Multidisciplinary Management of Patients with Advanced Rectal Cancer

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Abstract

The chance of lymph node involvement in T3 and T4 rectal cancers is 20% to 60%, a risk sufficiently high that most clinicians favor mesorectal excision rather than less aggressive approaches. Patients who have a complete clinical response of the primary lesions to neoadjuvant therapy may represent a special case. Total mesorectal excision can be accomplished without sacrifice of the anal sphincters, and continence can be preserved. Evolving understanding of patterns of tumor spread and mechanisms of anal continence have resulted in increased use of continence-preserving procedures. Removal of the anal sphincters seems to be advantageous only if the sphincters are directly involved. A few small series suggest that a segmental sphincter resection could result in good local control and continence preservation, even if the sphincters are involved. Areas of controversy currently include the role of neoadjuvant therapy for high rectal lesions, the role of lateral lymph node dissection, and methods of improving anal continence after rectal resection.

I would like to take a slightly different approach and express my thoughts about the multidisciplinary management of the patient with advanced rectal cancer. What I would like to share here is my thought process in patient evaluation.

Initial Patient Presentation

In my current practice, I begin every discussion with a patient with rectal cancer talking about genetics. Genetics has a significant effect on risk, therapy selection, and prognosis (1–4). We believe that genetics will help first to predict prognosis, and ultimately, therapeutic alternatives. For example, we base many decisions about chemotherapy on the profile of the tumor. Genetics should be more clearly incorporated into the care of patients nationally.

I then begin to think about preoperative staging. I believe that only a relatively small number of patients pose assessment difficulty. Most patients are easily assessed, and the therapeutic course is well defined. We do not often use computed tomography, magnetic resonance imaging, or positron emission tomography (1, 5, 6). Computed tomography would be used to look for disseminated disease, as opposed to trying to define regional disease. Lymphoscintigraphy has fallen into disfavor. We do use ultrasound, which is required for many of our protocols and has some value. Yet, under the best of circumstances, investigators in Minnesota have reported only 64% accuracy in judging nodal status, and even the T level is somewhat of an issue (6). I believe therefore that no test replaces a good clinical evaluation by an experienced physician.

At my institution, where we see a great number of patients with rectal cancer, our clinical judgment is as good as (or even a little better than) ultrasound. We use ultrasound to supplement—not replace—clinical decision-making.

After assessment of disease stage, a discussion of treatment can ensue. The first point I would like to make is that no variable is more important to patient outcome than the quality of the surgery. We have shown at our institution that survival improves by 15% if an experienced surgeon performs the procedure. Many other institutions have documented similar findings (7–11). Early in one's practice, outcome is related to training, but as time passes, outcome is based on experience and surgical volume. Most articles suggest that a surgeon must perform about 20 rectal cancer resections per year to be competent.

Our discussion turns now to T3 and T4 lesions. Because the risk of lymph node involvement is substantial with this level of mural invasion (i.e., this is more than mere mural disease), our focus must be on the entire rectal mesentery and how to deal with it. Good surgical technique will result in low local recurrence without any adjuvant therapy (12–14). Unfortunately, most adjuvant studies conducted in the United States have antedated the standardization of surgical technique and were predicated on local recurrence rates of 30% to 40%. Ideally, these adjuvant studies would be repeated with good surgical technique. Some of the studies have been redone, and data are provided here. Low tumors present more of a problem with regard to local recurrence than do higher tumors, thus, when we see tumors in the upper third of the rectum, we must rethink whether they require neoadjuvant therapy. If such tumors seem to be modest in size, we often will do surgery without neoadjuvant therapy, but routinely use neoadjuvant therapy for larger and lower tumors (15).

Neoadjuvant therapy offers a modest advantage over surgical technique. In a large Dutch study, local recurrence
improved by ~5% (16). Ninety-five percent of patients do not benefit from the routine use of neoadjuvant therapy. We do not automatically initiate neoadjuvant therapy, but rather try to assess the need for such therapy based on tumor size, grade, biology, and histologic features, as well as genetic analysis.

One of the reasons we choose to use neoadjuvant radiation selectively is that toxicity has been shown to be significant with such therapy in Swedish, Dutch, and German studies (17–20). Toxicity is greater when radiation is done postoperatively than preoperatively. Complications include increased blood loss and perineal complications. Postoperative mortality may be slightly increased, although it was not significantly so in the Dutch study. Radiation techniques varied in the above mentioned studies and may not have been optimal. Nevertheless, the best studies available suggest that the preoperative and postoperative use of radiation therapy is associated with significant toxicity (21, 22).

Radiation therapy is not a substitute for good surgical technique (23). If surgical margins are close, radiation is helpful in minimizing local recurrence; however, if the margins are positive, radiation therapy is not effective in sterilizing the margins. Positive surgical margins after rectal cancer resection are a serious adverse prognostic indicator.

What if a patient has a complete clinical response, there is no visible tumor, and the mucosa is normal after neoadjuvant therapy? The data in the medical literature are confusing. Several reputable studies suggest that a complete clinical response does not necessarily predict that all lymph nodes will be sterilized. Additionally, a complete pathologic response is not predicted. In these retrospective studies, a complete clinical or pathologic response may not predict a disease-free or overall survival advantage, compared with patients who do not have a complete mural response (24, 25).

Prospective data from a Brazilian study is the most current, and I believe, the most meaningful. This study was a prospective evaluation of a large number of patients, all of whom had relatively low lesions and neoadjuvant therapy (24). On an intent-to-treat basis, the investigators followed patients for >5 years, and ~25% of them had a complete clinical response. In such patients, local recurrence was 5%. Patients who did not have a complete clinical response to neoadjuvant therapy underwent standard mesorectal resection, and 22% of them had a complete pathologic response. In this prospective study, patients with a complete pathologic response had improved disease-free and overall survival, compared with those who did not have a complete response pathologically. We see this sort of patient with some frequency, and I tend to feel that we should offer patients an opportunity to be followed. In our practice, this means careful follow-up every 4 months, which includes history, physical examination, measurement of carcinoembryonic antigen, transrectal ultrasound, and proctoscopic examination. We are currently following 12 patients, and thus far, have not had a recurrence.

In patients who present with large obstructing tumors, we favor using a colonic stent as initial treatment. We do not know what effect a stent may have on radiation therapy, but the stent is a bridge, which increases therapeutic alternatives. We also use a stent for obstructing lesions for palliative purposes in patients with recurrent disease (26). We have abandoned preoperative mechanical bowel preps. Current data suggest that such preps actually increase anastomotic leak rates, wound infections, and mortality (27–29).

The lymphatic mapping of rectal cancer is not as clear as that of colon cancer, but I think that the advantage (or potential advantage) is greater (30, 31). There is no question that lateral pelvic lymph drainage from low rectal cancers occurs. Furthermore, Japanese investigators have shown that the routine performance of extrahypogastric lymph node dissection in stage III disease improves survival (32). This dissection is associated with increased morbidity, and most surgeons in the United States are not trained to work outside of hypogastric vessels; thus, the dissection is not routinely done here. Nonetheless, in certain cases, extrahypogastric lymph node dissection seems to improve survival. Because there is clearly a group of patients who might benefit from the procedure, it would be ideal if we could do some sort of lymph node mapping that would allow us to look in that area to decide which patients might be better managed by doing an extended dissection.

In preoperative patients, we have abandoned the 2-cm rule (and previously, the 5-cm rule) in tumors that are very close to the anus (33). As long as the anus is not directly involved, there is no advantage to performing an abdominal perineal resection. The entire lymph node dissection for a rectal cancer is done through the abdomen, regardless of tumor location. The only incremental tissue removed by an abdominal perineal resection is some ischiorectal fat, the anus, and a small portion of the levator muscle. These areas are not common sites of local recurrence. Because the entire lymphadenectomy is done through the abdomen, the only time that we would consider doing abdominal perineal resection is when the anus is directly involved and removal is necessary to obtain a margin around the primary tumor (34–40). If the tumor is ≥1 cm above the puborectalis, the sphincter muscles can routinely be preserved. There are even reports of taking out a segment of the sphincter along with the tumor, reconstructing the anal muscles, and restoring intestinal continuity by bringing the bowel back through the anus as a pull-through. Although we have done the procedure with no local recurrence, it is difficult to be enthusiastic about its routine use; nonetheless, the procedure is technically feasible.

To improve quality of life, we try to create a better reservoir when we do these very low anastomoses. Either a J-pouch or coloplasty helps to decrease bowel frequency and urgency in the postoperative period (41–43). A coloplasty may have a slightly higher leak rate (probably due to tension placed across a transverse anastomosis), but the function is good, and at 6 months, tends to be as effective as the J-pouch. In my own practice, I do not routinely incorporate a pouch if the sigmoid or descending colon is >33 mm in diameter because of risk of obstruction.

What about a protective stoma in patients with a low anterior resection? Many surgeons perform this procedure routinely, and I believe that there is some justification for doing so (44–46). Although a stoma does not prevent anastomotic leak, it does decrease surgical intervention if a leak occurs. Additionally, mortality is somewhat lower if patients are diverted than if not. However, stoma closure presents its own set of complications. Although between 85% and 90% of patients heal well and do not need this stoma, they will still be subjected to risks of stoma...
closure, including leaks, ileus, bleeding and wound infections, and a 2% mortality rate. For these reasons, we remain cautious in our use of stomas.

With larger T4 tumors that involve other pelvic structures, removing these structures with pelvic exenteration may be necessary. Intestinal continuity can be restored, even though a large tumor may involve the vagina, uterus, or bladder. Pelvic structures can be removed, a new rectum can be created, and in fact, a new bladder could also be created to preserve the continuity of the urinary tract. Pelvic exenteration is associated with significant complications and is a big operation that should not be undertaken lightly. Nonetheless, bowel continuity can be preserved in most patients (47–50). Several therapeutic options are available for large rectal cancers.

The next issue that must be considered is follow-up. An argument can be made that follow-up is not justified from a cost-benefit standpoint for early tumors (i.e., T1 tumors) because recurrence is so low. Follow-up is advantageous for patients with larger tumors, however, for several reasons (51). First, patients appreciate it (52). Although there is some anxiety associated with follow-up, patients generally have greater confidence in physicians and examinations, and there is improved survival in patients being followed. In a meta-analysis of follow-up studies, intense follow-up resulted in a 3-fold increase in survival and a greater number of curative resections (53–55).

Patients are followed for good reason: we have effective management for recurrent rectal cancer (25, 56). Hahnloser et al. (57) and Gunderson (58) have published data on intraoperative radiation therapy going back quite a while. Idrees et al. (59) have published more recent data on brachytherapy and the management of recurrent rectal cancer. We use a different type of brachytherapy (i.e., catheter placement occurs during surgery). After surgery, careful planning and high-dose rate brachytherapy can take place. This technique has minimum morbidity, and in patients with disease that cannot be fully resected, relatively good control and long-term survival, compared with any other alternative. We still have problems with disseminated disease, so I believe that such patients need adjuvant therapy afterwards, even though there is no evidence of disease (60).

Surgical management of T3 and T4 rectal cancer is an increasingly sophisticated endeavor with multiple diagnostic and therapeutic alternatives. More likely than not, multidisciplinary teams in specialized treatment centers will be necessary to effectively treat this disease.

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