



IMPACT OF COVID-19 PANDEMIC ON CANCER CARE – AN ONCOLOGIST PERSPECTIVE

Oncology

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ABSTRACT

The Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become the most talked-about clinical entity in early 2020. Health-care services are rapidly transforming their organization and workforce in response to the COVID-19 pandemic. These changes, and a desire to mitigate infection risk, are having profound effects on other vital aspects of care, including the care of patients with cancer. Difficult decisions are being made regarding the prioritization of both active treatments and palliative care, despite limited evidence that cancer is an independent risk factor for infection and mortality.

In this article, we tried to analyze the impact of COVID-19 on Cancer care. Management presents its own set of challenges deciding whether postponing cancer treatment until the infection resolves is going to benefit the patient and how to organize all aspects of patient care when social contact is as limited as it is for patients newly diagnosed with COVID-19.

KEYWORDS

COVID-19, SARS-CoV-2, Cancer Care, Palliative Care

INTRODUCTION:

The Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first described in Wuhan, China, in December 2019. After severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), SARS-CoV-2 is the third highly pathogenic and transmissible coronavirus. Since December, the virus has spread globally and has led to the implementation of some of the most serious policies around the world.

On January 30, 2020, the WHO declared the COVID-19 outbreak a public health emergency of international concern and, in March 2020, began to characterize it as a pandemic, in order to emphasize the gravity of the situation and urge all countries to take action in detecting infection and preventing spread [1,2].

The WHO has indicated three priorities for countries [3]:

- Protecting health workers
- Engaging communities to protect those at highest risk of severe disease (eg, older adults and those with medical comorbidities)
- Supporting vulnerable countries in containing infection

Since 31 December 2019 and as of 28 April 2020, **2 982 688 cases** of COVID-19 (in accordance with the applied case definitions and testing strategies in the affected countries) have been reported, including **210 193 deaths** [4].

Since start of pandemic, we have seen a number of consequences that have impacted people's lives. The economic impact has also been huge. Financial markets have been severely impacted; putting people's financial wellness at risk. The incubation period is not notably longer than for other viruses in the same family. However, the fact that people have been required to stay in isolation for 14 days has had a severe psychological impact on many affected individuals.

The most common clinical presentation is that of a mild upper respiratory tract infection, although a number of patients develop progressive respiratory failure. The most common co-morbidities of patients diagnosed with COVID-19 were hypertension and diabetes mellitus, while respiratory co-morbidities were comparably rare. The risk of intensive care unit (ICU) admission and death was significantly higher in older individuals and those with co-morbidities and the development of end-organ damage (acute respiratory distress

syndrome, acute kidney injury, cardiac injury). Many treatment regimens have been attempted including antivirals, antibiotics, corticosteroids.

In the COVID-19 crisis, cancer patients are regarded as a highly vulnerable group [5]. A recent investigation of 18 patients who had been previously diagnosed with cancer, from a nationwide cohort of 2007 COVID-19 cases, found that patients with cancer had a higher risk of severe clinical events than those without cancer. The case fatality rate reached 5.6% among cancer patients compared with 2.3% in the general population. [6,7]. However, with a relatively small sample size, limited clinical information, and high heterogeneity of the course of the disease, many critical issues concerning treatment principles of COVID-19-infected cancer patients remain unclear.

Delivering cancer care during this crisis is challenging given the competing risks of death from cancer versus death or serious complications from SARS-CoV-2, and the likely higher lethality of COVID-19 in immunocompromised hosts. Many patients with cancer are struggling to receive treatment for their cancers due to hospitals canceling or delaying surgeries and other procedures, including chemotherapy and radiation therapy.

There is also concern that patients who are otherwise healthy and have curable cancers that require timely implementation of surgery, chemotherapy, or radiation have unfortunately concluded that the risk of contracting COVID-19 may outweigh the benefits of cancer treatment. Inadequate supplies of personal protective equipment (PPE) for health care providers, limited hospital capacity, including intensive care units (ICUs), and lack of point-of-care testing further complicate the difficulty.

The purpose of this article is to analyze the impact of COVID-19 infection on cancer care including challenges and priority management.

Impact of COVID-19 on Cancer Care: Who is at specific risk?

So far, no systematic reports are available regarding a higher incidence of COVID-19 or SARS-CoV2 asymptomatic infections in patients with cancer. Recent limited data from China, and more recently from Italy and the US, do however seem to confirm a higher risk.

Available data indicate that older people are more vulnerable, with underlying health conditions such as chronic respiratory, cardiovascular or chronic kidney disease, diabetes, active cancer and more generally severe chronic diseases.

In cancer patients, categories at risk include:

1. People with some types of blood or lymphatic system cancer which damage the immune system, even if they have not needed treatment (for example, chronic leukaemia, lymphoma or myeloma).
2. People who have had bone marrow or stem cell transplants in the last 6 months, or who are still taking immunosuppressive drugs
3. Patients receiving chemotherapy, or who have received chemotherapy in the last 3 months,
4. Patients receiving extensive radiotherapy
5. Specific risk groups are cancer patients with an impaired immune system such as: Leukocytopenia, low immunoglobulin levels, Long lasting immunosuppression (steroids, antibodies) [10].

Impact on Cancer Screening:

It is likely that routine screening appointments, for example cervical screening tests and mammograms, will be cancelled or postponed for the foreseeable future.

Impact on Cancer Diagnostic and Staging procedures:

Tests to diagnose or stage cancer might be delayed if the risk of infection with coronavirus outweighs the benefits of the tests. This will be discussed on a case-by-case basis. In some patients, staging procedures may be limited to those that are the most crucial to guide treatment.

Impact of COVID-19 on Cancer Treatment:

Cancer treatment plan may be adapted in order to minimise the risks to health resulting from the COVID-19 pandemic. The adaptation strategy may differ depending on the therapeutic goal; for example, curative treatment is more likely to continue as planned to ensure the best chance of remission, whereas the risks of COVID-19 in patients undergoing palliative therapy may outweigh any potential benefits of treatment.

European Society for Medical Oncology (ESMO) has applied a tiered approach to guidance on the management of patients with cancer during the COVID-19 pandemic [10]. This approach considers the patient's condition, the urgency of the planned cancer treatment and its anticipated benefit in light of the potential risk of COVID-19 associated with the logistics of receiving treatment, as well as the available resources to safely provide treatment.

Using this approach, patients can be grouped into the following tiers:

Tier 1: High priority - This group includes patients whose condition is life threatening or clinically unstable and/or where the planned treatment is likely to result in a significant benefit (e.g. prolonging life or improving quality of life), making treatment a high priority.

Tier 2: Medium priority - This group includes patients whose condition is serious but not immediately life threatening and where a short delay in treatment can be considered. However, a delay of longer than 6–8 weeks could potentially impact on outcome and/or the amount of benefit derived, making treatment a medium priority.

Tier 3: Low priority - This group includes patients whose condition is stable enough that any treatment can be safely delayed for the duration of the COVID-19 pandemic. It also includes patients whose planned treatment is unlikely to provide a significant benefit (e.g. unlikely to prolong life or improve quality of life), making treatment a low priority.

A multi disciplinary team should review each individual patient in order to decide if any changes to treatment are needed. It is therefore very important to keep in contact with doctor or nurse via telephone or email to ensure you understand if, how and why treatment plan might be modified.

Chemotherapy:

Decision to delay, modify or interrupt chemotherapy should only be taken after weighing up the potential harm that could result from

delaying or interrupting chemotherapy versus the potential benefits of preventing COVID-19. The decision should be made on a case-by-case basis, taking into account the risk of cancer recurrence if chemotherapy is delayed or interrupted, the number of cycles of chemotherapy already completed and how well patients are coping with treatment.

Clinician can recommend a chemotherapy '**holiday**' if patients are on maintenance therapy and are in established remission.

Delaying or modifying adjuvant treatment (treatment given after surgery) may be recommended in some cases. If you are undergoing adjuvant treatment for resected high-risk disease, then your chemotherapy is likely to continue as planned. However, if the benefit of adjuvant chemotherapy is thought to be relatively small and non-immunosuppressive options are available, clinician should suggest using an alternative treatment to reduce your risk of complications from COVID-19.

Clinicians should think of switch to a chemotherapy regimen that requires less frequent infusions; for example, every 2/3 weeks rather than weekly.

You may be able to switch from an intravenous chemotherapy to an oral therapy, thus reducing the frequency of hospital visits.

If continue to receive chemotherapy, clinician should recommend that patients take prophylactic growth factors to help boost immune system and antibiotics to fight off any infections in order to make patients less vulnerable to serious complications of COVID-19.

Surgery:

In most countries, non-essential surgery is being postponed for the duration of the COVID-19 pandemic.

For patients with cancer, the potential risk of disease progression following a delay in surgery has to be balanced against the potential exposure to coronavirus and risk of serious complications from COVID-19.

In situations where **neoadjuvant therapy** (treatment given before surgery) is available but not routinely used (e.g. early-stage breast cancer), can offer neoadjuvant therapy as an alternative to upfront surgery (which could result in exposure to coronavirus) in order to delay your surgery. However, it's important to note that neoadjuvant therapy that is immunosuppressive or that requires clinic visits is also associated with a risk of infection and serious complications of COVID-19.

Therefore, clinician should discuss all of the options with patient to ensure optimal outcomes whilst minimising the risk of coronavirus infection.

Radio Therapy:

If patient have a rapidly progressing, potentially curable tumour, the risks of delaying radiotherapy may outweigh the risks associated with COVID-19 and so radiotherapy is likely to go ahead.

To reduce patient visits to the hospital, clinician should consider accelerated or hypo-fractionated radiotherapy schedules. This means that the total dose of radiotherapy is given over a shorter period of time or in fewer doses compared with standard radiotherapy.

A decision to alter or delay radiotherapy will only be made when medically justified and appropriate for patient. Clinicians should be able to discuss all of the options available to patient.

Endocrine Therapy:

Endocrine therapy does not suppress the immune system; therefore, it does not increase risk of severe COVID-19. This means it is usually safe to continue taking endocrine therapy during the pandemic.

Immuno Therapy:

If receiving immunotherapy, clinicians should adjust treatment schedule to reduce the frequency of hospital visits. It is important to note that immunotherapies can cause serious immune-related side effects; treatment-related pneumonitis is a particular concern as it may increase the risk of serious complications if patient develops COVID-19.

Stem cell transplant:

If patients are at high risk of serious complications from COVID-19, clinicians recommend delaying planned stem cell transplant, particularly if cancer is well controlled with other treatments.

There is currently no evidence to suggest that the new coronavirus is transmitted via blood transfusions, but in some areas potential stem cell donors should be tested for COVID-19 before stem cell collection. There may also be fewer stem cell donors available due to COVID-19 infection or logistical reasons (e.g. travel restrictions).

Association for Clinical Oncology announced an advocacy agenda for congress and the administration [4]. The agenda detailed 8 policy changes necessary to sustaining high-quality cancer through the remainder of COVID-19, including:

1. Continued support for telehealth and full reimbursement for audio-only visits.
2. Additional and immediate financial support for practices.
3. Passage of The Cancer Drug Parity Act, which would prohibit the currently unequal cost sharing between oral and IV drugs.
4. Action to prevent additional drug shortages.
5. Adapting clinical trials through models such as decentralization of trials.

Additionally, in order to re-establish cancer care following COVID-19, **American Society for Clinical Oncology (ASCO)** announced a "Road to Recovery" initiative, which they suggested will be informed by lessons learned in the current environment [5].

If patient develop symptoms of COVID-19, the medical priority should isolate and treat the COVID-19 infection rather than cancer. Cancer treatment will resume once recovered sufficiently from COVID-19.

Therefore, during the COVID-19 pandemic, the Benefit/Risk ratio of cancer treatment may need to be reconsidered in certain patients.

Two groups of patients:

"Patients off therapy" (A) who have completed a treatment or have disease under control (off therapy); and patients under treatment (neoadjuvant or adjuvant curative treatment or treatment for metastatic disease) (B) [10].

For all patients (A and B) it is mandatory to provide health education:

- a) Avoid crowded places;
- b) Wear PPE when you attend hospital for visits and treatments;
- c) Correctly wash your hands according to World Health Organization (WHO) indications;
- d) Do not have contacts with friends and relatives with COVID-19 symptoms or living in endemic zones;
- e) Guarantee social distancing with all people: protect yourself to protect others.

Special attention should be considered in case of recent new symptoms such as: Fever, Coughing, Sore throat, Difficulty breathing, Muscle pain, Tiredness, Anosmia, Dysgeusia. **In such situations, recommendations include:**

1. Test for confirmation if not already done
2. RT-PCR SRAS-CoV-2 testing should be proposed to all patients undergoing surgery, radiotherapy, chemotherapy or immunotherapy, if feasible and ideally before each treatment/ cycle
3. It should also be proposed to patients in follow-up or cancer survivors if they present with symptoms suggestive of COVID-19 infection
4. Serology (if available) should be proposed to identify previous COVID-19 infection in all cancer patients
5. If capacity is limited, RT-PCR SRAS-CoV-2 testing should be proposed to all patients with suggestive symptoms of COVID-19 infection, being in active treatment, in follow-up phase or a survivor
6. If serology is limited, it should be proposed to all patients undergoing surgery, radiotherapy, chemotherapy or immunotherapy, or any active anti-cancer treatment
7. Assess severity by clinical, radiological, lung function and biological tests
8. Evaluate the need for patients in terms of hospitalisation in

dedicated units

9. To minimise face-to-face contact, patient will be offered telephone or video consultations, particularly for pre-treatment meetings and follow-up appointments. If patient usually have blood tests done at a hospital, these may be relocated to a local centre instead. Medication may be delivered or a drive-through pick-up point may be arranged.
10. Repeat or electronic prescription periods are also being extended in many areas to allow patients to access their home-based cancer treatment (e.g. oral treatments) without the need for additional prescribing appointments during the pandemic [10].

Despite the relative scarcity of the available data due to the novelty of the SARS-CoV-2, it remains clear that the majority of experts recommend focusing on infection management over cancer management. It should be noted that most of the currently available articles used the data from Liang et al. and as Xia et al. pointed out, there are multiple issues with that study [8,9].

Clinicians should keep reporting any cases of cancer patients infected with SARS-CoV-2, their management, and the outcome in order to further our understanding of this complex issue.

CONCLUSIONS:

The outbreak of coronavirus disease 2019 (COVID-19) is of international concern. The currently available evidence seems to suggest that COVID-19 Pandemic is heavily impacting Cancer Care.

Attending hospital during the COVID-19 pandemic can put patient at risk of infection. Therefore, to keep patient safe, cancer care should be adapted while the pandemic is ongoing. It is quite possible that clinicians end up under treating a few patients which may compromise cancer outcomes in the long run, but this must be weighed against the clear threat from the COVID-19 which may also increase deaths short-term.

Reassessment of the relative risks and benefits of cancer therapies in the context of the COVID-19 pandemic is fundamental to the continued safe delivery of oncology management. Every effort should be made to avoid compromising the delivery of evidence-based cancer care when infection risks are outweighed by the benefits of treatment.

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