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· Review Article ·

Management of cancer patients during the COVID-19 pandemic: A narrative review

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Abstract **Objective:** We wrote this review with the objective of helping the physicians to manage patients with cancer during the COVID-19 pandemic. **Background:** In the absence of specific curative treatments, COVID-19 exerted worldwide a dramatic impact on public health and socio-economic aspects. Patients with cancer represent a vulnerable population when suffering from COVID-19 infection since they usually present a series of risk factors such as immunosuppressed state, older age, comorbidities (e.g., cardiovascular diseases, chronic lung disease, diabetes) and need for frequent hospitalizations and visits. A series of observational studies demonstrated that cancer patients infected with COVID-19, particularly with lung cancer, have a high rate of morbidity and mortality. **Methods:** We conducted a review of several observational studies and guidelines regarding the management of cancer patients in the context of COVID-19 infection. **Conclusions:** The oncologists, according to the main available recommendations, should carefully weigh risks/benefits when planning therapies and follow-up visits. They should defeat the "distraction effect" of the pandemic, which is represented by the risk of shifting attention away from standard therapeutic approach to COVID-19 only. In addition, health authorities should prioritize COVID-19 vaccinations for cancer patients with the aim of limiting the consequences of the pandemic in this particularly frail population.

Keywords COVID-19 pandemic; guidelines; cancer patients

At the beginning of 2020 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19) has reached pandemic levels. Among other reasons the absence of specific treatments notably led COVID-19 to exert worldwide a dramatic effect on public health and socio-economic aspects. Considering that the virus can spread via direct contact and respiratory droplets, in each country not only health care workers but everyone was recommended by national healthcare authorities to use personal protective equipment (PPE), as well as practicing frequent hand hygiene, environmental disinfection and cleaning, maintaining physical distances and averting unprotected contacts with persons presenting respiratory symptoms or fever. In this context patients with cancer represent a particularly vulnerable population since they usually present a series of risk factors such as immunosuppressed state, older age, comorbidities (e.g., cardiovascular diseases, chronic lung disease, diabetes) and need for frequent hospitalizations and visits. As we shall see later, a series of observational studies demonstrated that cancer patients, notably with lung cancer, have a high rate of morbidity and mortality when suffering from COVID-19 infection[1-2]. We wrote this review with the

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objective of helping the physicians to manage patients with cancer during the COVID-19 pandemic.

We present the following article in accordance with the Narrative Review reporting checklist (available at http://dx.doi.org/10.3978/j.issn.2095-6959.2021.08.001).

1 Methods

Information used to write this review was collected from several sources such as PubMed search, Embase and Web of Sciences using the following search terms: COVID-19 pandemic, guidelines, cancer. We evaluated the publications that were available on those databases up to April 30, 2021. We also considered data published online by several scientific associations of oncology.

2 Discussion

Chinese researchers were the first ones to observe that cancer patients infected with COVID-19 have poorer clinical course and prognosis than persons without cancer[3-5]. A subsequent analysis from the Italian national medical council reported the presence of 16.3% of cancer patients among the patients who have died from COVID-19[6]. Another study published by American researchers confirmed a high mortality rate among cancer patients with COVID-19[7]. More recently, a large report from the COVID-19 and Cancer Consortium (CCC19) including about 5,000 cancer patients with confirmed COVID-19 diagnosis, evaluated the correlation of clinical factors and antineoplastic therapies with COVID-19 severity[8]. In particular the authors observed that a series of clinical factors (e.g., obesity, male sex, older age, pulmonary and cardiovascular comorbidities, worse ECOG performance status, hematological malignancy, recent chemotherapy) and laboratory measurements (e.g., high neutrophil count, low or high lymphocyte count, low platelet count, abnormal troponin, LDH and creatinine) were associated with poor outcomes; they also suggested that caution should be adopted in administering particular antitumor therapies in these patients. A cohort study on 1,035 patients included in the CCC19 database found that the 30-day all-cause mortality was 13% in patients with prior or active cancer and COVID 19 infection[1]. The main factors correlated with a higher 30-day mortality were hydroxychloroquine plus azithromycin therapy, older age, male sex, former smoking status, comorbidities, ECOG performance status ≥2 and active cancer. The TERAVOLT study recruited 200 patients with thoracic malignancies mainly from Italy (76% with NSCLC, 74% while receiving an active anticancer treatment), with either confirmed or suspected COVID-19 infection[2]. The authors recorded high mortality (33%) and low admission to intensive care unit (only 10% of patients who met criteria for intensive care unit admission) in these patients. A pooled analysis of more than 50 registries published by Saini *et al*. reported a mortality of 25.6% in cancer patients with COVID-19[9]. Another recent meta-analysis including 16 studies (>4,000 patients) showed that delivering chemotherapy within one month of COVID-19 diagnosis may increase the mortality in cancer patients, while there was no safety concern for targeted therapies, immunotherapy, radiotherapy or surgery[10]. Finally, a large observational study evaluated the impact of the currently available COVID-19 treatments in cancer patients[11]. In this study only remdesivir demonstrated a potential benefit, while hydroxychloroquine or high-dose corticosteroids didn't show any significant 30-day mortality improvement.

In order to help physicians in their clinical practice several scientific associations developed peculiar guidelines or recommendations regarding the management of patients with cancer during the COVID-19 pandemic[12-16] (Table 1). First of all, cancer patients that are positive for COVID-19 should be admitted to specialized COVID units and not into oncology departments that, instead, should remain COVID-19 free zones. All healthcare professionals, patients and visitors should use PPE (masks, gloves, etc.). In addition, with the aim to limit the presence of patients in the hospital, several measures should be encouraged, such as the following ones: increase the use of telemedicine or phone calls, replacement of intravenous therapies with oral drugs or subcutaneous anticancer agents, adjustment of dosing schedules of chemotherapy or radiotherapy. To establish the intent of the anti-cancer treatment, the English National Institute for Health and Care Excellence (NICE) introduced a priority scale with six levels: level one includes curative treatments with more than 50% chance of success, while level 6 is reserved for palliative therapies[13]. Prioritisation decisions should

be adopted by a multidisciplinary team and should be clearly communicated to patients and their families. In case of COVID-19 positive patients, NICE suggests to continue systemic anticancer treatment only if it is necessary for an urgent control of the disease, otherwise it's advisable to wait for at least one negative test for COVID-19. The European Society of Medical Oncology (ESMO), recommends discussing with patients receiving active treatment the pros and cons of the therapy and identifying specific pathways to establish the timing of the treatment (e.g., prioritize adjuvant therapies in patients with a high-risk of recurrence)[14]. In addition, ESMO suggested a tiered approach for the categorization of patients into three levels of priority (high, medium and low) to receive cancer therapies during the COVID-19 pandemic. High priority indicates a life-threatening condition that requires an early intervention, while low priority is dedicated to patients with a stable clinical condition that do not require immediate attention or treatment. ESMO, as well as other scientific societies, released also statements to address the main issues and concerns about the use of vaccinations against COVID-19 in cancer patients[17-19]. In particular, according to ESMO recommendations, all cancer patients should receive COVID-19 vaccination with the aim of reducing their mortality; furthermore, patients receiving anticancer treatment should deserve a priority level in case of limited availability of vaccines.

Table 1 Summary of the main recommendations regarding the management of patients with cancer during the COVID-19 pandemic

Recommendations for physicians
Keep oncology units "COVID-19 free zones"
Increase the use of telemedicine/phone calls
Adopt a tiered approach for the categorization of patients into different levels of priority to receive active cancer treatment
Replacement of intravenous drugs with oral drugs
Weigh risks/benefits when planning cancer therapies and follow-up visits
Prioritize COVID-19 vaccinations for cancer patients
Defeat the "distraction effect" of the pandemic
Recommendations for patients
Limiting the access to the hospital for patient accompanists
Do not cancel monitoring visits, screening tests and administration of therapies
Recommendations for physicians and patients
Use of personal protective equipment (masks, gloves, etc.)
Frequent hand hygiene, environmental disinfection and cleaning
Repeal of unprotected contacts with persons with fewer or respiratory symptoms

3 Conclusions

It is proven that cancer patients have a high rate of morbidity and mortality in the context of COVID-19 infection. For all these reasons the oncologists, according to the main currently available specific guidelines, should carefully weigh pros and cons when planning anticancer therapies and follow-up visits and should defeat the "distraction effect" of the pandemic in order to reduce any possible deviations from the standard clinical approaches especially in cases of curative therapies[20]. Moreover, health authorities should prioritize COVID-19 vaccinations for these patients with the aim of limiting the effects of the pandemic in this particularly frail population.

Finally, the COVID-19 pandemic has also highlighted the limits of an individualistic society. For a long time, many people have thought only about themselves, forgetting the others: the pandemic should finally teach us that nobody saves themselves alone.

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Footnote

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