

Head and neck cancer: high-risk population for COVID-19

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Dear Dr. Hanna,
Since first identified in December of 2019, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has disseminated from Wuhan, China rapidly across the globe. On March 11, 2020, the World Health Organization deemed Coronavirus Disease 2019 (COVID-19) a worldwide pandemic, sending the global community into a state of emergency.¹ As of April 10, 2020, 1.6 million COVID-19 cases have been reported worldwide.² Case-fatality rate have ranged from 2% to 7%.³ Clinically, COVID-19 is initially characterized by a constellation of nonspecific symptoms such as cough, fever, and dyspnea. However, this can escalate quickly, with the median time from symptom onset to severe hypoxemia, necessitating ICU admission, seen to be from 7 to 12 days.⁴⁻⁶ It is clear certain populations such as patients with coexisting conditions, older age, an immunocompromised state, and a smoking history are at a high risk for severe disease as well as poor outcomes.⁷ Head and neck cancer patients are placed in a vulnerable state and may equally be of high-risk to the consequences of COVID-19, given their immunosuppressed state from cancer and corresponding treatment as well as high prevalence of the aforementioned risk factors. In this correspondence, we aim to discuss sequelae of severe COVID-19 disease, in addition to describing head and neck cancer patients as a high-risk population.

The majority of COVID-19 cases are of mild severity; however, 5% to 8%^{5,8} of COVID-19 patients may become critically ill, and experience respiratory failure, septic shock, and/or multi-organ failure. This necessitates admission into the intensive care unit (ICU). Two-thirds of these critically ill patients have met criteria for acute respiratory distress syndrome (ARDS) and require advanced respiratory support. The acute severity and rapid progression of COVID-19 is illustrated with over 63% patients requiring invasive mechanical ventilation in the first 24 hours of

admission into the ICU.⁹ Mortality of COVID-19 patients in the ICU has been estimated to be 50%.^{7,10} Of these, patients of age > 70 years old and with severe comorbidities were seen to have mortality rates of 68% and 59%, respectively.⁹ As defined by the Center for Disease Control's weekly morbidity and mortality report regarding COVID-19, these comorbidities may include diabetes mellitus, chronic lung disease, cardiovascular disease, chronic renal disease, and other chronic disease, of which a history of cancer falls under.¹¹

ARDS secondary to COVID-19 requires a longer time on mechanical ventilation than is usually required. Bhatraju et al⁷ reports a median of 10 days of time on mechanical ventilation before COVID-19 patients were extubated. This is in comparison to the 3 to 8 days seen on average for non-COVID related indications for mechanical ventilation.¹² Even then, most patients are unable to wean off mechanical ventilation, as seen by a tragically high mortality rate of COVID-19 patients on mechanical ventilation (Table 1). The Intensive Care National Audit & Research Centre (ICNARC) demonstrated a 67.3% mortality rate of patients receiving advanced (ie, noninvasive or invasive ventilation, tracheostomy or extracorporeal respiratory support) respiratory support.⁹ Studies from China examining critically ill COVID-19 patients placed on mechanical ventilation have reported mortality rates of 81% to 97%.^{4,5} A Seattle-based analysis of critically ill patients on mechanical ventilation saw a comparatively lower mortality rate of 50%, however, at the time of this study three were still on mechanical ventilation without recovery from COVID-19.⁷ These extraordinary high mortality rates of patients on mechanical ventilation, ranging from 50% to 97%, may reveal that full intensive care support and life-sustaining therapies still cannot overcome the poor prognosis of certain high-risk populations afflicted by

TABLE 1 Case fatality rate of patients on mechanical ventilation

Study	Country	Case fatality
Zhou	Wuhan, China	31/32 (97%)
Yang	Wuhan, China	19/22 (86%)
Bhatraju ^a	Seattle, Washington, United States	12/24 (50%)
ICNARC Report ^b	United Kingdom	261/388 (67.3%)

^aThree patients still receiving mechanical ventilation and disease course pending.

^bReports case fatality of patients on advanced respiratory support (noninvasive, invasive mechanical ventilation, ECMO).

COVID-19. Deterioration despite mechanical ventilation may be confounded by multi-organ system failure. Those who fail mechanical ventilation may be placed on extracorporeal membrane oxygen (ECMO) therapy as end of the line care; however, this is often accessible in most hospital systems. In fact, even with substantial cases of critically ill COVID-19 patients, ECMO therapy use has ranged from 6% to 12%.^{4,5}

As patients with cancer, especially those in active treatment or in the acute post-treatment phase, are in a particularly immunosuppressed conditions, elucidation of the course of COVID-19 in this patient population is paramount. Liang et al¹³ describe a cohort of 18 cancer patients (1 [6%] of which with head and neck cancer) having a higher risk of mechanical ventilation or death (39% vs 8%), compared to non-cancer patients. Cancer patients also more rapidly deteriorated, with a median time to a critical event taking 13 days as opposed to 43 days in non-cancer patients.

Multiple other studies have described cancer patients with COVID-19. Desai et al¹⁴ performed a meta-analysis of 11 studies describing clinical courses of COVID-19 cases and found a 2% prevalence of cancer in patients with COVID-19. Desai et al¹⁴ also discovered higher risk of severe events for patients recently treated with chemotherapy or surgery in the past 30 days, over non-cancer COVID-19 patients (75% vs 43%).

Zhang et al¹⁵ revealed clinical characteristics of 28 COVID-19 infected cancer patients in Wuhan China, of which 3 (11%) had head and neck cancer. Of this cohort, 10 (36%) of patients required mechanical ventilation and 8 (29%) patients died. If assumed these eight were on maximum respiratory therapy previous to death, a mortality rate of 80% can be extrapolated and is in line to mortality rates of critically ill non-cancer patients; this, however, is not explicitly validated in the study. Notably, stage IV disease was associated with higher rates of severe events (ICU admission, mechanical ventilation, or

death) than stage I-III disease (70% vs 44%). Zhang et al¹⁵ also revealed patients recently treated with chemotherapy, radiation therapy, and/or immunotherapy in the past 14 days had a four-times increased odds of developing a severe event than those who received any treatment >14 days prior.

From this, we can observe that (a) prevalence of cancer, active or in remission, in COVID-19 patients is higher than in the general population; (b) COVID-19 patients with cancer may deteriorate more rapidly than non-cancer patients; (c) active treatment of cancer may be associated with increased risk of severe COVID-19 sequelae than in patients not undergoing treatment; and (4) critically ill COVID-19 patients who have cancer may more likely develop end-stage respiratory failure or death than non-cancer critically ill patients, barring presence of other chronic illnesses. It is difficult to ascertain how cancer patients in remission may far in comparison to the general population, however it is clear patients undergoing active treatment may present as a high-risk population for severe illness following COVID-19 infection. These observations are based on limited data provided by retrospective studies of small sample sizes, and thus must be interpreted with caution.

Cancer patients present as a high-risk population for COVID-19 development as well as poorer outcomes. Head and neck cancer patients in particular may be susceptible to the deleterious effects of not only the viral pathogenesis of COVID-19 itself, but also the long-term psychosocial sequelae of intensive critical care, advanced respiratory treatment and other life-saving measures, all amidst a quarantined environment for a patient population characterized as having twice the suicide risk rate of other cancer patients. Given such high death rates of non-cancer patients on mechanical ventilation, the additive vulnerability from head and neck cancer may make severe or critical ill COVID-19 development quite fatal for our patients. Thus, more attention and perhaps additional testing for patients currently undergoing treatment may be warranted. As described in modified head and neck cancer treatment algorithms,¹⁶ treatment only for advanced head and neck cancers should proceed with full precautions (ie, COVID testing, PPE) and any possible methods to reduce nosocomial COVID-19 infection is warranted. We hope this correspondence provides insight into the high-risk of head and neck cancer patients for critical illness following COVID-19 infection.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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