrences. A 12.5% benign recurrence after TAE is reported; however, the average follow-up is only 25 months. Do you think that this is a long enough follow-up to conclude that you have seen all the benign recurrences which may be slow to recur? What is the time to recurrence? Is it relatively early or late? Occurring before or after 25 months? This will give some idea whether 25 months is an adequate time to judge the complete status of recurrence.

5. Margin status. I am concerned that in 9 of 40 excisions there was no information regarding resection margins. I feel that getting a negative margin is very important in these lesions, but in 25% of the patients, this information was not available. Why was this percentage so high? Also 2 of the patients had positive margins on pathology, but there is no mention of re-resection to obtain a negative margin. Why was re-resection not attempted in these patients?

6. Carcinoma in villous adenoma. Two of the patients treated transanally had T2 carcinoma in the villous adenoma but no additional therapy was recommended. Current data suggest that recurrence rate[s] with T2 lesions treated with simple excision alone are high and that additional therapy is warranted. This was reportedly done because of age and/or comorbidity. What would be your recommendation for further treatment in T2 lesions if the patient did not have any contraindications?

7. Endoscopic ultrasound. Ten of the lesions were called invasive carcinoma on EUS but only 5 patients actually had invasive carcinoma on final pathology. The positive predictive value was 50% and the specificity only 16%. These kinds of results I call the “flip the coin tests”; “heads, cancer; tails, benign,” since the results are no better then flipping a coin, but the tests are a lot more expensive. Also, I teach my residents not to order a test unless it directly benefits the patient or changes what you are going to do. However, in all these patients, in spite of the EUS results, excision/excision was still performed. With this data, are you still recommending preoperative EUS in rectal villous adenomas? Also have you looked into a simpler, less costly test and its correlation to postoperative pathology, that is, a rectal examination and the surgeon’s finger? Villous adenomas that are benign are characteristically soft and velvety and may even be missed on digital rectal examination. The presence of hard areas in the villous adenomas, in my experience, correlates with the presence of cancer. Is this your experience?

8. Statistics. In looking at the median prior attempts at excision in patients with no dysplasia/low-grade dysplasia vs high-grade dysplasia/cancer, the absolute numbers are 1 and 0 but the P value is .04. How can you get this probability from such small numbers? In general, the number of data points in the various comparisons is quite small leading to the possibility of β or type II errors in the reported probabilities. For example, in comparing patients with benign recurrence vs no recurrence (with only 4 patients recurring), it is stated that the average size of tumor that occurred was 3 cm and the average size with no recurrence was 2.8 cm with a probability of 0.10. This is almost a doubling in size between the 2 groups, but the lack of statistical significance may be a type II error. Even here a probability of 0.10 means only a 10% chance of random error and a 90% chance that the differences are real. Although it cannot be proved that these are statistically different, at the same time, it cannot be stated that they are statistically the same.

Dr Deveney: First, the comment regarding the extent of resection. Actually, that comment regarding APR was an error in the first draft. In my entire career, I believe that I have never done an APR for a benign lesion. But they were proctectomies, one of which was an actual LAR for an upper rectal lesion and the rest of them were proctectomies with coloanal pouches, some of those done by mucosectomy because the lesion extended very low in the rectum. Those were performed in lesions where the characteristics of the lesion precluded any other treatment because they were very geographically large lesions occupying the entire circumference or a very large percentage of the rectal mucosa, which actually answers question 2 as well. The selection of the procedure was indeed driven by the characteristics of the tumor as well as the suitability of the patient to undergo that procedure because of their comorbidities. In the patients in whom a proctectomy needed to be done, a TAE just was not deemed feasible.
Regarding the location of the lesion, that most definitely plays a role in what treatment should be performed. And again men vs women, anterior vs posterior lesions make a difference. A posterior lesion will be able to be removed more safely if it extends up higher from the anal verge and up to 10 or in some cases even 12 cm, whereas anteriorly the risk of entry into the peritoneal cavity as well as the difficulty in mobilizing the tissues and obtaining a secure closure will limit it to somewhat lower lesions. Being able to predict exactly how low the cul de sac extends and where the peritoneal cavity is, particularly in women in whom it extends lower, difficult and so maybe something that leads us to caution in attempting to resect lesions that are anterior.

Our follow-up is definitely not long enough. The recurrences that we had, which were all benign lesions, were early and some of the cases have had long enough follow-up to be able to be reasonably certain that recurrence will be unlikely. However, one of the patients who had been referred to us with a recurrence of a benign lesion had his initial resection done 25 years before. So I think that the length of time for recurrence may be extremely variable and that is a limitation of our paper. We need longer follow-up.

As far as our follow-up plan, I have the patients come back every 3 to 4 months for the first year and every 6 months thereafter until they have reached 5 years. This patient group did include a number of elderly people who were lost to follow-up after a few years.

With regard to the margin status not being available on some of the patients, it was really a matter of this being a retrospective study. The pathologists sometimes did not mention it in their final report.

Regarding the treatment of the T2 tumors, indeed these patients were very elderly and they had a lot of comorbidities. More aggressive treatment would not have been reasonable. If they were young and fit patients with a T2 lesion, I would favor transabdominal resection with a low anastomosis, and if they were not physically fit, then chemotherapy and radiation or observation.

The comment regarding EUS is a point I think very well taken. This test did not have any more effectiveness than a flip of the coin. We always do a digital rectal examination, and I agree totally with Dr O’Connell that the finding of any area in the tumor that is hard makes it likely that that might be a cancer. Any of our patients who had a villous adenoma who were found preoperatively to have a hard area or a biopsy of cancer were not included in this series because this series included only patients in whom a benign villous adenoma was the preoperative diagnosis. But that is a key aspect of the evaluation, and I would say more reliable than an EUS. There are some patients, however, whose lesions were above the digital examination or extended high enough that you could not feel the entire lesion, and as the experience with EUS increased in our hospital, I think that it is worthwhile to evaluate those patients who have a higher lesion with an EUS to have as much information as possible ahead of time.

Regarding the comments about the statistics, the Mann-Whitney U Test was used for comparisons per the advice of our statisticians, and I think in general our numbers are too small in some cases to reach statistical significance when you break it down into the small subgroups. We would need a larger number of patients to show true differences, but we did not have them.

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