Total Mesenteric Excision in the Surgical Treatment of Rectal Cancer

A Prospective Study

Richard B. Arenas, MD; Alessandro Fichera, MD; Debbie Mhoon, RN; Fabrizio Michelassi, MD

Background: Total mesorectal excision has been advocated in conjunction with low anterior or abdominoperineal resection as the optimal surgical treatment for rectal cancer. It involves removal of the entire rectal mesentry as an intact unit and maximizes the likelihood of obtaining a negative circumferential margin.

Objectives: To prospectively validate the efficacy of total mesorectal excision in obtaining locoregional control, to identify the perioperative factors influencing the selection of either a sphincter sparing or a sphincter ablating procedure, and to identify independent factors that may influence long-term prognosis in rectal cancers.

Settings: Tertiary referral center.

Patients: Seventy-three consecutive patients with rectal cancer located within 10 cm of the anal verge were treated from 1984 to 1997 by the senior author (F.M.). Sixty-five patients form the basis of our analysis after the exclusion of 7 patients who had their cancer removed transanally and 1 patient who had a permanent diverting stoma as the only procedure.

Results: Twenty-six patients underwent a sphincter ablating procedure; 39 underwent a sphincter sparing procedure. Operative mortality was 1.5%. Follow-up was complete in 64 patients (39±30 months; range, 3-126 months). Five-year actuarial survival rates were 88% for the 34 patients with stage I and II adenocarcinoma and 65% for the 22 patients with stage III adenocarcinoma. The local recurrence rate was 6.2% overall, but only 3.1% in the potentially curable group (stages I-III). When only patients who did not receive adjuvant chemoradiation therapy were considered (n=23), local recurrence rate was 8.3% overall and 0% in the potentially curable group. Tumor stage (P=.04) and vascular and/or lymphatic invasion (P=.002) were statistically significant in their association with survival. Circumferential lesions (P<.001), gross invasion of contiguous organs (P<.001) and distance from the anal verge of less than 5 cm (P=.01) were statistically significant in their association with the choice of a sphincter ablating procedure.

Conclusions: This study confirms the efficacy of total mesorectal excision in minimizing locoregional recurrence rates and confirms the well-established prognostic value of stage and microinvasion. Moreover, it indicates that circumferential lesions, distance from anal verge, and gross invasion of contiguous organs are significant perioperative factors in the selection of the type of surgical procedure.

Arch Surg. 1998;133:608-612

During the past 2 decades, the ratio of sphincter ablating procedures (SAP) to sphincter preserving procedures (SSP) has been reversed in the treatment of rectal adenocarcinoma. The widespread availability and use of modern stapling devices, the recognition that a shorter distal margin is adequate, and newer “ultralow” anastomotic and endoluminal techniques have all contributed to this progress. Yet, certain perioperative anatomic factors still limit the choice of surgical treatment to SAP.

The trend toward SSP has not been accompanied by a significant reduction in local disease recurrence. In 1994, Adam et al confirmed previous results that indicated the importance of adequacy of rectal excision by showing that involvement of radial resection margins after proctectomy for cancer was highly predictive of local recurrence. This concept has been echoed by Heald et al, who has consistently reported local recurrence rates lower than 3% to 5% using the technique of total mesorectal excision (TME).

Although nowadays optimal surgery allows a higher proportion of patients with rectal cancer to undergo SSP at a lower risk of local recurrence, cancer-related mortality has disappointingly remained stable. It is widely believed that, in the presence...
PATIENTS, MATERIALS, AND METHODS

Between October 1984 and February 1997, 73 consecutive patients with cancer located within 10 cm from the anal verge were operated on by the senior author (F.M.) at the University of Chicago Hospitals and Clinics, Chicago, Ill. Seven patients whose tumors were excised transanally and 1 patient who had a permanent diverting stoma as the only procedure were excluded from our analysis, leaving 65 patients to form the basis of this study.

Distance from the anal verge was measured with a graduated rigid proctosigmoidoscope with the patient in the genupectoral position. Surgical procedures were classified as SSP, which included low anterior resection with colorectal or coloanal anastomosis, or SAP, which included abdominoperineal resection and total proctocolectomy. The surgical technique for TME has already been described in detail. Complete removal of the mesorectum and the mesentery containing the inferior mesenteric artery and vein can be obtained en bloc by entering the avascular space between the visceral and parietal planes of the pelvic fascia. This can be done with preservation of the sympathetic and parasym pathetic nerves. Anteriorly, the peritoneum of the pelvis is incised 1 cm in front of the Douglas pouch and the dissection is continued anterior to the Denonvillier fascia, exposing the posterior wall of the prostate gland or the posterior vaginal wall. Laterally, the mesorectum is sharply dissected away from the parasympathetic and sympathetic nerves where they join together along the pelvic side wall. All our patients underwent TME as described, although in the earlier years of the study, the plane of dissection included the parietal fascia.

Clinical data (tumor stage, morphology, size and distance from the anal verge, presence of synchronous colonic pathologic abnormalities, invasion of contiguous organs, and adjuvant treatment) and follow-up data (local recurrence, development of metastatic disease, and survival) were collected prospectively by the senior author and a dedicated nurse-clinician (D.M.) and were complete up to March 1997. Tumors were staged according to the modified Astler-Coller classification. Sixty-five patients (25 men and 41 women; mean age, 61.5 years; range, 28-81 years) underwent a proctectomy for their rectal cancer and were included in our study. Preoperative workup included colonoscopy with biopsy in 63 patients (97%) and barium enema in 10 (17%). Complete preoperative colonic evaluation, by either colonoscopy or barium enema, was obtained in 64 (98%) of the 65 patients. Seventeen cancers (26%) were located less than 5 cm from the anal verge. Ten cancers were found to involve the rectum circumferentially. Forty-two patients (65%) received chemoradiation therapy either preoperatively (n=18) or postoperatively (n=24).

In all patients, TME was performed en bloc in conjunction with a proctectomy. Twenty-six patients (40%) underwent an SAP and 39 patients (60%) underwent an SSP. Sphincter sparing procedures included low anterior resection either with a colorectal (n=26) or coloanal (n=13) anastomosis. Twenty-eight patients (42%) had a proximal diverting stoma, in most cases a temporary loop ileostomy, to protect the anastomosis. Of anatomic extent of cancer, there is no doubt that additional factors may independently influence outcome. Other factors need to be identified and verified to sharpen our prognostic classification.

The aim of this prospective study is to review our experience with patients with cancers located in the rectum, to validate the efficacy of TME in obtaining locoregional control, to identify perioperative factors influencing the selection of the surgical procedure, and to identify independent factors that may influence long-term prognosis.

RESULTS

Table 1. Determinant Factors for the Choice of a Sphincter Ablating Procedure (SAP) or Sphincter Sparing Procedure (SSP)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total</th>
<th>SSP</th>
<th>SAP</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>62.7</td>
<td>59.6</td>
<td>.30</td>
<td></td>
</tr>
<tr>
<td>Circumferential tumor</td>
<td>2 (5)</td>
<td>8 (31)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Local invasion</td>
<td>3 (8)</td>
<td>4 (15)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Distance &lt;5 cm</td>
<td>2 (5)</td>
<td>17 (65)</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td>Preoperative radiation therapy</td>
<td>9 (23)</td>
<td>9 (35)</td>
<td>.43</td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>1 (3)</td>
<td>1 (4)</td>
<td>.21</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>22 (57)</td>
<td>10 (38)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>12 (31)</td>
<td>10 (38)</td>
<td>.22</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>4 (11)</td>
<td>5 (19)</td>
<td>.32</td>
<td></td>
</tr>
</tbody>
</table>

The surgical technique for TME has already been described in detail. Complete removal of the mesorectum and the mesentery containing the inferior mesenteric artery and vein can be obtained en bloc by entering the avascular space between the visceral and parietal planes of the pelvic fascia. This can be done with preservation of the sympathetic and parasym pathetic nerves. Anteriorly, the peritoneum of the pelvis is incised 1 cm in front of the Douglas pouch and the dissection is continued anterior to the Denonvillier fascia, exposing the posterior wall of the prostate gland or the posterior vaginal wall. Laterally, the mesorectum is sharply dissected away from the parasympathetic and sympathetic nerves where they join together along the pelvic side wall. All our patients underwent TME as described, although in the earlier years of the study, the plane of dissection included the parietal fascia.

Clinical data (tumor stage, morphology, size and distance from the anal verge, presence of synchronous colonic pathologic abnormalities, invasion of contiguous organs, and adjuvant treatment) and follow-up data (local recurrence, development of metastatic disease, and survival) were collected prospectively by the senior author and a dedicated nurse-clinician (D.M.) and were complete up to March 1997. Tumors were staged according to the modified Astler-Coller classification. Sixty-five patients (25 men and 41 women; mean age, 61.5 years; range, 28-81 years) underwent a proctectomy for their rectal cancer and were included in our study. Preoperative workup included colonoscopy with biopsy in 63 patients (97%) and barium enema in 10 (17%). Complete preoperative colonic evaluation, by either colonoscopy or barium enema, was obtained in 64 (98%) of the 65 patients. Seventeen cancers (26%) were located less than 5 cm from the anal verge. Ten cancers were found to involve the rectum circumferentially. Forty-two patients (65%) received chemoradiation therapy either preoperatively (n=18) or postoperatively (n=24).

In all patients, TME was performed en bloc in conjunction with a proctectomy. Twenty-six patients (40%) underwent an SAP and 39 patients (60%) underwent an SSP. Sphincter sparing procedures included low anterior resection either with a colorectal (n=26) or coloanal (n=13) anastomosis. Twenty-eight patients (42%) had a proximal diverting stoma, in most cases a temporary loop ileostomy, to protect the anastomosis. Of anatomic extent of cancer, there is no doubt that additional factors may independently influence outcome. Other factors need to be identified and verified to sharpen our prognostic classification.

The aim of this prospective study is to review our experience with patients with cancers located in the rectum, to validate the efficacy of TME in obtaining locoregional control, to identify perioperative factors influencing the selection of the surgical procedure, and to identify independent factors that may influence long-term prognosis.

Factors such as the patient age, preoperative radiotherapy, stage, local invasion, distance from the anal verge, and tumor morphology were examined by multivariate analysis to identify variables that determined the type of resection. Circumferential involvement (P<.001), extension of the tumor beyond the rectum (P<.001), and distance from the anal verge less than 5 cm (P=.01) were strong determinants for performing an SAP (Table 1). Age, preoperative radiation therapy, and stage did not seem to influence the type of resection.
Operative mortality occurred in 1 patient (1.5%) who suffered a postoperative myocardial infarction. Sixty-four patients (98%) were available for follow-up. Mean duration of follow-up was 39±30 months (range, 3-126 months; median, 36 months). In 34 patients (52%), the tumor was confined to the bowel wall.

Local recurrence occurred in 4 patients (6.2%), all of whom underwent SSP. One patient has since undergone a salvage abdominoperineal resection and remains free of disease. Two of the 4 recurrences were in patients who initially presented with liver metastasis and underwent a palliative resection. Therefore, the local recurrence rate in patients who underwent resection for curative intent is 3.1%. Delivery of preoperative or postoperative radiation therapy (n=42) did not seem to influence the local recurrence rate, as 2 recurrences occurred in the group of patients who did not receive adjuvant therapy (n=23) and 2 in the group of patients who did (n=42) (8.3% vs 5%, respectively). When only patients who did not receive adjuvant chemoradiation therapy were considered, the local recurrence rate was 8.3% overall and 0% in the potentially curable group.

Characteristics of patients with local recurrence are listed in Table 2. Distance of the tumor from the anal verge (P=.2) or its stage (P=.09) had no statistically significant association with local recurrence. Despite local recurrences occurring solely within the SSP group, there was no significant association between local recurrence and type of surgical procedure (P=.2).

Forty-seven patients are alive to date, with an overall survival rate of 72%. Five-year actuarial survival rates are 88% for patients with node-negative disease (stages I and II, n=34) and 65% for those with node-positive disease (stage III, n=22). Multivariate analysis identified stage (P=.04, Figure 1) and microinvasion (P=.002, Figure 2) as statistically significant variables, while distance from the anal verge, tumor morphology, involvement of contiguous organs, and size were not significant prognosticators.

### COMMENT

This study confirms the efficacy of TME in minimizing the locoregional recurrence rate. In addition, it confirms the well-established prognostic value of stage and microinvasion and indicates that circumferential lesions, distance from the anal verge, and direct invasion of contiguous structures are significant factors in the selection of the type of surgical procedure.

Pelvic recurrence rates reported in the literature vary widely, from 3% to 50%. This wide discrepancy in recurrence rates has generated controversy regarding whether surgery alone for rectal cancer can achieve acceptable local recurrence rates. In 1995, McCall et al reviewed the surgical literature for articles published between 1982 and 1992 to objectively evaluate the available data regarding failure rates after surgery alone for rectal cancer. To be accepted in their review, articles had to report follow-up on at least 50 patients surviving rectal excision with curative intent; articles were excluded if adjuvant therapy was used in more than 10% of patients. A total of 52 articles were included in the study. The median local recurrence rate for all series was 18.5%. More than 1000 patients from 8 series were identified as having undergone TME, with local recurrence rates varying between 3% and 13%. Our series validates these results, with a local recurrence rate of 8.3% overall when no adjuvant chemoradiation therapy was used, and gives support to the concept that TME affords optimal surgical treatment for rectal cancer.

Forty-two patients in our series received preoperative or postoperative radiation therapy to the pelvis, potentially influencing the observed local recurrence rate.

### Table 2. Characteristics of Patients With Local Recurrences

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Stage</th>
<th>Distance, cm</th>
<th>Procedure*</th>
<th>Radiation Therapy</th>
<th>Time to Recurrence, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C2</td>
<td>7</td>
<td>LAR</td>
<td>Postoperative</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>B2</td>
<td>9</td>
<td>LAR</td>
<td>Postoperative</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>D</td>
<td>9</td>
<td>LAR†</td>
<td>No</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>D</td>
<td>9</td>
<td>LAR†</td>
<td>No</td>
<td>12</td>
</tr>
</tbody>
</table>

* LAR indicates low anterior resection. † With liver resection.

### Figure 1. Survival according to stage. Multivariate analysis identified stage (P=.04) as a statistically significant prognostic variable.

### Figure 2. Survival according to lymphatic and/or vascular microinvasion. Multivariate analysis identified microinvasion (P=.002) as a statistically significant prognostic variable.
In published control trials with adjuvant radiation therapy, the local recurrence rate in the surgery alone group has always exceeded 20%, well above what can be accomplished in experienced hands. Thus, how much additional radiation therapy reduces local recurrence rates after optimal surgery is not known. In our series, patients controlled for stage had similar local recurrence rates with or without adjuvant radiation therapy, suggesting that radiation therapy may not be necessary and may actually represent harmful overtreatment.

Since Dukes proposed a pathologic classification for rectal cancer, surgeons and pathologists have attempted to refine their prognostic skills. Better prognostic capabilities would allow us to offer adjuvant therapy only to patients who most need it and to better administer our follow-up resources. Over and over again, pathologic stage has been confirmed as the most accurate independent prognostic factor. In 1988, we suggested that lymphatic and/or vascular microinvasion was an independent prognostic factor in addition to stage. Our current prospective series confirms this finding, opening the way to the search for prognostic systems in which the integration of multiple independent factors will help predict outcome with a higher degree of accuracy.

Circumferential involvement, extension of the tumor beyond the rectum, and distance from the anal verge less than 5 cm continue to be strong determinants for performing an SAP. Despite concerns regarding bowel function of elderly patients after low anterior resection, especially when followed by coloanal anastomosis, age did not appear to influence the type of resection. The broad distribution of stage in either the SSP or SAP groups demonstrated no significant bias towards one type of procedure or the other.

In summary, proper selection of SSP or SAP for patients with rectal cancer requires precise preoperative evaluation to assess the extent and the location of the disease within the rectum and pelvis. Total mesenteric excision in association with proctectomy offers optimal surgical radicality to achieve adequate locoregional control and can be performed with either SSP or SAP. Patients' prognosis can be better defined when lymphatic and/or vascular microinvasion is considered along with pathologic stage.

Presented at the 105th Scientific Session of the Western Surgical Association, Colorado Springs, Colo, November 18, 1997.

Reprints: Fabrizio Michelassi, MD, Department of Surgery, The University of Chicago, 5841 S Maryland Ave, MC 5094, Chicago, IL 60637.

REFERENCES


DISCUSSION

Robert D. Madoff, MD, Minneapolis, Minn: In 1990, the National Institutes of Health promulgated a consensus statement regarding the adjuvant therapy of rectal cancer that recommended adjuvant chemotherapy and radiation therapy for T3 or N1 lesions. Little recognized at that time were the very high local recurrence rates on which that recommendation was based, ranging from 25% to 35% in most of the cooperative trials. Meanwhile, the success or failure of rectal cancer excision was proven to be a technically driven issue, as several groups demonstrated wide surgeon-to-surgeon variability in local recurrence rates. Against this backdrop came the proposal, largely from Bill Heald in Basingstoke, England, that complete excision of the entire mesorectum was capable of dropping the local recurrence rates to a level that was virtually unimaginable by the cooperative group trials—in Mr Heald’s hands, 4%. More recent TME alone series have reported local recurrence rates ranging from 3% to 13%, still well below the average 25% reported in combined controlled series. The Achilles’ heel of this approach, at least in Mr Heald’s hands, was a very high anastomotic leak rate that seemed related to a partially devascularized rectum. This led to a standing policy in Basingstoke of diverting stomas after TME.

Total mesorectal excision has 2 components; a lateral dissection and the distal dissection. We have just heard a few words about the lateral dissection, and there is really no room for debate in this area. The presence of a positive lateral margin—the margin that none of our pathologists are willing to give us because it is too labor-intensive—is probably the strongest indicator available today for the local recurrence of rectal cancer. The other part of TME is a complete distal dissection of the mesorectum all the way down to the level of the levators. The evidence supporting this part of the approach is spottier. There is evidence from several patients that metastatic deposits can be identified in the mesorectum distal to the primary tumor, but it has not been well documented how far distal to the primary tumor these lie, or if these are simply markers for widespread and incurable disease.

We have just heard the results of what is really an outstanding personal series with local recurrence rates that any surgeon in this room should be very proud to have. However, there are several unanswered questions that I have for the authors. Sixty-two percent of the patients in the series received radiation therapy and probably associated chemotherapy either before or after their surgery. The authors state in their manuscript that local recurrence rates were similar with or without radiation therapy, but presumably the patients with more advanced cancers had received the adjuvant therapy. If the results are in fact based on a series in which more than half of the patients received radiation, how do you conclude that TME alone is responsible for the excellent results shown?
Second, TME mandates removal of the major blood supply to the rectum down to the levators. This means that the surgeon must either perform an anastomosis at the levators or dissect back up the rectum and perform a higher anastomosis to devascularize the rectal stump. Which of these did you choose? At what level was your anastomosis? What was the leak rate? And were diverting stomas necessary?

Finally, patients who have low anastomoses have not only higher leak rates but also inferior functional results. Before an entire generation of surgeons and patients is committed to TME, how do we know that it is not as good to dissect the mesorectum with the good lateral dissection, say 3 to 5 cm below the tumor, transect the mesorectum perpendicularly at that level, and perform an anastomosis there? If you start with the tumor at 7 to 10 cm before mobilization and mobilize it, this will leave a lot of usable rectum and probably a safer and more functional anastomosis.

Merrill T. Dayton, MD, Salt Lake City, Utah: Mesorectal excision has really not been done or has not been emphasized during the entire 13 or so years that this study was conducted. Did you do mesorectal excisions during the entire period of this study? What about postoperative morbidity, particularly sexual dysfunction and urinary dysfunction? Is overall morbidity higher in this more thorough and detailed anastomosis.

Armando Giuliano, MD, Santa Monica, Calif: Dr Madoff asked about the difficulty in judging the efficacy of this operation because of the use of radiation therapy. I wonder if Dr Michelassi could clarify for us what his indications for radiation therapy are, and when to use preoperative radiation therapy rather than postoperative radiation therapy.

Gilbert Hermann, MD, Denver, Colo: The average follow-up was between 1 month and 126 months. I would like to know, because the time for recurrence may be 2 years or longer, what the median follow-up was. How many patients were followed up more than 3 years out of the whole group?

Dr Michelassi: The first important question focused on how we could ascribe our results to TME alone when close to two thirds of our patients received preoperative or postoperative chemoradiation therapy. Obviously, we cannot. There have been several controlled trials in which preoperative or postoperative radiotherapy has been compared with surgery alone in the past 10 to 15 years and many of these studies have shown a statistically significant decrease in the rate of local recurrence in the irradiated group. Yet in all these trials the local recurrence rate in the surgery alone group has always exceeded 20% to 25%. Thus, how much additional radiotherapy reduces local recurrence rates in the presence of optimal surgery is just unknown. One can suggest indeed that if you perform optimal surgery and you have a local recurrence rate in the mid single digits, adding radiation therapy may represent overtreatment and the morbidity caused by the radiation therapy may indeed nullify its benefits. In our study, 23 patients did not receive radiation therapy. 42 did. In both groups, 2 patients developed local recurrence. This difference was not statistically significant.

The second question was whether all anastomoses were at the level of the pelvic floor. While this is certainly the case for the occasional small rectal cancer in the lower third of the rectum that can be treated with a proctectomy and coloanal anastomosis and usually the case for middle rectal cancers, it is not invariably the case for rectal lesions, located 9 to 10 cm from the anal verge. With these lesions, it is sufficient to divide the mesorectum and the rectum 4 to 5 cm distal to the lowest palpable edge of the cancer without any “coning down.” As a consequence, the level of the anastomosis really varies in relation to the level of the primary cancer and it is not necessarily on the levators. Because of the fear of clinical complications associated with a pelvic anastomotic dehiscence, a temporary defunctioning stoma, usually a loop ileostomy, was employed in about two thirds of cases, all of whom had their anastomosis located less than 5 cm from the anal verge.

There was one question regarding postoperative sexual and urinary function. During the past 8 years, a deliberate attempt was made to identify and preserve both the sympathetic and parasympathetic nerve plexus during the dissection. This has been possible in all patients unless the tumor was invading the nerve plexus or unless adverse clinical situations, such as a very large tumor or obesity, were found. About 15 male patients were so treated in the group that underwent a sphincter-sparing procedure: considering that some were impotent at that time because of age and some became impotent after preoperative radiation therapy and before surgery, the remaining number is too small to derive any definitive conclusions as to the efficacy of the pelvic nerve-sparing technique on sexual function. There was no deterioration of urinary function.

For the first 6 years of the study, we performed an extended pelvic lymphadenectomy in association with each proctectomy. This lymphadenectomy, which is carried lateral to the parietal fascia, adds an aortoiliac lymph node dissection to the TME. Thus, for the purpose of the study, all patients received at least a TME.

Finally, what are my indications for radiation therapy in conjunction with surgical treatment of rectal cancers? I feel that in the absence of a prospective study analyzing radiation therapy with optimal surgery, we still have to consider the validity of those studies suggesting that there is an advantage in complementing the surgical treatment with radiation therapy. In dealing with a tumor located in a position where a coloanal anastomosis may be possible, I opt to deliver preoperative radiation therapy to avoid the need for postoperative radiation therapy, which may adversely affect the patient’s functional results. When dealing with a rectal cancer that is better approached with an abdominoperineal resection, I opt to proceed with surgery and defer the decision for radiotherapy after analysis of intraoperative and pathologic factors. This approach avoids an increase in postoperative perineal wound complications associated with delivery of preoperative radiation therapy and spares the morbidity of radiation therapy to patients who may not need it. Obviously, if the cancer appears to be fixed to the pelvic wall or to other organs, a course of preoperative radiotherapy is selected to attempt downstaging of the lesion, independent of the final surgical procedure.