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In Brief

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There have been significant advances in the multidisciplinary management of rectal cancer over the last few decades, with further changes and improvements on the horizon. Changes to surgical treatment, including new techniques for performing both minimally invasive local excision and oncologic proctectomy, have increased options for patients and bring into question the balance of oncologic and functional outcomes. Advances in radiation and chemotherapy have resulted in decreased risk of local recurrence and are raising the possibility of eliminating surgery completely for select patients. The constantly changing landscape of rectal cancer management has led to significant variation in treatment and outcomes, prompting the creation of an accreditation program for institutions that care for patients with rectal cancer.

Surgical resection is considered definitive treatment for patients diagnosed with low-risk early-stage rectal cancer, while patients with locally advanced rectal cancer, defined as stage 2 or stage 3, additionally benefit from multimodality treatment with radiation, chemotherapy, or both. Patients who are identified as having metastatic disease at the time of diagnosis may still be eligible for curative resection depending upon the extent and pattern of spread of the cancer and the response to preoperative chemotherapy.

Because the treatment strategy for rectal cancer varies considerably depending upon the stage at diagnosis, it is critical that patients are accurately staged prior to beginning treatment. Clinical staging provides the physician and the patient with data regarding evidence of local and distant disease, allowing for an informed discussion on the survival and risk of recurrence. Standard staging evaluation is defined by the National Comprehensive Cancer Network (NCCN) and also supported by the American Society of Colon and Rectal Surgeons practice parameters for the management of rectal cancer. Along with routine laboratory tests (eg, complete blood count, chemistry panel), it is recommended that carcinoembryonic antigen level be assessed to estab-

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lish a baseline that can be followed post-treatment for active surveillance. CT scans of the chest and abdomen asses for systemic metastatic disease, which most commonly occurs in the liver or lungs.

Staging of rectal cancer differs from colon cancer in that it is important to assess for locally advanced disease, which is an indication for treatment with chemotherapy and/or radiation prior to surgical intervention. Magnetic resonance imaging of the pelvis with specific rectal cancer protocol is the current standard of care to assess for local tumor advancement and lymph node involvement. Although the details of the protocol may vary between institutions, they typically include an oblique sequence. The oblique sequence allows for more accurate measuring of distance to the mesorectum and to the top of the anal canal, as the rectum is not a transverse structure. Endorectal ultrasound (EUS) or transrectal ultrasound (TRUS) play a complementary role in locoregional staging of rectal cancer, as they are able to visualize the layers of the rectal wall and distinguish between T1 and T2 tumors.

Local excision of early-stage rectal cancer is an attractive treatment option because it is significantly less invasive than radical oncologic resection and maintains intestinal continuity without the changes in bowel function associated with low anterior resection. Because local excision involves full-thickness excision of the tumor and wall of the rectum but specifically does not include oncologic lymphadenectomy, complete pathologic staging cannot be performed. As a result, local excision is associated with a higher risk of local recurrence compared to radical surgical resection. Rectal cancers with clinical staging consistent with T1N0 are best suited for local excision, in the absence of adverse pathologic features. Such features include lymphovascular invasion, poorly differentiated histology, high level of tumor budding, and distal location in the rectum, which are all poor prognostic signs with increased risk of occult lymph node metastases. Given the high risk of local recurrence, patients with rectal cancers who have adverse pathologic features should be considered for formal oncologic resection with proctectomy and lymphadenectomy rather than local excision.

Transanal local excision has traditionally been performed with an open technique. This confers limitations with how proximal the surgeon is able to reach, typically limited to approximately 8 cm or less from the anal verge. Newer techniques such as transanal endoscopic microsurgery and transanal minimally invasive surgery have revolutionized local excision for rectal cancer. These techniques allow more proximal reach, up to the rectosigmoid junction. With these advanced platforms, full-thickness excision is possible, but a specialized surgeon skillset is required.

Other advances in rectal cancer care in the last 20 years include the standardization of oncologic surgical resection, including total mesorectal excision (TME). TME requires the mesorectum and the rectum to be removed with the fascia propria of the mesorectum intact. This mesorectal package can be graded as complete or incomplete. Completeness is a valuable item to assess the oncologic safety of the surgical resection, as it is a predictor of local tumor recurrence in the pelvis. TME improves the chances of having a negative circumferential resection margin, which is associated with improved long-term survival. Thus, these pathologic outcomes are used to measure the quality of rectal cancer surgery.

There are currently multiple approaches to rectal cancer surgery, including open, laparoscopic, robotic, and transanal total mesorectal resection. Regardless of the approach, the oncologic principles of rectal cancer surgery do not change. The advantages of laparoscopic surgery include less blood loss, less postoperative pain, earlier return of bowel function, shorter hospital stay, and reduced cost of care. The disadvantages of laparoscopy include the technical challenges associated with advanced laparoscopy in the confined space of the pelvis, longer operative times, and a longer learning curve to accomplish these advanced laparoscopic techniques. There have been multiple clinical trials looking at the safety and oncologic outcomes of a minimally invasive approach to rectal cancer surgery. These studies show that laparoscopic surgery in patients with rectal cancer without invasion of adjacent tissues is oncologically safe and is associated with improved patient recovery. The most recent advance in the surgical technique, transanal total mesorectal resection, still requires randomized controlled clinical trial data to prove safety and efficacy.

A number of multi-institutional trials conducted in the 1990s confirmed that the addition of chemoradiation to radical resection could improve at the least locoregional control of these tumors. Both adjuvant and neoadjuvant approaches seem to be superior to surgery alone. The German Rectal Cancer Trial convincingly demonstrated that the neoadjuvant approach was superior to postoperative regimens in terms of locoregional control and preservation of gastrointestinal tract continuity rates. Based primarily on that trial, neoadjuvant chemoradiation therapy followed by radical resection became the standard treatment for locoregionally advanced mid to distal cancers in most places throughout the world starting in the early 2000s. Since the 1990s, the standard treatment paradigm for locally advanced rectal cancer, which includes stage 2 and stage 3 disease, has included neoadjuvant chemoradiation, followed by surgical resection, and finally adjuvant chemotherapy (for node positive disease). This approach, along with improvements in the surgical technique, has resulted in substantially lower rates of local failure from pelvic recurrence. However, systemic recurrence remains a significant risk, with up to 30% of patients developing distant metastatic disease. Moving systemic chemotherapy to the neoadjuvant setting has thus been proposed as a means of addressing the unidentified micrometastatic disease present at the time of diagnosis sooner in the treatment plan. This approach of delivering all chemotherapy and radiation up front with surgical resection as the final step is termed total neoadjuvant therapy (TNT) and is currently recommended by the NCCN as a treatment option for locally advanced rectal cancer.

The greatest perceived risks of TNT are overtreatment due to imprecise clinical staging and the potential for disease progression in patients who do not respond to neoadjuvant treatment. However, advances in imaging technology should continue to improve our ability to accurately identify, treat, and monitor patients with locally advanced rectal cancer. The benefits of improved compliance with chemotherapy are well accepted, as is the likelihood of a shortened period of time with an ostomy—an important quality of life factor for patients.

Increased adoption of TNT will also likely facilitate broadening the selection of patients who may be eligible for a nonoperative approach. Prior to the 1990s, radical resection alone with low anterior or abdominoperineal resection was the mainstay of treatment. Recognition of the fairly high local and systemic recurrence rates with surgery alone, as well as the risk of functional loss associated with these operations, led to significant interest in finding effective adjunctive therapy to improve care for patients with these cancers. As the above approach became the standard of care, reports started to surface identifying patients who had undergone therapy who appeared to have complete clinical responses (CCR). As has been true for other cancers treated with neoadjuvant therapy, such as anal cancer, legitimate questions were raised regarding the necessity of proceeding with potentially major and morbid radical surgery in patients with no measurable residual disease following neoadjuvant therapy. One of the largest early studies supporting the safety of a nonoperative, or “watch and wait” approach, for these patients with a CCR was reported by Habr-Gama et al, who reported favorable rates of local and systemic failure in patients who were followed after receiving chemoradiation rather than proceeding with major resection. Although randomized clinical trial data are not available, multiple retrospective single-institutional studies have reported experiences with the watch-and-wait strategy and several prospective trials are currently accruing patients. Although forgoing surgery in favor of a watch-and-wait strategy may be a reasonable and attractive option for select patients achieving a CCR after neoadjuvant treatment, the appropriate role of watch-and-wait within the standard of care for patients with rectal cancer is not yet definitively defined.

It is estimated that approximately 11%-24% of nodal metastases in rectal cancer are found in the lateral pelvic sidewall. A retrospective study in Japan reported that the incidence of lateral pelvic lymph nodes (LPLN) in patients with T3/T4 rectal cancers was 18%. This is primarily due to the drainage pattern of the mid- to low rectum, which can either spread upward along the superior rectal vessels or laterally along the middle rectal vessels and then to the internal iliacs. Extended lymphadenectomy (EL), particularly in the context of mid- to low rectal cancers, refers to the dissection and removal of the LPLN, which are defined as the lymph nodes that travel along the common iliac, internal iliac, external iliac, and obturator arteries. Recent guidelines put forth by the Japanese Society for Cancer of the Colon and Rectum (JSCCR) recommend

that surgical resection for rectal cancers located above the peritoneal reflection should include TME, whereas resection of those below the peritoneal reflection should include both TME and LPLN dissection as the standard of care. In contrast, centers in the United States and Europe do not routinely perform LPLN dissections for rectal cancers, even in advanced disease, primarily because pelvic lymph node metastases outside the mesorectal fascia are considered to be systemic disease which is best treated with chemotherapy. LPLN dissections are therefore rarely performed due to the potential associated morbidity with little perceived oncologic benefit. Currently, inclusion of LPLN dissection in the treatment algorithm for rectal cancer appears to be regionally dependent, without a clear international consensus. It is clear that both treatment strategies offer patients much-improved rates of local recurrence and overall survival. However, the guidelines and criteria for routine utilization of LPLN dissection in this country are currently undefined.

There have been several significant advances in the management of patients with rectal cancer in recent years, which together make the care of these patients complex. Management that follows evidence-based guidelines is associated with decreased rates of recurrence and improved survival. However, in the United States, outcomes for patients diagnosed with rectal cancer vary considerably depending upon the institution where the patient is treated, with up to one half of patients with rectal cancer not receiving guideline-recommended staging and treatment. As a result, significant disparities exist for important outcomes such as postoperative morbidity and mortality, sphincter preservation with bowel continuity vs permanent ostomy, local recurrence, and long-term survival. To address this variation in outcomes and broadly improve the quality of rectal cancer care, the American College of Surgeons Commission on Cancer recently established the National Accreditation Program for Rectal Cancer (NAPRC). Design of the program is modeled after rectal cancer accreditation programs in Europe that have successfully decreased cancer recurrence rates and improved survival by standardizing care. Central elements of accreditation include strict requirements for multidisciplinary cancer conferences (including regular attendance by a set group of specialists with rectal cancer expertise), development of a standards manual of evidence-based protocols, and an external audit of compliance with protocols. Leaders involved with the development of the NAPRC acknowledge that many hospitals will find accreditation excessively resource intensive, especially low-volume centers. Thus, there is a critical need to develop alternative strategies that will improve care across a wider range of institutions and ensure that disparities in care delivery are not exacerbated.