Local Excision of Rectal Carcinoma

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Hypothesis: Selected clinicopathologic characteristics of locally treated rectal cancers are predictive of recurrence.

Design: Case series review with median follow-up of 6 years.

Setting: University medical center.


Main Outcome Measures: Local and distant recurrence rates and overall survival.

Results: Overall local recurrence rate was 14% (8 patients). There were no local recurrences among patients treated with chemotherapy or radiation. Of patients not treated, local recurrence rates were 33%, 5%, 45%, and 25% for T0, T1, T2, and T3 tumors, respectively. No clinicopathologic factor predicted local recurrence. Two patients developed distant recurrence. Overall survival was 98%, 93%, and 84% at 1, 3, and 5 years, respectively.

Conclusion: In selected patients, outcomes for local excision combined with additional therapy may be equivalent to those for radical resection.


Rectal carcinoma traditionally has been treated by radical resection. Recent improvements in surgical techniques have allowed more patients to undergo sphincter-sparing operations. However, for tumors of the distal third of the rectum, many patients still require an abdominoperineal resection. This operation, despite having dramatically reduced mortality, has significant morbidity\(^1\,2\) and requires the patient to have a permanent colostomy.

In general, local recurrence rates for rectal cancer have decreased with attention to surgical techniques\(^3\,4\) and adjuvant therapy.\(^5\,6\) Despite excellent local control, however, patients still develop distant metastases, and aggressive surgical management of local disease has had only a limited impact on long-term disease-free survival.\(^3\) Local excision of distal rectal tumors is an alternative for patients who have early lesions, refuse to have an abdominoperineal resection, have other medical problems that contraindicate a major abdominal operation, or have evidence of metastases with limited life expectancy. Local excision offers these patients less operative morbidity and mortality,\(^7\,8\) and long-term outcome is better than expected.\(^9\,10\) Increasing evidence,\(^9\,11\) based on locoregional recurrence and survival rates, supports the use of local excision as a primary treatment modality in selected patients, especially when combined with adjuvant therapy.

The aim of this study was to review our experience with locally excised rectal cancers, to find morphologic and pathologic characteristics that were predictive of local recurrence, and to calculate survival after limited resection.

RESULTS

MORPHOLOGIC CHARACTERISTICS

Tumors ranged from 1 to 10 cm in greatest dimension, with a mean ± SD size of 3.3 ± 1.6 cm. Only 8 patients had tumors larger than 5 cm. Mean ± SD distances from the distal edge of the tumor to the dentate line and the anal verge were 3.2 ± 2.2 cm (range, 0-8.0 cm) and 5.4 ± 2.1 cm (range, 1.5-10.0 cm), respectively. Forty-one (71%) of 58 tumors were polypoid, 34 (59%) were ulcerated, and 44 (76%) were mobile on digital rectal examination. Tumors were evenly distributed around the...
PATIENTS AND METHODS

Between February 1, 1982, and December 31, 1998, 58 patients with rectal carcinomas were treated by local excision at the Department of Surgery, University of California, San Francisco, by 1 of 2 colorectal surgeons (T.R.S. and M.L.W.). The 26 women and 32 men in the group had a mean age of 65.7 years (age range, 40-87 years). The primary initial symptom was bleeding (47%; 27 patients), followed by a change in bowel habits (15%; 8 patients) and occult blood in the stool (8%; 5 patients). In 7 patients (12%), the tumor was found during routine examination or endoscopy. Four patients were referred to our institution because of recurrence after treatment elsewhere.

All patients underwent routine preoperative evaluation with history intake, physical examination, laboratory tests, and chest radiographs. Additional workup in selected patients included sigmoidoscopy or colonoscopy (97%; 56 patients), barium enema (24%; 14 patients), computed tomographic scan (53%; 32 patients), magnetic resonance imaging (12%; 7 patients), endorectal ultrasound (22%; 13 patients), and bone scan (3%; 2 patients). Eleven patients had no further workup aside from the routine evaluation.

Fifty-six patients were treated with curative intent. However, 3 of them had medical problems that precluded an abdominal operation, and 1 refused an abdominoperineal resection. Two patients were treated for local palliation. All patients received perioperative antibiotic drugs and preoperative bowel preparation, and had full-thickness excision of the rectal wall with an attempt to obtain a 1-cm margin around the tumor.

Mean length of stay in the hospital was 4.5 days, time to oral intake averaged 1.6 days, and median follow-up was 6 years (range, 0-16.6 years). Recurrence was detected in a variety of ways, including digital rectal examination, rigid sigmoidoscopy, colonoscopy, and imaging studies.

Univariate analysis was used to evaluate the importance of the following variables on local and distant recurrence rates: age, sex, tumor size and shape, presence of ulceration, mobility, location, TNM stage, differentiation, status of margins, vascular or lymphatic invasion, and use of neoadjuvant or adjuvant therapy. Independent prognostic factors for recurrence were determined using multivariate logistic regression modeling. Survival was estimated by Kaplan-Meier analysis. A log-rank test was used to compare survival curves. P<.05 was considered significant. Statistical analysis of all data was performed using statistical software (JMP Statistical Discovery Software, v3.1; SAS Institute Inc, Cary, NC).

rectal circumference, with 38% anterior (n = 22), 36% posterior (n = 21), 14% lateral (n = 8), and 12% not specified (n = 7). Univariate analysis did not show any morphologic characteristics to be predictive of local or distant recurrence.

PATHOLOGIC CHARACTERISTICS

The distribution of tumor (T) stages is shown in Figure 1. Nine patients had 1 or more lymph nodes in the specimen, all of which were negative (N0). One patient with N1 preoperatively based on computed tomographic imaging received neoadjuvant radiation therapy, but a lymph node excised with the tumor was negative histologically. All other patients (n = 48) were NX. Three patients had metastases on radiographic studies at initial evaluation and were, therefore, M1. Thirty-two patients were M0, based on results of imaging, and 23 were MX.

Most tumors (90%; n = 52) were well to moderately differentiated adenocarcinoma; 3 tumors (5%) had moderately poor differentiation. There were no poorly differentiated tumors. Twenty-nine tumors (50%) had negative margins, 7 (12%) had positive margins, and 21 (36%) had margins less than 5 mm from the tumor and were considered close. Average distance from the tumor to the close margin was 2.9 mm. Five tumors had vascular invasion and 3 had lymphatic invasion. On univariate analysis, histological characteristics did not correlate with local or distant recurrence rates, except for T staging, which predicted distant recurrence (P = .03). Both patients who developed distant metastases had T3 tumors.

NEOADJUVANT AND ADJUVANT THERAPY

Nineteen patients received additional therapy: 5 had neoadjuvant treatment with either chemoradiation (n = 4) or external beam radiation alone (n = 1), and 14 had adjuvant therapy with chemoradiation (n = 9), radiation (n = 4), or chemotherapy (n = 1). Similar numbers of patients in the treated and untreated groups, when compared according to T stage, had differentiation, margin status, and lymphatic or vascular invasion. The only exception was that all 3 patients with tumors of moderately poor differentiation had adjuvant therapy. Four patients had additional therapy at the time of recurrence and salvage operation. The incidence of local recurrence was significantly higher in the untreated group (20%; n = 8) than those who received neoadjuvant or adjuvant therapy (0%) (P = .03).
LOCAL RECURRENCE

Overall local recurrence rate was 14% (8 patients) and the distant recurrence rate was 3% (2 patients). Median time to recurrence was 1.25 years (range, 1.00-3.25 years). No patient who received neoadjuvant or adjuvant therapy had local recurrence. Recurrence rates by stage and treatment are shown in Table 1. When all the clinicopathologic characteristics were analyzed by multivariate logistic regression modeling, the only factor that was independently prognostic of recurrence was the lack of neoadjuvant or adjuvant therapy ($P = .02$).

SALVAGE

All 8 patients who developed local recurrence had salvage operations. Another 4 patients had immediate reoperations because of pathologic characteristics considered unfavorable, and 1 had a resection of liver metastases within 1 month of initial surgery. No patient who underwent operation—immediately or after local recurrence—developed local disease again. Treatment and follow-up of patients who developed recurrence are shown in Table 2.

SURVIVAL

Overall survival rates at 1, 3, and 5 years were 98%, 91%, and 88%, respectively. The T stage–specific 5-year survival rates were 100%, 95%, 83%, and 57% for T0, T1, T2, and T3 tumors, respectively. The survival curve for patients who underwent salvage operation was comparable to that for patients who did not at 5 years (87% vs 84%) (see Figure 2 and Figure 3).

Although advances have been made in surgical techniques and the oncologic management of carcinoma of the distal one third of the rectum, the overall outcome remains unsatisfactory. Radical operations, including low anterior resection, coloanal anastomosis, and abdominoperineal resection, have been the standard of care for many years, and local recurrence rates are reportedly as low as 4%. Unfortunately, these patients succumb to distant disease, and overall survival has not significantly improved. This is especially true of patients with T2 and T3 stage tumors.

Local excision with curative intent is considered only for patients who have early lesions with favorable morphologic and histological characteristics. This restriction is supported by data showing certain characteristics to be predictive of lymph node metastasis and local recurrence. The use of adjuvant therapy in this setting has reduced the local recurrence rate by sterilizing tissue with higher risk of residual disease even in more advanced tumors with unfavorable characteristics.

Our study, which spans 16 years, includes all locally excised rectal cancers treated with or without additional therapy. We did not demonstrate any morphologic or histological factor to be a predictor of local recurrence. The most important predictor of local recurrence was the absence of (neo)adjuvant treatment with local excision. No patient who had neoadjuvant or adjuvant therapy developed a local recurrence, and patients who did not receive additional therapy had an unacceptably high rate of local recurrence for T2 (46%) and T3 (25%) tumors. T1 tumors had an acceptable rate of recurrence at 5%, and only 3 patients had T0 tumors, 1 of which recurred, explaining the 33% recurrence rate. This patient had a villous adenoma with adenocarcinoma that was excised, and then had a recurrent villous adenoma with adenocarcinoma. Only patients with T3 tumors developed distant metastases, 1 of whom was treated surgically for local and distant recurrence and died of distant disease without evidence of local failure. Even in patients with T3 tumors, no local recurrences occurred when patients received adjuvant therapy.

### Table 1. Recurrence Rates (Percentages) by Stage and Adjuvant Therapy

<table>
<thead>
<tr>
<th>Stage</th>
<th>Yes</th>
<th>No</th>
<th>Local</th>
<th>Distant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>0/1</td>
<td>1/3 (33)</td>
<td>1/4</td>
<td>0/4</td>
<td>1/4 (25)</td>
</tr>
<tr>
<td>T1</td>
<td>0/3</td>
<td>1/21 (5)</td>
<td>1/24</td>
<td>0/24</td>
<td>1/24 (4)</td>
</tr>
<tr>
<td>T2</td>
<td>0/9</td>
<td>5/11 (46)</td>
<td>5/20</td>
<td>0/20</td>
<td>5/20 (25)</td>
</tr>
<tr>
<td>T3*</td>
<td>1/6</td>
<td>1/4 (25)</td>
<td>1/10</td>
<td>2/10</td>
<td>2/10 (20)</td>
</tr>
<tr>
<td>Total</td>
<td>1/19 (5)</td>
<td>8/39 (21)</td>
<td>8/58</td>
<td>2/58</td>
<td>9/58 (16)</td>
</tr>
</tbody>
</table>

*One patient with a T3 tumor developed both local and distant recurrence.

### Table 2. Salvage Operations in 9 Patients With Local or Distant Recurrence

<table>
<thead>
<tr>
<th>Stage</th>
<th>Site of Recurrence</th>
<th>Time of Recurrence, y</th>
<th>Operation</th>
<th>Follow-up, y</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>Local</td>
<td>0.75</td>
<td>LE</td>
<td>13.5</td>
<td>Died, DF</td>
</tr>
<tr>
<td>T1</td>
<td>Local</td>
<td>1.00</td>
<td>LE</td>
<td>7.0</td>
<td>Died, DF</td>
</tr>
<tr>
<td>T2</td>
<td>Local</td>
<td>1.25</td>
<td>LAR/ADJ</td>
<td>8.0</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T2</td>
<td>Local</td>
<td>1.25</td>
<td>LE</td>
<td>2.2</td>
<td>Died, DF</td>
</tr>
<tr>
<td>T2</td>
<td>Local</td>
<td>1.00</td>
<td>APR/ADJ</td>
<td>9.1</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T2</td>
<td>Local</td>
<td>3.25</td>
<td>LE</td>
<td>7.2</td>
<td>Alive, no follow-up</td>
</tr>
<tr>
<td>T2</td>
<td>Local</td>
<td>2.10</td>
<td>LAR/ADJ</td>
<td>3.4</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T3</td>
<td>Local/met</td>
<td>3.00</td>
<td>APR/L/ADJ</td>
<td>5.8</td>
<td>Died, liver mets</td>
</tr>
<tr>
<td>T3</td>
<td>Met</td>
<td>1.00</td>
<td>X</td>
<td>2.0</td>
<td>Died, pulmonary mets</td>
</tr>
</tbody>
</table>

*LE indicates local excision; LAR, low anterior resection; ADJ, adjuvant therapy; APR, abdominoperineal resection; X, no salvage surgery performed; DF, disease free; and met, distant metastasis.*
Limitations of this retrospective study are the small size of our series and that not all patients were treated by the same protocol. Four patients with unfavorable pathologic characteristics were operated on immediately for salvage; no patients had poorly differentiated tumors, and only 8 patients had tumors larger than 5 cm. All these factors play a role in the lack of any pathologic correlation of local recurrences with the pathologic characteristics affecting recurrence rates.

Many management issues evolved during this study. Patients have better preoperative staging with use of imaging studies so that less invasive tumors without nodal disease can be selected for this therapeutic modality. Our practice now includes routine use of computed tomographic scanning and endorectal ultrasound for candidates for local excision; this was not the case in previous years. We also perform local excision as a mode of diagnosis and therapy for patients whose tumors cannot be precisely staged by imaging but are clearly not T3 or T4 tumors. Regimens for adjuvant therapy have also changed during this 16 years. Chemoradiation and radiation therapy are used routinely for T2 and T3 tumors. We currently use 5040 Gy, with or without 5-fluorouracil. Patients are now followed up every 3 months for the first 2 years, and our short interval from operation to recurrence supports this approach. In earlier times, follow-up was performed with several different tests that have now been standardized.

Despite these inadequacies, local recurrence and overall survival rates compare favorably to those reported in the literature for patients who have local excisions or more radical resections. Although there is concern regarding the disease-free survival of patients treated by local excision who develop locally recurrent disease, results of this study show that patients who undergo salvage operations for local recurrence have the same chance of survival as those who did not experience recurrence.

In light of these issues, local excision of selected rectal cancers—with the appropriate use of neoadjuvant or adjuvant therapy—may allow patients to choose to avoid the physical and psychological impact of a colostomy without compromising their long-term survival.

Presented at the 70th Annual Session of the Pacific Coast Surgical Association, San Jose del Cabo, Baja California Sur, February 14, 1999.

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REFERENCES

I have 2 questions for the authors. First, I would like to know how they follow these patients following transrectal excision of the tumor? Is there a role for these patients in positron emission tomography? Second, I would like to know if they currently have a protocol that they follow as far as the use of neoadjuvant or adjuvant chemoradiation therapy. Is this based on any preoperative staging techniques?

Karen E. Deveney, MD, Portland, Ore: I appreciate the fact that this study spanned a long period of time during which the diagnostic studies changed quite a bit. In 1999, what are your criteria for deciding whether transanal excision is the appropriate treatment? In addition to preoperative staging with CT scan and endorectal ultrasound, what size boundaries would you use as consideration, for one thing? I notice that there were 8 patients who had what I consider to be quite large tumors of over 5 cm, even as large as 10 cm. It seems to be a fairly daunting enterprise to excise a known rectal cancer of that size transanally. Was it possibly not known that, in some of these patients the lesions were malignant preoperatively and thought to be villous adenomas, and that, only on the pathology were they found to be invasive malignancies. Or, were they all known preoperatively to be rectal malignacies and would you set any size boundaries as to the upper limits of what you attempt transanally? Would you possibly consider the role of neoadjuvant chemoradiation therapy with a coloanal pouch instead of transanal excision?

Theodore X. O’Connell, MD, Los Angeles, Calif: Although I believe the results of this study and do this on a regular basis in my own practice, I have a difficult time getting any firm conclusions from the paper, except that it can be done. This is because there are really no controls. This is not a randomized prospective study of radical vs local excision or even a historical matched control. So it is very hard to say that this study has proved it better or equal to more radical therapy due to the lack of controls—although I do believe it works in selected cases.

Second is a problem with selection. There are only 4 patients per year for 2 colorectal surgeons. Either the colorectal surgeons had a meager practice over that time or they are selecting very, very stringently. Although they describe in detail the patients they operated on, I am even more interested in the ones they didn’t operate on by local excision because I think their selection criteria is utmost in the success of their study.

Third, although they say patients had polypoid, mobile, or ulcerative lesions in varying amounts and some had 2 of these simultaneously, both polypoid and mobile are considered good prognostic indicators; indication for local excision while ulcerated is considered by many to be a contraindication. So, how are these factors mixed? Do patients have both mobile and ulcerated? They have successes and failures, but I really did not hear a good description of which preoperative factors differentiate their successes from failures. What kinds of criteria did you see in the failures that were different than the successes to help select our patients?

Finally, although the authors state that adjuvant radiation or adjuvant radiation chemotherapy is good and has a positive effect, it looked as if it was used randomly in early- and late-stage patients, and those in between. I really want to know how they choose chemoradiation: by grade, depth, endoscopic ultrasound, etc? What kind of criteria do they use? Certainly the patients with the best, most curable lesions can be treated with local excision alone and do not need this modality, which does have significant morbidity.

John MacFarlane, MD, Vancouver, British Columbia: I think that, as a study in evolution, this study has brought forward some interesting and pithy points of discussion, many of which have already been made. I think that if you look carefully, it seems as if the tumors that were over T2 in size would ultimately be the ones not appropriately managed with local ex-
cision. This may be the beginning of a selection criteria for this kind of treatment. The other issue is the preoperative evaluation with ultrasound, and clearly that wasn’t possible before the test was available, as has already been pointed out. I would suggest looking carefully at the use of MRI in this setting. We have been impressed. We have not had a lot of experience with MRI, but in the ones that we have been able to do, I think that, using 1.5 T, really does provide a very good evaluation of the local disease, depth of invasion, and, more importantly, the lymph nodes in the mesorectum. So I would encourage you, while organizing your prospective study, to include that as part of your evaluation.

Hernan Vargas, MD, Torrance, Calif: It has recently been our practice to do transanal excisions in selected patients. My question is, how do you select your patients for transanal excisions? I am concerned about transanal excision for deeper lesions, not necessarily by size, but by depth of the invasion. T3 tumors can technically be resected with a local excision but have a deeper level of invasion. You had only 8 T3 lesions in 16 years, so I presume those are being excluded.

As a word of caution, 1 of your conclusions was that the pathologic criteria were not predictive of recurrences, but in the presentation, it was pointed out that 22 out of 50 some patients did not have accurate statement of lymphatic or vascular invasion. I think this should really be seen with caution.

Jeffrey Pearl, MD, San Francisco: I raise the same last point as the previous discussant. Perhaps the pathologist could be asked to go back and review those 22 cases and the information be used to further stratify the results.

Dr Welton: Actually, this paper was presented to provoke discussion, and I am glad it did because some of the standard criteria that I have strongly felt we need to meet prior to our review, I’m no longer sure have to be met. So I think this adds grist to the mill for individuals who think there should be a national trial to do a randomized, prospective study. Certainly we can’t do this in a single institution with the slow accrual of rectal cancers.

Regarding Dr Russell’s comments or questions, these patients are “well-selected,” but it became less clear to me with this review as to what well-selected patients means. The standard dogma is 3 cm in size or less, not ulcerated, not tethered, not fixed, and a well-differentiated tumor. While the majority of our tumors were ulcerated, they were anywhere from moderately to moderately well to well differentiated, but they all weren’t just well differentiated. The depth of invasion with a T2 or T3 lesion may have been tethered. So patients would have been excluded before, and now, after reviewing our data, I am not so sure we should be excluding all of those patients because certainly, ulcerated morphology and size actually do not predict local failure in our retrospective review. Our follow-up, as Dr Varma commented on at the end, is on a 3 monthly, 4 monthly basis to perform digital exams, which is still the gold standard. Multiple studies have shown that preoperative ultrasound is only as good as the experienced colorectal surgeon, so for those of us who are junior and not quite as experienced, ultrasound may be better. However, once you get a few more years under your belt, the digital exam may be equivalent. Post-operatively, however, ultrasound is useless. It is not a good test to follow in these patients. So you need to perform a digital exam, anoscopic exam, look at the scar, see that it is healthy, see that you don’t have any evidence of recurrence; if you think you do, biopsy that. We are getting CT scans on a 6-month interval to look at the nodal disease in the mesorectum.

Chemoradiation therapy is standard. Chemoradiation therapy is 5-FU with 5040 cGy, 4500 to the whole pelvis, and the tumor bed is boosted to 5040.

Dr Deveney, the 10-cm tumor was a villous adenoma with cancer. Therefore, we did not undertake transanal excision of a 10-cm cancer. Before this review of our own data, the rule was that tumors 3 cm or less could be excised. Well, we are taking out 4 and 5 cm tumors all the time, and not really realizing it preoperatively. As Dr Russell pointed out, on the digital exam you try to get your finger above it, move it around, and think, well, it feels like about 3 cm. You get it out and pin it out, and it is a 5-cm tumor. So I am not sure that the 3-cm cutoff is set in stone, and I think that on a national level, we should reevaluate exclusion criterion.

I do think that neoadjuvant therapy and coloanal pouch is a good option for some of these patients. The 1 caution there, and I hear this discussed frequently, is to deliver radiation therapy up front to shrink the tumor, in particular away from your distal margin. So if your tumor was 1 cm from the distal margin before chemoradiation therapy, it may shrink to 3 cm from the distal margin. You can’t come through where the tumor was previously, and this mistake will lead to high local failure rate. Shrinking large tumors to allow radial dissection is okay, but you cannot change your distal margin.

Dr O’Connell, there are no controls, and this is certainly not a randomized, prospective double-blind trial. The CALGB had a trial looking at this issue and it accrued so poorly they closed it. The bottom line is that you either believe this is an adequate therapy or you don’t. If you believe it is an adequate therapy, you won’t commit your patients to a colostomy.

I am standing up here as 1 of the 2 surgeons. I have only been here 5 and one-half years. The vast majority of the work has been done by Dr Schrock, and he really deserves all of the credit for the outstanding numbers.

What predictors do we have as far as success or failure? We came up with no predictors from histology, size, ulceration, digital exam, and thought we would. Much to our surprise, if you gave the patients chemoradiation therapy, there were no local failures. That was a take-home message. We had T3 lesions treated with chemoradiation that did not fail in the pelvis. I did not expect that. I thought they would fail in the pelvis after these “less-than-adequate” operations, but because of medical comorbidities and patient refusal, you end up giving chemoradiation when you want to perform an abdominoperineal resection. So a small number, but a provocative thought.

Dr MacFarlane, as far as whether T2 lesions are appropriately managed with local excision and chemoradiation therapy, I believe they are. A T3 lesion is a questionable patient, and I generally would bring those patients on to abdominoperineal resection. But again, based on the study, maybe we should be readdressing this. The published data suggest that, for T1 lesions, local excision alone is adequate. It used to be said there was a 3% local failure rate. It is now reported as approximately 8%. For T2 lesions without chemoradiation therapy, the local failure rate is now reported as 18% to 20%. For T2 lesions with chemoradiation, the local failure rates are around 7%, which is acceptable.

Ultrasound, particularly done by the surgeon who knows the question, is a better way of looking at the tumor than is MRI. The data in the literature on MRI is that it is less sensitive than ultrasound. The 3-D ultrasound is really the way that should be done. The pathologist could be involved. It adds grist to the mill for individuals who think there should be a national trial to do a randomized, prospective study. Certainly we can’t do this in a single institution with the slow accrual of rectal cancers.

In selecting out the T3 lesions, we definitely did select out those in our series. There are also no poorly differentiated tumors; they were selected out preoperatively. The ones that we thought might be T3 were not done unless they had metastatic disease, there were medical comorbidities that prohibited abdominoperineal resection, or it wasn’t recognized preoperatively. If we thought we had a T2 and we found a T3, then we had T3s. But generally, we did try to exclude those, and it is a good point. The lymphatic and vascular invasion: if you go back to the path reports from 10 years ago, it’s not mentioned. It’s a newer feature and maybe we can get a gastrointestinal pathologist interested to rereview that. Dr Pearl echoed the same comments.