Accurate Staging, Selective Preoperative Therapy and Optimal Surgery Can Deliver a Good Oncological and Functional Outcome in Low Rectal Cancer

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The primary surgical objective in a patient with rectal cancer is to perform a mesorectal excision achieving macroscopically clear proximal, distal and radial (circumferential or CRM) margins while restoring intestinal continuity wherever feasible.

In this month's journal, Pricolo et al. [1] report their experience of the impact of the length of the distal resection margin on outcome in rectal cancer. Fifty-three patients with advanced rectal cancer (T3/4 N0/N1) on endoscopic ultrasound (EUS) or MRI underwent neoadjuvant chemoradiation (5-fluorouracil and 50.4 Gy). Thirty-three patients (62%) underwent low anterior resection with a distal margin ranging from 1 to 74 mm (mean 18 mm) excluding the anastomotic rings. At a mean follow-up of 49 months, there was no evidence of locoregional recurrence [1].

This paper illustrates several important points: the evolution in the understanding of the biology of distal tumor spread in rectal cancer, the importance of accurate tumor staging, the value of meticulous surgical technique and the deployment of neoadjuvant therapy in appropriately selected patients to optimize outcome.

Histopathological studies have demonstrated that intramural submucosal spread, present in 40% of patients, extends more than 10 mm in only 4–6% of patients with rectal cancer [2]. Such reports led to the revision of the traditional 5-cm distal resection margin rule and to the recommendation of a 2-cm distal margin where feasible

[3, 4]. Subsequent work has shown that in appropriately selected cases a distal margin of 10 mm does not increase the local recurrence rate or compromise survival [5]. The lower rectal and anorectal anatomy provides a challenge both from a staging and therapeutic standpoint in rectal cancer. In low rectal cancer (defined as the area below the insertion of the levator muscle), the mesorectal volume is reduced, and in anorectal tumors there is no mesorectal plane, as the rectal tube lies against the pelvic floor before passing through the external anal sphincter. The mesorectal fascia tapers as it fuses with the endopelvic fascia overlying the levator muscles, which in turn fuses with the muscles of the external anal sphincter. The intimate relationship between the mesorectum, levator muscle and external anal sphincter renders it essential to rule out tumor impingement of the sphincter complex, especially if an intersphincteric dissection is being contemplated. Indeed these lowest tumors are at the highest inherent risk of circumferential margin involvement regardless of stage by virtue of these anatomic relations.

The first step in the management of a patient with low rectal cancer is to assess the tumor in terms of its stage and its relationship to the anal sphincter complex. Both EUS and MRI are employed to determine the size of the tumor (T stage) and lymph node status (N stage) as well as the preoperative stage of the tumor. In low rectal cancer close to the sphincter complex, additional information is required to assess the possibility of performing

sphincter-saving surgery and the need for neoadjuvant therapy. It is essential to assess the distance between the tumor and the sphincter complex and its relationship to the levators. EUS has been reported to be accurate in the assessment of histological infiltration of the external anal sphincter or levator ani muscle in patients with low rectal cancer, having a sensitivity of 100%, negative predictive value of 100%, specificity of 87% and positive predictive value of 53% when predicting sphincter infiltration [6]. High-resolution MRI is the ideal imaging modality in the preoperative staging of low rectal cancer as it can accurately define the tumor distance to the sphincter complex and the ability to clear radial and distal margins [7]. The MERCURY study, using a 1-mm threshold for a positive CRM, reported accuracy for the prediction of clear margins of 91% and a negative predictive value of 93% in patients who underwent primary surgery after MRI [8]. Thus the modality can identify patients at an increased risk of a positive resection margin (CRM or distal) who may benefit from neoadjuvant therapy due to a close or compromised resection margin but who may not be offered it on the basis of local tumor size (T) and nodal (N) staging such as in the case of a T2N0 tumor on EUS which is demonstrated to have a threatened margin on MRI. Salerno et al. [9] have also reported on a cohort of patients with low rectal cancer (within 5 cm of the anal verge) with pre- and post-MRI assessment following neoadjuvant therapy. They observed that patients with little or no treatment response on the post-treatment MRI tended to have a subsequent positive histological margin. This raises the intriguing question of whether such patients could be offered second-line neoadjuvant therapy in an attempt to achieve further downstaging or whether the absence of downstaging simply indicates 'poor biology' and therapeutic unresponsiveness and should mandate a more aggressive surgical resection in an attempt to reduce the risk of a positive resection margin.

Although short-course preoperative radiotherapy (SCPRT) and combined long-course chemoradiation treatment are efficacious in reducing the risk of local recurrence, combined long-course treatment offers the potential to downsize and downstage the tumor which may facilitate sphincter preservation. Subset analysis of patients with low rectal cancer ($n = 188$) from the German Rectal Cancer Trial found that patients who had preoperative chemoradiation therapy had twice the sphincter preservation rate (39%) compared with surgery alone (19%) ($p = 0.004$) [10]. These findings are countered by data from the Polish RCT, which is the only study published to date comparing SCPRT and combined chemo-

radiation. The combined chemoradiation arm demonstrated a significantly lower pathologically complete response rate (16.1 vs. 0.7%) and a significant downstaging effect (tumors were 19 mm smaller than in the SCPRT group), which is not surprising, as SCPRT is not employed to induce downstaging. However, there was no difference in the primary study endpoint, which was the rate of sphincter preservation, with 39% of patients in the SCPRT group undergoing abdominoperineal resection (APR) compared to 42% in the chemoradiation arm ($p = 0.57$) [11]. These discordant findings may be related to clinical reluctance to alter the operative strategy to perform an APR which was formulated prior to chemoradiation rather than amending the surgical approach in light of apparent tumor downsizing after neoadjuvant therapy.

In patients with a low rectal tumor extending to within 2 cm of the upper part of the sphincter, the necessary distal resection margin may only be achieved by resection of a variable part of the internal sphincter utilizing the intersphincteric dissection technique or APR. Chamblou et al. [12] reported on a series of 90 patients with low tumors (median distance of 35 mm from the anal verge) that underwent neoadjuvant therapy and an intersphincteric dissection with partial or complete excision of the internal anal sphincter and a coloanal handsewn anastomosis. The median distal resection margin was 12 mm while the local recurrence rate was 6.6% at a median follow-up of 56 months.

While we should always strive to offer a patient sphincter-saving surgery, a technically proficient but functionally poor result may not be in the best interests of the patient. Patients with low rectal tumors who undergo neoadjuvant therapy and a low stapled or coloanal anastomosis have a high incidence of the functional symptoms of low anterior resection syndrome. It is interesting to note that in the study by Chamblou et al. [12] 24% of the patients at follow-up reported incontinence with a mean Wexner score of 15. Careful patient assessment and education are essential in counseling the patient on the risks and benefits of therapy.

Patients with low rectal cancer represent a staging and therapeutic challenge as the surgeon needs to balance the often competing requirements for an oncologically sound procedure with the desire to perform a sphincter-sparing procedure. Such a patient will benefit from multidisciplinary team input as accurate preoperative imaging; the judicious use of neoadjuvant therapy and reassessment after therapy will help determine the appropriate surgical approach. This approach will help optimize the individual patient's function and outcome.

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