Cancer in the context of COVID-19: Summary of emerging evidence (14)

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The CRI presents a selection of emerging research articles and clinical practice guidelines related to cancer and COVID-19, with a summary of their key findings/recommendations (links to the articles are embedded as hyperlinks in the titles). This is the 14th of our weekly compilation, which we plan to update and disseminate as the pandemic evolves globally and nationally.

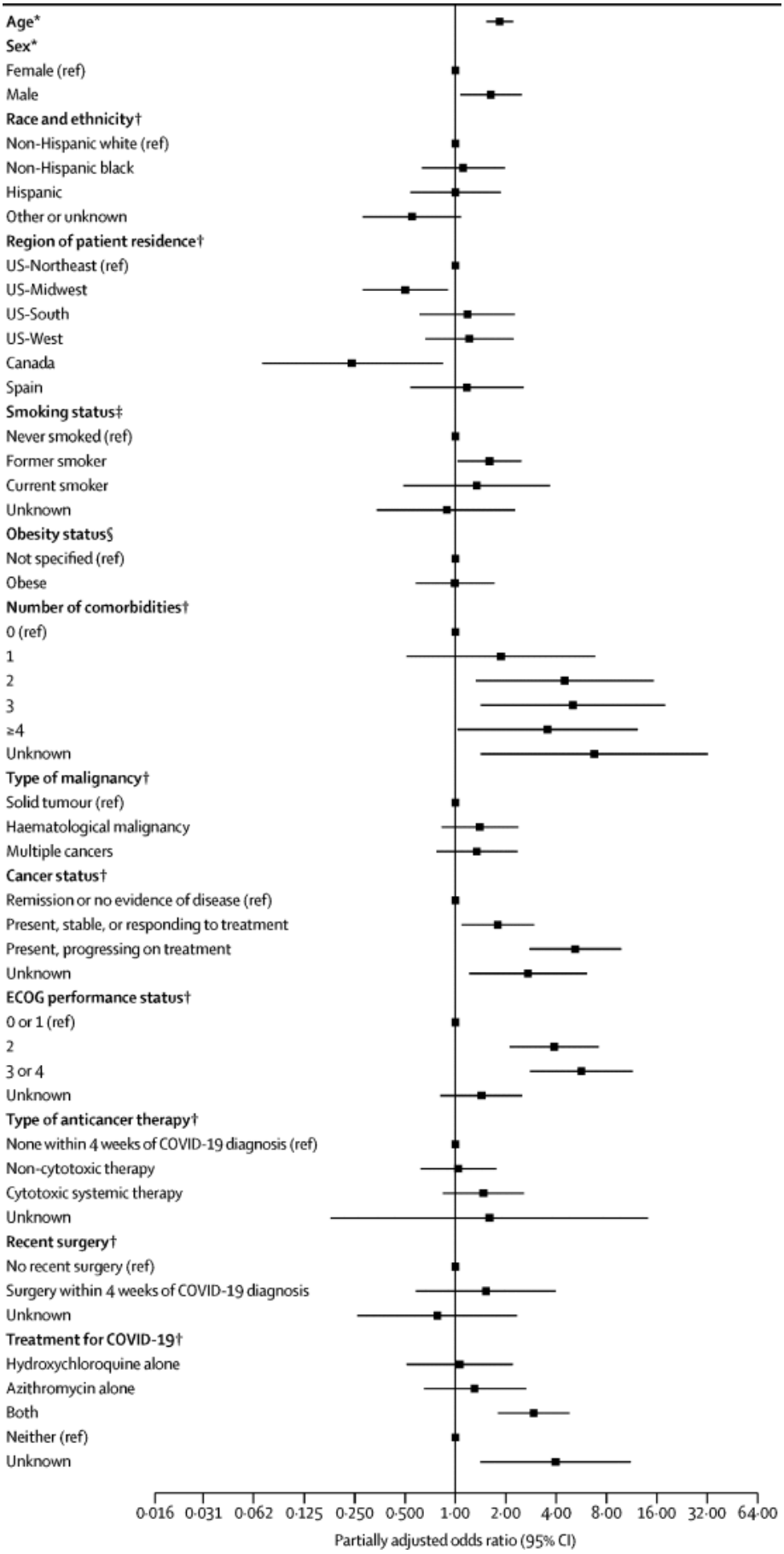
This week, we highlight the latest research and evidence related to oncology services in COVID-19 outbreak contexts globally, with a focus on African and other low- and middle-income country (LMIC) contexts. We hope that insights from these pieces of evidence will help guide how we rethink cancer prevention, treatment and care in the context of the ongoing pandemic, in view of its unprecedented implications for patients, healthcare providers and the community in general. We are keen to include research and guidelines from African and other low- and middle-income settings and will profile these as they become available. Previous weeks' editions can be found on the **CRI website,** as well as on **our Twitter page (@UctCri)**.

Kuderer et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. The Lancet. DOI: 10.1016/S0140-6736(20)31187-9.

Country Context: USA, Canada, Spain

This cohort study characterises the outcomes of a cohort of patients with cancer and COVID-19 and identify potential prognostic factors for mortality and severe illness. A total of 928 patients met inclusion criteria for the study. Their median age was 66 years, 30% were aged 75 years or older, and 50% were female. The most prevalent malignancies were breast (21%) and prostate (16%) cancer. About 40% were on active anticancer treatment, and 43% had active (measurable) cancer. Within the follow-up period, 121 (13%) patients had died. Independent factors associated with increased 30-day mortality were: increased age, gender, smoking status,, number of comorbidities, Eastern Cooperative Oncology Group performance status, active cancer (progressing *vs* remission), and receipt of azithromycin plus hydroxychloroquine (*vs* treatment with neither). The figure below is a Forest plot of factors associated with 30-day all-cause mortality in the cohort:

Forest plot of factors associated with 30-day all-cause mortality

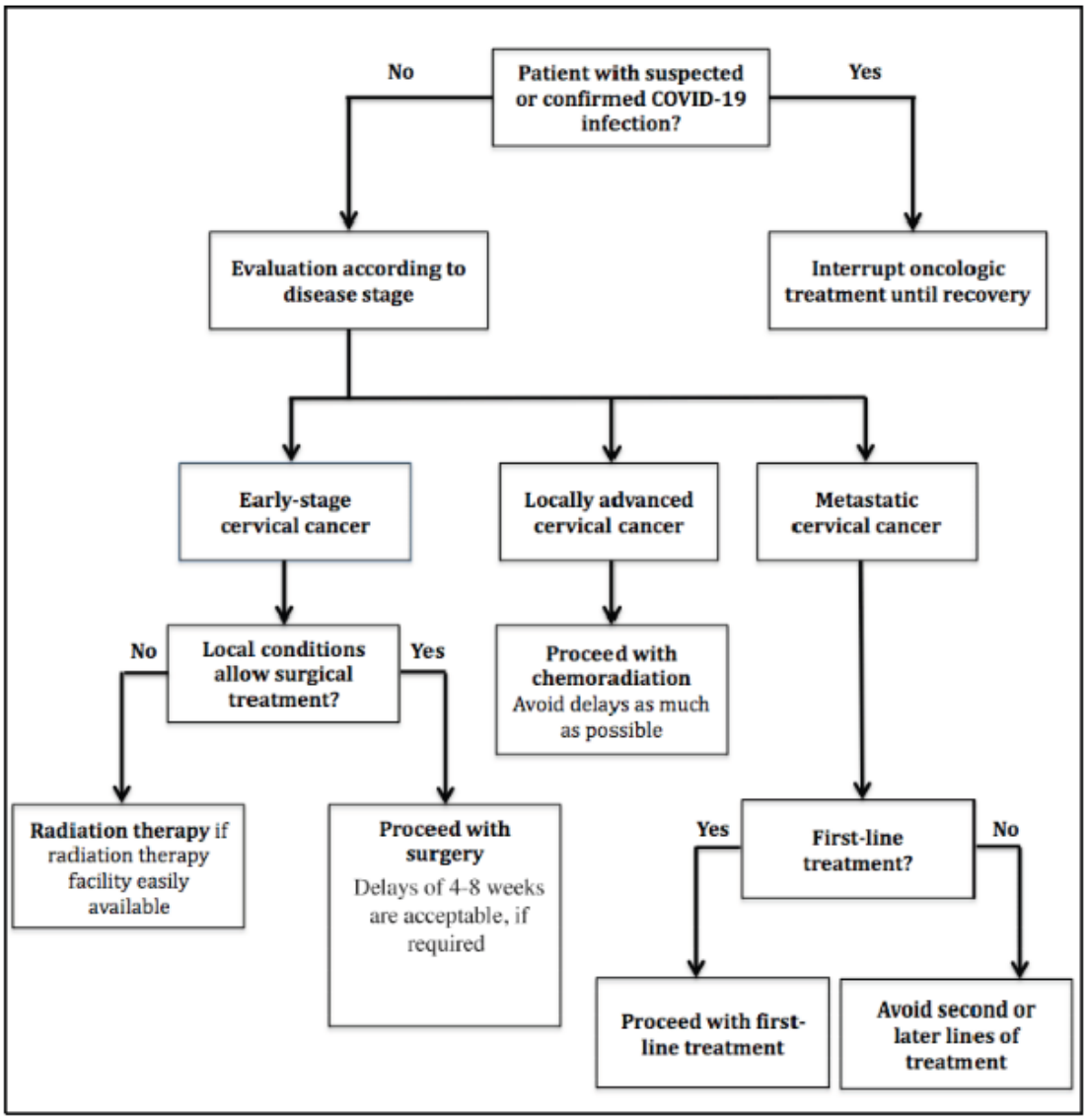


Estevez-Diz et al. Management of cervical cancer patients during the COVID-19 pandemic: a challenge for developing countries. Ecancer. DOI: 10.3332/ecancer.2020.1060

Country Context: LMICs

In this review paper, the authors discuss the cervical cancer landscape in LMICs and provide recommendations for its management during the COVID-19 pandemic. Generally, they recommend that whenever possible, cancer treatment should be done in the outpatient setting to avoid unnecessary hospitalisations; and that treatment interruptions should be considered for patients with active COVID-19 infection until recovery with resolution of symptoms, especially in cases of immunosuppressive treatments such as cytotoxic chemotherapy**.** They consider localised, potentially curable cervical cancers (stages I-IVA) as cancer treatment priorities. The flowchart below illustrates the authors' recommendations for the management of cervical cancer patients on active treatment during the COVID-19 pandemic:

Recommendations on priority and non-priority procedures for cervical cancer management during COVID-19 pandemic.



Elzembely et al. Providing Care for Pediatric Cancer Patients in the COVID-19 Era: Rapid Response Recommendations From a Developing Country. Pediatric Blood and Cancer. DOI: 10.1002/pbc.28467

Country context: Egypt

In this editorial correspondence, the authors propose a framework for managing paediatric cancer in the COVID-19 era within developing country contexts. It makes the following recommendations:

Screening and surveillance: All patients and their caregivers should be screened. Suspected cases should be immediately isolated in an area separate from other patients. Medical workers caring for isolated patients should not care for regular patients in the oncology ward.

Social distancing: Should be applied through isolating patients in separate rooms and if not possible arrange patients' beds with 2 meters distance at least; only one caregiver is allowed during hospital admission or in outpatient clinic; no visitors are allowed; and keep patients in the waiting area by at least 2 meters distance.

Prioritisation of paediatric cancer care: For newly diagnosed cases, patients should proceed with their diagnostic procedures without delay. Diagnostic procedures should be performed as an outpatient procedure unless otherwise required by the treating physicians. For patients on active curative treatment, modification of the treatment protocols is required to decrease hospitalisation and neutropenia duration without survival impairment.

Acute lymphoblastic leukemia: Patients should be treated according to the modified St. Jude total XV protocol. Specifically, the authors propose:

- Giving granulocyte colony stimulating factors (GCSFs) during induction chemotherapy if BMA at day 19 is in complete remission and after induction chemotherapy.
- Delaying consolidation and giving weekly methotrexate (MTX)/6-mercaptopurine (MP) for two weeks as interim continuation if BMA at the end of induction is minimal residual disease (MRD) negative.
- During consolidation, reduction of the 6 MP dose by 50% with a close assessment of total leucocytic counts.
- During continuation: specific treatments quidelines are provided for low- and high-risk patients.

Acute myeloid leukemia (AML): Patients should be treated according to the modified St. Jude AML 02 protocol, with the following specific recommendations:

- Induction chemotherapy: Omit etoposide so that induction consists of Ara-C and doxorubicin based on the Medical Research Council AML 15 clinical trial.
- The use of G-CSF during induction chemotherapy and 24 hours after chemotherapy if BMA at day 15 less than 5%.

Non-Hodgkin lymphoma including mature B ALL: the use of growth factors preemptively 24 hours after the completion of chemotherapy is recommended.

Hodgkin lymphoma, classic type: Patients should be treated according to the EuroNet-PHL-CI clinical trial. The use of OEPA and COPDAC chemotherapy as multiple-day regimens on outpatient basis is also recommended.

Solid tumors: The following are recommended:

- Use of growth factors preemptively 24 hours after the completion of chemotherapy.

- Shift of chemotherapy protocols as a daycare outpatient therapy if possible, without endangering patients with possible adverse effects as nephrotoxicity.
- Delay all therapies beyond first-line therapy unless there is an urgent clinical situation.
- Delay imaging procedures to monitor response to treatment unless an urgent clinical condition.

Patients on palliative care therapy: Palliative care patients need to be evaluated case by case as delay in care may result in more suffering and subsequently more hospitalisation.
Follow-up patients: Disease-free patients should not visit the hospital. Where feasible, use telemedicine for communication with pediatric cancer survivors.

Parasole et al. Collateral effects of COVID-19 pandemic in pediatric hematooncology: Fatalities caused by diagnostic delay. Pediatric Blood and Cancert. DOI: 10.1002/pbc.28482
Country context: Italy
In this letter to the editor, the authors share their experiences on how paediatric hemato-oncology services are being affected in the context of a COVID-19 outbreak. They report that paediatric emergency services rendered in March 2020 were only one-fifth of those registered in the same month in 2019. They illustrate the cases of three children who arrived at the hospital with life-threatening conditions at the onset of acute lymphoblastic leukemia (ALL). The children had presented late and arrived at the hospital in critical conditions, most likely as a consequence of fear of COVID-19 and movement restrictions. Sadly, two of them had fatal outcomes. Based on these, and considering the relatively lower risks of COVID-19 incidence, morbidity and mortality in children, the author are of the view that delays in diagnosis, chemotherapeutic treatments, and treatment of chemotherapy complications are collateral effects of the pandemic, which may be worse than those posed by the disease (COVID-19) itself.

Fregatti et al. Breast Cancer Surgery During the COVID-19 Pandemic: An Observational Clinical Study of the Breast Surgery Clinic at Ospedale Policlinico San Martino - Genoa, Italy. In Vivo. DOI: 10.21873/invivo.11959
Country context: Italy
This study assessed the effectiveness of a patient-tailored, healthcare resource re-allocation programme for the prevention of COVID-19 infection among patients with breast cancer undergoing surgery and healthcare workers (HCWs). A total of 91 patients were selected for elective surgery by means of: i) Pre-hospital screening aimed at avoiding hospitalisation of symptomatic or suspicious COVID-19 patients, and ii) prioritisation of surgical procedure according to specific disease features. Most of the patients (93.4%) were fit for surgery, while the rest were temporarily excluded through triage. Of the patients who were fit for surgery, 83.5% were diagnosed with invasive cancer, most of whom were undergoing breast-conserving surgery. The mean in-hospital stay was 2.2 days. After hospital discharge, no patient needed re-admission due to post-operative complications; moreover, no COVID-19 infection among patients or HCWs was detected. The authors conclude that his preliminary clinical experience shows that elective breast cancer surgery can be safely pursued with careful preservation of both patient and HCWs health status.

Abratt R. Patient care and staff well-being in oncology during the coronavirus pandemic – Ethical considerations. South African Journal of Oncology. DOI: 10.4102/sajo.v4i0.129

Country context: South Africa

This editorial discusses some of the ethical issues related to considerations for modifying oncology treatment and care practices, such as the use of hypofractionation, triaging and rationing of cancer treatment services during the pandemic.

The author suggests the following principles for guiding critical decision making:

- Medical insights are required to both tailor treatments and balance available resources. A structured approach towards medical benefit might use a priority points system and consider benefit in terms of 'life years' gained.
- Binary decisions should be avoided as much as possible. Time often brings clarification as we understand the trajectory of the disease.
- Factors such as perceived social worth should be disregarded, while clinical factors that will affect the well-being of patients should be given due consideration.
- Consider not only current but future patients.
- Consider the broader institutional resources and capacity for supporting and sustaining services.

Moskowitz et al. Implications for Design and Analyses of Oncology Clinical Trials During the COVID-19 Pandemic. JAMA Oncology. DOI: 10.1001/jamaoncol.2020.2370

Country context: Global

This commentary discusses the implications of the COVID-19 pandemic for oncology clinical trial design and analyses of end points, specifically from ongoing trials that critically depend on serial data collection. It draws attention to the need for further guidance from regulatory agencies and review boards for navigating these implications, while calling on the oncology community to think carefully about the implications, not only for current trials, but for future clinical trial design as well.