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Follow-up and management of head and neck cancer patients during the 2019 novel coronavirus (SARS-CoV-2) disease pandemic --Manuscript Draft--

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Follow-up and management of head and neck cancer patients during the 2019 novel coronavirus (SARS-CoV-2) disease pandemic

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ABSTRACT

The SARS-CoV-2 pandemic has significantly impacted healthcare delivery around the world. Elective procedures and routine follow-ups have been cancelled and/or converted to tele-health visits by many systems. In this article, we focus on recommendations for the surveillance of head and neck cancer patients during and following radiotherapy treatment. We synthesized information from clinical evidence, existing recommendations from the NCCN, and variations in practice between multiple academic tertiary cancer centers to develop the proposed guidance.

INTRODUCTION

The COVID-19 pandemic which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has upended normal life around the world. Cancer patients constitute a particularly vulnerable population during this outbreak due to their potentially compromised immune system and the frequency of their healthcare visits. Significant risk factors for death in patients with SARS-CoV-2 infection include older age (>60) and those with other serious ailments including chronic respiratory disease and cancer¹. The United States Centers for Disease Control and Prevention (CDC) estimates a 3-11% fatality for persons aged 65-84 years and 10-27% for persons aged ≥ 85 years². Several groups have shared their approach to managing cancer patients during this global outbreak^{3,4}. These recommendations focus on the management of patients currently undergoing cancer therapy. Filippi and colleagues, reporting on their experience in Italy, recommend that follow-up visits be postponed³.

Based on the experiences in outbreak epicenters (Wuhan city in China and the Lombardy region in Northern Italy), and outbreak projections, it is likely that social distancing restrictions will be in place for several months. Many hospitals are cancelling all non-urgent clinic visits, operations, procedures, and imaging studies for patients with cancer. Physicians are being asked to prioritize their schedules and determine who can be safely postponed, converted to a telehealth visit, and who requires in-person follow-up in addition to being encouraged to consider hypofractionated regimens, single fraction palliative treatments, and approaches to minimize the required visits while still providing appropriate treatments⁵⁻¹⁰. Such recommendations require a disease-specific approach, since the risk and trajectories for tumor recurrences differ between the cancer types. An explicit example would be the follow-up for prostate versus head and neck cancer (HNC) patients.

HNC patients have several unique considerations compared to other cancer sites. First, some centers are seeing an increase in radiation therapy volume for HNC patients due to the shuttering of operating rooms for both elective, and in some cases, curative HNC operations deemed urgent/level 3a by the Centers for Medicare and Medicaid Services¹¹. Second, in-person management of acute toxicities must now be done via telemedicine where possible and is a challenge if patients require intensive symptom control, adjustment of maxillary/oral prostheses, and speech language pathology assessments, to name a few. Additionally, the standard H&N physical exam, including mirror exam and nasopharyngolaryngoscopy (NPL), is an aerosolizing procedure and must be reserved for only those cases in which the information to be gained is essential to the care of the patient. There are many other HNC-specific management challenges discussed below.

Here, we sought to share our approach to these issues in head and neck cancer patients to provide insight into some approaches to prioritization during this and future epidemics.

PROPOSED APPROACH

During treatment

Conventional radiotherapy regimens for adjuvant or curative treatment of head and neck cancer extend for 6 to 7 weeks. On-treatment visits (OTVs) are a critical component in the management of the acute toxicities of radiation therapy treatment. Mucositis, odynophagia, and dermatitis are common consequences of radiation and can be severe, requiring close

surveillance and supportive care. OTVs occur weekly and often occur in conjunction with in-person visits with a nurse, a dietician, and a speech/language therapist. Patients with HNC often have or develop a cough or sore throat during treatment which trigger screening protocols for COVID-19. Given recent changes in recommendations for mask use in the US it is reasonable for all HNC patients to wear a mask when in public ¹².

Several opportunities to minimize face-to-face contact exist. Especially during the first few weeks of treatment, patients can be managed via phone visits either in the department or out of the department. As some cancer centers restrict entrance to the patient only, phone visits conducted when the patient is at home, allow for participation of family members and minimize hospital-based exposure; video-calls enable a limited exam as well to assess dermatitis and mucositis. Phone visits may need to be supplemented by an in-person assessment by a clinician in the clinic to perform a focused exam or provide medications. It is important, where possible, to have an on-site clinician: whether a nurse, physician, or advanced practice provider to address any urgent patient concerns when they present to the radiation therapy department. Any provider with close patient contact should use proper PPE (the definition of this is rapidly changing as incidence of SARS-CoV-2 infection and availability of PPE evolves). Using a phone or dedicated telehealth visit, health care providers can offer medical advice relating to oral hygiene, nutrition, and speech/swallow rehabilitation. The on-site therapist or nursing staff can supplement these visits and provide daily feedback to the physician about changes in the patient's symptoms. If need be, verbal orders for step 1 analgesia (i.e. non-opioid analgesics) and oral and skin care can be given by the physician to the patient or via the front-line staff in the clinic on that day such as therapist/nurse/on-site physician as an intermediary over the phone. Later in the treatment course (week 4 onwards), with the expected incremental toxicities to radiotherapy, the consultations with the physicians can be converted to face-to-face visits, while dietician can be safely and easily maintained as telehealth visits. Speech and language pathology visits can be maintained over the phone but face the challenge of being unable to visually assess the patient such as the cough response to swallowing various consistencies.

During the face-to-face consults, appropriate protective measures must be in place to avoid patient-to-health care worker (HCW) transmission ^{13,14}. In this instance, the level of protective measures will depend on whether the patient is suspected of being infected by SARS-CoV-2 and if invasive procedures (NPL, brachytherapy, biopsy, etc.) have to be performed ¹⁵. These scenarios would be considered high-risk for SARS-CoV-2 transmission, and the HCW consulting the patient would require full personal protection equipment (PPE) consisting of N95 mask, surgical gowns, gloves, and goggles/face shields ¹⁶. The ability to perform such aerosolizing procedures will be influenced by the availability of PPE which is currently in short supply in many centers. A shortage of appropriate PPE may lead to an over-reliance on imaging, or require referral to a site with a negative pressure room and available PPE.

Post-treatment Follow-up

Following the completion of treatment any patient with direct contact with a SARS-CoV-2 infected individual or who has personally tested positive or has symptoms of COVID-19 should not be seen in an oncology clinic for a follow-up visit. The management of these patients is a

rapidly evolving area and physicians should refer to local guidelines regarding testing and return to routine care in the absence of cancer-related symptoms. The following recommendations will need to be weighed against the local prevalence of SARS-CoV-2 infection and patient risk factors for severe morbidity and/or mortality associated with infection;

Within 1 month of treatment completion

The majority of patient visits during this time can be managed at home. Depending on the treatment intensity, some head and neck cancer patients will require close surveillance in the immediate period after radiotherapy. While not all clinics routinely schedule follow-up visits in the 3-6 weeks following completion of treatment, these visits should be carefully considered. Patients treated with concurrent chemoradiotherapy will likely require close monitoring for wound recovery secondary to severe dermatitis, hydration status due to poor intake from severe mucositis, and pain control. Intravenous hydration will require in-person interaction with the health care team. However, for many patients and particularly for the subset of patients who are treated with radiotherapy alone in the adjuvant setting (e.g. salivary cancers), or with a short course radiotherapy to a small target volume (e.g. T1N0 glottis cancer) telehealth visits are preferred to minimize risk to the patient and the health care team. Based on telehealth visits, patients can be recalled for in-person visits based on medical necessity. Where possible, video capability is helpful to visually assess the patient.

8-12 weeks after completion of treatment

For patients treated with definitive radiotherapy or chemoradiotherapy or those undergoing re-irradiation, this is a typical time-frame for post-treatment imaging studies to evaluate the adequacy of tumor response to treatment, and determine whether post-treatment neck dissection or surgical salvage is required^{17,18}. Given the importance of the data obtained at this time-point, it is our opinion that effort should be made to complete post-treatment imaging that has the potential to influence treatment decision making. Any delay in imaging beyond standard 12 week post-treatment timing, should be limited. It is possible that the imaging studies will provide sufficient information to forgo a physical exam, like in the instance of a definitive complete response. When it is challenging to distinguish between post-treatment edema and residual tumor on imaging, a detailed physical exam including endoscopy may be required, and as aforementioned, full PPE is required to protect the HCW from transmission of SARS-CoV-2 through aerosolization during NPL. This exam should not be undertaken lightly during the SARS-CoV2 outbreak. If an endoscopic exam is required, we recommend that this is coordinated with the relevant clinician who may be involved in the patient's next phase of care to minimize the number of times the procedure is performed. For example, if post-radiation surgery may be required, the endoscopic exam should be coordinated with the head and neck surgeon.

For patients treated with adjuvant radiation/chemoradiation, the importance of this visit is less well-defined, since there is limited guidance on the value of imaging in the adjuvant setting. Data from multiple randomized studies indicates that about half of patients who recur after receiving adjuvant radiation do so in the first 6-12 months¹⁹⁻²². In these patients, it is reasonable to delay an in-person visit until the pandemic in the local environment has subsided. This decision should be individualized to each patient's risk and symptoms. However, in the

high-risk subgroup of patients who had a positive resection margin or features of extracapsular extension on surgical pathology there should be a very low threshold for an in-person visit in patients who report symptoms during a telehealth follow-up.

Follow-up from 3-24 months

A comprehensive physical exam, and to a lesser extent imaging, is a critical part of standard follow-up for head and neck cancer patients. However, given the risk of NPL, we propose that it may be reasonable to alternate surveillance methods between physical examination and imaging during an outbreak. NCCN guidelines recommend follow-up every 1-3 months in year 1 and every 2-6 months in year two (7). Many centers alternate these visits between radiation oncology and otolaryngology. In the short term, it is reasonable to convert in-person evaluations to tele-health visits. The presence of any symptoms that are concerning for recurrence should warrant urgent in-person evaluation. During the first year, patients should be seen face-to-face no less than every 6 months, and at the earliest indication of pandemic disease control in the community, all patients should return to regular follow-up intervals.

Follow-up years 2-5

The majority of recurrences in head and neck cancer patients occur within the first two years. Postponing visits in years 2-5 post-treatment is reasonable - if the next follow-up is scheduled within 8 months of a previous in-person visit, it is reasonable to see the patient at this time. If more than 8 months will elapse between visits, we would recommend scheduling a follow-up at the next available time.

Table 1. Evaluation and follow-up of head and neck cancer patients and alternative approaches to in-person visits. Medical acuity during treatment refers to management of side effects. Medical acuity post-treatment refers to both side effect management and cancer control monitoring.		
Timepoint	Medical acuity 0 - very low 5 - very high	Alternatives to in-person
During treatment	3-5	Telehealth, especially during the first several treatment weeks may be appropriate. Because patients are available daily, a low threshold to convert to an in-person visit is recommended.
0-1 month	0-2	Telehealth check-in to assess nutrition and recovery from therapy
2-3 month	Definitive - 4-5 Adjuvant - 1-2	Imaging only for appropriate patients, clinical correlation requires in-person visit,

		reschedule in-person for next reasonable timeframe
4-24 months	3	Alternate imaging and physical exam, reschedule in-person for next reasonable timeframe
25-60 months	0-1	Telehealth and reschedule in-person for next reasonable timeframe
>60 months	0	Telehealth, reschedule in-person for next reasonable timeframe

Endoscopy and mirror exams

Fiberoptic endoscopy (i.e. NPL) plays a key role in the evaluation of head and neck cancer patients. Due to the respiratory tropism of the SARS-CoV-2 virus, these exams likely involve a higher risk of transmission than do most physical exams. Many hospitals are now requiring all patients undergoing aerosolizing procedures (often defined as intubation or bronchoscopy) to test negative for SARS-CoV-2 infection prior to the procedure. We are currently unaware of any clear recommendations regarding this issue for HNC patients but this is a clearly rapidly evolving area and it is our opinion that this should be strongly considered. It is important for head and neck oncologists to use appropriate PPE during these exams including appropriately sized N95 respirators, face shields, gloves, and gowns. Any equipment covered in sputum expectorated during the exam of patients should be sterilized or disposed of appropriately. Until additional guidelines are developed, fiber optic equipment should be sterilized according to institutional best practices. Due to the persistence of viral particles in the air after aerosolizing procedures, six full air exchanges on a closed-door room are recommended before unmasked individuals should be allowed back within ²³. Providers are encouraged to discuss airflow measurements of individual rooms with their institution’s environmental services to determine best practices for room decontamination.

We are not aware of any formal guidelines regarding PPE for mirror exams. However, due to the risk of mirror exam induced cough, it is our opinion that these exams should follow similar protection practices to fiberoptic exams. Appropriate PPE should be worn and exams should be deferred at the discretion of the treating physician.

DISCUSSION and CONCLUSION

The rapid rate of human-to-human transmission of SARS-CoV-2 is unprecedented, and consequently, healthcare systems globally are now facing the need to manage patients with mild to severe SARS-CoV-2 symptoms. To curb the pace of this outbreak, measures ranging from tight infection control procedures in the hospital, to social distancing in the community are being implemented. However, the surge of SARS-CoV-2 cases had also inadvertently affected the delivery of other critical healthcare services, with varying implications across the different medical disciplines. For patients with cancer, a delay in diagnostic and staging work-up, and

treatment will have a detrimental impact on survival. Herein, we focused on the impact of this pandemic on the management of head and neck cancer patients who are undergoing or have completed radiation treatment. Guidelines on treatment aspects of surgery and radiotherapy have been covered by others⁵⁻¹⁰. Thus, we focused on the surveillance of patients whilst they are undergoing treatment, and at the different time-points following treatment. Different sets of considerations take precedence for the respective phases; toxicity symptom management and supportive care are more important issues during the early time-points, while early and prompt detection of residual or recurrent disease is crucial in the later time-points. We synthesized the information borne from clinical evidence and existing recommendations from NCCN, taking into account the variations in practice between multiple academic tertiary cancer centers, and proposed some guidance on improvisations to practice. The fundamental rationale underpinning our proposed approach is simple - to reduce the number of hospital visits for head and neck cancer patients, thereby mitigating the risk of patient-to-patient and patient-to-HCW virus transmission in this vulnerable group of patients, who are also at risk of more severe illness¹. While it is plausible that the acute phase of this pandemic could dissipate in the next 3-4 months, as of early April 2020, the path forward remains quite foggy. Fauci et al. recently presented 4 pillars to end an epidemic that includes diagnosing all individuals with the disease as early as possible post infection, treating rapidly and effectively to achieve sustained viral suppression, preventing new at-risk individuals from acquiring the infection, and rapidly detecting and responding to emerging clusters of an infection to further reduce new transmissions²⁴. Current data also suggests the possibility of recurrent new waves of human-to-human SARS-CoV-2 transmission within communities, and thus it is difficult to accurately predict the end of this pandemic. Hence, we believe that it is prudent to formulate a set of guidelines that are safe and sensible to integrate into our clinical practice longer term in the face of a prolonged COVID-19 pandemic or future outbreaks of novel diseases.

As the global community struggles to contain this pandemic, continuous efforts are needed to understand the ever-changing clinical course of this disease, as the virus evolves with each subsequent outbreak cluster. Nonetheless, the oncology community ought to take this opportunity to rethink the necessity for some existing processes and review potential ways of leveraging technological innovation to streamline management of patients in the clinic. These new measures are likely to persist in the aftermath of this infectious disease crisis.

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