

Oncology Practice During the COVID-19 Pandemic

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In just a few short weeks, the coronavirus disease 2019 (COVID-19) pandemic has transformed health care delivery around the globe. The crisis has dismantled how care is delivered and forced clinicians to make difficult triage decisions about what types and components of care have limited immediate value and which are essential for optimal outcomes. Because some malignancies could pose an immediate threat to survival, cancer provides a lens into the major shifts currently underway in clinical care. Cancer and cancer-related treatments frequently cause immunosuppression, and patients with cancer have excess mortality risk from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The magnitude of this risk is not yet known but early reports suggest a substantial increased risk of death associated with COVID-19 infection among patients with cancer, perhaps highest among those older than 60 years and those with pulmonary compromise.^{1,2}

The prevailing clinical approach in medicine, the in-person visit between patient and physician, has been upended. To flatten the growth curve of the COVID-19 pandemic, physicians have postponed or canceled nonacute procedures and transitioned millions of visits to telehealth. The technology used to effect this transformation is not new, but COVID-19 has forced widespread adoption of remote encounters by video applications, patient portals, or phone calls. Patients and oncologists have rapidly adapted to this new way of communicating and many have found this approach satisfactory and sometimes preferred. Barriers to remote care previously precluded by entrenched culture or billing hurdles have quickly been surmounted.

In this unprecedented context, what frameworks should be used to inform decisions about how to modify cancer treatment based on patient and cancer-specific factors? Oncology care generally falls into 4 categories: First is care that is not time sensitive, can be delivered remotely, or both. This includes survivorship and surveillance visits for patients who have completed cancer treatment and have no acute symptoms to suggest recurrence. Low-risk patients receiving hormonal or oral chemotherapy also can usually be evaluated remotely, and, in most cases, blood work and imaging studies could be deferred until health system capacity has recovered.

Second is care that cannot be delivered remotely but for which treatment omission or delay has a marginal effect on quality or quantity of life. A sizeable proportion of oncology care involves systemic chemotherapy for patients with advanced cancer. When clinical trial data demonstrate that the incremental survival benefit of this therapy is limited, then omission or delay is appropriate given the balance of potential benefit of treatment vs the risk if the patient becomes infected with SARS-CoV-2. For example, for most metastatic solid tumors, chemotherapy beyond the third regimen does not improve sur-

vival for more than a few weeks; therefore, oncologists are advising supportive care instead. For patients receiving adjuvant therapy for curable cancers, delaying initiation or abbreviating the number of cycles is appropriate. Oncologists are postponing initiation of adjuvant chemotherapy for some estrogen receptor-negative stage II breast cancers by 8 weeks and administering 6 rather than 12 cycles of adjuvant chemotherapy for stage III colorectal cancers. Because screening for breast, colorectal, lung, and prostate cancer has been halted, the proportion of screen-detected early-stage cancer is expected to decline over the next several months. Although some patients are willing to undergo treatments for small benefits, the pendulum of risk related to immunosuppression and exposure at a health care facility tip the risk-benefit ratio away from treatment. Low-grade tumors include many prostate cancers, carcinoid and neuroendocrine tumors, some thyroid cancers, some central nervous system tumors, and some lymphomas, for which treatment usually can be safely postponed by 8 to 12 weeks or longer. The COVID-19 crisis is forcing elimination of low-value treatments that were identified by the Choosing Wisely campaign, even though uptake of recommendations to eliminate these treatments has previously been adopted slowly.³

During the pandemic, triage decisions require even more interspecialist coordination and communication than usual. Postponing surgery and administering neoadjuvant therapy as a bridge can decrease risk to the patient and preserve health care resources. Similarly, radiation oncologists may omit, delay, or use shorter courses to reduce the number of visits.

Third, and most challenging, are situations for which delay has a moderate clinically important adverse influence on quality of life or survival. For example, randomized trial evidence demonstrates that 3 years of maintenance rituximab after autologous transplant for mantle cell lymphoma improves overall survival by 9%.⁴ Although treatment omission increases the chance of relapse, some oncologists are omitting or delaying this treatment. The incremental benefits of treatments with higher risk of infection become deprioritized, and for many cancer types, oncologists are reasonably prescribing marginally less effective regimens that have lower risk of precipitating hospitalization. Oncologists are also using white cell growth factor, more stringent neutrophil counts for proceeding with a next cycle of therapy, and omitting use of steroids to manage nausea. When possible, oncologists are substituting oral for intravenous agents and myriad other modifications to minimize visits and hospitalizations.

Fourth, and more clear, is cancer treatment that has the potential to cure and cannot safely be delayed. This includes most patients with new diagnoses of acute leukemia, high-grade lymphoma, and those with

chemotherapy-responsive tumors such as testicular, ovarian, and small cell lung cancer. Despite the risks, oncologists are not modifying such treatments because these cancers are likely more lethal than COVID-19. For example, most allogeneic transplants cannot be safely postponed. Both donors and recipients are undergoing SARS-CoV-2 testing before induction starts.

Once a patient's cancer and perceived risk of contracting SARS-CoV-2 infection are determined, the next step is to consider the capacity of the local health care system to meet existing and projected needs. This requires knowledge about whether the system is in the preparatory, acute, or crisis phase of the pandemic. In the preparatory phase, the health care workforce is intact and hospital beds and equipment including ventilators are available. In the acute phase, the workforce has limited capacity but is functional and through strategic reorganization, there is some ability to deliver routine cancer care. In the crisis phase, the health care system is overwhelmed with COVID-19 cases and has no surplus capacity with respect to hospital beds, equipment, or staff.

In the first weeks of April 2020, oncologists in epicenters like New York City and Detroit are often opting for regimens with lower efficacy but lower risk of hospitalization, whereas oncologists in Denver and Raleigh have confidence—at least for the moment—that beds will be available and therefore have not yet had to make as many modifications. Although accrual to therapeutic trials has slowed dramatically and acquisition of biospecimens for correlative studies has largely stopped, oncologists remain focused on ensuring that clinical trial participants can continue to receive their protocol-directed therapy and evaluations where it is safe to do so. The twin goals are to minimize harms to research participants and to ensure that disruptions from the COVID-19 pandemic do not prevent the ability to test study hypotheses. Ensuring that the pandemic does not exacerbate existing disparities for cancer patients based on race, ethnicity, and class and access to specialty care is also a priority.

Oncologists report unprecedented levels of cooperation and collegiality across borders. Clinicians in Milan and Barcelona are sharing their experiences with those in Boston and San Francisco. The oncology community has united to share strategies, formulate guidance, collect data, and design and execute treatment protocols. Clinicians report deriving comfort and professional solidarity from these interactions. Consortia to identify which patients are most at risk of infection, determine how antineoplastic therapies influence the course of COVID-19 illness, and understand when it may be safe to resume treatment have proliferated with remarkable speed and receptivity.

Many patients with cancer are concerned that their needs will be overlooked or marginalized during the COVID-19 crisis. Attending to these legitimate concerns has become, and should be, a focus. Balancing the value of cancer treatments with competing risks during a time of declining resources will increasingly present ethical and logistical challenges to clinical standards and humanism. Because most hospitals and outpatient infusion centers now prohibit visitors from accompanying patients, there is intense attention on clarifying advance directives, health care proxies, and end-of-life care preferences. Oncologists and patients must prioritize these conversations.⁵ However, the essential empathy of oncology practice will continue to transcend the new physical barriers presented by masks and telehealth.

In the space of a month, approaches and accepted norms of cancer care delivery have been transformed of necessity. Most of these changes would not have occurred without the pandemic. Although the immediate priority is to save lives, in the aftermath and recovery phase, evaluating the effects of COVID-19 on cancer mortality will be a priority. Planning for resuming cancer treatment and screening to mitigate harms is already underway. It is also likely that some changes provoked by the crisis will permanently transform how to treat cancer, in some cases perhaps for the benefit of both patients and their physicians.

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