

Nonoperative Strategies for Rectal Cancer Following a Complete Clinical Response to Preoperative Chemoradiation: A Few Considerations

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Although the current standard treatment for patients with locally advanced rectal cancer is preoperative chemoradiotherapy followed by total mesorectal excision, concerns have been raised over the functional sequelae and possible overtreatment of rectal cancer patients.

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Current standard treatment for patients with locally advanced rectal cancer is preoperative chemoradiotherapy (CRT) followed by total mesorectal excision. Although this multimodality approach is supported by randomized trials, concerns have been raised over the functional sequelae and possible overtreatment of rectal cancer patients. In this issue of ONCOLOGY, Sabbaga et al review the nonoperative “watch-and-wait” approach for clinical complete responders after CRT and conclude that defining conservative strategies should be one of the most important goals in the management of patients with rectal cancer.[1] Their proposal for nonoperative management of patients with locally advanced rectal cancer experiencing a complete clinical response after CRT is timely and reasonable. However, certain aspects of the discussion require further clarification.

In their introduction, the authors describe the difficulties with evacuation and incontinence that patients with distally located rectal cancer experience following a sphincter-saving resection. Although we agree that surgical removal of the rectum accounts for the majority of the “low anterior resection syndrome” that patients experience following preoperative CRT and resection, we also acknowledge the detrimental effect that preoperative radiotherapy has on long-term anorectal function and quality of life. It is precisely for this reason that a trial of neoadjuvant chemotherapy without routine use of radiotherapy was conducted. The encouraging results from this pilot study[2] have led to a randomized phase III trial using selective preoperative radiotherapy (the PROSPECT trial).

The authors describe the clinical “paradox” of a pathologic complete response (pCR) after CRT, since a pCR can only be definitely confirmed based on pathologic analysis of the resected specimen. The authors point out the lack of data to support utilization of digital rectal examination, endoscopic findings, histopathologic assessment of rectal biopsy, and imaging studies such as magnetic resonance imaging or positron emission tomography (PET) for predicting a pCR. However, in their review of the literature, they do not include several recent, large studies that address this issue in a prospective fashion. For example, in a prospective study of 94 patients, there was only 22% concordance between pathologic assessment of response to preoperative CRT and clinical assessment based on DRE and sigmoidoscopy, both prior to and after CRT.[3] In terms of imaging, in a prospective study of 121 patients, neither PET nor CT had a predictive value adequate to be clinically useful in distinguishing a pCR from an incomplete response.[4] Lastly, Glynne-Jones et al[5] also reviewed 218 phase I/II and 28 phase III trials of preoperative radiotherapy or CRT and concluded that a clinical and/or radiologic response does not correlate with a pathologic response sufficiently to recommend a “wait-and-see” approach for patients who are presumably complete clinical responders following preoperative therapy.

Since the results of randomized trials with long-term, close observation are not available, some investigators caution against wide adaptation of this approach.[6,7] We agree that it is most appropriate for patients to be assessed in the setting of a research protocol designed to carefully and systematically follow them and capture meaningful data on clinical features associated with pathologic response. Outside of a clinical trial, patients who experience a clinical response following preoperative CRT and choose to pursue a watch-and-wait approach may do so if they are made to understand the risk of occult residual mural or mesorectal lymph node disease and physicians’ inability to detect clinical disease in this setting in a timely, curative fashion.

In the section of the article discussing local excision as a surgical option after CRT, the authors write that with the oncologic benefits of neoadjuvant CRT in patients with locally advanced rectal cancer,

several retrospective case series and some prospective studies (Garcia-Aguilar et al[8]; Lezoche et al, 2008[9]; Pucciarelli et al[10]) suggest that CRT before local excision reduces recurrence to a level comparable to TME. Although important, these prospective studies do not support the conclusion of Sabbaga and colleagues that the results of a local excision of a locally advanced rectal cancer treated with neoadjuvant CRT is comparable to a TME resection. The study by Garcia-Aguilar et al (Z6041) is a phase II trial of patients with clinical T2N0 rectal cancer who received preoperative CRT. It was not designed to study locally advanced rectal cancer, nor is it a comparative study. The study by Lezoche et al enrolled 70 patients with T2N0 early cancer, not locally advanced tumor. The study by Pucciarelli et al is a sequential two-stage phase II investigation, not a comparative trial. Overall, the authors should be commended for addressing a very complex, controversial, and evolving topic. We agree with their conclusion that defining strategies that would achieve organ preservation with survival rates comparable to those achieved with standard treatment is one of the most important goals in the care of patients with rectal cancer.

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