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

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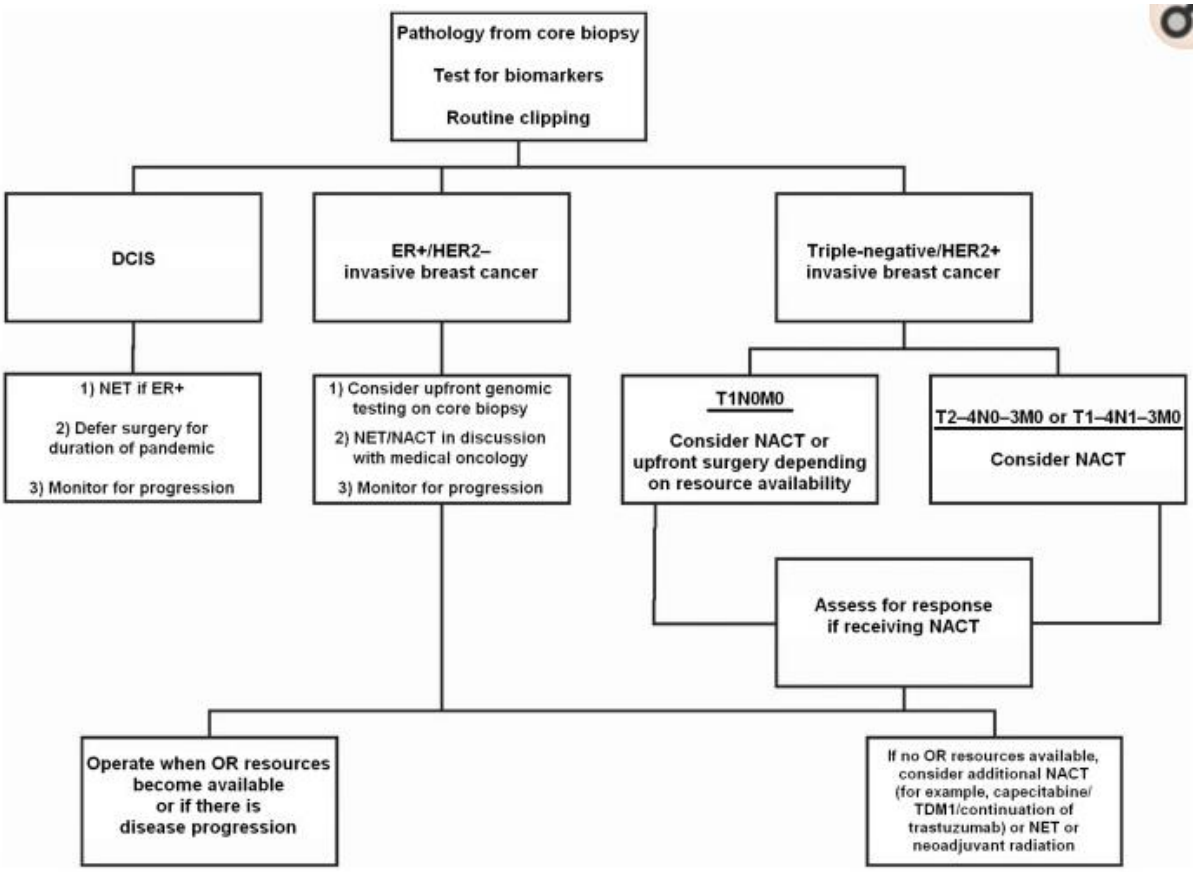
The CRI presents a selection of emerging research articles and clinical practice guidelines related to cancer and COVID-19, with a summary of their key findings/recommendations (links to the articles are embedded as hyperlinks in the titles). This is the 19th of our weekly compilation, which we plan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

Berger-Richardson et al. Preparing for the renaissance: treating breast cancer during the COVID-19 pandemic and planning for a safe re-emergence to routine surgical care within a universal health care system. Current Oncology. DOI: 10.1002/cncr.33075.

Country context: Canada

In this report, the authors summarize current treatment recommendations and precautions for breast cancer management, estimate the burden of accumulating untreated disease, and explore strategies to safely and gradually reintroduce surgical management once or resources become available. The flowchart highlights their breast cancer management approach during the pandemic:



Flowchart of breast cancer management during pandemic. DCIS = ductal carcinoma *in situ;* ER = estrogen receptor; HER2 = human epidermal growth factor receptor 2; NET = neoadjuvant endocrine therapy; NACT = neoadjuvant chemotherapy.

The authors outline principles to be considered in preparing for a safe return to care.

Bailey et al. Cancer Research: The Lessons to Learn from COVID-19. Cancer Discovery. DOI: 10.1158/2159-8290.CD-20-0823.

Country Context: Global

In this commentary, the authors explore the effect of the pandemic on the clinical trials landscape in both COVID-19 and cancer, and highlight some of the innovation that can be taken forward. Some of the innovative approaches in adapting to the restrictive environment include adopting remote practices to facilitate recruitment, patient contact, site visits, training, and institutional review board communications. Other include the permission of protocol deviations, which may allow increased flexibility in the design and conduct of new trials.

Garg et al. Discordance of COVID-19 guidelines for patients with cancer: A systematic review. Journal of Surgical Oncology. DOI: 10.1002/jso.26110

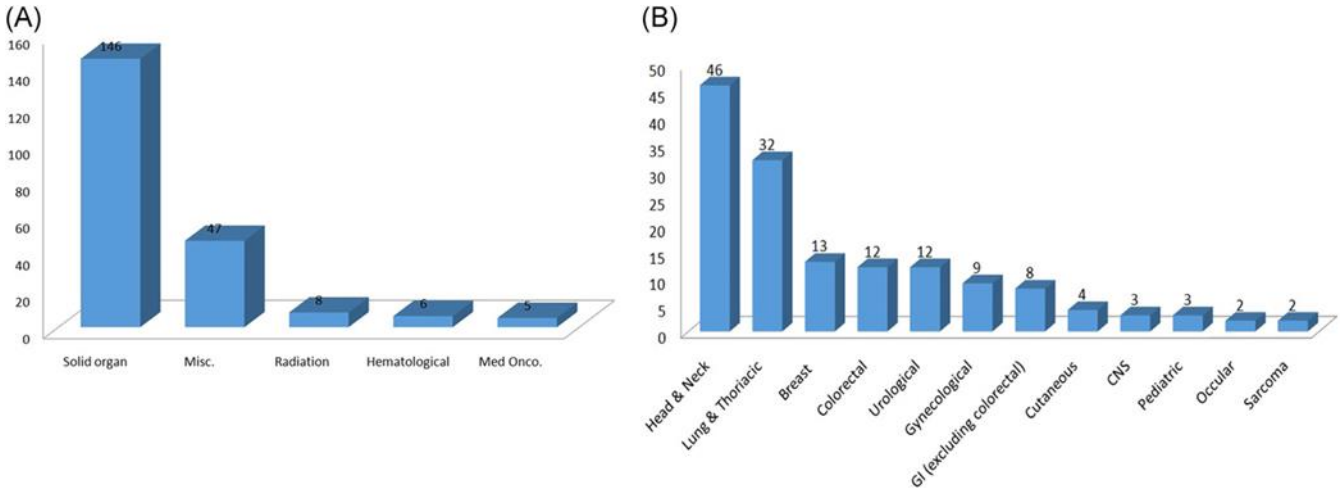
Country context: Global

This systematic review evaluated the available literature on the impact of COVID-19 on cancer care and to critically analyse the diagnostic and therapeutic strategies suggested by various healthcare providers, societies, and institutions. From a total of 212 articles included (published since the inception of the pandemic through 2 May 2020), the review found that

the majority of guidelines for various types of cancers favoured a delay in treatment or a non-surgical approach wherever feasible. The bar-charts below (A and B) describe the number of publications per cancer domain and per type of solid malignancy. The article includes a set of tables that summarize the guidelines/recommendations for the following cancers: head and neck, lung and thoracic malignancies, breast, gynaecological , urological, colorectal and haematological. The review demonstrated that these guidelines are based on a low level of evidence and have significant discordance for the role and timing of cancer surgery, especially in early tumours. The postulated reasons for discordance among the guidelines are as follows:

- A rapid response to the pandemic—various institutional policies were formulated without multicentre discussion.
- Paucity of literature—The outcomes of oncological treatments in form of delaying surgery, chemotherapy/immunotherapy or radiation therapy in the patients with active or latent SARS-CoV-2 infection is currently an unfathomed territory.
- Differences in the national healthcare systems (single-payer system, government-run care, hybrid system, etc.), which have a considerable impact while formulating any guidelines.
- Demographic profile of the nation as well as the percentage of population affected by COVID-19 and the relative proportion of healthcare resources available.
- Lack of mental preparedness and unanticipated clinical outcomes of the pandemic.
- All the guidelines/consensus statements are framed in a relatively short period of time without multilevel comprehensive discussions supported by the sufficient evidence.

All the guidelines/consensus statements clearly mention that they can be subjected to constant evolution and dynamism in light of emerging new evidence.



Bar-charts depicting the (A) number of publications in various domains of cancer and (B) distribution of publications as per the type of solid organ malignancy

Vatansev et al. COVID-19 infection can cause chemotherapy resistance development in patients with breast cancer and tamoxifen may cause susceptibility to COVID-19 infection. Medical Hypotheses. DOI: 10.1016/j.mehy.2020.110091

Country context: Global

In this letter to the editor, the authors report their observation that the use of tamoxifen increased the susceptibility to COVID-19 infection in their breast cancer patients. They

speculate that tamoxifen may increase the COVID-19 risk due to its anti-oestrogen and P-glycoprotein inhibitory effects. They note that oestrogen can have a protective effect against COVID-19 by increasing the release of interferon I and III from T lymphocytes which alleviate COVID-19 infection. Conversely, tamoxifen treatment causes down-regulation, mutation, or loss in oestrogen receptors. The authors also noted that tamoxifen as a P-glycoprotein inhibitor suppresses T cell functions and interferon release, independent of its effect on oestrogen receptors. Based on these considerations, the authors think that the use of tamoxifen may increase the risks of COVID-19 infection and severity in cancer patients.

Mozaffar Aznabl. Evaluation of COVID 19 infection in 279 cancer patients treated during a 90-day period in 2020 pandemic. International Journal of Clinical Oncology. DOI: 10.1007/s10147-020-01734-6.

Country context: Iran

This study investigated the outcome of COVID-19 in cancer patients who needed treatment, within a 90-day period. Cancer patient who required treatment, were evaluated for potential COVID-19 infection in a 90-day period, starting from beginning of the epidemic in Iran. A total of 279 patients were followed up. COVID-19 infection was observed in 7 cancer patients, including those with colon cancer, lung cancer, brain tumours, ovarian cancer, Hodgkin's disease, acute leukaemia and multiple myeloma.

Lee et al. Innovative countermeasures can maintain cancer care continuity during the coronavirus disease-2019 pandemic in Korea. European Journal of Cancer. DOI: 10.1016/j.ejca.2020.06.021

Country context: South Korea

This study compared the status of cancer management before and after COVID-19 and analysed how cancer care continuity was maintained in South Korea. The authors assessed the medical records on the number of cancer diagnosis, cancer surgery, radiation therapy and scheduled chemotherapy conducted in Korea University Anam Hospital from January 1 to April 30, 2019 and from the same period in 2020. A 14.7% decrease was observed in the number of new cancer diagnosis (from 1694 in 2019 to 1445 in 2020). Cancer surgery performed fell from 830 to 800 cases, while radiation therapy decreased from 185 to 140 cases. However, the number of systemic chemotherapies for metastatic cancer patients treated in department of medical oncology increased from 2555 to 2878 cases. Among hospitalised patients, emergency centre visit, intensive care unit admission, discharge after recovery and death reveal no drastic changes. The table below summarizes the findings.

Comparison the status of routine cancer care between 2019 and 2020 (January to April).

	2019					2020				
	Total	**January**	**February**	**March**	**April**	**Total**	**January**	**February**	**March**	**April**
Cancer diagnosis	1694	503	365	418	408	1445 (85.3%)	425 (84.5%)	381 (104%)	325 (77.8%)	314 (77.0%)
Cancer surgery	830	240	177	190	223	800 (96.4%)	202 (84.2%)	199 (112%)	233 (122%)	166 (74.4%)

		2019					2020				
		Total	January	February	March	April	Total	January	February	March	April
Radiation therapy		185	46	49	36	54	140 (75.7%)	31 (67.4%)	37 (75.5%)	43 (119%)	29 (53.7%)
Chemotherapy	Outpatient	657	182	158	157	160	1136 (173%)	283 (155%)	259 (164%)	286 (182%)	308 (193%)
	Inpatient	1896	506	416	467	507	1742 (91.9%)	425 (102%)	361 (86.8%)	466 (99.7%)	490 (99.6%)
	Total	2555	688	574	624	667	2878 (113%)	708 (103%)	620 (108%)	752 (121%)	798 (120%)
Foreign patients		64	15	10	19	20	49 (76.6%)	12 (80%)	20 (200%)	12 (63.2%	

William Hamilton. Cancer diagnostic delay in the COVID-19 era: what happens next? Lancet Oncology. DOI: 10.1016/S1470-2045(20)30391-0

Country context: UK

In this article, the author discusses the disruption of cancer diagnostic services by the COVID-19 pandemic in the UK, particularly with the suspension of cancer screening since late March, 2020. The article highlights how this has left around 8500 patients with a positive colorectal screening test and a cancer risk of around 10%, uninvestigated, while leading to a decrease in 2-week-wait referrals of approximately a quarter for possible breast cancer cases. The author also points out that the 2 UK studies (including that of Sud et al summarized below) modelling cancer mortality due to a delay in cancer diagnosis possible may be underestimates in one and over estimates in the other, but notes that perhaps a precise figure is not required but rather a plan for the large loss of life noted whichever modelling study is used. Possible ways forward are proposed for re-adapting and catching up on missed diagnoses in the post-COVID-19 era.

Sud et al. Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study Lancet Oncology. DOI: 10.1016/S1470-2045(20)30392-2

Country context: UK

This modelling study examined the impact of different scenarios of lockdown-accumulated backlog in cancer referrals on cancer survival, and the impact on survival per referred patient due to delayed diagnosis versus risk of death from nosocomial COVID-19 infection. It predicts that delays in presentation via the 2-week-wait pathway over a 3-month lockdown period could result in 181 additional lives and 3316 life-years lost as a result of a backlog of referrals of 25%, 361 additional lives and 6632 life-years lost for a 50% backlog of referrals, and 542 additional lives and 9948 life-years lost for a 75% backlog in referrals. Compared with all diagnostics for the backlog being done in month 1 after lockdown, additional capacity across months 1–3 could result in 90 additional lives and 1662 live-years lost due to diagnostic delays for the 25% backlog scenario, 183 additional lives and 3362 life-years lost under the 50% backlog scenario, and 276 additional lives and 5075 life-years lost under the 75% backlog scenario. Based on these, the authors recommend prompt provision of additional capacity to

address the backlog of diagnostics to minimise deaths as a result of diagnostic delays. They also recommend the prioritisation of patient groups for whom delay would result in most life-years lost warrants consideration as an option for mitigating the aggregate burden of mortality in patients with cancer.