

# Should Local Excision After Neoadjuvant Therapy Be Included in the National Guidelines for the Treatment of Locally Advanced Rectal Cancer?

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The American Society of Colon and Rectal Surgeons recently published its clinical guidelines for the management of advanced rectal cancer.<sup>1</sup> The guidelines stated that a watch and wait (WW) management approach can be considered in the context of a protocolized setting for highly selective patients if complete clinical response (CCR) is achieved after neoadjuvant therapy (NAT). We agree with this position; however, we also believe that full-thickness local excision (FTLE) after NAT and demonstration of CCR, also in a protocolized setting, should be added to the guidelines.

The case for organ preservation with FTLE is actually stronger than with WW. The safety of FTLE compared to that of total mesorectal excision (TME) was proven in a randomized trial by Rullier et al.<sup>2</sup> Although this study did not restrict randomization to only tumors in CCR after NAT, which may cause the appearance of a bias in favor of FTLE, we do not expect that the result would have been different had randomization been limited to only tumors in CCR because of the low recurrence rates in both arms and the inclusion of some tumors with stages >ypT1 in the FTLE data.

Multiple prospective and retrospective reviews have indicated that the incidence of local failure after

FTLE and the confirmation of ypT0 status is <5%.<sup>3,4</sup> Completion TME can be performed shortly after the acquisition of a false-negative result of the presumed preoperative CCR when residual microscopic disease is detected after FTLE. This avoids the possibility of missing residual cancer for a prolonged period of time, which may result in a higher incidence of distant recurrence, as suggested in the case of regrowth during the follow-up period of WW cases.<sup>5</sup> Of course, FTLE is not expected to alter other mechanisms of distant spread.

Another concern related to the WW approach (compared to FTLE) is the complexity of the follow-up protocols required to detect early regrowth, the rates of which can be as high as 20%. The close follow-up period should be at least 2 to 3 years. This requirement may not be suitable for patients who are not completely compliant or who are likely to move frequently during the initial follow-up period. Another potential hurdle to appropriate follow-up and continuity of care is the ever-changing insurance “in-network” participation by both institutions and physicians. These difficult follow-up protocols may prevent some centers from implementing an organ preservation strategy,<sup>6</sup> thus depriving their patients of an opportunity to make their own choice regarding whether to enroll in protocols that could potentially result in significant quality of life improvement. In comparison, the local failure rate after FTLE for ypT0-ypT1-R0 disease is much lower; therefore, the frequency of follow-ups and the anxiety levels of both patients and physicians can be decreased.

We assume the reason, at least in part, that FTLE was not considered in the guidelines is the perception of the frequent and severe toxicity associated with FTLE performed after NAT. Examples of severe complications include wound dehiscence, severe perineal pain, rectal bleeding, and fistula formation.<sup>7,8</sup> These complications can result in prolonged hospital stays, stool diversion, and premature closure of clinical trials. It should be

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noted that other authors have reported much lower adverse side effects with acceptable toxicity profiles.<sup>9</sup> We recently published our experience with FTLE after neoadjuvant NAT and reported a favorable complication rate.<sup>10</sup> Our approach with FTLE in this clinical scenario is similar to that reported by Stipa et al.<sup>11</sup> We consider FTLE simply as an excisional biopsy to confirm the microscopic absence of potential residual disease. Therefore, there is no need to excise any normal-appearing tissue surrounding the residual mucosal abnormality (RMA). We termed this modified procedure limited full-thickness local excision (LFTLE). Studies of the microscopic residual cancer pattern after NAT have shown that the bulk of residual disease is always detected in the rectal wall directly beneath the RMA.<sup>12</sup> Similarly, data from our center have confirmed that in all cases of ypT-positive disease, malignant cells are always found directly under the RMA. There are no studies that reported the presence of residual microscopic cancer outside the RMA without its presence directly underneath it. Some reports that exhibited high complication rates demanded at least a 1-cm margin around the RMA to ensure complete eradication of any residual disease. In this setting, the FTLE goal should not be the excision of all cancer cells (this can be done later by completion TME); it should only be to determine the ypT status. We believe that excising a margin of normal tissue around the RMA is unnecessary and will not increase the accuracy of the pathological assessment of the presence or absence of residual malignancy and will result in increased postoperative complications.

We believe that organ preservation with LFTLE can be more easily adopted than that with the WW approach by centers that are currently not considering organ preservation protocols.

Clearly, FTLE has its shortcomings. The Table summarizes some of the commonly raised concerns. In the

absence of randomized trials comparing WW to FTLE, we will have to balance the merits and problems of each procedure according to each individual patient's circumstances. Both approaches can be offered to different patients treated in the same center, as is the practice of our group. Patients with very distal tumors—namely, 3 to 4 cm from the anus—are offered the WW strategy to avoid the potential postoperative complications discussed above. Habr-Gama's group<sup>8</sup> proposed a reasonable theory related to the lack of tissue elasticity and different innervation to explain the increased toxicity when FTLE is performed for tumors extending into the anal canal. Patients with higher tumors are offered LFTLE to obtain the certainty of tumor response and the instant prediction of a long-term very high control rate. We believe that tailoring the preservation strategy according to each clinical situation is valuable to our patients.

We urge the members of the Rectal Cancer Practice Guideline Committee and the readership of *Diseases of the Colon and Rectum* to rediscover FTLE/LFTLE.

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**TABLE.** Reported FTLE-associated areas of concern

Areas of concern	Comments
Management of local recurrence	Incidence of local recurrence is very small. More of a theoretical concern, not well demonstrated clinically. Use of LFTLE is expected to mitigate.
Loss of opportunity to perform a sphincter-saving operation after completion TME	The need for completion TME is decreased by selecting only tumors in CCR for FTLE. Limiting FTLE/LFTLE to tumors >3 cm from the anus will ameliorate this concern.
Rectal function may be better after WW than after FTLE	Limiting FTLE to tumors >3 cm from the anus will improve the resulting rectal function. Demonstrated in only a few series.

CCR = complete clinical response; FTLE = full-thickness local excision; LFTLE = limited full-thickness local excision; TME = total mesorectal excision; WW = watch and wait.

- chemoradiation therapy is associated with significant immediate pain and hospital readmission rates. *Dis Colon Rectum*. 2011;54:545–551.
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