



# Cancer or COVID-19? A Review of Guidelines for Safe Cancer Care in the Wake of the Pandemic

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## Abstract

In the wake of the COVID-19 pandemic, due to reasons beyond control, health care workers have struggled to deliver treatment for the patients with cancer. The concern for otherwise healthy patients with curable cancers that require timely intervention or therapy is the risk of contracting COVID-19 may outweigh the benefits of cancer treatment. Lack of international guidelines leaves health care providers with a case-to-case approach for delivering optimal cancer care in the wake of the pandemic. Transition to telemedicine has somewhat bridged the gap for in-office visits, but there is a continuing challenge of delays in cancer screening or significant decline of new diagnoses of cancers due to the pandemic. We aim to propose a balance in risk from treatment delay versus risks from COVID-19 with emphasis on treatment modality (surgery, radiation, and systemic therapy) as well as supportive care for cancer patients, and therefore have reviewed the publications and recommendations from international societies and study groups available as of October 2020.

**Keywords** Cancer care · COVID-19 pandemic · Disruption in oncology care · Resumption of elective surgeries · Supportive cancer care · Re-planning radiation therapy · Medical oncology treatments · Prevention of SARS-CoV-2 infection · International society guidelines · Literature review

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## Key Points

- Patients with confirmed SARS-CoV-2 infection within 7 days before or 30 days after surgery had an overall 30-day mortality of 24%.
- Prioritization of treatments and testing of patients prior to institutional procedures should be implemented as standard protocol.
- Radiation therapy for head-neck, nasopharyngeal, and lung fields should be actively monitored, possibly owing to the unknown effect on respiratory complications associated with COVID-19.
- Patients that have tested negative for SARS-CoV-2 are recommended to continue anticancer therapy that might be critical for tumor control.
- The risk of in-hospital COVID-19 death was significantly higher for non-hematologic malignancies diagnosed 1 to 5 years prior to SARS-CoV-2 infection and the risk for hematologic malignancies continued to remain high even after 5 years.
- Mental and physical health of clinicians should be given utmost importance as they are the ones at high risk for stress and fatigue breakdown during the pandemic.

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## Introduction

The acute pandemic of (coronavirus disease 2019) COVID-19 since its declaration in March 2020 by the World Health Organization has impacted not only medical care but most aspects of daily life. Disease spread may be intervened by physical distancing, hand and respiratory hygiene, and national stay at home guidelines.

Health systems are posed with a challenge to deliver care for diagnosed patients with cancer during this crisis, given the risks of serious complications from SARS-CoV-2 as compared with mortality from cancer. Reports with likely higher severity of COVID-19 in immunocompromised patients add the challenge [1, 2]. Due to reasons beyond control, health care workers have struggled to deliver treatment for the patients with cancer. Reasons are not limited to lack of resources and diverting workforce towards the pandemic response—forcing hospitals to cancel or delay surgeries or limit inpatient admissions, including chemotherapy and radiation therapy. Nationwide lockdowns have limited patient's access to travel to their health care facility. The concern for otherwise healthy patients with curable cancers that require timely intervention or therapy is the risk of contracting COVID-19 may outweigh the benefits of cancer treatment [3].

Demands for personal protective equipment, greater hospital capacity, and ventilator equipped intensive care units have resulted in insufficiency in the demand need.

Transition to telemedicine has somewhat bridged the gap for in-office visits, but there is a continuing challenge of delays in cancer screening or significant decline of new diagnoses of cancers due to the pandemic [4–6]. Lack of international guidelines leaves health care providers with a case-to-case approach for delivering optimal cancer care in the wake of the pandemic. We aim to propose a balance in risk from treatment delay versus risks from COVID-19, and reviewed the publications and recommendations for cancer groups as of October 2020.

## Routine Precautions for Outpatients

In addition to general guidance provided by the Centre for Disease Control (CDC), USA, emphasis in the American Society of Clinical Oncology (ASCO) for cancer patients visiting the outpatient clinics include the following [7]:

- Training for cancer patients in proper hand hygiene.
- Information regarding the symptoms of COVID-19 and minimizing exposure to sick contacts and large crowds.
- To wear a mask or cloth face cover when exposed to public or hospital environments, not necessarily a N95 mask (lack of evidence to suggest benefit in low exposure risk population).

- Most institutions implement requirements for all personnel—health care workers, patients, and visitors—to wear a surgical face mask when on campus, regardless of symptoms.
- Postponement of in-person visits if not associated with additional risk to the patient. Postponement also directed towards routine follow-up visits to assess post treatment disease status/surveillance which may be substituted with locally available investigations, self-examination, and teleconsultation.
- Screening via telemedicine for COVID-19 symptoms and exposure history (48 to 72 h prior to treatment cycles or every in-person visit) [8].
- Pro-active medical assessment for patients with symptoms of infection or fever, considering the overall higher risk of routine infections in immunocompromised cancer patients.
- For prevention of infection to other patients and health care personnel, guidelines suggest that the status of patient screening and positive COVID-19 status be documented prior admission of the patient to the institution/treatment facility [7].

**Cancer Diagnosis and Staging** Conservation of resource in areas where infection is an ongoing issue, the CDC as well as National Comprehensive Cancer Network (NCCN) and other expert guidelines recommend postponement of in-person visits for cancer screening for the general public [9–12]. Postponement of screening procedure would not only conserve resources and manpower for these facilities but also minimize patient exposure to the health care environment [13] until a time where infection spread is under control [13–16]. This also reserves facilities for patients with symptoms requiring assessment for monitoring progression or new diagnosis of cancer [17–19].

## Challenges in Cancer Therapy

### Cancer Surgery

**Elective Surgeries Delayed/Deferred** While the World Health Organization suggests that “elective surgeries” and inpatient facilities should be rescheduled unless unavoidable, individual case-based assessment on the potential outcomes from delaying essential cancer-related surgery needs to be discussed by the clinicians and their patients. Memorial Sloan Kettering Operating Room COVID-19 Subcommittee have characterized a subset of “essential cancer surgery,” primarily tumor surgeries that cannot be delayed, including surgical management of brain tumors, as well as breast, colon,

stomach, pancreas, liver, bladder, kidney, and lung resections [20].

This approach has been corroborated by the American College of Surgeons with emphasis on cases that may progress in delaying or in the absence of treatment are the ones that should be performed. This is aimed to offer a more planned procedure as compared with an emergency procedure that may arise from delay in timely surgery. Such unplanned and complicated emergencies are likely to consume more resources in the restricted setting. Another category of essential surgeries is selective palliative procedures being performed for acute relief of pain and suffering or acute neurologic deficits that are not manageable by other means [20]. Institutional protocols require the specification whether a surgical procedure will require postoperative intensive care unit (ICU) admission (planned or inadvertent complications); the decision to undertake such a procedure must be considered in conjunction with availability of ICU beds.

Neoadjuvant therapies have been used as a means of performing surgery at a later and relatively better equipped date. Neoadjuvant chemotherapy (e.g., rectal cancers), hormonal therapy (e.g., breast, prostate cancers), chemoradiotherapy (e.g., rectal, prostate cancers), or pre-operative radiotherapy (e.g., soft tissue sarcomas) as opposed to upfront surgery are possible in a spectrum of cancers as a means for delaying surgery without allowing the disease to remain unchecked [21]. However, this may not be applied as a rule, and disease management groups should weigh the risk of delay in definitive surgery against the risk of COVID-19 exposure or the probable more complex surgical resection if the tumor progresses while on interim neoadjuvant therapy [22, 23]. Neoadjuvant therapies requiring in-person visits or immunosuppressive therapies must take into account the potential incremental risks to the patient.

An international cohort study observed the outcomes of surgery during the early part of the pandemic from 1 January 2020 to 31 March 2020 and 1128 patients with confirmed SARS-CoV-2 infection within 7 days before or 30 days after surgery had an overall 30-day mortality of 24%. Most common complication resulting in mortality was pulmonary complications (83%). Mortality in adjusted analysis was associated with male sex, age > 70 years, poorer physical status (ASA grades 3–5), malignant lesions, and emergency procedures or major procedures [24]. The poorer outcomes exceed those seen in major surgeries in the pre-COVID era. Hypotheses suggest inflammatory and prothrombotic states associated with COVID-19 severity as a result of poor surgical outcomes [25]. Therefore, this reinforces the rationale for delaying elective surgeries for limitation of viral spread, and minimizing risks, particularly of postoperative infection.

**Resumption of Elective Surgeries?** A joint statement from the group of surgeons, anesthesiologists, and hospital associations

[26] in USA and similar guidelines from UK [27] recommend that elective surgeries be scheduled when

- There is a persistent downward trend of SARS-CoV-2 infection rates for two or more weeks in the referral zone catered to by the hospital/institution.
- Calibration of resource distribution and return to optimal utilization of ICU bed, PPEs, and blood bank adequacy for surgery needs, over and above the requirements of the institution for catering to COVID-19 patients.
- Prioritization of surgical cases and testing of patients prior to surgery is standard protocol. Testing of employees is recommended and may be considered.

**Special Precautions: Head and Neck and Upper Respiratory/Digestive Tract Procedures** Particular higher risk of droplet contact through respiratory or upper digestive tract procedures, namely diagnostic/therapeutic scopes, head-neck, and ENT surgeries [28] with safety recommendations suggesting two tests at > 24-h intervals for SARS-CoV-2 infection prior to undertaking such procedures [29, 30] or exploration of alternative intervention through image/computed tomography guidance, etc., where feasible.

**Radiation Therapy** Consideration for receiving radiation therapy (RT) is with respect to the risk of COVID-19 exposure and may be slightly higher than the outpatient exposure associated with frequency and duration of radiation treatment, and this has been noted in the targeted response from the international radiation oncology group (Global Radiation Oncology Group) [31]. There is no independent documented risk of radiation therapy affecting COVID-19 severity or higher infection risk. However though, recommendations for certain cancers that may be placed on systemic therapy suggest delay in radiation therapy [32] or substitute with hypo-fractionated radiotherapy [33] for head-neck, nasopharyngeal, and lung fields possibly owing to the unknown effect on respiratory complications associated with COVID-19. Proceeding with radiation delivered with curative intent or for rapidly progressive tumors outweighs the risks of COVID-19 exposure and infection [34]. For active ongoing treatments, the decision to continue or delay requires careful consideration of indications, dose already delivered, and risks and benefits.

**Systemic Anticancer Treatments** Direct evidence to support changing or withholding systemic therapy in cancer patients is lacking [35]. Therefore, patients that have tested negative for SARS-CoV-2 are recommended to continue anticancer therapy that might be critical for tumor control. The potential harms from interrupting or delaying initiation of treatment when compared with possibility of preventing SARS-CoV-

2-19 infection are uncertain. It is essential that an individualized decision takes into consideration patient and tumor-related factors, namely, curability from the cancer, risk of local or distant cancer recurrence possible with delay in treatment or modification/interruption, the phase of therapy (induction or maintenance, neoadjuvant or adjuvant etc.) already completed, and the current tolerance versus the expected tolerance to systemic treatment at a later date considering some progression of disease in the absence of a therapeutic check. As discussed earlier, status of patient screening and COVID-19 status be documented prior admission of the patient to the institution/treatment facility [7] at every cycle or visit for drug administration. An international collaboration of medical oncologists [36] has suggested guidelines from expert opinions that are in sync with recommendations from the National Institute for Health and Care Excellence (NICE), UK. However, lack of evidence-based guidelines requires individual centers to adapt and modify to support their health care infrastructure.

**Chemotherapy** Ability to isolate the chemotherapy unit from the COVID-19 care facility (patient flow as well as teams of health care workers), though challenging, may serve as a protective barrier to provide chemotherapy administration as intended. As agreed upon by multiple expert groups, treatment with curative intent would be best continued as directed by the physician with the acceptance of SARS-CoV-2 infection threat during therapy. However, an individualized treatment modification with reduction in admission duration by administering shorter duration of therapy or ensuring hydration and premedication at a local or home care facility may be implemented where feasible.

Palliative therapy alteration in the wake of COVID-19 is a fine balance with the challenges of worsening of disease status leading to deterioration of symptoms and physical performance status. Loss of opportunity to treat may be taken into account prior to modification/delay in palliative regimens [37].

ASCO recommendations [7] for chemotherapy treatment includes some of the following:

- Omission of chemotherapy in consideration of risk of COVID-19 for patients expected to have a small benefit over non-chemotherapy or non-immunosuppressive therapy (e.g., receptor-positive breast cancers in early stage or prostate cancers may benefit from hormonal therapy).
- Home care–assisted infusion of drugs in consultation with primary care physician, though available in certain countries [38, 39] may not a feasible option for infusion chemotherapy or monoclonal antibody infusions without adequate safety protocols or clinical supervision, but may be adequate to minimize admissions for need of hydration, antiemetics, etc.

- Adaptation of inpatient regimens to outpatient administration may reduce burden on hospital resources, while increasing the frequency of visits to the outpatient clinic by the patient and therefore must be judiciously considered. The NCCN toolkit is available as a guide for shifting regimens for hematological malignancies to an outpatient setting [40].

**Immunotherapy: Immune Checkpoint Inhibitor** Conflicting data in published literature regarding checkpoint inhibitor immunotherapy and its effect on the severity of COVID-19, especially in the instance of treatment-related pneumonitis associated with ICI, needs to be assessed in further detail [41–43].

### **Immunomodulatory Agents: Anti-CD20 Monoclonal Antibodies**

B cell–mediated immunity has been extensively studied in the COVID-19 population, and serological evidence of antibodies as host response to SARS-CoV-2 infection has been documented [44–46]. It is therefore essential to re-evaluate the risk-benefit balance for drugs (anti-CD20 monoclonal antibodies) inhibiting B cells and resulting in lymphopenia [47, 48].

**Glucocorticoids** While glucocorticoid and steroidal compounds are essentials in multiple cancer therapeutic regimens, the lack of evidence-based recommendations does not justify withholding glucocorticoid use in otherwise healthy cancer patients and data regarding its effect on host immunity for the SARS-Cov-2 infection is limited [35].

### **Type-Specific Guidelines and Literature for Cancers**

Various society guidelines and literature reports (Table 1) from study groups for specific cancer types are represented in table. An algorithmic and conceptual approach towards decision making on cancer management during the ongoing pandemic of COVID-19 requires balancing attempts between cancer progression due to treatment delay vs. risk of infection and morbidity from COVID-19. A framework for this has been proposed by an international collaborative group [49], but case-based decisions are imperative [50].

A summary compiled by an international group of international recommendations was made available in 23 languages to overcome the language barrier for dissemination of knowledge [51].

**Table 1** Various society guidelines and literature reports from study groups for specific cancer types

| Cancer type                     | Society guidelines  | Literature from study groups |
|---------------------------------|---|------------------------------|
| Breast cancer                   | American College of Surgeons<br>Surgical Society of Oncology<br>American Society of Breast Surgeons<br>European Society of Medical Oncology (ESMO)<br>NCCN  | [52–57]                      |
| Gastrointestinal cancers        | American College of Surgeons<br>Surgical Society of Oncology<br>ESMO<br>NCCN<br>US Colorectal Cancer Alliance   | [58–60]                      |
| Genitourinary cancers           | ESMO<br>European Association of Urology [64]<br>Canadian Group [65]<br>British Guidelines [66]  | [61–63]                      |
| Gynecological cancers           | ESMO<br>American College of Surgeons<br>Society of Gynecologic Oncology [71, 72]<br>International Gynecologic cancer society<br>American society for colposcopy and cervical pathology  | [67–70]                      |
| Head and neck cancers           | ESTRO-ASTRO [73]<br>French society—joint consensus [77]   | [74–76]                      |
| Hematologic malignancy          | American Society of Hematology<br>American Society of Transplantation and Cellular Therapy<br>European Society for Blood and Marrow Transplantation<br>ESMO<br>Australian/New Zealand consensus statement [84]<br>Brazilian task force [85]<br>International Lymphoma Radiation Oncology Group<br>International Society of Amyloidosis [86] | [78–83]                      |
| Liver malignancy                | ESMO<br>International Liver Cancer Association<br>American Association for the Study of Liver Diseases  | [87, 88]                     |
| Brain and neurological cancers  | American Association of Neurological Surgeons [89]<br>ESMO [93]   | [90–92]                      |
| Endocrine/neuroendocrine tumors | North American Neuroendocrine Tumor Society (NANETS)<br>UK and Ireland Neuroendocrine Tumor Society<br>Society of Surgical Oncology   |                              |
| Skin cancers                    | ESMO<br>Society of Surgical Oncology<br>NCCN  | [94–96]                      |
| Sarcomas                        | Society of Surgical Oncology<br>ESMO<br>French Sarcoma Group [97]   |                              |
| Lung cancer                     | American College of Surgeons<br>Thoracic Surgery Outcomes Research Network [100]<br>ESMO<br>International Association for the Study of Lung Cancer (IASLC)<br>NCCN  | [98, 99]                     |

**Table 1** (continued)

| Cancer type            | Society guidelines  | Literature from study groups |
|------------------------|---|------------------------------|
| Pediatric malignancies | ESTRO-ASTRO [101]<br>International Consensus group [9]<br>International Society for Pediatric Oncology<br>Children's Oncology Group<br>Childhood Cancer International [102]<br>French Society for the Fight against Cancers and Leukemias in Children and Adolescents [103] |                              |

**Cancer Survivors** Limited studies have addressed the risk of COVID-19 severity and complications in patients that have received treatment for cancer, some considerations resulting from persistent immunosuppression, toxicities from systemic therapy agents, radiation-induced changes, limitation in physical activity status after major surgeries, etc., or even those on long duration of maintenance therapy [104].

- The UK group recorded national registry data adjusted for hematological and non-hematological cancers. The risk of in-hospital COVID-19 death was significantly higher for non-hematologic malignancies diagnosed 1 to 5 years prior to SARS-CoV-2 infection, and the risk for hematologic malignancies continued to remain high even after 5 years [105].
- Higher psychological and social distress resulting from isolation and distancing among cancer survivors in fear of worse COVID-19 infections may add to their overall risk to mental and physical health in adolescent and young adults [106].

### Cancer and Patient Support

Prophylaxis for COVID-19 infection in the general population remains controversial without equivocal evidence to suggest for or against the use of certain agents (e.g., hydroxychloroquine, antiviral compounds, etc). The use of specific antiviral agents as prophylaxis for the immunocompromised subset of patients undergoing cancer therapy remains ambiguous too.

- Supportive care includes care of chemoports which may be over intervals as long as 10 to 12 weeks (as compared with the routine 4–6-week schedule) [107], with the possibility of trained home care personnel providing aseptic port care without requiring visit to the hospital facility.

- Scarcity of blood donations and increased demand for blood transfusions for COVID-19 patients with severe disease may lead to a shortage of blood and blood-product availability for cancer patients receiving therapy. Anticipation and pre-emptive stimulation with erythropoietin stimulation/colony-stimulating factors may be administered. Anemia from bleeding may need aggressive intervention with embolization, etc.
- Relatively staged surgical procedures may offer the patients an opportunity to arrange for donor transfusions from family and friends to sustain or replenish the personal requirement.
- In patients with advanced cancer, counseling and documentation of the counseling for end-of-life preferences and physicians orders for life-sustaining treatment (POLST) must be carried out in the event the cancer or COVID-19 may affect the other, worsening outcomes and chances of survival [108, 109].
- Pneumonitis associated with medica agents (checkpoint inhibitor immunotherapies, gemcitabine, etc.) needs to be assessed and differentiated from COVID-19 symptoms. COVID-19 testing should be recommended in any event of suspicion. Lymphangitic spread, radiation pneumonitis, and lung infiltrates may also resemble respiratory changes associated with COVID-19 [110]. Need for this distinction is essential due to inadequate data on worsening of pneumonitis in COVID-19 to vice versa.
- Deferred treatment in the wake of the pandemic may lead to vulnerability in cancer patients that are already anxious and fearful of disease progression or local/distant recurrences. Social isolation combined with mixed depression and anger from constrained resources and helplessness needs to be identified and addressed by counseling/education and reassurance by reaching out through telemedicine [111, 112].
- Stress and anxiety are not only limited to the patients but also affect the clinicians isolating from family and friends,

exceedingly demanding work schedules and challenges in patient care [113]. There is therefore a need for resources to help and enhance the physical and mental health of frontline workers.

## Summary

- It is imperative to balance the result of delayed cancer therapy as compared with risk of COVID-19 in the potential increased vulnerable population with cancer.
- SARS-CoV-2 infection does not interfere with, nor does it have an effect on the diagnosis or staging of cancer as available from current evidence.
- Elective surgeries may be delayed with staged treatment strategies in attempt to conserve of resources, limit exposure to hospital and high viral environment thereby minimizing risks, particularly of postoperative infection which may be life threatening.
- There is no direct evidence to support changing or withholding radiotherapy, chemotherapy, or immunotherapy in patients with cancer, and routinely withholding critical anticancer or potentially immunosuppressive therapy is not recommended for those who do not have COVID-19.
- Port care may be available at local/home facilities and at extended intervals as is documented to be effective as well as safe.
- Patients with advanced cancer who are at elevated risk for COVID-19 must be counseled for end-of-life choices and POLST.
- Teleconsultations for routine follow-up and disease surveillance may be implemented. In-person visits required for physical examination, investigations, etc., need to be streamlined with physical distancing, minimal waiting times, limiting accompanying persons, and visits to emergency for care that may be available locally.
- Guidelines on use of face masks must be implemented as a rule for all persons, at least within the hospital campus. Identification of risk zones/procedures and recommendations for risk-specific PPE use should allow optimal use of limited resources.
- Mental and physical health of clinicians should be given utmost importance as they are the ones at high risk for stress and fatigue breakdown during the pandemic.

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**Data Availability** Not applicable.

## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Ethics Approval** Not applicable, no patient data presented.

**Consent to Participate** Not applicable.

**Consent for Publication** Not applicable.

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