Journal of Oncology Research and Therapy
Carbonara R, et al. J Oncol Res Ther 7: 10139.
www.doi.org/10.29011/2574-710X.10139
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Mini-Review

Impact of COVID-19 Pandemic on Radiation Oncology Practice: An Overview of Recent Higher Quality Reports

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Citation: Carbonara R, Ciliberti MP, Gregucci F, Surgo A, Caliandro M, et al. (2022) Impact of COVID-19 Pandemic on Radiation Oncology Practice: An Overview of Recent Higher Quality Reports. J Oncol Res Ther 7: 10139. DOI: 10.29011/2574-710X.010139

Received Date: 16 June, 2022; **Accepted Date:** 22 June, 2022; **Published Date:** 29 June, 2022

Abstract

Worldwide, the COVID-19 pandemic seems to significantly impact on cancer care due to emergency-related conditions. Aim of the present editorial is to synthesize the emerging changes in multiple fields of Radiation Oncology, reporting an overview of high-quality clinical experiences and recommendations published since the beginning of the emergency period of COVID-19 pandemic. **Methods:** Based on this background, a brief review of the literature was performed according to a Pubmed search via P (population) I (intervention) C (comparison) O (outcome). Only higher quality reports were included. **Results:** Among a total of 290 titles, 18 higher quality reports in RO were selected and evaluated: 6 Systematic Reviews, 3 Clinical Trials and 9 Practice Guidelines (English version). The remarked endpoint of published works was the balance between the risk of oncological disease progression and ill from COVID-19. **Conclusions:** The evaluation of patient-specific risk factors and a multidisciplinary management remain crucial steps of diagnostic-therapeutic care pathways.

Mini-Review

Worldwide, the COVID-19 pandemic seems to significantly impact on cancer care due to emergency-related conditions [1]. Aim of the present editorial is to synthesize the emerging changes in multiple fields of Radiation Oncology (RO), reporting an overview of high-quality clinical experiences and recommendations published since the beginning of the emergency period of COVID-19 pandemic.

Based on the latter background, a Pubmed search via P (population) I (intervention) C (comparison) O (outcome) was performed using the following terms: P (Cancer patients and Covid) and I (Radiotherapy). Only higher quality reports according to study design (Systematic Reviews, Clinical Trials and Practice Guidelines) were selected and analyzed.

Among a total of 290 titles, 18 higher quality reports in RO were selected and evaluated: 6 Systematic Reviews, 3 Clinical Trials and 9 Practice Guidelines (English version) [2-19]. In particular, international expert consensus recommendations and proposals for managing cancer patients during COVID-19 pandemic were published with specific regard to the following tumors: breast and digestive cancers, as well as thoracic, hematological and gynecologic malignancies. Additionally, as an interestingly non-oncological result, whole-lung irradiation in a single fraction of 0.5 Gy was reported to obtain a response rate of 80% in a clinical trial enrolling oxygen-dependent patients with COVID-19 pneumonia [20,21]. Tables showed all the main results for cancer patients and covid related pneumonia in terms of radiotherapy: Table 1 reported clinical trials and review/metanalysis data, while Table 2 reported the Expert panel/scientific societies data.

Author, year	Study design	N. pts	Patients category	Other anti-cancer therapy assessed	Main results
Wang B, 2020	Systematic review and meta-analysis	3581 (including other anti-cancer therapies)	Cancer patients with COVID-19	Yes (surgery, targeted therapy, chemotherapy, immunotherapy)	RT was not associated with increased risk of exacerbation and mortality (p-value > 0.05)
Yekedüz E, 2020	Systematic review and meta-analysis	35301; 111 patients in RT group	Cancer patients with COVID-19	Yes (surgery, targeted therapy, chemotherapy, immunotherapy)	RT did not increase the severe disease and death risk (OR: 0.82; 95% CI:0.50-1.37; p = 0.46). Chemotherapy increased the risk of death from COVID-19
Gupta T, 2020	Literature review	641	Non-nasopharyngeal Head and neck squamous cell carcinoma	Yes-RT combined with systemic therapy	Curative-intent hypofractionated-accelerated RT schedule delivering 55 Gy in 20 fractions over 4 weeks is a suitable alternative to standard fractionation
Liu Y, 2021	Systematic review and meta-analysis	3268 (including other anti-cancer therapies)	Cancer patients with COVID-19	Yes	Recent anti-cancer treatments do not increase mortality
Thomson DJ, 2020	Systematic Review of the Quality of Evidence and Recommendations		Cancer patients treated during COVID-19 pandeminc	Yes	Hypofractionated RT schedules are recommended across numerous major disease sites
Venkatesulu BP, 2020	Systematic review and meta-analysis	23.736 (including other therapies)	Cancer patients with COVID-19	Yes	There was no association between receipt of a particular type of oncologic therapy and mortality
Ameri A, 2020	Clinical trial	5	Oxygen-dependent patients with COVID-19 pneumonia		Whole-lung irradiation in a single fraction of 0.5 Gy had a response rate of 80%
Huang SH, 2020	Clinical trial	2039	Head and Neck squamous cell carcinoma (HNSCC) cases (oropharynx/ larynx/ hypopharynx)	Yes – RT alone or combined with systemic therapy	RT-hypofratcionated could be considered in place of standard fractionated RT for HPV+ T1-T3N0-N2c (TNM-7) HNSCCs, HPV- T1-T2N0 HNSCCs, and select stage III HNSCCs during the COVID-19 pandemic

Dai M, 2020	Clinical trial	105 patients with cancer and 536 age-matched noncancer patients	Cancer patients with COVID-19		Unlike surgery, RT did not increase the risk of severe events

Table 1: Clinical trials and review/metanalysis data.

Summarizing data, an exponential increase in the COVID-19 publications, also including literature in RO fields, has been observed. The remarked endpoint of published works was the balance between the risk of oncological disease progression and ill from COVID-19. In general, the use of RADS (Remote, Avoid, Defer, Shorten) principles has been proposed since the beginning of pandemic period, taking into account the necessity of personalized therapeutic approaches and pandemic containment (e.g. managing elderly or COVID-19 positive patients).

Group/Expert panel	Tumor site, district	Other anti-cancer therapy assessed	Main results
French intergroup, 2020	Digestive cancer	Yes	As far as possible, no therapeutic modification should be carried out. If necessary, therapeutic adjustments may be considered if they do not constitute a loss of chance for patients. Considering the level of evidence all therapeutic modifications need to be discussed
German Hodgkin Study Group and the German Lymphoma Alliance, 2020	Hematological malignancies	Yes	Omission of RT was only considered in a minority of cases if alternative treatment options were available. Hypofractionated regimens and reduced dosages may be used for indolent lymphoma and fractures due to multiple myeloma. Panelists agreed to start emergency RT for typical indications (intracranial pressure, spinal compression, superior vena cava syndrome) within 24 hours
International Society of Geriatric Oncology (SIOG) COVID-19 Working Group, 2020	Elderly cancer patients	Yes	In selected cases is required to defer or omit surgery, RT or systemic treatments, especially if benefits are marginal and alternative safe therapeutic options are available
French High Council for Public Health, French-Language Society of Pulmonology (SPLF)/French-language oncology group, 2020	Thoracic malignancies	Yes	Situation should be examined case-by-case depending on the histology, tumor stage and patients characteristics. Initiating treatment in new patients must be discussed in multidisciplinary team meetings. A clear benefit and rare settings (clinical trial) with no treatment alternatives must be prioritized.
An international committee of ten experts in gynecologic radiation oncology, 2020	Gynecologic malignancies	Yes	Hypofractionated RT should be used when feasible and recommendations regarding radiation dose, timing, and technique have been provided for external beam and brachytherapy treatments. Concurrent chemotherapy may be limited in some countries, and consideration of radiation alone is recommended.

European Society for Medical Oncology (ESMO), 2020	Breast cancer	Yes	According to clinical prioritisation, immediate RT should be initiated in patients with acute spinal cord compression, symptomatic brain metastases not improving with steroidal medication and any urgent irradiation or a modifying effect on the risk of disabling sequelae and/or quality of life. Post-operative RT for high-risk patients (eg, inflammatory breast cancer, node-positive or high-risk biology) should be scheduled as high priority, also proposing alternative (shorter) radiation regimens(hypo-fractionated schedules). Accelerated partial breast irradiation should be proposed for low-risk patients. Where the expected clinical benefit of irradiation is very low, as in the older population with low-risk breast cancer under adjuvant endocrine therapy, deferral is possible or omission could even be considered in some circumstances.
ESTRO-ASTRO consensus statement, 2020	Lung cancer Non Small Cell Lung Cancer (NSCLC) Small Cell Lung Cancer (SCLC)	Yes	In the early phase of the COVID-19 pandemic, decisions on delay of treatment depended on the clinical case. There was a strong consensus not to postpone curative treatment for stage III NSCLC, LS SCLC and palliative NSCLC. In contrast, there was a strong consensus to postpone treatment for post-operative RT NSCLC and a prophylactic cranial irradiation SCLC. Postponement or interruption of radiotherapy treatment of COVID-19 positive patients is generally recommended. In the early phase of the COVID-19 pandemic, there was consensus not to universally change radiotherapy practice to more hypofractionated regimens. In contrast, there was strong consensus to change to more hypofractionation in palliative NSCLC. In stage III NSCLC hypofractionated RT is appropriate in RT alone or sequential radiochemotherapy (there was consensus against hypofractionation in concomitant radiochemotherapy). Various fractionations were considered as appropriate, with total doses between 50 Gy and 66 Gy delivered in 15–30 fractions.
International Lymphoma Radiation Oncology Group (ILROG), 2020	Hematological malignancies	Yes	Using alternative hypofractionation RT regimens when RT cannot be omitted or delayed is to be considered with the aim of maintaining high cure/palliation rates without undue toxicity (RT alternative schedules are reported). When there is no or little expected adverse effect on outcome from the delay, delaying RT is to be considered for asymptomatic localized low-grade lymphomas, localized nodular lymphocyte-predominant Hodgkin lymphoma, in a palliative setting for low-grade lymphomas in stable patients and for patients who develop COVID-19
FRANCOGYN group of the National College of French Gynecologists and Obstetricians (CNGOF), 2020	Gynecologic malignancies	Yes	If a patient with a gynecologic cancer presents with COVID-19, surgical management should be postponed for at least 15 days. For cervical cancer, RT and concomitant radiochemotherapy could replace surgery as first-line treatment and the value of lymph node staging should be reviewed on a case-by-case basis.

Table 2: Expert panel/scientific societies data.

Results of systematic reviews and meta-analyses suggested no increased risk of mortality in cancer patients affected by COVID-19 who receive recent anti-cancer treatments (radiotherapy (RT), as well as surgery, targeted therapy, chemotherapy, immunotherapy). Only one review [3] showed a relationship between chemotherapy and mortality in COVID-19 patients; similarly, only one study [8] suggested higher risks of severe events for patients who received surgery.

As preliminary knowledge, RT seems to be safe in SARS-CoV-2-infected cancer patients (Table 1). As showed in tables, taking into account patient's and disease's specific conditions, the use of hypofractionated regimens has been generally encouraged across numerous tumor presentations. For selected cases, defer RT could be considered only if clinically appropriate, while avoid RT could be proposed exclusively if marginal advantages are demonstrated and alternative validated approaches are available.

Conclusion

In conclusion, the evaluation of patient-specific risk factors and a multidisciplinary management remain crucial steps of diagnostic-therapeutic care pathways.

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