Oncology and COVID-19

People who have cancer are at risk for multiple health problems. Active treatment of the disease with chemotherapy can lead to immune suppression, failure to thrive, a decrease in physical and cognitive function, and other treatment-related toxicities. Some patients who have been previously treated for cancer are also predisposed to an increased incidence of cardiovascular disease, abnormal kidney function, and pulmonary insufficiency, all of which may affect the severity of coronavirus disease 2019 (COVID-19) infection and complications. The COVID-19 pandemic has highlighted the issue of whether patients with cancer, either receiving active treatment or having survived cancer, are more vulnerable to the virus and its sequelae than people without cancer. Due to the complexity of health issues in patients with cancer, the diversity of malignancies and treatments, and the limited number of individuals with both COVID-19 infection and cancer, the risk of death and serious complications due to the virus has been a challenge to define. Oncologists and their patients have had to make difficult decisions aimed at limiting potential exposure to the COVID-19 virus that have influenced treatment choices and, in some cases, clinical outcomes based on scant evidence.

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A major clinical concern is whether patients with cancer, if they become infected with COVID-19, are more likely to develop life-threatening complications and die from the disease. One multicenter cohort study evaluated the clinical characteristics of any COVID-19-infected individual who died within 28 days of hospitalization in the intensive care unit. The study assessed 2215 adults at 65 hospitals across the US over a 1-month period.1 One hundred twelve of the patients had active cancer as defined by malignancy treated within the last year (5.1% of the study population). Overall, there were 784 deaths at 28 days, of which 60 deaths (7.7%) were among patients with active cancer, and 724 deaths (32.7%) were among those without cancer. In a multivariable model, active cancer was associated with increased mortality (odds ratio [OR], 2.15 [95% CI, 1.35-3.43]).

Subsequent cohort studies have focused specifically on patients with cancer in an attempt to identify potential subgroups of individuals who may be at the highest risk of complications and death from COVID-19 infection. A multi-institution study collected data on patients with active or previous malignancy who had confirmed COVID-19 infections manifesting as severe acute respiratory syndrome.2 The primary end point of the analysis was all-cause mortality within 30 days of the COVID-19 diagnosis. Of the 928 adult patients with cancer enrolled, 39% were currently receiving cancer therapy and 43% had measurable disease. Twenty-two percent of patients had hematologic malignancies, and the remainder were solid tumor patients. During the 2-month study period, 13% of patients died. Patient characteristics associated with increased 30-day mortality were older age (per 10 years) (partially adjusted OR, 1.84 [95% CI, 1.53-2.21]) and male sex (OR, 1.63 [95% CI, 1.07-2.48]) as has been previously reported, being a former smoker (OR, 1.60 [95% CI, 1.03-2.47]), the number of comorbidities (≥2) (OR, 4.50 [95% CI, 1.33-15.28]), Eastern Cooperative Oncology Group performance status 2 (OR, 3.89 [95% CI, 2.11-7.18]) or greater (OR, 5.66 [95% CI, 2.79-11.47]), and progressive cancer (defined as no longer responding to treatment) (OR, 5.20 [95% CI, 2.77-9.77]). Cancer type, specific anticancer therapy the patient was receiving, or any recent surgery were not associated with increased COVID-19-related mortality. Although this study was retrospective and did not adjust for multiple comparisons, the data suggest that patients with multiple comorbidities, progressive cancer, and those with a physical decline due to their malignancy may be at a greater risk of death if they contract COVID-19. However, having had cancer may not be an important risk factor.

Several theoretical reasons may help explain why receiving active cancer treatment may make a patient more vulnerable to infection. Since the start of the pandemic, many assumptions have been made about the role of anticancer therapy in increasing the risk for severe complications from COVID-19 infection. Chemotherapy can induce neutropenia and lymphopenia, potentially predisposing the patient to a greater chance of becoming infected. Immune checkpoint inhibitor therapies, a common treatment for malignancies such as melanoma and lung cancer, could increase the risk for hyperinflammatory syndromes and acute COVID-19 respiratory disease. In addition, radiotherapy may also limit bone marrow reserve and can cause pneumonitis, which could lead to increased complications if a patient developed COVID-19–related lung disease.

Very little clinical data are available to support these assumptions. Investigators from 55 centers in the United Kingdom published a prospective observational study of 800 patients with cancer and documented COVID-19 infection.3 Approximately half the patients (412 [52%])...
had a mild disease course. Twenty-eight percent (n = 226) of patients died. The risk of death was significantly associated with similar clinical characteristics as reported in other studies: older age, male sex, and the presence of comorbidities such as diabetes and cardiovascular disease. A unique aspect of the study was that 35% (n = 281) of patients had recently been treated with cytotoxic chemotherapy within 4 weeks of their COVID-19 diagnosis. After adjustment for the other risk factors, there was no significant association between receiving chemotherapy and mortality from COVID-19 infection when compared with patients who had not received chemotherapy (OR, 1.18 [95% CI, 0.81-1.72]; P = .38). Whether the patients were receiving adjuvant chemotherapy or palliative bxchemotherapy, the risk was still not significantly different from those patients who were not receiving treatment. Moreover, there was no significant association with mortality if patients received immune therapy, targeted therapies, hormonal therapy, surgery, or radiotherapy within 4 weeks of diagnosis. These data support the conclusion that active cancer treatment may not adversely affect survival related to the virus in patients with cancer with COVID-19. However, in this study, 22% (n = 172) of patients reported that their anticancer treatments were interrupted due to the COVID-19 pandemic, although detailed information of the type of treatment disruption was not collected.

Treatment disruptions, modifications, or delayed cancer diagnoses that result from self-isolation due the COVID-19 pandemic will require further evaluation to determine the clinical consequence, if any, that has occurred for these patients. Thoracic oncologists at McGill University prospectively assessed the clinical management plan of 211 patients receiving active treatment for lung cancer from the beginning of March 2020 until the end of May 2020. Fifty-seven percent (n = 121) of patients underwent at least 1 change in their lung cancer treatment plan with 9% having more than 1 change. While some of the changes were of low clinical importance, such as lengthening the time interval for pembrolizumab infusion from every 4 weeks to every 6 weeks, other alterations could be significant. Palliative chemotherapy was delayed in 40% of patients, stopped in 15% of patients, and treatment was stopped permanently in 3% of patients. Adjuvant chemotherapy was delayed a mean of 42 days in 2.5% of patients. Changes in the dosing and schedule of chemotherapy occurred in 26%.

Cancer treatment alterations are increasingly being reported during the pandemic for many malignancies. One study, conducted via survey and involving 609 patients with breast cancer, identified treatment delays in as many as 44% of patients, with changes being the most common in young patients (ie, age 45 years or younger). Cancer surgeries and radiation treatment have also been delayed. It will be imperative to establish a systematic method to capture cancer treatment alterations as the pandemic progresses. The ability to determine what changes resulted in adverse clinical outcomes will be critical to be able to prospectively recommend alterations in therapy that would be acceptable and safe to clinicians and patients who should widespread self-isolation be reinstituted due to a resurgence in COVID-19 infections.

The studies published to date have refined the current understanding of the clinical characteristics of patients with cancer that identify those at highest risk of death from COVID-19 and have demonstrated that among patients with active cancer, the pandemic has resulted in significant health effects related to their malignancy. Several important questions remain. Are patients with cancer more likely to contract the virus, and if so, will their response to anti–COVID-19 therapy be similar to those individuals without cancer? Will patients with cancer be able to be effectively immunized once a vaccine has been developed, or will specific vaccine schedules and doses need to be defined for this population? As the COVID-19 pandemic progresses, rapid answers to these questions will be needed to develop the most effective treatment plans to keep patients living with cancer safe.

ARTICLE INFORMATION
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REFERENCES