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Challenges for Cancer Care During the Coronavirus Disease 2019 Pandemic

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Abstract

With this current pandemic, it is crucial to synthesize information that will be useful to frontline healthcare providers, particularly our nurses who are taking care of vulnerable populations. This short commentary describes the common manifestations and current management of COVID-19 infection based on recent publications, aiming to equip nurses and other healthcare providers, especially those taking care of cancer patients, with basic information about the signs and symptoms of COVID-19 infection and updated practice recommendation.

Keywords: COVID-19, Cancer, Coronavirus

Introduction

In early 2020, the World Health Organization (WHO) officially recognized the novel coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2) that causes the coronavirus disease 2019 (COVID-19).[1] Since the first known case of atypical pneumonia was reported on November 16, 2019 in China,[2] there have been nearly 200 million confirmed cases with more than 4 million deaths worldwide.[3] The most recent meta-analysis of immunocompromised patients (e.g., cancer patients, organ transplant patients) have higher rated of hospitalization and poorer hospital outcomes compare to general population.[4] The risk of death in cancer patients who were older than 60 years old was 47% if hospitalized with COVID-19.[5] The outbreak of this novel virus has created an enormous clinical and public health crisis. While an army of nurses and healthcare providers on the frontlines is fighting against this pandemic, scientists and researchers are working on increasing our understanding of the virus, clinical features and its impact on individual's health and the healthcare system.

While everyone is at risk for contracting COVID-19, there are serious concerns for patients with cancer and cancer survivors. Cancer patients are more vulnerable than the general population to severe COVID-19 infection due to their immunocompromised states from cytotoxic treatments.[6] Given the high severity and infection rates of SARS-Cov-2, recommendations have been put forward by several organizations for patients with cancer,

based on past experiences with this virus. Activities including face-to-face consultations with caregivers and visitors present were remodulated to ensure that cancer patients were not exposed to SARS-CoV-2. A recent study found that nearly 90% of cancer centers faced challenges in providing cancer care.[7] The COVID-19 vaccines are being distributed with more than 3 billion doses administered to date worldwide.[3] However, some countries are facing with vaccines shorting and distribution challenges. In Southeast Asia, percent of fully vaccinated people per country population range from 0.3% (Vietnam) to 49.8% (Singapore).[8] Majority of countries in this region has less than 10% vaccination Myanmar (2.9%), Timore-Leste (3.2%), Philippines (4.5%), Brunei (4.8%), Thailand (5.1%), Indonesia (6.1%) and Laos (9.1%).[8] The reports of new variants and mutations are concerning. The duration and course of this pandemic are uncertain, so it is important to ensure the efficient delivery of cancer care. This commentary provides an overview of what we have learned about COVID-19, its impact on the people with cancer, and existing practice recommendations.

Manifestations of COVID-19

The list of distinct symptoms observed in people infected with COVID-19 include fever, shortness of breath, dry cough, loss of sense of taste and smell.[9–11] In addition, some may report chest tightness, diarrhea, and myalgia.[12,13] Severe signs associated with COVID-19 infection include an observable lung abnormality from computerized tomography (CT) images[12,14,15] and thromboembolism from the fibrinolysis shutdown and hypercoagulation, especially among patients with severe/critical COVID-19.[16–19] Fifty percent of hospitalized COVID-19 patients have thromboembolism either on admission or within the first 24 hours of hospitalization.[20] The underlying mechanism of this thromboembolic state is unclear. Autopsies of patients with COVID-19 have shown diffuse microthrombi in the kidneys and lungs, leading to organ failure and death.[21] The incidence of thromboembolic events is associated with poor clinical outcomes. The Chinese Center for Disease Control (CDC) divided clinical manifestations of COVID-19 infection into mild disease with none to mild pneumonia (approximately 81% of the cases), moderate disease with fever, respiratory distress, and hypoxia (14% of the cases), and severe/critical disease with respiratory and multiple organ dysfunction (5% of the cases).[2,22]

The Risk for Oncology Patients

A study of COVID-19 patients in Asia revealed that approximately 1% of cases (n=1,590) had cancer or a history of cancer (Liang et al., 2020). Compared to non-cancer COVID-19 patients, patients with cancer were older and had a history of smoking (22%). Liang and colleagues (2020) reported that cancer patients had 30% more risk of severe events (defined as being admitted to the intensive care unit, or requiring invasive ventilation, or even death) compared to non-cancer patients (seven [39%] of 18 patients vs 124 [8%] of 1,572 patients; Fisher's exact p=0.0003). Moreover, the conditions of COVID-19 patients with cancer deteriorated faster to an average of 13 days compared to 43 days in non-cancer patients (p <0.0001).[11] A systematic review and meta-analysis of 15 COVID-19 studies from Asia, United Kingdom, Europe, United States, and Canada (total 3,019 patients) reported similar findings that the case mortality rate of COVID-19 patients with cancer (23.4%) was higher than COVID-19 patients without cancer (5.9%).[6]

Earlier in the pandemic, several studies found associations between recent cancer treatment with COVID-19 severity and death;[23–25] however, a recent meta-analysis found no association between increased risk of severity or mortality and the receipt of anti-tumor treatments, including immunotherapy,

hormonal therapy, or radiotherapy in the months before COVID-19 infection.[26]

Clinical Practice Recommendations for Prevention

In response to these published data, many medical organizations have instituted procedures to reduce the risk of COVID-19 infection in cancer patients. It is important to note that those currently undergoing cancer treatment, or even those with a history of cancer, are more likely immunocompromised and more susceptible to infections. Many groups of oncologists developed clinical guidelines for anti-cancer treatment decision-making. Specifically for radiotherapy, a group of radiation oncologists from the United States and the United Kingdom conducted a systematic review and recommended a RADS (remote visits, avoidance, deferral, and shortening) framework to be used for radiotherapy during the pandemic.[27] The group recommended that all hospital visits be transitioned to telehealth visits using phone and/or video calls; active surveillance, deferral, and that shortening of the treatment should be considered based on the patients' clinical condition, safety, and cancer staging.

International collaborative groups of oncologists have recommended that cancer patients on active anticancer treatment should remain vigilant for COVID-19 symptoms.[28] The infection prevention measures recommended by the Centers for Disease Control and Prevention (CDC), including frequent and proper hand hygiene, maintaining physical distancing (6 feet), covering of mouth and nose, and that frequent cleaning and disinfecting of touched surfaces should be routinely followed in all cancer centers.[29] A radiotherapy center in China reported using "infection control zoning" and a new radiotherapy workflow to manage and screen patients and caregivers.[30] They partitioned and labeled the clinical area into (a) clean zone (e.g., administrative offices, staff area, and dosimetry offices); (b) semi-contaminated zones (e.g., patients waiting areas); and (c) contaminated zones (e.g., front desk, mold room, CT room, console areas, and treatment vaults, etc.). In addition to following the CDC guidelines for staff training, use of personal protective equipment, and surface disinfection, Wei and colleagues (2020) suggested that the new radiotherapy workflow include masks and temperature checks for all patients and caregivers entering the medical areas. A chest CT and a nucleic acid amplification test (nasopharyngeal or oropharyngeal swabs) for COVID-19 are performed for all patients and caregivers. Patients with confirmed positive tests for COVID-19 infection will be referred to the designated COVID-19 units.[30] In the outpatient units, patients who received daily treatment will have a daily physical examination to ensure that all clinical indices are within the normal limits (blood oxygen saturation $\geq$ 95% and temperature <37.3 C).[30] For cancer patients with positive tests for COVID-19, a group of German and Dutch radiation oncologists recommended that treatments should only be postponed, interrupted, or terminated for COVID-19 positive patients who are critically symptomatic, while those with asymptomatic or mild symptoms can continue the treatment as planned.[31] However, other precautionary measures should be employed to minimize the risk of transmission to other patients and medical staff. In April 2020, the National Comprehensive Cancer Network (NCCN) published the "NCCN Best Practice Guidelines on Management of COVID-19 Infection in Patients with Cancer" based on the guidelines published previously by other specialty societies and organizations.[32] These guidelines discussed recommendations in several areas including

1. COVID-19 testing. NCCN recommended Reverse Transcription Polymerase Chain Reaction (RT-PCR) test to be performed in acute symptomatic

patients. Positive Antigen testing must be confirmed with the RT-PCR and serology testing is not currently recommended for cancer patients.

2. Isolation and precautions. Recommendations include
    a. All cancer patients regardless of COVID-19 status should wear a face marks when interacting with the health care providers and others. N95 respirators are required for health care providers when performing aerosol generating procedure.
    b. Hospitalized cancer patients with COVID-19 should be isolated in the negative pressure room or single-person room with dedicated bathroom and close door (if negative pressure rooms are limited). If the single rooms are not available, cohorting patients with confirmed COVID-19 is acceptable.
    c. Isolation and precaution can be discontinued 10 days after the symptom onset and resolution of the fever without fever reducing medication for at least 24 hours. Immunocompromised patients (e.g., receiving intensive chemotherapy, prolonged neutropenia) may require up to 20 days after COVID-19 symptom onset.
    d. Same as recommendation for general population, cancer patients who have a significant exposure to a person with known COVID-19 will require a14 days quarantine.
3. The recommendations for cancer treatments for SARS-CoV-2-positive patients are based on type of cancer and symptoms severity.
    a. Hematologic cancer patients
        i. mild/moderate symptoms: Chemotherapy should be delayed until symptoms resolve and at least 10 days after symptoms onset
        ii. Severe symptoms: chemotherapy should be delayed until all symptoms are resolved and at least 20 days after symptoms onset.
    b. All other type of cancer and asymptomatic patients. Chemotherapy should be delayed for a minimum of 10 days after the first positive RT-PCR test for SARS-CoV-2 RNA. However, the treatment should be administered without delay at the judgement of attending physician if the cancer treatment is urgently needed to control cancer.
4. Treatment for COVID-19 among cancer patients. NCCN recommended the use of the following treatment
    a. Monoclonal antibody products (e.g., bamianvimab, imdevimab, casirivimab, etesevimab) for outpatients with mild and moderate COVID-19 symptoms who are at risk of severe disease (e.g., undergoing chemotherapy, older than 65 years old, diabetes) only. These products are not recommended for asymptomatic and hospitalized patients.
    b. Antiviral medication (e.g. Remdesivir) is recommended for hospitalized patients with pneumonia and hypoxia who are not requiring mechanical ventilator or extracorporeal membrane oxygenation (ECMO). a Janus kinase JAK inhibitor drug such as barcitinib can be considered as an addition to the remdesivir.
    c. Glucocorticoids (Dexamethasone 6 mg/day or prednisone 40 mg/day or hydro-

cortisone 150 mg/day x 10 days) are recommended for cancer patients hospitalized for COVID-19 pneumonia with hypoxia with caution in those with diabetes mellitus.

d. Convalescent plasma can be considered as a adjunctive treatment for hospitalized patients especially in patients who have impaired antibodies production.

5. COVID-19-related complications in cancer patients: Co-infections including fungal infection or COVID-19-associated pulmonary aspergillosis (CAPA), bacterial infection (e.g., *Mycoplasma pneumoniae, Pseudomonas aeruginosa, Haemophilus influenzae, Staphylococcus aureus, and Streptococcus pneumoniae),* viral infection (e.g., influenza A or B, Respiratory Syncytial Virtus [RSV], rhinovirus, enterovirus, and others) should be routinely monitored and treated.

Recovering and Symptom Management

After the acute onset (4 weeks following the onset of symptoms or a RT-PCR-positive test), patients are encouraged to resume their daily activities, as tolerated. Persistent physical symptoms such as fatigue, dyspnea, chest pain, cough, and psychological and cognitive complaints such as anxiety, depression, poor memory, and concentration were commonly reported by COVID-19-recovered patients.[33] The regular assessment of the patient's symptom severity, duration, and trajectory is important to determine the timing, frequency, and type of follow-up assessment and management. Most management is based upon the management of symptoms following similar illnesses. The following are current management guidelines for these common persistent symptoms.

Fatigue and weakness: Fatigue is the most common symptom experienced by COVID-19 survivors, which can last for longer than 3 months in some patients. The profound fatigue may impact exercise capacity and functional status. General guidelines for managing persistent fatigue include energy conservation, adequate rest, good sleep hygiene, maintaining nourishment and hydration, and performing regular light physical activity.[34]

Shortness of breath/dyspnea: In addition to pharmacotherapy for underlying cardiac or pulmonary disease, breathing exercises (deep breathing and pursed-lip breathing exercises) are recommended for patients with a Borg score ≤ 3 (mild symptoms without cardiac etiology).[35] Moreover, positions such as high side lying, forward lean sitting, forward or backward lean standings are recommended to help with difficulty breathing.[36]

Chronic cough: Most clinicians use supportive therapy including cough suppressants (e.g., dextromethorphan) and inhaled bronchodilator or glucocorticoids, as needed. Some nonpharmacological interventions such as hydration, steam inhalation, warm honey, and lemon can help with the cough.[36]

Cognitive impairment: Some COVID-19 survivors have reported memory and concentration problems. While this cognitive impairment can be temporary and minor, it may indicate more severe neurological and neurocognitive complications of acute COVID-19. Therefore, some clinical settings screen for cognitive impairment using the Montreal Cognitive Assessment (MoCA) to assess the attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation, and refer patients for neuropsychological evaluation when the scores indicating moderate to severe cognitive impairment (i.e., score <18).[35]

Altered taste and smell: These symptoms resolve slowly over several weeks without intervention; however, in some cases, education regarding food and home safety may be needed. Especially home isolated patients who may not smell the gas leakage or smoke

and may not be able to differentiate the taste of rotten foods and drinks or contamination of hazardous chemicals in foods or drinks

Insomnia: Post-COVID-19 sleep disturbance is common. Sleep hygiene consultation, relaxation technique, and stimulus control are recommended.[35]

Psychological and emotional issues: Evaluation of mood, anxiety, isolation, and stress levels is vital to determine appropriate management. In 2020 and 2021, many studies are investigating the effectiveness of various intervention both online and home visits on COVID-19 psychological and emotional issues including mindfulness meditation, exercise, online consultation, however, it is too early to report the results of these clinical trials.

Coronavirus Vaccine and People with Cancer
Although there are limited data for COVID-19 vaccines in patients with cancers, patients with cancer are at increased risk of complications from COVID-19 infection. The NCCN COVID-19 Vaccination Advisory Committee recommends that cancer patients, caregivers and household/close contacts should be immunized when any vaccine has been authorized for use by the Food and Drug Administration (FDA) is available to them, with the specific recommendation to delay vaccination at least 3 months after receiving hematopoietic cell transplantation (HCT) or engineered cellular therapy (e.g., chimeric antigen receptor [CAR] T-cells), and vaccination at least a few days before or after surgery[37]

Currently available vaccines have been shown to be safe and effective in the general population.[38] The most common side effects of most COVID-19 vaccines include local injection site pain, fever, chills, myalgias, headaches, and fatigue.[38] These symptoms usually resolve in a few days. To date, there is no report on unique or significant adverse events of any vaccines specifically to the immunocompromised patients, which would require a specific guideline for this population. However, in some patients, palpable unilateral axillary and cervical lymphadenopathy may occur. Lymphadenopathy is a known side effect of vaccines such as influenza and human papillomavirus vaccine. The reported rate among patients who receive mRNA vaccines (Pfizer/BioNTech, Moderna) is higher.[39] Among cancer patients, to avoid potential unnecessary concerns on disease progression, the NCCN advisory committee recommends the delay of imaging studies by 4-6 weeks after receiving the second dose of COVID-19 vaccine, especially the mRNA vaccine, and documenting the vaccination date, injection site and vaccine type in the medical record.

Conclusion

Since this COVID-19 pandemic is on-going and ever-changing, we expect more articles and research findings to advance our understanding of the short- and long-term consequences of COVID-19 infection, especially among the most vulnerable, such as patients with cancer. It is imperative to continue synthesizing available information to assist nurses and other healthcare providers as we continue to address and mitigate this common, existential threat.

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