Cancer in the context of COVID-19: Summary of emerging evidence (15)

Compiled by Chukwudi Nnaji and Jennifer Moodley

Date: 30 June 2020

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 15th 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)**.

Amaoui et al. Organization of a Radiotherapy Service During the COVID-19 Epidemic: Experience of Regional Center of Oncology of Agadir, Morocco. Radiography. DOI: 10.1016/j.radi.2020.06.008

Country context: Morocco

This study proposes a strategy for organising radiotherapy services during the COVID-19 pandemic period. Reliable circuits for staff as well as for patients are installed and treatment protocols are adapted to the current COVID-19 situation. The following are proposed to deal with any subsequent pandemic situation:

Zoning of the radiotherapy department: During this pandemic period we proposed to divide the radiotherapy department according to the risk of contamination into three zones:

- Clean area: Represents the circuit where the risk of contamination is low. It includes the administrative offices, the dosimetry room and the staff rest room.
- Semi-contaminated area: This is the circuit where the probability of contamination is medium. It includes locker rooms, patient corridors, washrooms and waiting rooms.
- Contaminated area: This is the circuit where the risk of contamination is high. It includes the simulation room, the accelerator console, and the treatment room.

Disinfection of areas: For the purpose of good environmental hygiene, good ventilation must be maintained and a disinfection procedure for each area must be clearly defined. The disinfection by area will be carried out as follows:

- For the clean area: All surfaces must be cleaned daily with 75% ethanol.
- For the semi-contaminated clean area: A final disinfection at the end of the consultation and at the end of the treatment must be applied.
- For the contaminated area: Disinfection twice a day.

Access to the service: To access the service during this pandemic period, two entrances were installed. One door is reserved exclusively for staff and another for patients.

- Staff circuit in the service: At the entrance to the staff door each team member who has suspicious symptoms must report them to the staff monitoring committee. The nursing staff are provided with surgical masks (to be changed every 4-6 hours) and a hydro-alcoholic gels in Pocket format. The movement of personnel between units will be done in an internal circuit without any contact with the patients
- Patient circuit in the ward: At the entrance to the patient door a screening unit was installed. An interrogation on the symptoms of COVID-19 as well as the taking of temperature will be carried out for the patient. For suspicious cases the patient is referred to the COVID-19 specialised medical unit for further diagnosis.

Adjustment of treatment protocols with the pandemic: The strategy adopted favours hypo-fractionated protocols according to the recommendations of the Moroccan Society of Cancerology. Patients treated curatively with tumours in place (cervix; head and neck; and lung) were prioritised. For lung cancer, a protocol was adopted based on the concomitant radioechemotherapy combination with carboplatin rather than cisplatin and hypo-fractionated radiotherapy of 55 Gy in 20 fractions instead of the usual standard protocol of 60-66 Gy in classic fractionation.

Management of human resources in the event of a worsening of the epidemic state: Divide the staff of the center into two teams. One team consists of three radiation oncologists, one medical physicist and three RTTs. Each team performs the work for two weeks and then alternates with the other team in order to reduce the risk of staff contamination. In case of human resources needs, the Radiotherapists, Medical Physicists and Radiation technicians (RTTs) of the region can be called upon.

Guckenberger et al. Practice Recommendations for Lung Cancer Radiotherapy During the COVID-19 Pandemic: An ESTRO-ASTRO Consensus Statement. International Journal of Radiation Oncology Biology and Physics. DOI: 10.1016/j.ijrobp.2020.05.012.

Country Context: high-income countries

In this report, an international group of experts in lung cancer radiotherapy present their practice recommendations pertaining to whether and how to adapt radiotherapy for lung cancer in the COVID-19 pandemic. To arrive at these recommendations, 32 experts in lung cancer radiotherapy contributed to a modified Delphi consensus process by assessing potential adaptations of radiotherapy in two pandemic scenarios. The first, an early pandemic scenario of risk mitigation, is characterised by an altered risk benefit ratio of radiotherapy for lung cancer patients due to their increased susceptibility for severe COVID-19 infection, and minimisation of patient travelling and exposure of radiotherapy staff. The second, a later

pandemic scenario, is characterised by reduced radiotherapy resources requiring patient triage. The recommendations are highlighted below:

Fractionation recommendations

Would you recommend hypofractionating beyond your usual fractionation?			
Case	Standard fractionations	Response	Maximum degree of hypofractionation supported
Case 1: stage I NSCLC	SBRT: 45–54 Gy in 3 Fx, 48 Gy in 4 fractions	Yes: 50% No: 50%	30–34 in 1 Fx[17]: 90% support if choosing hypofractionation **(strong consensus)**
Case 2: stage III NSCLC	Radiochemotherapy: 60–66 Gy in 30–33 Fx over 6–6.5 weeks	Yes: 46% No: 54%	
Case 3: PORT NSCLC	PORT: 50–60 Gy over 5–6 weeks	Yes: 29% **No: 71% (consensus)**	
Case 4: LS SCLC	Radiochemotherapy: 60–66 Gy in 30–33 Fx over 6–6.5 weeks, or 45 Gy in 30 Fx over 3 weeks using BID fractions of 1.5 Gy	Yes: 33% **No: 67% (consensus)**	
Case 5: PCI SCLC	PCI: 25 Gy in 10 Fx over 2 weeks	Yes: 7% **No: 93% (strong consensus)**	
Case 6: Palliative NSCLC	30 Gy in 10 Fx over 2 weeks	**Yes: 89% (strong consensus)** No: 11%	Favored fractionations: 20 Gy in 5 Fx (30%)[18] 17 Gy in 2 Fx (37%)[19] 8–10 Gy in 1Fx (33%)[20]

Recommended hypofractionation regimens based on availability/use of concurrent and sequential radiochemotherapy, or radiotherapy alone

Would you consider hypofractionated radiotherapy as appropriate?		
Case 2 stage III NSCLC	Response	Maximum degree of hypofractionation supported
Radiotherapy only	**Yes: 97% (strong consensus)** No: 3%	60 Gy in 15 Fx (33%)[21,22] 60 Gy in 20 Fx (27%)[23] 60–66 Gy in 24–30 Fx (2.2–2.75 Gy/day) (23%)[24] 55 Gy in 20 Fx (13%)[25] None (3%)
Sequential radiochemotherapy	**Yes: 97% (strong consensus)** No: 3%	60–66 Gy in 24–30 Fx (2.2–2.75 Gy/day) (27%)[24] 55 Gy in 20 Fx (27%)[25] 60 Gy in 15 Fx (23%)[21,22] 60 Gy in 20 Fx (20%)[23] None (3%)
Concomitant radiochemotherapy	Yes: 27% **No: 73% (consensus)**	See footnote*

* Although there was consensus not to recommend hypofractionation, the respondents supportive of hypofractionation (n = 11) were asked which fractionation(s) they would support, with multiple answers allowed. The favored options were 60–66 Gy in 22–30 Fx, given at 2.2–2.75 Gy/day, (75%) and 55 Gy in 20 Fx (63%).

Recommendations on delay or interruption of treatment in COVID-19 positive patients

Patient case	Time patient is diagnosed as COVID-19 positive	Postpone or interrupt RT?
Case 1: Stage I NSCLC	Start of Tx	**Yes: 96% (Strong consensus)**
	After start of Tx	Yes: 54%
Case 2: Stage III NSCLC	Start of Tx	**Yes: 100% (Strong consensus)**
	After start of Tx	Yes: 57%
Case 3: PORT NSCLC	Start of Tx	**Yes: 96% (Strong consensus)**
	After start of Tx	**Yes: 68% (Consensus)**
Case 4: LS SCLC	Start of Tx	**Yes: 89% (Strong consensus)**
	After start of Tx	Yes: 48%
Case 5: PCI SCLC	Start of Tx	**Yes: 93% (Strong consensus)**
	After start of Tx	**Yes: 67% (consensus)**
Case 6: Palliative NSCLC	Start of Tx	**Yes: 74% (Consensus)**
	After start of Tx	**Yes: 78% (Consensus)**

Prioritisation of lung cancer patients and factor for triaging of patients

Prioritization of lung cancer patients			
Rank	Case*	Relative Priority Compared All Other Types Cancer Cases in Department**	Top 5 factors for triaging patients across all radiotherapy cases
1.	Stage III NSCLC	Very high/high (71% consensus)	1. Potential for cure
2.	LS-SCLC SCLC	Very high/high (78% consensus)	2. Relative benefit of RT vs. other treatment options
3.	Stage I NSCLC	High/average (near consensus: 65%)	3. Active COVID-19 infection (absence thereof)
4.	Palliative NSCLC	No consensus. Widely dispersed responses.	4. Life expectancy
5.	PORT NSCLC	Low/very low (68% consensus)	5. Performance Status
6.	SCLC PCI	Low/very low (81% consensus)	

* The six cases were ranked, with 6 points given for a #1 ranking, 5 points for #2, etc, and the average number of points was determined. The average scores, in order of ranking as listed in the table, were 5.2, 4.9, 4.1, 3.0, 2.1 and 1.7, respectively.

** Respondents were asked to prioritize each case as very high, high, average, low, or very low, corresponding to quintiles of priority (e.g. very high = top 20%, very low = bottom 20%), compared to all types of cancers treated in their department. Adjacent categories were combined to determine consensus.

Kartik et al. Implications of Reduced Health Care Services for Cancer Patients in India and Similar Resource-Limited Health Care Systems During COVID-19 Pandemic. Asia Pacific Journal of Public Health. DOI: 10.1177/1010539520937103

Country Context: India

In this letter to the editor, the authors discuss the implications of the COVID-19 pandemic for health care and oncology services for cancer patients in resource-limited settings. They recommend the following:

- Segmentation of health care into 2 parts, where one is focused on COVID-19–related care and the other continues to provide care to other health care.
- Limiting patients and visitors accompanying them.
- Telemedicine can be an effective tool for consultations with patients who would otherwise be seen in an outpatient setting. Another approach that is under consideration is adapting alternate treatment regimens that reduce patient visits; however, the implications of this are still uncertain.
- Strategies to minimise interruption of cancer treatment, particularly in patients being treated with curative intent and proactive end-of-life and palliative care discussions with patients who have a poor prognosis.

Ding et al. Delayed Cancer Diagnoses and High Mortality in Children During the COVID-19 Pandemic. Pediatric Blood and Cancer. DOI: 10.1002/pbc.28427

Country context: USA

In this editorial correspondence, the authors report five cases of children who presented critically ill to two tertiary referral centers in April 2020. All of them tested SARS-CoV-2 negative and experienced delays in cancer diagnosis due to the impact of the COVID-19 pandemic on help-seeking behaviour and oncology services. Each patient required emergent life-saving interventions shortly after presentation, including resuscitation following cardiac arrest (2 children), emergent intubation (4 children), and emergent pericardiocentesis for tamponade (one child). Sadly, two of the children died within days of presentation. The authors conclude that these cases illustrate the indirect impact of the pandemic on morbidity in COVID-19–negative patients for whom care delays can be fatal. They recommend further work to quantify these consequences and to develop solutions that protect severely ill but treatable children, while also balancing public health and the needs of those infected during the COVID-19 pandemic.

Leones et al. Caring for the Carers: Safeguarding Oncologists' Mental Health in the Time of COVID-19. Ecancer. DOI: 10.3332/ecancer.2020.1057

Country context: The Philippines

The authors report how their hospital responded to the challenges posed by the COVID-19 pandemic, including the increased workload as well as the attendant anxiety and fear of infection. The following measures were taken to safeguard the mental health of staff: 1) use of psychological support materials; 2) initiation of a psychological intervention programme and 3) establishment of peer support programmes. They conclude that caring for the carers through evidence-based interventions ensures the delivery of quality care to our cancer patients despite the challenges during these trying times.

Yarza et al. SARS-CoV-2 Infection in Cancer Patients Undergoing Active Treatment: Analysis of Clinical Features and Predictive Factors for Severe Respiratory Failure and Death. European Journal of Cancer. DOI:10.1016/j.ejca.2020.06.001

Country context: Spain

This study aimed to describe the disease characteristics and morbidity of COVID-19 in cancer patients undergoing active oncologic treatment and to determine predictive factors for poor outcome in terms of severe respiratory distress (acute respiratory distress syndrome [ARDS]) or death. A total of 63 patients were included in the study, 34 of whom developed ARDS. Levels of lymphocytes, serum albumin, lactate dehydrogenase (LDH) and C-reactive protein (CRP) were predictors of respiratory failure. Mortality rate was 25%, significantly higher among ARDS, neutropenic patients and in those with bilateral infiltrates. Multivariate logistic analyses model confirmed the predictive value of severe neutropenia, bilateral infiltrates and tumour lung involvement. The authors recommend that the assessment of neutropenia, lung involvement and bilateral pneumonia at diagnosis are essential for the management of this high risk population.

Multivariable logistic predictive model for respiratory distress and mortality outcomes

n (%)	ARDS			Mortality		
	OR	CI 95%	*p value*	OR	CI 95%	*p value*
Age, >65 years	1.17	0.42–3.2	0.76	1.59	0.5–4.99	0.42
Sex, Female = 1	0.98	0.35–2.74	0.98	0.88	0.28–2.73	0.83
Smoking habit						
Former smoker	0.81	0.27–2.45	0.72	0.89	0.25–3.11	0.86
Current smoker	2.4	0.48–11.8	0.28	2.48	0.5–12.54	0.27
Comorbidities						
Hypertension[a]	1.5	0.5–4.43	0.46	2	0.68–5.88	0.21
Diabetes[a]	2.4	0.63–9.44	0.19	1.15	0.34–3.9	0.81
CKD[a]	3.5	0.46–26.18	0.22	2.39	0.29–19.85	0.42
COPD[a]	0.79	0.18–3.34	0.75	0.35	0.05–2.23	0.26
Previous VTED[a]	1.79	0.48–6.7	0.39	4.82	1.14–20.3	0.03
Chronic anaemia[c]	2.76	0.62–12.3	0.18	1.32		
ACEI/ARBsI[b]	0.64	0.11–3.5	0.6	0.23	0.02–2.23	0.2
COPD[d]	1.69	0.33–8.62	0.52	1.43	0.25–8.33	0.68
Radiol infiltrates bilateral=1	21.4	4.2–108.55	<0.001	32.83	3.51–307	0.002
Neutropenia[e]						
<1500	0.46	0.13–1.58	0.21	0.62	0.16–2.37	0.43
<500	10.36	0.93–114.52	0.056	16.54	1.43–190.9	0.025
Primary tumour[f]						
Overall lung cancer	1.81	0.49–6.7	0.37	2.35	0.58–9.51	0.22
Colorectal cancer (lung=1)	1.65	0.1–16.97	0.81	2.33	0.17–30.94	0.52
Breast cancer (lung=1)	0.9	0.12–6.54	0.9	2.47	0.17–34.23	0.5
Genitourinary cancer (lung=1)	1.56	0.17–14.13	0.69	2.29	0.17–30.73	0.53
Other tumours (lung=1)	1.86	0.37–9.19	0.44	2.13	0.42–10.82	0.36
Metastatic disease[g]	1.11	0.23–5.38	0.88	1.88	0.19–18.19	0.58
Visceral metastatasis[h]	0.7	0.21–2.25	0.54	1.32	0.38–4.55	0.44
Pulmonary involvement[i]	1.96	0.63–6.14	0.24	4.34	1.26–14.95	0.02
Cancer Treament[j]						
Chemotherapy alone	1.36	0.4-4-56	0.68	1.6	0.4–6.33	0.5
Immunotherapy + Chemo	0.97	0.14–6.45	0.95	1,96	0.29–13.18	0.49
Immnunotherapy alone	0.26	0.03–1.88	0.18	0.15	0.01–1.65	0.12

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; VTED, venous thromboembolic disease; ACEi/ARBs, angiotensin converting enzyme inhibitor/angiotensin receptor blockers; ECOG, Eastern Cooperative Oncology Group; OR, odds ratio; CI, confidence interval.

[a] Adjusted by age, sex, hypertension, diabetes, CKD, COPD, previous VTE, smoking habit.
[b] Adjusted by age, sex, hypertension, diabetes, CKD, COPD, smoking habit.
[c] Adjusted by age, sex, hypertension, diabetes, CKD, COPD, Previous VTE, smoking habit, oesophagogastric tumour.
[d] Adjusted by age, sex, cardiopathy, previous VTED.
[e] Adjusted by age, sex, hypertension, diabetes, CKD, COPD, Previous VTE, smoking habit.
[f] Adjusted by age, sex, CT.
[g] Adjusted by age, sex, COPD, previous VTE, metastasis, ECOG.
[h] Adjusted by age, sex, previous VTE, pulmonary involvement.
[i] Adjusted by age, sex, ECOG, metastasis, previous VTE.
[j] Adjusted by age, sex, ECOG, metastasis, previous VTE, COPD.

Amegan-Aho et al. Coronavirus disease-2019 and childhood cancers in developing countries: A hurdle in the hope to attain the WHO 2030 targets? Cancer Res Stat Treat. DOI: 10.4103/CRST.CRST_203_20

Country context: Ghana

This letter to the editor discusses the impact of the COVID-19 pandemic on developing countries, and particularly the challenges it poses to the achievement of the target of 60% childhood cancer survival rate by 2030 in countries that report hardly more than 20% long-term survival. In addition to issues such as limited access to healthcare facilities, delay in diagnosing new cases, relatively increased workload, avoidance of essential treatment components, rationalization of supportive care, shortage of drug supply, reduced support from partners, and difficulty to start or continue clinical trials; the authors have identified the following as important challenges that need to be addressed to meet the 2030 target:

- Limited access to healthcare because of a reduction in the caregivers' purchasing power due to low economic activities.

- The diversity of symptoms of COVID-19 among children may confuse the primary healthcare personnel, who may miss the diagnosis of childhood cancers, especially in areas where personnel knowledge on the topic is already low
- Pediatric oncology staff are diverted toward the care of patients with COVID-19 and are stationed away from their healthcare facility, thus compounding the staff shortage
- Increase in substandard medicines for cancer and supportive care in the developing countries on account of shortages due to major disruptions in production and supply chain
- The reduction in the numbers of voluntary donors may increase the risk of transfusion-related infections due to lapses in transfusion safety procedures
- Continued restrictions in economic activities may collapse businesses, thus endangering critical fund-raising activities, which many pediatric oncology units/centers in the developing countries heavily rely on to operate.

.

Harris AL. COVID-19 and Cancer Research. British Journal of Cancer. DOI: 10.1038/s41416-020-0960-1

Country context: Global

This editorial summarises some of the major effects on cancer patients and impacts on cancer research. For instance, it highlights how cancer research funding could be severely depleted, due to the fact that much of the research in cancer is funded by charities or governments, many of which re-prioritised their financial commitments. The author proposes how these challenges can be mitigated by appropriate and timely responses from governments, research funders, cancer programmes, universities, industry and the public.