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Multivisceral Resection in Rectal Cancer

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Introduction

The treatment of locally advanced rectal cancer (T3/4 or N1/2) is challenging and requires a multidisciplinary approach including diagnostic radiology, medical oncology, pathology, radiation therapy, and surgery. Unlike many solid tumors, locally advanced or locally invasive rectal cancer is not necessarily unresectable (Lopez 2001). Indeed, over the past 30 years, it has been shown that a significant percentage of even large colorectal tumors remain localized and do not metastasize; therefore, en-bloc resection with clear margins can lead to cure (Lopez 2001; Gebhardt et al. 1999; Nakafusa et al. 2004; Lehnert et al. 2002; Klaassen et al. 2004; Govindarajan et al. 2006). In a study by Spratt and Spjut involving examination of more than 1,000 colorectal tumors, two-thirds of the large or locally invasive tumors had reportedly not metastasized to even locoregional lymph nodes (Spratt and Spjut 1970). However, it is important to recognize that up to 15% of rectal cancer tumors will be adherent to or invasive into adjacent pelvic organs. Since the surgeon cannot easily differentiate a malignant fistula from an inflammatory adhesion (Gebhardt et al. 1999), and because separation of a malignant fistula can lead to local tumor dissemination and recurrence, multivisceral resection should be considered. Advanced planning, with strict adherence to the principles of surgical oncology, is necessary when treating these difficult cases.

Although multivisceral resection, compared with standard resection, can improve outcome of advanced lesions, these are complex procedures associated with increased morbidity and even perioperative mortality (Birkmeyer et al. 2003, 2007). It is critical to anticipate the need for assistance in order to mobilize a large, multidisciplinary surgical team, which may include colorectal, urologic, gynecologic, orthopedic, neurosurgical, and plastic surgeons. In addition, it is important to recogn ize the need for perioperative care including radiologists, intensivists, and specialized nurses as well as occupational and physical therapists (Madoff 2006). Multivisceral pelvic resections are a challenge not only for surgeons, but also for the patient and the healthcare system. For these reasons, it is both rational and necessary to treat such advanced lesions at specialty centers (Madoff 2006).

This chapter provides a general overview of the role of multivisceral resection during treatment, as well as strategies and guidelines to be used when approaching patients with locally advanced rectal cancer.

Preoperative Procedures

Staging and Imaging

Proper staging of rectal cancer is imperative, not only in planning the proper operation, but also

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in selecting those patients who will benefit from neoadjuvant treatment. Early in the workup process, it is important to differentiate, those patients who have early rectal cancers and can be treated with immediate surgery from those with locally advanced tumors that may require chemoradiation prior to resection (Klaassen et al. 2004). It is also necessary to identify those patients who already have distant metastases, in order to avoid any unnecessary and potentially morbid treatment.

Physical Examination

Although many consider modern imaging modalities to be the most effective means of tumor staging, the importance of a proper physical examination and digital rectal exam cannot be overlooked. An experienced surgeon may gain valuable information regarding the extent of the tumor, as well as its fixation to adjacent organs and the bony pelvis. This information can also help guide the radiation oncologist in determining the necessity of preoperative chemoradiation. A thorough pelvic exam may be the simplest, most direct method of determining the feasibility of a sphincter-sparing operation or the necessity of multivisceral resection. Complete colonoscopy should be done to rule out the possibility of synchronous primary tumors (Lopez 2001).

Radiologic Imaging

Contrast-enhanced computed tomography (CT) scanning remains the most commonly utilized imaging modality for assessing the extent of tumor and the presence of metastases. Although CT scans can provide an approximate idea of tumor size, it is often difficult to accurately differentiate tumor margins from surrounding viscera. Since obtaining adequate circumferential resection margins is paramount to a curative resection, CT scanning may not always be adequate in patients with locally advanced tumors. In the setting of T3 or T4 lesions, magnetic resonance imaging (MRI) may provide a better assessment of pelvic involvement and the potential need for multivisceral resection. Several published studies have compared CT with MRI in predicting extrarectal involvement. One study found that MRI, although demonstrating only moderate accuracy in predicting tumor stage, provided a consistent and highly accurate prediction of the circumferential resection margin compared with final histologic findings (Beets-Tan et al. 2001). Other studies have shown that in the setting of T3 and T4 lesions, possible invasion of the mesorectal fascia was better predicted by MRI, with a sensitivity of 80%, a specificity of 84%, and a negative predictive value of 96% (Klaassen et al. 2004; Mathur et al. 2003).

Endorectal ultrasound (EUS) is another imaging tool that may be used to assess the local extent of rectal tumors. Early and mobile transmural bowel lesions can be accurately gauged by EUS (Lopez 2001). However, in the setting of locally advanced tumors, EUS is less accurate (Klaassen et al. 2004). EUS tends to understage larger lesions due to limited resolution (Siddiqui et al. 2006). Also the accuracy of EUS, as for all imaging modalities, in staging of rectal cancer is markedly reduced after radiation therapy as a result of postradiation edema, inflammation, necrosis, and fibrosis. Studies have indicated that the accuracy of EUS in assessing T-stage after radiation is only 50%, with a 40% rate of overstaging (Siqqiqui et al. 2006). See Fig. 2.1 for examples of all three imaging modalities in the same patient.

Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) is a newer imaging modality that is becoming more valuable in the preoperative staging of locally advanced rectal cancer. FDG-PET is a powerful, noninvasive tool for imaging tumor metabolic activity and can be used to assess changes in tumor glucose metabolism (Cascini et al. 2006). Identifying nodal disease remains a challenge for all imaging modalities. A prospective study of 104 patients by Llamas-Elvira et al. compared FDG-PET and conventional CT. FDG-PET was vastly superior in identifying metastatic disease, showing a sensitivity of 89% vs. 44% for CT. FDG-PET revealed previously unknown metastatic disease in 19% of patients, changed staging in 13%, and modified the scope of surgery in an additional 12% (Llamas-Elvira et al. 2007). However, both FDG-PET and CT demonstrated poor sensitivity in detecting regional lymph nodes (21% and 25%, respectively). Another potential use of FDG-PET is identifying recurrent disease. EUS, CT, and MRI are poor at differentiating viable tumor from scar or inflammatory tissue. FDG-PET appears to have a role in differentiating scar from viable tumor (Cascini et al. 2006).

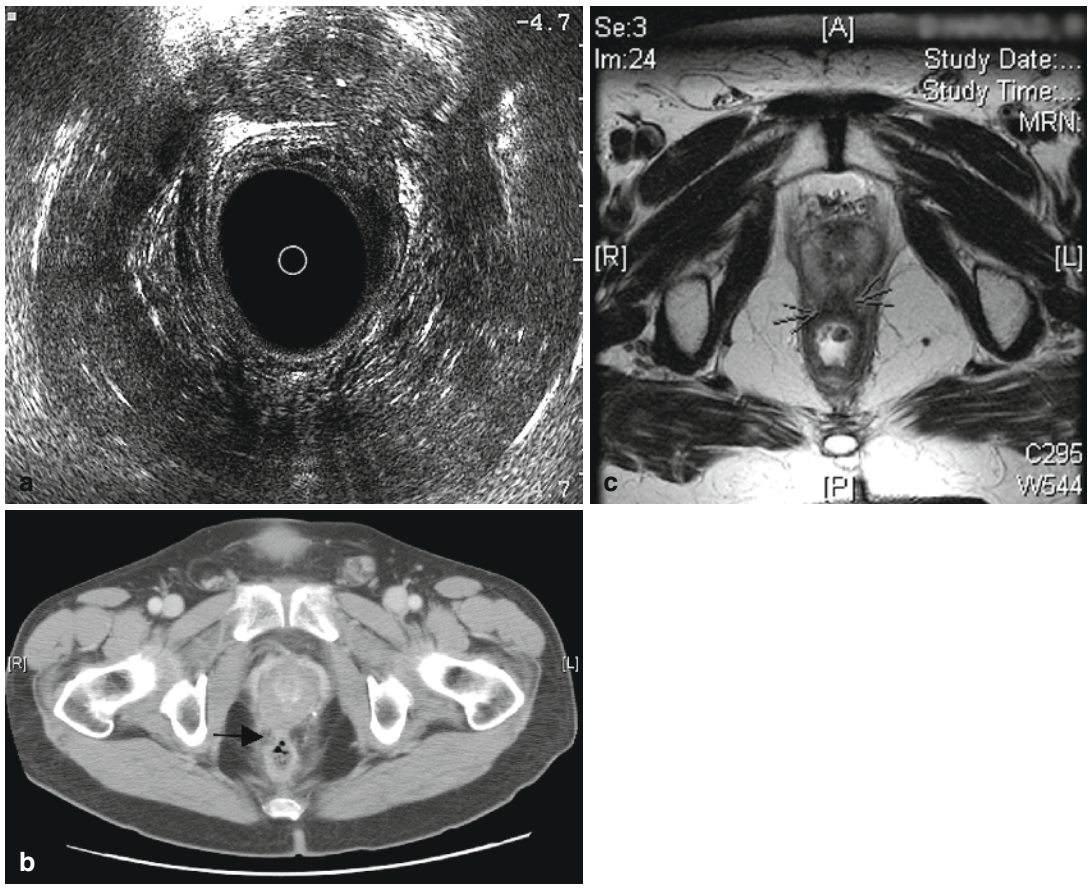

Figure 2.1. A comparison of EUS (**a**), CT (**b**), and MRI (**c**) in a patient who has rectal cancer with prostate invasion.

Although no single imaging modality yet exists that can accurately and consistently stage locally advanced rectal cancers, technology is quickly evolving. Newer imaging tools such as PET-CT may soon be changing the way we stage these difficult cases (Gearhart et al. 2006).

Neo-Adjuvant Therapy

The single most important factor in the cure of rectal cancer remains complete excision of the tumor, with negative macroscopic and microscopic margins. Multimodality therapy is often the best method for achieving this goal.

Over the last two decades, the introduction of adjuvant and neoadjuvant therapy has helped to decrease local recurrence rates and improve long-term survival rates. Postoperative chemoradiation has been found to improve survival. In a landmark randomized trial conducted by the North Central Cancer group, chemotherapy was shown to enhance the efficacy of pelvic radiation (Krook et al. 1991). The National Institutes of Health Consensus Development Conference on Adjuvant Therapy for Patients With Colon and Rectum Cancer resulted in a National Cancer Institute Consensus Statement released in 1990, which recommended that adjuvant therapy, combining chemotherapy and radiotherapy, should be used to improve local control and survival in Stage II and Stage III patients ([No Authors Listed]1990).

With preoperative radiation therapy, potential tumor downsizing may help ensure an R0 resection and may downstage the tumor so that a sphincter-preserving procedure may be undertaken and postoperative quality of life improved. The Colorectal Cancer Collaborative

Group published a meta-analysis in 2001 combining the data from 22 randomized trials and comparing the results of preoperative radiotherapy, postoperative radiotherapy, and no radiotherapy for rectal cancer ([No Authors Listed] 2001). They found that the yearly risk of local recurrence was 46% lower in those who had preoperative treatment than in those who had surgery alone, and 37% lower in those who had postoperative treatment than in those who had surgery alone. They also demonstrated that fewer patients treated with preoperative radiotherapy died of rectal cancer than those treated with surgery alone (45% vs. 50%, respectively) (Krook et al. 1991).

Although preoperative radiotherapy and postoperative chemoradiation have become the standard of care for advanced rectal cancers, chemotherapeutic regimens as well as use of preoperative chemotherapy vary among institutions. A recent study by Bosset et al. investigated the potential benefits of preoperative vs. postoperative chemotherapy. The study enrolled 1,011 patients, divided into four treatment groups as follows: (1) preoperative radiotherapy alone; (2) preoperative chemoradiotherapy; (3) preoperative radiotherapy and postoperative chemotherapy; (4) preoperative chemoradiotherapy and postoperative chemoradiotherapy. They found no significant difference in overall survival between the groups receiving chemotherapy preoperatively or postoperatively. The combined 5-year survival rate was 62.5%. Although overall survival rates were not altered, local recurrence rate were. The 5-year cumulative incidence rate for local recurrence varied from 7.6 to 9.6% in those receiving chemotherapy, and was 17.1% in those receiving radiotherapy alone (Bosset et al. 2006). These findings corroborated those of the German Rectal Cancer Study Group, which assessed preoperative vs. postoperative chemotherapy in patients with T3 or T4 disease. In that study, overall survival was not affected by preoperative vs. postoperative radiotherapy; however, local recurrence rates were significantly decreased in the group receiving preoperative treatment (6% vs. 13%) (Sauer et al. 2004).

Intraoperative Procedures

The goal of any cancer operation is an R0 resection. Positive margins, particularly grossly positive margins, greatly increase the risk of local recurrence, and few patients benefit from such incomplete resections (Madoff 2006). Meticulous and thorough preoperative assessment of the patient will hopefully provide the surgeon with adequate information for a successful procedure.

Surgical Treatment

Lateral Invasion

As Klaassen and colleagues have shown, total mesorectal excision (TME) can still be performed after neoadjuvant treatment, when tumor extends in the direction of the radial margin; however, if tumor penetrates the mesorectal fascia and invades surrounding pelvic structures, en-bloc resection of the pelvic autonomic nerve plexus should be attempted in a plane lateral to the nerves. Direct extension into the pelvic wall, including the iliac vessels, necessitates resection lateral to the internal iliac as well as ligation of the gluteal vessels and the ventral branches of S2–S4 (Klaassen et al. 2004).

Posterior Invasion

Invasion into the sacrum, requiring an abdominosacral resection, is more often seen in recurrent cases than in advanced primary cases (Klaassen et al. 2004). The idea of an abdominosacral resection was advanced in the early 1980s by Wanebo and Marcove (1981). The major problems they found with these resections were: (1) the technical considerations of extensive surgery; (2) potential for iatrogenic sequelae such as neurologic defects involving bladder, bowel, and sexual functioning; (3) potential musculoskeletal defects as a result of instability caused by high sacral resection [21]. Some believe that the major morbidity and decrease in quality of life (QOL) associated with abdominosacral resection are mainly due to the high amputation of the sacrum, as resections are extended to the sacral promontory or sciatic notch. Moriya et al. concluded that a less extensive sacral amputation led to acceptable QOL, with similar survival rates (61% at 3 years and 46% at 5 years). Although the survival rates quoted by Moriya et al. were slightly higher than others in the published literature, local rerecurrence and lung metastasis occurred in more than 90% of the patients in their series

(Moriya 2006). Surgery may still be an option in these settings, but the low patient survival rate must be weighed carefully alongside the high morbidity of this procedure.

Anterior Invasion

Klaassen et al. demonstrated that in extensive resection for rectal cancer, the presence of a dedicated urology team is critical in preoperative evaluation of the urinary system as well as postresection reconstruction. When the ureter is involved unilaterally, it can be resected en-bloc and repaired with a psoas hitch procedure (Klaassen et al. 2004). In the setting of tumor involving the base or trigone of bladder or prostate, total pelvic exenteration (TPE) with resection of the bladder, lower ureters, and internal genital organs may be required. As Vermaas et al. have noted, since its introduction in 1948, TPE has been viewed as a very difficult procedure associated with poor QOL and considerable morbidity and mortality (Vermaas et al. 2007). Over the years, however, technique, technology, and experience have improved to the point where TPE may now provide a good chance of survival as well as adequate QOL. Vermaas and colleagues found 5-year local control and overall survival rates of 88% and 52%, respectively, in patients with primary advanced rectal cancer. In patients with recurrent rectal cancer, 3-year local control and survival rates were 60% and 32%, respectively (Vermaas et al. 2007). Ike et al. reported a 5-year survival rate of 66% in patients with T3 lesions, and 39% in those with T4 lesions (Ike et al. 2003). Although morbidity rates vary greatly, depending on the study (anywhere from 13 to 75%), the high chance of a potential cure makes TPE a viable option for carefully selected patients (Vermaas et al. 2007; Ike et al. 2003). Male patients with lesions involving the prostate and seminal ve sicles may benefit from total or partial prostatectomy and/or seminal vesiculectomy in addition to resection of the primary lesion. A study by Poggio et al. performed at Memorial Sloan-Kettering Cancer Center found a 2-year local and distant recurrence rate of 83% and 70%, respectively, and a 5-year overall survival rate of 49% in this population of patients (Poggio et al. 2007).

In female patients, anterior invasion of the tumor may be simpler to deal with since the uterus creates a barrier to the urinary system. Klaassen et al. point out that vaginal invasion

Figure 2.2. A patient with rectal cancer involving the posterior vagina.

necessitates resection of the involved vagina and its paracolpium, with subsequent reconstruction (Fig. 2.2) (Klaassen et al. 2004). This anatomic "barrier" may be why women are four times more likely to receive multivisceral resection than men (Govindarajan et al. 2006). Unfortunately, some surgeons may be reluctant to perform a more aggressive resection in men for fear of the potential morbidity associated with a complex genitourinary resection – thus leaving the patient with an incomplete resection and a high likelihood of recurrence (Lopez 2001).

Pelvic Reconstruction

Reconstruction of the pelvis after an extensive resection constitutes another facet of treatment for these patients. As Madoff has stated, the major goals of reconstruction are simple: to optimize healing, to avoid complications, and if possible, to restore function (Madoff 2006). In most cases, a rectal anastomosis is not possible, and the surgeon must confront a large, irradiated pelvic space prone to wound healing complications. Usually, an omental pedicle graft can be used to fill the pelvis, but some patients may benefit from more complex reconstruction such as a vertical rectus abdominus myocutaneous flap (Madoff 2006; Klaassen et al. 2004; Bell et al. 2005). If a cystectomy is performed, options for urinary diversion include the traditional ileal conduit or an orthotopic bladder substitution. Large vaginal defects may also be reconstructed with a rectus abdominus flap (Bell et al. 2005), or a neovagina may be created; however, at this point in time little is known about the long-term anatomical and functional results of this type of reconstruction (Madoff 2006).

Intraoperative Decisions

Although accurate anticipation of the exact degree of tumor invasion and total scope of the planned resection is ideal, intraoperative surprises cannot always be avoided. In these instances surgical expertise and proper intraoperative decision-making become crucial. On entering the abdomen, a thorough search for distant metastases should be performed, as the presence of metastasis would preclude an en-bloc resection. Additionally, tumor adherence to adjacent organs may represent either malignant invasion or simply inflammatory adhesions. Every effort must be made to avoid finger fracture of adhesions leading to tumor dissemination and the possibility of an incomplete resection. The reported incidence of histologically proven malignant adhesions is 49–84% (Nelson et al. 2001). If it is not possible to reliably differentiate a malignant adhesion from an inflammatory adhesion, en-bloc resection should be performed.

Intraoperative Radiation Therapy (IORT)

Substantial progress has been made in recent years in the experimental, technical, and clinical application of intraoperative radiotherapy (IORT) as a treatment modality for various cancers. A major goal of all radiation oncologists is to increase the dose delivered to the tumor relative to that delivered to the normal adjacent tissues. As Willett and colleagues have noted, this has led to the use of field-shaping techniques with multileaf collimation, multiple field techniques, and intensity-modulated radiation therapy, as well as intracavitary and interstitial brachytherapy (Willet et al. 2007). Two alternative but complementary IORT techniques have evolved using this philosophy of achieving higher effective doses of irradiation in the tumor: intraoperative electron radiation (IOERT) and high-dose rate brachytherapy (HDR-IORT). Delivery of radiation during surgery means that normal tissues can actually be moved aside or physically shielded. Additionally, because the tumor can be visualized, it is possible to more accurately define areas at risk for tumor involvement (Willet et al. 2007).

Since IORT is not widely practiced, no randomized trials have been conducted to evaluate its impact on survival; however, experiences from single large institution studies indicate that IORT may positively influence local control and survival (Willet et al. 2007). In a study performed at the Massachusetts General Hospital, Nakfoor et al. assessed 101 patients with locally advanced primary rectal cancer who underwent preoperative radiation and IOERT. They found that patients undergoing margin-negative (R0) resection had a 5-year local control rate of 89% and a disease-specific survival of 63%. Patients with microscopically involved margins had a local recurrence rate of 68%; and those with gross disease had a local recurrence rate of 57% (Nakfoor et al. 1998). A similar study at the Mayo clinic found an improvement in local control and survival with the addition of IOERT. Five-year overall survival was reportedly 46%, and 3-year overall survival improved from 24 to 55% (Gunderson et al. 1997). In another study at Memorial Sloan-Kettering Cancer Center, Alektiar et al. investigated the effects of HDR-IORT in the management of locally recurrent colorectal cancer (Fig. 2.3). In a series of 74 patients, the 5-year local control rate was reportedly 39%, with a distant metastasis disease-free rate of 39%. Overall 5-year survival was 36% in those patients with R0 resections (Alektiar et al. 2000). Although further studies are needed to justify the routine use of IORT, preliminary studies are encouraging, and use of IORT should be considered in select cases.

Morbidity of Multivisceral Resection

As expected, the morbidity of multivisceral resections is higher than that of standard resections owing to the increased complexity inherent in these procedures, as well as increased blood loss. Morbidity rates vary widely depending on the source, but Lopez quotes a general morbidity rate of 30% in extended resections (Lopez 2001). Poggio et al. found that patients undergoing partial or total prostatectomy had a 79% chance of erectile dysfunction and those undergoing seminal vesiculectomy alone had a 43% chance of erectile dysfunction. In their series of pelvic exenterations, Gannon et al. found an overall complication rate of 43%, with a third of those being major complications

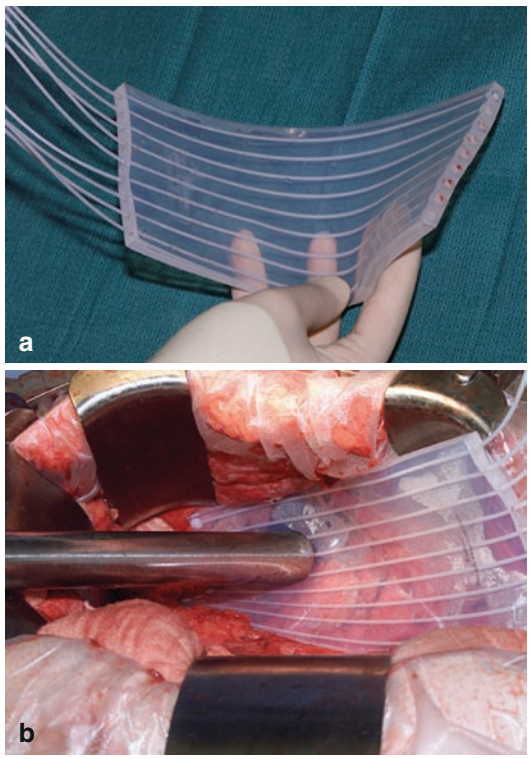

Figure 2.3. HDR-IORT HAM-setup used at Memorial Sloan-Kettering Cancer Center. (Photo courtesy of Dr. Karyn Goodman)

(enterocutaneous fistula, respiratory failure with pneumonia, urinary conduit leaks) requiring a hospital stay >20 days (Gannon et al. 2007).

With a 5-year postoperative survival rate approaching 50%, multivisceral resections warrant more consideration. With thorough preoperative planning, meticulous intraoperative technique, and wide anatomic resection, multivisceral surgeries may result in cure, which should remain our chief objective. The most important factor in preventing local recurrence is obtaining a tumor-free resection margin, as patients rarely benefit from an incomplete resection. However, as Lopez points out, multivisceral resections are not standardized procedures, and not all surgeons should attempt them. The best course for a surgeon unwilling or unable to perform extensive multivisceral resection in the setting of unexpected intraoperative findings is to seek immediate consultation with a more experienced colleague, or else to close the abdomen and refer the patient to a specialty center with significant expertise in this type of complex surgery. This is far better than compromising patient care by performing an incomplete operation (Lopez 2001).

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