

Brief Opinion

Management of Locally Advanced Rectal Cancer During The COVID-19 Pandemic: A Necessary Paradigm Change at Memorial Sloan Kettering Cancer Center



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Abstract

The COVID-19 pandemic will consume significant health care resources. Given the concerns for rapidly increasing infection rates in the United States, impending staffing shortages, and the potential for resource reallocation, we rapidly reevaluated our rectal cancer practice policies during this public health emergency. Before the pandemic, we commonly used total neoadjuvant therapy with a strong preference for long-course chemoradiation. In the setting of the ongoing pandemic, we now mandate short-course radiation therapy (SCRT). Despite multiple randomized trials demonstrating no difference in locoregional recurrence, distant recurrence, or overall survival between SCRT and long-course chemoradiation, the adaptation of SCRT in the United States has been low given concerns for less tumor downstaging and increased toxicity. In the setting of the ongoing and likely prolonged COVID-19 pandemic, we feel that these concerns must be reevaluated, because SCRT presents a well-validated alternative that will allow us to meet the needs of a greater number of potentially curable patients at a time when resources are severely and acutely constrained.

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Perspective

Early reports from China suggest that patients with cancer who are diagnosed with coronavirus disease 2019 (COVID-19) have an increased need for intensive care unit admission and ventilator use and a higher mortality compared with patients without cancer who are not infected.¹ The risk of severe complications was even greater for patients with cancer who underwent surgery or received cytotoxic chemotherapy within 1 month of

documented severe acute respiratory syndrome coronavirus 2 infection.¹ Robust predictors of outcome are still being determined, but patients undergoing active oncologic therapy are likely at an elevated risk for morbidity and mortality from COVID-19.^{1,2}

The pandemic will consume significant health care resources, even with conservative estimates forecasting that COVID-19–related health needs will exceed the capacity of the US health care system and that of other developed countries.³ Given the legitimate concerns for impending staffing shortages, resource reallocation, and rapidly increasing infection rates in the United States, we rapidly reevaluated our rectal cancer practice policies during this public health emergency. Multidisciplinary experts in rectal cancer at our high-volume comprehensive cancer center worked together (electronically, due to the need for social/physical distancing) to establish new institutional guidelines for rectal cancer treatment during the COVID-19 pandemic.

Before March 2020, our standard approach for patients with locally advanced rectal cancer favored total neoadjuvant therapy (TNT), which incorporated preoperative long-course chemoradiation.^{4,5} Chemoradiation was delivered in 25 to 28 fractions using either 3-dimensional conformal radiation therapy (RT) or intensity modulated RT with concurrent capecitabine. The sequencing of chemoradiation and chemotherapy varied depending on the clinical scenario, but induction chemotherapy followed by consolidative chemoradiation was our most common approach.⁴ Given the pandemic conditions, the utility of long-course chemoradiation therapy (LCCRT) was questioned owing to concerns for increased infectivity rates of severe acute respiratory syndrome coronavirus 2 among our patients and staff, increased risk for infectivity with prolonged and frequent visits, and contingent planning if reallocation of institutional resources is required.

The ability of preoperative RT to prevent locoregional recurrence for locally advanced rectal cancer has been well established for both short-course RT (SCRT)⁶⁻⁸ and LCCRT.⁹ SCRT has been shown to be a noninferior alternative to LCCRT,¹⁰ with multiple randomized trials demonstrating no difference in locoregional recurrence, distant recurrence, or overall survival.¹⁰⁻¹² SCRT is delivered in 5 fractions using either 3-dimensional conformal or intensity modulated RT to protect adjacent normal tissue. Importantly, given the higher dose per fraction, no concurrent chemotherapy is used with SCRT. Concerns have been expressed, in the absence of randomized data, that SCRT may result in less tumor downstaging, especially for patients with low rectal tumors (ie, <5 cm from anal verge) and bulky tumors with a close or involved circumferential resection margin, and a higher rate of late toxicity (especially among patients with tumors abutting the anal canal).^{12,13} However, the Stockholm III trial evaluated SCRT with immediate

surgery, SCRT followed by delayed surgery, and LCCRT with delayed surgery and found no difference in locoregional recurrence, distant metastasis, and overall survival. SCRT with delayed surgery compared with SCRT with immediate surgery resulted in greater tumor downstaging and higher acute toxicity, but decreased surgical and postoperative complications.¹⁰ A longer interval from radiation to surgery results in greater tumor downstaging for both SCRT¹⁰ and LCCRT.¹⁴ Furthermore, the incorporation of SCRT into TNT has been evaluated with promising results,¹⁵⁻¹⁹ and although still under active investigation,^{20,21} our colorectal disease management team concluded that delivering TNT with SCRT off-trial is reasonable and necessary given the ongoing COVID-19 pandemic. Admittedly, other potential differences between SCRT and LCCRT have not yet been fully understood (eg, in the context of nonoperative management and long-term anal sphincter function).

In the setting of an ongoing pandemic, SCRT has the potential to provide efficient and quality oncological care for patients; significantly decrease patient exposure with repeated RT appointments for LCCRT; decrease the likelihood of a patient being diagnosed with COVID-19 during treatment; decrease immunosuppression by omitting concurrent chemotherapy; decrease resource utilization in a setting where RT capacity may be sharply curtailed or reallocated; provide at least partial therapy in the event that surgery or chemotherapy need to be delayed; and reinforce federal, state, and city mandates to encourage social and physical distancing while still addressing the active cancer for each patient. After careful consideration of the risks and benefits, we have now mandated that at Memorial Sloan Kettering Cancer Center, all patients with locally advanced rectal cancer are to be treated with SCRT until the current COVID-19 epidemic passes. This mandate benefits patients by reducing the number of exposures to other potentially infected patients and health care workers and lowering the chances that treatment would be interrupted or terminated if they were diagnosed with COVID-19. This mandate is also in the best interest of our patient population as a whole given the decreased utilization of health care resources, allowing 5 patients to be treated instead of 1 patient in a setting where we expect to have substantial reductions in available staff to administer treatment owing to expected staff illness from the epidemic.

Despite being shown to be more cost effective than LCCRT,²² SCRT has been used in <1% of patients receiving neoadjuvant radiation for rectal cancer in the United States due, in part, to strong physician bias regarding diminished downstaging and increased toxicity.^{23,24} In the setting of the ongoing and likely prolonged COVID-19 pandemic, we feel that these concerns must be reevaluated because SCRT presents a well-validated alternative that has been shown in randomized studies to result in noninferior oncologic outcomes. Rectal cancer radiation is unique and presents 2 well-

established and substantially equivalent options for locally advanced disease. Under COVID-19 pandemic conditions, SCRT has important nononcologic benefits that justify making SCRT the standard regimen for locally advanced rectal cancer, such as limiting the potential for patients with rectal cancer to contract COVID-19 and significantly reducing the utilization of health care resources, which allows us to meet the needs of a greater number of potentially curable patients at a time when resources are severely and acutely constrained.

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