The COVID-19 pandemic will consume significant health care resources. Given concerns for rapidly rising infection rates in the US, impending staffing shortages, and potential for resource re-allocation, we rapidly re-evaluated our rectal cancer practice policies during this public health emergency. Previous to the pandemic we commonly utilized total neoadjuvant therapy (TNT) with a strong preference for long course chemoradiation (LCCRT). In the setting of the ongoing pandemic we now mandate short course radiation therapy (SCRT). This mandate allows us to treat 5 patients instead of 1 in a setting in which we expect to have substantial reductions in available staff to administer treatment, due to expected staff illness from the epidemic, and decreases risk for patient infection by limiting frequent unnecessary visits. Despite multiple randomized trials demonstrating no difference in locoregional recurrence, distant recurrence, or overall survival between SCRT and LRCCT, 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 re-evaluated, as 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 our resources are severely and acutely constrained.
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 concerns for rapidly rising infection rates in the US, impending staffing shortages, and potential for resource re-allocation, we rapidly re-evaluated our rectal cancer practice polices during this public health emergency. Previous to the pandemic we commonly utilized total neoadjuvant therapy (TNT) with a strong preference for long course chemoradiation (LCCRT). 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 LRCCT, 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 re-evaluated, as 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 our resources are severely and acutely constrained.

PERSPECTIVE:

Early reports from China suggest that cancer patients diagnosed with coronavirus disease 2019 (COVID-19) have increased need for intensive care unit admission and ventilator use and a higher mortality compared to non-cancer COVID-19 patients\(^1\). The risk of severe complications was even greater for cancer patients who underwent surgery or received cytotoxic chemotherapy within one month of documented severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection\(^1\). Robust predictors of outcome are still being determined, but it seems likely that patients undergoing active oncologic therapy are at an elevated risk for morbidity and mortality from COVID-19\(^1,2\).

The pandemic will consume significant health care resources, with even conservative estimates forecasting that COVID-19-related health needs will greatly exceed the capacity of the United States (US) health care system and that of other developed countries\(^3\). Given legitimate concerns for impending staffing shortages, resource re-allocation, and rapidly rising infection rates in the US, we rapidly re-evaluated our rectal cancer practice polices during this public health emergency. Multidisciplinary rectal cancer experts 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.

Prior to March, 2020, our standard approach for patients with locally advanced rectal cancer favored total neoadjuvant therapy (TNT), which incorporated pre-operative long-course chemoradiation\(^4\). Chemoradiation was delivered in 25-28 fractions using either three-dimensional conformal radiotherapy (3D-CRT) or intensity modulated radiation therapy (IMRT) with concurrent capetabine. The sequencing of chemoradiation and chemotherapy varied depending on clinical scenario, but induction chemotherapy followed by consolidative chemoradiation was our most common approach\(^4\). Given pandemic conditions, the utility of long-course chemoradiation (LCCRT) was questioned given (1) concerns for increased infectivity rates of SARS-CoV-2 among our patients and staff, (2) increased risk for infectivity with prolonged and frequent visits, and (3) contingent planning if reallocation of institutional resources is required.

The ability of pre-operative radiation therapy to prevent locoregional recurrence for locally advanced rectal cancer has been well-established for both short-course radiation therapy (SCRT)\(^6,8\) and LCCRT\(^8\). SCRT has been shown to be a non-inferior 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 3D-CRT or IMRT.
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 (i.e. <5cm 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. 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 as compared to SCRT with immediate surgery resulted in greater tumor downstaging and higher acute toxicity, but decreased surgical and post-operative complications. A longer interval from radiation to surgery results in greater tumor downstaging for both SCRT and LCCRT. Furthermore, incorporation of SCRT into TNT has been evaluated with promising results and while it is still under active investigation, our colorectal disease management team concluded it is reasonable and necessary to deliver TNT with SCRT off-trial given the ongoing COVID-19 pandemic. Admittedly, other potential differences between SCRT and LCCRT have not yet been fully understood, for example in the context of non-operative management and long-term anal sphincter function.

In the setting of an ongoing pandemic, SCRT has the potential to (1) provide efficient and quality oncological care for patients, (2) significantly decrease patient exposure with repeated radiation therapy appointments for LCCRT, (3) decrease the likelihood of a patient being diagnosed with COVID-19 during treatment, (4) decrease immunosuppression by omitting concurrent chemotherapy, (5) decrease resource utilization in a setting where radiotherapy capacity may be sharply curtailed and/or reallocated, (6) provide at least partial therapy in the event that surgery and/or chemotherapy need to be delayed, and (7) 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 HOSPITAL, patients with locally advanced rectal cancer be treated with SCRT. This mandate benefits patients by reducing the number of exposures to other potentially infected patients and health care workers and lowering the chances that their 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 decreased utilization of healthcare resources, allowing us to treat 5 patients instead of 1 in a setting in which we expect to have substantial reductions in available staff to administer treatment, due to expected staff illness from the epidemic.

Despite being shown to be more cost effective than LCCRT, SCRT has been used in less than 1% of patients getting neoadjuvant radiation for rectal cancer in the US, due in part to strong physician biases regarding diminished downstaging and increased toxicity. In the setting of the ongoing and likely prolonged COVID-19 pandemic, we feel that these concerns must be re-evaluated, as SCRT presents a well-validated alternative that has been shown in randomized studies to result in non-inferior oncological outcomes. Rectal cancer radiation is unique in presenting two well-established and substantially equivalent options for locally advanced disease. Under COVID-19 pandemic conditions, SCRT has important non-oncolgic benefits that justify making it the standard regimen for locally advanced rectal cancer, namely limiting the potential for rectal cancer patients to contract COVID-19, and significantly reducing utilization of healthcare resources, thereby allowing us to meet the needs of a greater number of potentially curable patients, at a time when our resources are severely and acutely constrained.

REFERENCES:


