



Impact Of Covid-19 On Radiotherapy Protocol For Cancers Of The Head And Neck Region: A Scoping Review

¹Dr. Neha Anand Khaire, ²Dr. Radhika Thakkar, ³Dr. Anshul, ⁴Dr. Damandeep Kaur Mander, ⁵Dr. Anil Managutti, ⁶Dr. Rahul Tiwari

¹Senior Lecturer, Department of Prosthodontics, Crown & Bridge, K. M. Shah Dental College and Hospital, Sumandeep Vidyapeeth, Pipariya, Taluka: Waghodia, Vadodara, Gujarat, India

²Resident, Eastman Institute for Oral Health, University of Rochester, NY

³Lecturer, Dept of Oral Medicine and Radiology, PDM Dental College, Bahadurgarh, Haryana, India

⁴BDS, MDS, Dept. of Oral and Maxillofacial Surgery, Reader, Rayat Bahra Dental College, Kharar, Punjab, India

⁵Prof. & HOD, Dept of OMFS, Narsinhbhai Patel Dental College and Hospital, Sankalchand Patel University, Visnagar, Gujarat, India

⁶PhD Scholar, Department of Oral and Maxillofacial Surgery, Narsinhbhai Patel Dental College and Hospital, Sankalchand Patel University, Visnagar, Gujarat, India

Corresponding Author: Dr. Neha Anand Khaire,
drnehakhaire@gmail.com

ABSTRACT

Covid-19 has hit the world population and the ultimate aim now is survival. At risk groups are being defined by age, comorbidities, and risk of exposure. We must also keep the immunocompromised patients in mind. The critically ill patients cannot afford a delay in treatment. This scoping review was planned to delineate treatment of cancer patients with Radiation therapy. While surgeries are being postponed this seems to be a practical and viable option. It limits exposure to clinical environments that could be contaminated. It also makes them less reliant on the availability of hospital beds which are mostly being reserved for Covid-19 patients. It relieves the burden on the existing medical equipment, infrastructure, and resources, medical and paramedical staff. Electronic research databases i.e. Cochrane, PubMed, Medline, Web of Science, Scopus and Ebsco were scanned for related articles. In total 11 articles were shortlisted by two reviewers. They were narrowed down to 5 after full scale assessment After a review of the newly recommended guidelines, the available data was tabulated. New guidelines based on what has been learnt about the virus have been provided. Protocols are evolving with each new input around the virus. An institution based planning and approach is needed to help patients in dire need of treatment. Decisions depend on case to case basis and existing research on the effect of radiotherapy for each type of tissue involved.

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CONTRIBUTIONS TO THE LITERATURE

1. Effect of COVID-19 on essential medical services has been grave; the terminally ill patients like those suffering from cancer are hit worse.
2. The lockdowns imposed in across most countries has lead to a shortage of personnel and resources required to administer radiation therapy.
3. Cancer patients are immune compromised as such and exposure to medical facilities may expose them to Covid-19 increasing mortality rate.
4. The above-mentioned points serve as template for any emergency/pandemic situations in the future.
5. The information provided in the article is appropriate for your journal as it encompasses the effect of the pandemic on public health services for cancer patients.

INTRODUCTION

The world changed as Covid-19 began and humankind grapples with new realities. The medical fraternity has embarked on resetting treatment modalities for every known ailment. “Triage” has become the norm in clinical scenarios. It is best not to risk the chance of nosocomial infection. Therefore, patients suffering from minor illnesses are advised to remain home. All kinds of healthcare workers, hospital beds, personal protective equipment, relevant medications, and medical apparatus are reserved for a common enemy. The virus has exposed the vulnerabilities of embittered healthcare systems. However, the ever adapting human race, molds and researches for survival. Obviously Corona positive patients with signs and symptoms are given top most priority now. Everything and everyone else takes a step back.

In this infectious environment it is best to safeguard those that are particularly susceptible to contracting Covid-19. These include patients with diminished immune systems. We consider the regular culprits in this case i.e. autoimmune diseases, the senile, children, patients on long term immuno-suppressive therapies etc. We must spare a thought for patients in need of critical care like cancer patients. Their life depends on access to regular chemo/radiation therapy and hospital visits. In most cases of Head & Neck Cancer, surgical intervention is the first line of action. In the present scenario such patients are deemed unfit. They cannot be exposed to hospitals where the risk to their lives is grave.

The oncology team now has to re-strategize to provide the best care to such patients. The need has emanated not only from Covid-19 but also the lack of resources.¹ Treatment prioritization is the key now.² As reported by Li Zhang³ the main problem for a cancer patient is the availability of relevant medical facilities. They also mention the need for online medical counseling to assess the need for critical care. It helps prevent the progression of malignancies. The quality and duration of care has also been detrimentally affected by Covid-19.³

In India the issue related to Head and Neck malignancies is significant. These are one of the most common within the subcontinent. This is due to the high consumption of Tobacco particularly among the lower socio-economic strata. Comorbidities in such patients are mostly related to the respiratory tract. This makes them susceptible to Covid-19 and increases mortality rates. There is a rampant rise in the burden on the health sector. It is the need of the hour to modify the mode of treatment for cancers of the Head and Neck region.⁴ Recommendations for modification of protocols have poured in from all over the world. Since time is of the essence a scoping review was planned. These allow a foundation for further research into the selected field. The endeavor of a scoping review is to provide a cross sectional impression of available data. We have therefore, not analyzed the quality of data. Only the presentation of information as gathered from relevant literature is presented here.

MATERIALS & METHODS

There are various documented methodologies for such reviews. This review has utilized the Arskey and O'Malley⁵ strategy for reviews in healthcare. **It follows the following steps:**

1. Identifying the research question
2. Identifying relevant work
3. Study selection
4. Charting data
5. Collating, summarizing and reporting the results
6. Consultation with stake holders.

The research question examined the guidelines for modified regimens of Radiation therapy for cancers of the Head and Neck region pertaining to Covid-19. The key words used were

Radiotherapy in Head and Neck Cancer during Covid-19, Protocols for Radiation therapy during Covid-19, Changes in Radiation protocol for Head and Neck cancer during Covid-19. The inclusion criteria incorporated the strategies outlined by various organizations such as ASTRO/ESTRO and other individual contributions. Based on this need for data, electronic databases of Cochrane, PubMed, Medline, Web of Science, Scopus and Ebsco were explored.

A total of 11 articles were identified as relevant to the research criteria. However after further evaluation of full text of the articles, 5 were analyzed for fulfillment of the review. The proposed guidelines for administration of Radiation Therapy under the impact of Covid-19 were summarized. The results were tabulated (Table 1) for reporting. Consultation with stake holders is not applicable under the parameters of this scoping review.

RESULTS

Tom Roques and Robin Prestwich¹ recommend that every treatment centre modify their protocol. This will depend upon the availability of resources to provide radiotherapy and the relative risk of infection from Covid-19. They emphasize pre and post treatment assessment of ability of the patient to swallow and avail nutrition. To reduce hospital visits, Hypofractionated regimens of radiotherapy are vital. To reduce treatment durations; 65 Gy in 30 fractions is recommended. Previous evidence from UK suggests 55 Gy in 20 fractions over 4 weeks⁵. Concurrent chemotherapy may also be administered but it increases the susceptibility to infections. It should be avoided in older patients. Accelerated fractionation without administering chemotherapy is optional however feasibility issues arise. Depending upon local resource potential concurrent Cisplatin/Carboplatin may be effective. They suggest omitting adjuvant radiotherapy if risks are higher than the overall benefit. For palliative care, they propose short fractionation schedules. 20 Gy in 5 fractions over one week to 30 Gy in 6 fractions with IMRT over a period of 2 weeks or even a one-time 8 Gy fraction; as dictated clinically. It is best to postpone radiotherapy if patient tests positive for Covid-19. Thomson et al² in their unpublished survey among the American Society of Radiation Oncology (ASTRO) and European Society for Radiotherapy and Oncology (ESTRO) and few Asia Pacific countries also recommend hypofractionated radiotherapy schedules. These pertain to local factors like availability of resources, staff and knowledge of the altered fractionation, and dose constraints. Factors relevant to patient's fitness like age and presence/absence of comorbidities govern the risk of exposure. They abstain from disrupting Radiotherapy for Covid-positive patients with minor symptoms. This is to avoid tumor repopulation. However, severely symptomatic Covid-19 positive patients need to discontinue Radiation therapy.

Where resources to provide Radiotherapy are severely diminished treatment prioritization on case to case basis is imperative. In decreasing order of priority ranking was enlisted as follows OP+, OP-, LX, OC+, GLOT, HXpal,OC. They agreed that HXpal needs to be prioritized over GLOT and LX over OP- to prevent airway obstruction, keeping Covid-19 in mind. Further, due to inability to open operation rooms, radical chemo-radiotherapy be considered instead of surgery. In case of cancers of the oral cavity; where toxic effects of radiotherapy are worse; a waiting period of 8 weeks for T1-2 and 4 weeks for T3-4 cancers was suggested. This is to accompany close clinical monitoring.²

According to Kochhar et al⁶ patients receiving radiation/chemotherapy for oral cancer must maintain their oral hygiene. Dentists should counsel patients to abide to the prescribed medicated oral rinses and dentifrices. This aids in avoiding the side effects of Radiation therapy like mucositis, xerostomia and dysgeusia. The mineralization of teeth needs to be maintained and carried risk has to be reduced. Hence home care measures are essential. Tele-dentistry is an essential tool in the pandemic enslaved world.

Day et al⁷ advocate primary radiotherapy with chemotherapy for advanced sinonasal or T4a laryngeal mucosal squamous cell carcinoma patients. Although, the results as compared to surgery maybe poor. The combination will most likely preserve the possibility of cure. Re-radiation maybe considered for salvaging patients who have had long periods of remission. However, toxicity due to these treatments will be higher. Radical-intent radiotherapy can be considered for patients with advanced cutaneous squamous/basal cell carcinomas.

Evidence based recommendations by Patil V et al⁴ include: **for stage I-II oral cancer** inoperable due to medical comorbidities; immediate radical radiotherapy should be administered (delay of up-to 37 days is acceptable). Adjuvant radiotherapy is advised post operatively where high risk features exist like grade is poor, invasion of lymphovascular space, or perineural invasion.¹⁰ Chemoradiation (CRT) is suggested where margins are positive or even close to improve survival rate.⁸ Again, toxic effects are high. For **locally advanced resectable cancers of the oral cavity** adjuvant radiotherapy can be avoided on T3N0 and T1-T2N1 however it is recommended for salvaging such patients with recurrence.

Concurrent CRT improves survival where margin status is positive and there is perinodal extension or more than 2 lymph nodes are positive. 3-4 cycles of NACT will help avoid radiotherapy in 40% patients. This reduced the load on radiotherapy units during the pandemic. IMRT should be reserved for patients where it will be useful in reducing toxicity and sparing critical organs. 3D conformal radiation may be administered to decrease the load on depleting resources.⁴

For **locally advanced borderline resectable oral cancer** SRT should be deferred if possible; unless margins are positive and perinodal extension exist with 2 or more lymph nodes being involved. For **oropharyngeal/laryngeal cancers** radiation is preferred to preserve the swallowing apparatus in stage III-IV (CRT plus cisplatin). Surgery is unavoidable in **stage III-IV laryngeal/hypopharyngeal resectable malignancies**. Adjuvant radiation therapy is advised if deemed necessary. For the **unresectable** ones, radiation following NACT is preferred to limit nosocomial exposure. In **cancers of the nasopharynx**, radiation for stage I should not be delayed and IMRT for stage II-IV is advantageous. Radiation therapy should be tailored to the needs of the patients with **recurring salvageable/non salvageable malignancies**.

Table 1: Author Recommended Guidelines For Administration Of Radiation Therapy Depending Upon Staging And Location:

| S.No | Title/Author | Recommendations |
|------|--|--|
| 1. | Roques T. Prestwich R et al. Head and Neck Cancer and Covid-19. ¹ | <p>Hypofractionated Regimens: 65 Gy in 30 fractions/55 Gy in 20 fractions over 4 weeks Concurrent chemotherapy (Cisplatin/Carboplatin) Omit adjuvant radiotherapy if risks are higher</p> <p>Palliative Care: 20 Gy in 5 fractions over one week - 30 Gy in 6 fractions with IMRT over a period of 2 weeks or even a one-time 8 Gy fraction</p> <p>6. Postpone radiotherapy if Covid-POSITIVE</p> |
| 2. | Thomson D. Palma D. et al. Practice Recommendations for Risk-Adapted | Hypofractionated Radiotherapy Schedules |

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|----|---|---|
| | Head and Neck Cancer Radiation Therapy During the COVID-19 Pandemic: An ASTRO-ESTRO Consensus Statement. Int J Radiation Oncol Biol Phys, 2020, Vol. 107;4(618-27). ² | Continue radiotherapy in Covid-positive with Minor symptoms Discontinue radiotherapy in Covid positive with Severe symptoms Treatment Prioritization: HXpal over GLOT and LX over OP- Radical Chemo-Radiotherapy instead of surgery Waiting Period of 8 weeks for T1-2 and 4 weeks for T3-4 Oral cancers |
| 3. | Kochar A. Bhasin R, et al., Provision of continuous dental care for oral oncology patients during & after COVID-19 pandemic. ⁶ | Patients receiving radiation/chemotherapy for oral cancer must maintain Oral Hygiene Tele-dentistry is an essential |
| 4. | Day A. Sher D, Head And Neck Oncology During The COVID-19 Pandemic: Reconsidering Traditional Treatment Paradigms In Light Of New Surgical And Other Multilevel Risks. ⁷ | Primary Radiotherapy + Chemotherapy for advanced sinonasal or T4a laryngeal mucosal squamous cell carcinoma Re-Radiation in recurring malignancies after long term remission Radical-Intent Radiotherapy in advanced cutaneous squamous/basal cell carcinomas. |
| 5. | Patil V. Noronha V. COVID-19 and head and neck cancer treatment. Cancer Research, Statistics, and Treatment / Volume 3 / Supplement 1 / April 2020 ⁴ | For Inoperable stage I-II oral cancer: Immediate radical radiotherapy Adjuvant radiotherapy (post operative in high risk) CRT (positive margins) For locally advanced resectable oral cancers: adjuvant radiotherapy -avoid for T3N0 and T1-T2N1 -recommended in recurrence. CRT (positive margins) NACT IMRT - reduce toxicity 3D conformal radiation locally advanced borderline resectable oral cancer- defer SRT unless positive margins oropharyngeal/laryngeal cancers - radiotherapy preferred stage III-IV laryngeal/hypopharyngeal resectable malignancies- Surgery is unavoidable + Adjuvant radiation stage III-IV laryngeal/hypopharyngeal un-resectable malignancies- radiation + NACT cancers of the nasopharynx – STAGE I - radiotherapy STAGE II-IV - IMRT |

DISCUSSION

Werner et al⁹ concur that the Covid-19 pandemic will cause a disruption in the treatment process. Evidence suggests that most head and Neck tumors double in volume over a period of 1-3 months. This is irrespective of location or size at the time of initiation.⁸ Data suggests that the longer the interval between surgery and post operative radiation therapy, the lower the overall survival rate. Delaying treatment; surgical/radiation will significantly impact the survival rate as well. They suggest that HPV related cancers be treated with definitive radiotherapy because endoscopic procedures generate aerosols.¹⁰

Under the impact of Covid-19, Higgins et al¹¹ (New South Wales) noted an 8% rise in 20 fraction regimen for head and neck cancer patients. The 30 fraction regimens have increased by 12% and 0% attendance was noted for 35 fraction regimen.

Nagar et al¹² have pointed out the harmful effects of postponing radiotherapy in the current setting. Delay in delivery of radiotherapy can compromise not only the control over local invasion of the tumor but also the overall survival of the patient. They affirm a definite worsening of survival outcome.

Radiotherapy is an irreplaceable part of cancer treatment. For head and neck cancer it is essential for limiting local invasion of critical organs and improving the survival rates. An important part of triage during Covid-19 is weighing the pros and cons. Is it practical to expose immunocompromised patients to radiation units? On the other hand, surgery involves procedures which generate aerosols so radiation is safer. Institutions have to re-design resource and personnel-based protocols depending on availability.

CONCLUSION

This scoping review has attempted to congregate the available recommendations from various sources. The aim was to provide a comprehensive glance at the Radiation therapy protocols that need to be modified according to the restrictions imposed by Covid-19. With new information pouring in everyday extensive research is warranted. It is suggested that future research should explore the effects of Covid-19 on patient care pre and post radiation therapy.

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