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Brief Opinion

Palliative Radiation Therapy for Oncologic Emergencies in the Setting of COVID-19: Approaches to Balancing Risks and Benefits

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Abstract

Palliation of metastatic disease compromises a significant portion of radiation treatments in the United States. These patients present a unique challenge in resource-limited settings, as expeditious treatment is often required to prevent serious morbidity. In order to reduce the risk of infection with severe acute respiratory syndrome coronavirus-2 and maximize the benefit to patients, we present evidence-based recommendations for radiation in patients with oncologic emergencies. Radiation oncologists with expertise in the treatment of metastatic disease at a high-volume comprehensive cancer center reviewed the available evidence and recommended best practices for the treatment of common oncologic emergencies, with attention to balancing the risk of infection with severe acute respiratory syndrome coronavirus-2 and the potential morbidity of delaying treatment. Many prospective trials and national guidelines support the use of abbreviated courses of radiotherapy for patients with oncologic emergencies. As such, in the setting of the current coronavirus disease 2019 pandemic, the use of hypofractionated radiation therapy for patients requiring palliation for oncologic emergencies achieves desirable functional outcomes without compromising care.

Introduction

Radiation therapy (RT) is critical for the treatment of oncologic emergencies, including neurologic injury from cord compression or brain metastases, airway compromise, and bleeding.[1-4] Palliative RT for patients with limited functional status is crucial for providing effective care and limiting morbidity from disease progression. The current coronavirus disease 2019 (COVID-19) pandemic has heightened our awareness of resource constraints, prompting institutions to create guidelines to delay treatments whenever possible and prioritize cases that are clinically urgent.[5-8]

Recent data from China and Italy have demonstrated that cancer patients have a higher risk of contracting the virus and a higher case-fatality rate.[9-12] It is therefore imperative to be judicious in the use of RT and to consider shorter courses of palliative RT for oncologic

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emergencies. Existing recommendations, such as those from the Choosing Wisely campaign, support the use of short-course RT as a component of value-based care.[13] However, its use in the United States has been limited, and therefore cancer centers are less equipped to optimally manage patients considered for palliative radiation.[8,14,15] Here, we aim to provide a more detailed departmental approach to triaging and shortening RT for oncologic emergencies at a major comprehensive cancer center in New York City, an epicenter of COVID-19 in the United States.

Methods and Materials

Radiation oncologists with expertise in the management of metastatic disease and inpatient oncologic emergencies at a high-volume comprehensive cancer center in the epicenter of the current COVID-19 outbreak convened to discuss best practices for this time. We reviewed high-impact evidence, prior systematic reviews, and national guidelines to compile recommended practices for the treatment of common oncologic emergencies. Although this was not a comprehensive systematic review of the literature, we discussed our individual institutional best practices in the unique circumstances of this global pandemic. Specific attention was given to balancing the risk of infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and the potential morbidity of delaying treatment.

Suggested considerations

Clinical evaluation

In response to departmental guidance to limit clinical exposure and maximize single-use personal protective equipment, the majority of patient assessments, including history of present illness, performance status, current symptoms, and imaging are being evaluated virtually via telemedicine. Prior studies have shown the feasibility and efficacy of assessing symptoms and performance status through electronic and telemedicine platforms.[16-18] When in-person physical examination is crucial to treatment decision-making, including neurologic evaluation and pain assessments, patient encounters are limited to a single radiation oncologist or an advanced practice provider.

We recommend discussion of the patient's overall prognosis and goals of care with the patient, the primary medical oncologist, and supportive care specialists before determining a radiation plan that uses the provider's preferred validated prognostic models.[19-21] For patients with an estimated life expectancy of days to weeks, best supportive care with medical therapies alone is encouraged.

For subsequent on-treatment visits and follow-ups, our institution has implemented telemedicine visits as default to reduce the risk of exposure. For patients needing urgent supportive care while receiving RT, a nursing visit or physician visit can be arranged with the designated rotating radiation oncology health care providers of the day. When face-to-face evaluation is clinically indicated, we recommend that all patients, caregivers, and providers adhere to institutional policies and Centers for Disease Control recommendations on social distancing, handwashing, assessment of personal risk factors, and use of appropriate personal protective equipment to mitigate risk of exposure of patients and staff.[22]

Patient triage

In the setting of the COVID-19 pandemic, our department developed and implemented a 3-tiered system to identify clinically urgent cases in which delaying treatment would result in compromised outcomes or serious morbidity. For patients with metastatic cancer requiring palliative RT, patients with oncologic emergencies are assigned with the tier 1 designation (Table 1). This includes patients with cord compression, symptomatic brain metastases requiring whole brain RT, life-threatening tumor bleeding, and malignant airway obstruction (Table 2). Tier 2 includes patients with symptomatic disease, exclusionary of oncologic emergencies for which RT is the standard of care, and patients with asymptomatic disease for which RT is recommended to prevent impending functional deficits. Tier 3 includes patients with symptomatic or asymptomatic disease for which RT is one of the effective treatment options.

Need for urgent RT is guided by a simple triage flowsheet that includes active symptoms that can be addressed with RT, prognosis, goals of care, and tier 1 designation (Fig 1). The following management recommendations pertain to patients with oncologic emergencies, which are departmentally categorized with tier 1 designation.

Table 1 Assignment of radiation tiers based on treatment indication

Tier 1 (highest priority)	Patients with oncologic emergencies (neurologic compromise, tumor bleeding, airway compromise, etc) requiring palliative RT
Tier 2	Patients with symptomatic disease exclusionary of oncologic emergencies for which RT is the standard of care Patients with asymptomatic disease for which RT is recommended to prevent impending functional deficit
Tier 3 (lowest priority)	Patients with symptomatic or asymptomatic disease for which RT is one of the effective treatment options

Abbreviation: RT = Radiation therapy.

Table 2 Hypofractionated palliative regimens

Indication	Treatment	References
Brain metastases requiring whole brain RT	4 Gy × 5 daily fractions steroids alone	Rades et al[24]: 20 Gy/5 fx well tolerated QUARTZ[26]: Steroids alone for patients with poor performance status
Cord compression	8 Gy × 1 daily fraction	Maranzano et al, SCORAD III, ICORG 05-03[30-33]: Similar effect on OS and post-RT motor functions. Retreatment is safe.
Tumor bleeding	3.7 Gy × 4 twice daily fractions 4 Gy × 5 daily fractions	RTOG 8502, RTOG 7905[34,35,43]: "Quad Shot" is safe and effective. Avoid bid fractionation for COVID + patients.
SVC syndrome airway obstruction	8.5 Gy × 2 weekly fractions 4 Gy × 5 daily fractions	Sundstrom et al[36,37]: Equivalent symptom relief and no difference in survival compared with standard fractionation Exercise caution with COVID + patients
Bone metastases	8 Gy × 1 daily fraction	RTOG 9714[13,38-40]: 8 Gy × 1 similar efficacy in pain relief with less acute toxicity. Retreatment is safe.

Abbreviations: COVID = coronavirus disease; ICORG = Cancer Trials Ireland (formerly All Ireland Cooperative Oncology Research Group); OS = overall survival; RT = radiation therapy; QUARTZ = Quality of Life after Treatment for Brain Metastases; RTOG = Radiation Therapy Oncology Group; SCORAD = Single-fraction Radiotherapy Compared to Multifraction Radiotherapy; SVC = superior vena cava.

Management of oncologic emergencies

Brain metastases

The management of brain metastases has been an evolving clinical paradigm for which patient prognosis, histology, age, competing risks, and neurologic symptoms must be considered. For patients with favorable prognosis and for whom stereotactic radiosurgery is appropriate, we continue to provide stereotactic radiosurgery for patients and treat all or the dominant lesion(s) that are most likely to cause morbidity to delay or potentially avoid whole brain radiation. However, for patients with urgent indications, such as progressive neurologic symptoms from multiple brain metastases or leptomeningeal disease, whole brain radiation is often indicated. For these patients, particularly those who are hospitalized, 10-fraction treatment increases the risks for patients and staff exposure to SARS-COV-2. Thus, although several dose options are available, we favor 20 Gy in 5 fractions, which has been safely used in multiple studies.[23,24] Standard fractionation (30 Gy in 10 fractions) with memantine could be considered for patients in whom longer term survival is expected in order to limit neurocognitive complications.[25] For patients with limited prognosis, the Quality of Life after Treatment for Brain Metastases study demonstrated similar rates of overall survival and quality of life with steroids and best supportive care alone compared with whole-brain RT,[26] and therefore observation is likely preferred to limit unnecessary exposure to SARS-COV-2.

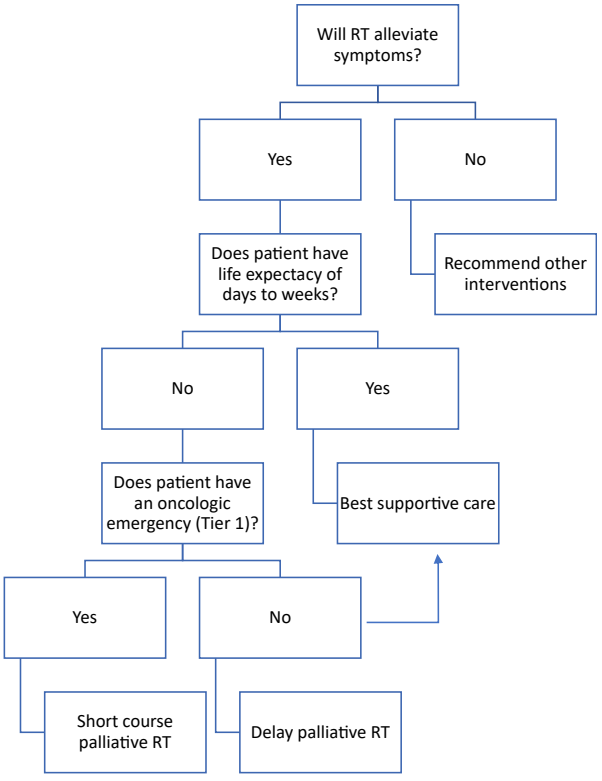

Figure 1 Triaging a patient with an oncologic emergency.

Spinal cord compression

The management of patients with spinal cord compression requires multidisciplinary discussion especially with neurosurgery, and evaluation of several factors including degree of spinal cord compression and presence or absence of spinal instability. We used the Neurologic, Oncologic, Mechanical, and Systemic paradigm to facilitate selection of optimal treatment.[27] If radiation is indicated, over 30 studies have shown equivalent functional outcomes of single-fraction radiation treatment instead of multifraction radiation treatment,[4,28] with

recent meta-analysis of 3 randomized clinical trials demonstrating preserved motor response with no clinical difference between single-fraction radiation treatment (8 Gy × 1 fraction) and multifraction treatment at a 2-month timepoint.[29-33] However, there is conflicting evidence regarding the role of single-fraction RT for spinal cord compression, particularly given that the Single-fraction Radiotherapy Compared to Multifraction Radiotherapy III study did not meet its prespecified noninferiority endpoints, although the absolute difference of ambulatory status at 8 weeks was small (69.3% in the single-fraction group vs 72.7% in the multifraction group).[33] Nevertheless, 8 Gy × 1 provides acceptable rates of palliation and allows for safe retreatment with either conventionally fractionated or stereotactic body radiation therapy approaches if warranted. In the setting of the COVID-19 pandemic, the risk for nosocomial infection from patient daily exposure and prolonged hospitalizations and the potential exposure to staff and other patients must be balanced against the potential benefit of multifractionated treatment.

Tumor bleeding

Uncontrolled tumor bleeding is a life-threatening condition that can be effectively relieved with palliative radiation. Radiation Therapy Oncology Group 8502 used 10 Gy × 1 to palliate advanced pelvic malignancies, but due to frequent late gastrointestinal toxicities (grade 3-4 late toxicities in 49% of patients), it was closed prematurely and replaced with 3.7 Gy × 4 fractions twice daily, repeated at 3-week intervals for a total of 3 courses.[34] This "Quad Shot" regimen has also been effective in head and neck malignancies.[35] Owing to potential increased risk of nosocomial SARS-COV2 exposure, our center has recommended limiting treatment of patients with COVID-confirmed or suspicious cases to a single treatment machine at the end of the day to facilitate disinfection and risk reduction procedures. As such, it may be logistically preferable to avoid twice-daily treatments and instead favor 4 Gy × 5 as an alternative.

Superior vena cava syndrome/airway obstruction

Superior vena cava syndrome can present with clinically severe airway and neurologic or hemodynamic compromise. Radiation can be effective in relieving hemoptysis but has limited utility for relieving dyspnea and cough. Sundstrøm et al[36,37] reported excellent outcomes with 8.5 Gy × 2 fractions given a week apart for patients with central airway emergencies, although our institutional practice favors 4 Gy × 5 daily fractions. Although 8.5 Gy × 2 1 week apart may offer logistical advantages, particularly for inpatients who may be discharged after the first fraction, we felt that this must be balanced with concerns for spinal cord toxicity, especially in patients with prior radiation treatments and those who may need future treatments.

For patients with airway obstruction from a lung or mediastinal tumor, there are no data at this time on the effect of RT exposure to lung in patients with SARS-COV-2 infection. Given the danger of acute respiratory distress syndrome, the possible need for mechanical ventilation, and the potential for structural and obstructive lung disease, a multidisciplinary discussion is recommended for patients requiring RT palliation for malignant airway obstruction.

Painful bone metastases

Although not an oncologic emergency, patients with painful bone metastases frequently require radiation oncology consultation for symptom management. Per National Comprehensive Cancer Network guidelines for supportive care, many medical strategies can also be considered for the management of bone metastases.[38] If patients have an impending fracture, we recommend a multidisciplinary discussion with orthopedic surgery or interventional radiology to decide on mechanical stabilization and a potential role for RT. The risk of prolonged hospitalization from pathologic fracture may expose the patient to potential hospital-acquired infections including SARS-COV-2, and thus planned surgical intervention should be considered for patients with impending fracture. Otherwise, radiation should be considered if it is anticipated that localized pain from a metastasis would result in potential admission for pain crisis. If radiation is indicated, several studies and the Choosing Wisely campaign support 8 Gy × 1 fraction treatment for uncomplicated bone metastases.[13,39,40] Additionally, for patients with less urgent symptoms who are able to wait for complex treatment planning, single-fraction stereotactic body RT may also be an appropriate way to provide faster and more durable palliation still in a single treatment session, based on randomized evidence.[41]

Conclusions

Palliative RT plays a critical role in the prevention of serious morbidity for patients with metastatic cancer in the setting of oncologic emergencies, even in the midst of the current COVID-19 pandemic. For patients with metastatic cancer, prognosis must first be clearly estimated and communicated with the patient, followed by a goals-of-care conversation. Data from China suggest that 40% of patients with active cancer diagnoses required either intubation or died, although the authors report that they are only presenting a small sample size and acknowledge the presence of other comorbidities such as age and smoking history.[9] Patients who have prognostic awareness are less likely to choose and therefore receive aggressive oncologic treatments in the last month of life.[42] As such, these patients may opt for medical

supportive care. For patients suitable and requiring palliative RT, an abbreviated course of treatment is of particular importance to reduce the risk of viral exposure to all patients and staff, without compromising functional outcomes. Furthermore, as staffing and clinical treatment capacity remain at risk for fluctuation, abbreviated RT courses better allow for treatment completion without delay. Fortunately, there is high-level evidence supporting these courses for oncologic emergencies to maximize patient benefit and resource allocation. As such, hypofractionated regimens for palliative radiation are preferred to reduce risk and maximize benefit for both individuals and the population during the COVID-19 pandemic.

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