

Impact of COVID-19 Pandemic on Patterns of Care and Outcome of Head and Neck Cancer: Real-World Experience From a Tertiary Care Cancer Center in India

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PURPOSE The COVID-19 pandemic has caused unprecedented health, social, and economic unrest globally, particularly affecting resource-limited low-middle-income countries. The resultant curfew had made the access to and delivery of cancer care services an arduous task. We have reported the patterns of care and 1-year outcome of head and neck squamous cell carcinoma (HNSCC) treatment before and during COVID-19 lockdown at our institution.

MATERIALS AND METHODS Patients who underwent radiation therapy (RT) for nonmetastatic HNSCC between March 1, 2020, and July 31, 2020, were included in the COVID-RT group, and those who were treated between October 1, 2019, and February 29, 2020, were included in the preCOVID-RT group.

RESULTS A total of 25 patients were in the COVID-RT group, and 51 patients were in the preCOVID-RT group. An increase in the incidence of locally advanced cancers across all subsites was observed in the COVID-RT group. There was a steep increase in the median overall RT treatment duration (52 v 44) and median break days during RT (10 v 2) in the COVID-RT group. The median follow-up period of all patients was 18 months. The progression-free survival at 1 year in the COVID-RT group and preCOVID-RT group was 84% and 90%, respectively ($P = .08$), and overall survival at 1 year was 86% and 96%, respectively ($P = .06$).

CONCLUSION Our study elucidates the adverse impact of the COVID-19 curfew on cancer care and has demonstrated safe delivery of RT for HNSCC without major acute adverse effects. Despite a significant increase in treatment breaks, early outcome data also suggest that 1-year progression-free survival and overall survival are comparable with that of the pre-COVID-19 times; however, longer follow-up is warranted.

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INTRODUCTION

The novel coronavirus (SARS-CoV-2) outbreak emerged in December 2019 and was later labeled officially by the WHO as COVID-19. On January 30, 2020, the WHO formally announced that COVID-19 is a worldwide health emergency, and coincidentally, India reported its first COVID-19 case on the same day. On March 11, 2020, the WHO declared the COVID-19 outbreak a pandemic that was predicted to cause unprecedented global unrest, especially in densely populated low-middle-income countries (LMICs) such as India. Subsequently, with the rising cases, the Government of India instituted a series of nationwide lockdowns that began on March 24, 2020.¹

India's national lockdown, which was considered one of the world's strictest lockdowns, and stringent travel restrictions were a necessary evil that eased out the emergent first wave in 2020.² Several areas of health care, including oncology services, were adversely affected

during the pandemic. Even before the pandemic, reports suggest that a substantial group of patients in India travel outside their domicile region for cancer care, which was significantly affected during the lockdown.³ The access to cancer care was severely affected as a majority of cancer centers in India are located in tier 1 cities. Some cancer centers were partially or entirely converted to COVID-19 treatment facilities. Data from cancer centers across the world and India have reported that oncology services have been considerably disrupted during the COVID-19 pandemic.⁴ Various hospitals and cancer centers were forced to defer elective surgeries, restrict non-COVID-19 admissions, and redirect resources toward COVID-19 care.^{5,6}

Head and neck cancers are the second most common cancer by incidence in India and are often locally advanced, warranting multimodality management.⁷ Radiation therapy is a cornerstone in head and neck squamous cell carcinoma (HNSCC) treatment, as around 70% of patients would require radiation

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CONTEXT

Key Objective

What are the real-world impacts of the COVID-19 pandemic and resultant restrictions on head and neck cancer management?

Knowledge Generated

We have compared patterns of care and outcomes of patients treated during the first wave of the pandemic (COVID-RT) and just preceding the pandemic (preCOVID-RT). Because of significant disruption to the access to cancer care during the pandemic, more advanced stages of cancer increased overall radiotherapy treatment duration and breaks during radiotherapy were noted. These factors are proven to have an adverse impact on survival.

Relevance

The 1-year survival rates are comparable in the two groups; however, diverging trends were noted in the survival curve, suggesting that a longer follow-up is needed before drawing any significant conclusion on the outcome. A global preparedness initiative is warranted with the emerging outbreaks worldwide without compromising the delivery of cancer care.

during the course of their disease. Resectable oral cavity cancers and laryngeal cancer with thyroid cartilage involvement are often managed with primary surgery, and radiation therapy is added as an adjuvant whenever indicated. However, definitive radiotherapy with or without chemotherapy is the treatment modality of choice in other subsites of HNSCC.⁸ A plethora of practice guidelines for cancer management had emerged during the pandemic recommending to defer immunosuppressive chemotherapy and major surgeries because of the risk of aerosolization and contracting COVID-19 infection.⁹⁻¹¹ As the pandemic evolved over time, various guidelines and consensus documents for radiotherapy practice were published from across the world and India during the second half of 2020. Unlike chemotherapy or surgery, the use of radiation therapy was never discouraged whenever indicated, but various measures such as hypofractionation and disinfection protocols were advocated to reduce infection rates.¹²⁻¹⁵ Because of the diverse oncologic infrastructure across the country, it is well recognized that such one-size-fits-all strategies cannot be implemented everywhere.¹⁶

Although a handful of reports on patterns of care and radiotherapy practice during the COVID-19 pandemic are available, almost all of them lack outcome data. Therefore, our study aims to report the practice changes, patterns of care, and outcomes of patients treated during the early phase of the COVID-19 pandemic when the national curfew was most stringent.

MATERIALS AND METHODS

In this study, data of all patients age older than 18 years who underwent radiation therapy for nonmetastatic HNSCC in our tertiary care institution were retrospectively collected and divided into two groups. Patients treated between March 1, 2020, and July 31, 2020, were included in the COVID–radiation therapy (COVID-RT) group, and those who were treated between October 1, 2019, and February 29, 2020, were included in the preCOVID-RT group (Fig 1). Patients diagnosed with nasopharyngeal carcinoma,

cutaneous squamous cell carcinoma, and nonsquamous histology were excluded from the study.

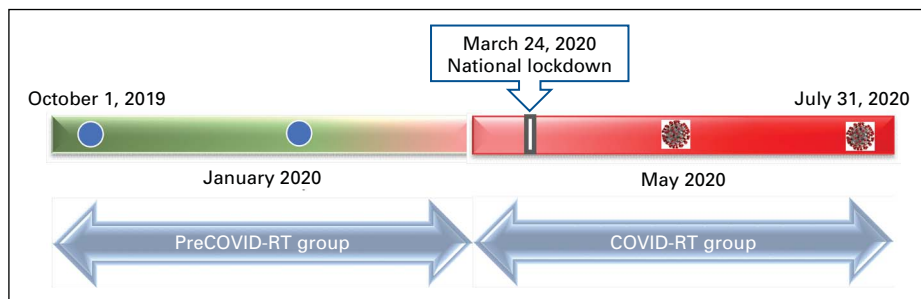
Data were collected from electronic medical records, including imaging and laboratory reports. Clinical information such as age, sex, tumor site, stage, treatment details, and follow-up data were retrieved. Baseline characteristics, patterns of care, sequencing of treatment, treatment protocol, radiotherapy details, compliance, toxicities, and follow-up data were compared between the two groups. Patients who were lost to follow-up after treatment were contacted over the phone. Given the study's retrospective nature, approval from the institutional ethics committee was not required as part of our institutional protocol, and the need for obtaining written informed consent was also waived.

Descriptive data were presented as mean or median values with ranges or absolute numbers with percentages and proportions, as appropriate. Chi-square test was used to compare proportions, and the Student T-test was used to compare continuous data between the two groups. Overall survival (OS) and progression-free survival (PFS) rates were calculated using the Kaplan-Meier method. Follow-up data of the preCOVID-RT group was censored on March 30, 2021, to compare the 1-year outcome. Univariate analysis of prognostic variables was performed using a log-rank test, and Cox proportional hazards regression models were used to assess the predictors of PFS and OS on multivariate analysis. A two-sided P value $\leq .05$ was considered statistically significant. All statistical analyses were performed using IBM SPSS software (Version 25, Armonk, NY).

RESULTS

A total of 76 patients were included in the study; 25 patients were included under the COVID-RT group and 51 patients under the preCOVID-RT group. Baseline patient characteristics of both groups are tabulated in Table 1. There was a substantial decrease of 49% in the number of patients subjected to head and neck radiotherapy in the COVID-RT group. Median age was 50 years and 56 years for the

FIG 1. Timeline used for stratification of the study groups. COVID-RT, COVID–radiation therapy; preCOVID-RT, preCOVID–radiation therapy.



COVID-RT group and the preCOVID-RT group, respectively. Compared with the preCOVID-RT group, a 15% increase in the use of radical radiotherapy in oral cavity subsites was noted in the COVID-RT group (49% v 34%), whereas in the preCOVID-RT group, radiotherapy was predominantly used postoperatively for oral cavity cancers (50% v 61%). A significant drop in the presentation of early-stage laryngeal cancers was noted in the COVID-RT group (12% v 33%). A global increase in the incidence of locally advanced cancers across all subsites was observed in the COVID-RT group.

Treatment details are tabulated in [Table 2](#). Patients referred for RT after surgery or induction chemotherapy had a

median delay of 34 days before initiation of RT in the COVID-RT group, whereas it was 22 days in the preCOVID-RT group. A noticeable shift was observed in using radical radiotherapy with concurrent chemotherapy in subsites and stages where surgical intervention or induction chemotherapy would have been otherwise used. Because of the higher incidence of early-stage laryngeal and oral cancer, the indication of chemotherapy was also relatively lesser in the preCOVID-RT group. Only 24% of patients received the planned cycles of chemotherapy in the COVID-RT group. Intensity-modulated radiotherapy with simultaneous integrated boost technique was used in all patients treated with curative intent, and 3D conformal radiotherapy

TABLE 1. Patient Characteristics

Characteristic	COVID-RT (n = 25)	PreCOVID-RT (n = 51)	P
Age, years			
Range	35-71	19-78	
Median	50	55	
Sex, Frequency (%)			.57
Male	21 (82)	40 (78)	
Female	4 (18)	11 (22)	
Site, Frequency (%)			.051
Oral cavity	17 (68)	23 (45)	
Oropharynx	4 (16)	3 (6)	
Larynx	3 (12)	17 (33)	
Hypopharynx	0 (0)	5 (10)	
Sinonasal	1 (4)	3 (6)	
Stage, Frequency (%)			.32
I	2 (8)	7 (14)	
II	2 (8)	7 (14)	
III	5 (20)	10 (19)	
IV A	15 (60)	22 (43)	
IV B	1 (4)	5 (10)	
Intent of RT, Frequency (%)			.93
Radical	15 (60)	29 (57)	
Adjuvant	9 (36)	19 (37)	
Palliative	1 (4)	3 (6)	

Abbreviations: COVID-RT, COVID–radiation therapy; PreCOVID-RT, PreCOVID–radiation therapy; RT, radiation therapy.

TABLE 2. Treatment Characteristics

Characteristic	COVID-RT (n = 25)	PreCOVID-RT (n = 51)	P
Overall RT duration, days			.068
Median	52	44	
Range	10-71	12-68	
Break during RT (excluding weekends), days			< .001
Median	10	2	
Range	4-24	0-12	
Treatment defaults (after initiation of RT), Frequency (%)	4 (16)	3 (6)	.353
Symptomatic COVID-19 during RT, Frequency (%)			
Yes	3 (12)	NA	
No	21 (88)	NA	
Chemotherapy, Frequency (%)			.073
Concurrent	6 (24)	17 (33)	
Neoadjuvant	7 (28)	6 (12)	
Chemotherapy not indicated	7 (28)	25 (49)	
Chemotherapy indicated, not given	5 (20)	3 (6)	

Abbreviations: COVID-RT, COVID–radiation therapy; NA, not available; PreCOVID-RT, PreCOVID–radiation therapy; RT, radiation therapy.

was used for palliative intent. Hypofractionation (2.2-2.5 Gy per fraction) was adopted in five patients (20%) in the COVID-RT group to an appropriate equivalent dose at 2 Gy per fraction. Hypofractionated radiotherapy was not associated with increased treatment-related toxicity or breaks during RT. We observed a steep increase in the median overall RT treatment duration (52 v 44) and breaks during RT (10 v 2) in the COVID-RT group, predominantly between the third week of March and the fourth week of May 2020. The treatment breaks observed in the preCOVID-RT group were because of treatment-related toxicity such as grade 3 mucositis, dermatitis, or neutropenia. However, in the COVID-RT group, it was predominantly because of travel restrictions and COVID-19 infection. Overall treatment default rates after initiation of RT were similar in both groups. Three patients who developed symptomatic COVID-19 during radiotherapy had significant breaks of 23, 26, and 30 days, respectively. As per the government health department's protocols, radiotherapy was interrupted, and all of these patients were quarantined in COVID-19 care centers for a minimum of 21 days. Radiotherapy was restarted after two reverse transcription polymerase chain reaction–negative tests and treatment gaps were compensated with extra fractions.

The median follow-up period of all patients was 18 months (range, 3-20 months). Median PFS and OS were not reached in the study population. The OS and PFS at 1 year of all patients are depicted in the Kaplan-Meier curves (Figs 2 and 3). The PFS at 1 year in the COVID-RT group and preCOVID-RT group was 84% and 90%, respectively ($P = .08$). The OS at 1 year in the COVID-RT group and preCOVID-RT group was 86% and 96%, respectively ($P = .06$; Table 3). Disease progression was reported in five patients (20%) in the COVID-RT group and eight patients

(16%) in the preCOVID-RT group ($P = .64$). Four patients died in the COVID-RT group during the follow-up period, of which one patient, who was in remission, died because of severe COVID-19 infection. Hypofractionated radiotherapy, use of chemotherapy, overall treatment time, and breaks during radiotherapy did not significantly affect survival.

DISCUSSION

The COVID-19 pandemic has affected more than a billion people and resulted in unprecedented challenges globally. The resultant widespread mortality and newer variants of the virus have exposed the frailties of health care systems worldwide. India's health care system had crippled during the massive second wave, resulting in the loss of thousands of lives. On the brighter side, more than five billion vaccine doses have been administered globally, which serves as our beacon of hope in reducing the mortality associated with COVID-19 and possible protection from the infection. However, the emergent highly infectious and vaccine-resistant mutant strains suggest that the complete eradication of the COVID-19 virus may take many years. Various restrictions were enforced to curb the spread of the virus, including but not limited to a strict travel ban, stay-at-home curfew, and restructuring of health care systems to prioritize COVID-19 care. Several reports worldwide have suggested a possible increase in non-COVID-19 deaths (heart disease and cancer) during the COVID-19 pandemic, possibly because of lack of access to appropriate care.^{17,18} A predictive model-based outcome analysis on cervical cancer from India has also estimated a likelihood of excess cervical cancer deaths due to pandemic-related delays in diagnosis and treatment compared with COVID-19 deaths averted by the nationwide restrictions.¹⁹ Another audit from

TABLE 3. Outcome Characteristics

Outcome	COVID-RT (n = 25)	PreCOVID-RT (n = 51)	P
Disease progression, No. (%)	5 (20)	8 (15)	.64
Deaths, No. (%)	4 (16)	5 (10)	.432
Death because of cancer, No. (%)	3 (12)	5 (10)	.214
1-year PFS, %	84	90	.08
1-year OS, %	86	96	.06

Abbreviations: COVID-RT, COVID-radiation therapy; OS, overall survival; PFS, progression-free survival; PreCOVID-RT, PreCOVID-radiation therapy.

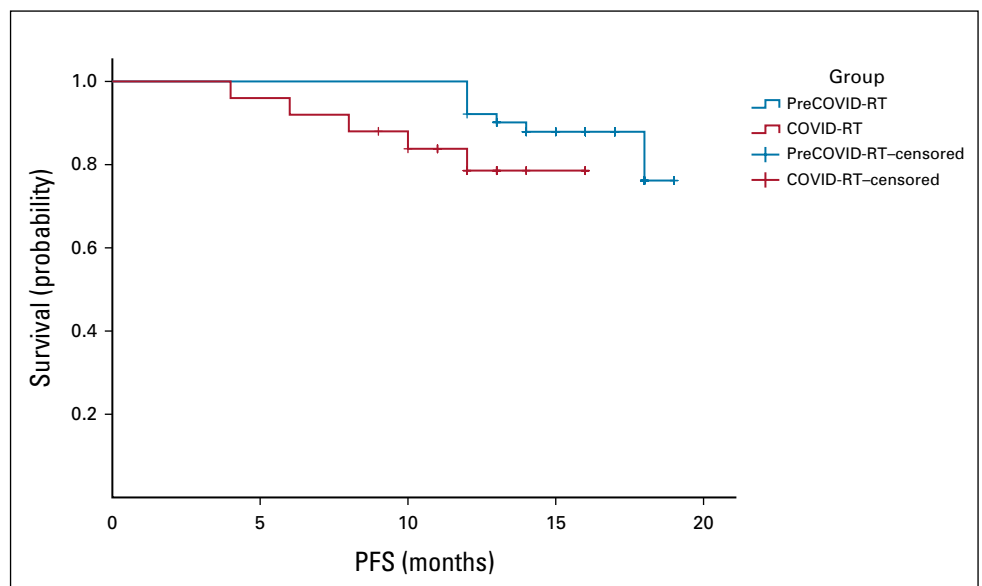
India, similar to ours, conducted on the management of gynecologic malignancies, also highlights the challenges faced in delivering cancer care during the lockdown.²⁰ Reports such as ours, on real-world experience with cancer management during COVID-19, are essential to formulate robust oncology practice guidelines during such crisis situations.

Travel restriction, lack of public transportation, and hesitancy of the patients because of the fear of contracting the virus from hospitals further complicated the existing debilitated health care access in the country. A significant reduction in the number of patients availing cancer care services was observed across countries, irrespective of the nation's income status. A pan-Indian multicentric study also observed an average decrease of 45% in patients undergoing radiotherapy, which was consistent with a 49% reduction reported by us.⁴ This delayed access to care probably contributed to the significant increase in the locally advanced HNSCC across all subsites in the early phase of the pandemic. Although emergency procedures were performed, major surgical procedures for HNSCC were deferred as they were considered high aerosol-generating, increasing the risk of infection to the surgical team and requiring the use of critical resources such as the intensive care unit. Radiotherapy was used with a radical

intent in early oral cavity cancer or stage T4a laryngeal cancer, whereas in normal circumstances, surgery would take precedence. Although there is a lack of large randomized studies comparing the outcome of surgery versus radical chemoradiation in oral cavity subsites, a large retrospective analysis of locally advanced HNSCC of oral cavity showed improved survival with surgery as the initial treatment modality.²¹ In the first couple of months of the lockdown, there existed a hesitancy for the use of chemotherapy as neoadjuvant or concurrently with radiotherapy, which reflects in the number of patients who did not receive chemotherapy when indicated. However, the use of chemotherapy was resumed with appropriate precautions subsequently.

Overall treatment time and treatment breaks during radiotherapy are among the crucial factors predicting the outcome of radiotherapy in HNSCC. A systematic review showed that delays during RT may result in a decline in locoregional control as high as 12%-14% per week.²² This was further reiterated in a national cancer database study, where the authors reported that prolonged radiation therapy treatment time of more than 8 weeks (hazard ratio, 1.25; 95% CI, 1.14 to 1.37; $P < .001$) was associated with a worse OS.²³ Unfortunately, during the pandemic, a significant five-fold increase in the median number of days of

FIG 2. Kaplan-Meier survival curves of PFS between the two groups. COVID-RT, COVID-radiation therapy; PFS, progression-free survival; preCOVID-RT, preCOVID-radiation therapy,



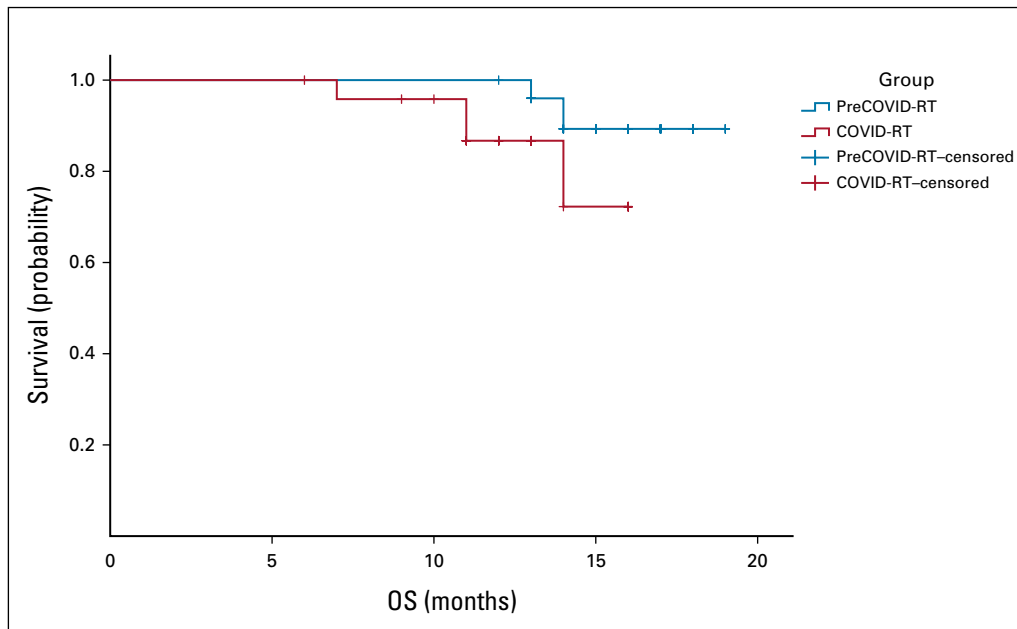


FIG 3. Kaplan-Meier survival curves of OS between the two groups. COVID-RT, COVID–radiation therapy; OS, overall survival; preCOVID-RT, preCOVID–radiation therapy.

interruption during radiotherapy was observed, which also reflected in the prolonged overall treatment time. Albeit, the treatment default rate in our study was similar to the pre–COVID-19 times, which was reassuring. This could be attributed to regular teleconsultations and communication with the patients on treatment by the doctors, radiation therapists, and support staff (Fig 4). Hypofractionated radiotherapy was used as a part of the simultaneous integrated boost in a few selected patients during the study period. Although very little safety data exist on the use of moderate hypofractionation with concurrent chemotherapy, because of

the lack of robust outcome data and limited toxicity management resources, hypofractionation was sparsely used.^{24,25} However, the recent PET NECK trial update provided solidarity toward using hypofractionated radiotherapy with concurrent chemotherapy without compromising local control, OS, and quality of life.²⁶

Despite extensive patient education and safety measures, unfortunately, three patients developed mildly symptomatic incurrent COVID-19 infection. Although various international guidelines suggest noninterruption of

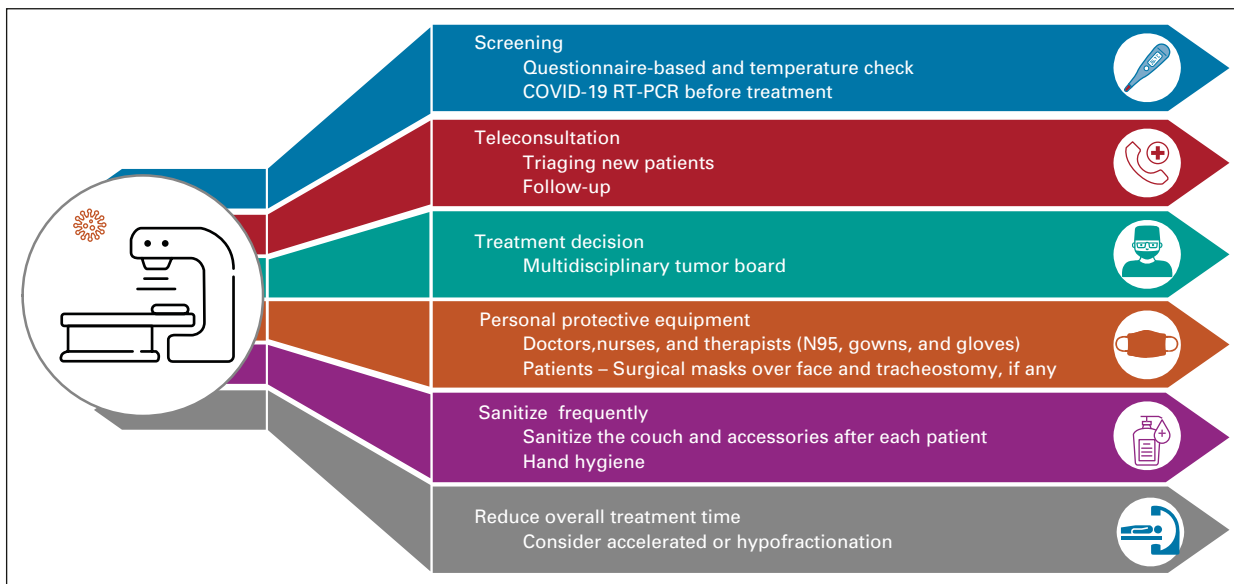


FIG 4. COVID-19–appropriate protocol for radiotherapy during the pandemic. RT-PCR, reverse transcription polymerase chain reaction.

radiotherapy by treating these patients with adequate personal protective equipment at the end of the day in a dedicated vault, implementing the same in a resource-limited setting is not feasible. We did not find a statistically significant difference in the PFS or OS at 1 year among patients in the COVID-RT and preCOVID-RT groups. However, a decrease in survival trend was noted, which perhaps may be because of more advanced-stage disease at presentation and prolonged break in treatment in the COVID-RT group. A global preparedness initiative is warranted with the emerging outbreaks worldwide, even in vaccinated populations because of newer variants. Initiatives taken to curb the spread of COVID-19 infection are paramount but should not be at the cost of compromising treatment for other debilitating illnesses such as cancer. This is a very prevalent issue and is widely under-reported in LMICs. Public health measures have to be taken to improve the accessibility of patients to cancer care and ensure delivery of standard-of-care treatment.

Our study, because of its relatively small, retrospective design, has several inherent limitations such as treatment biases associated with single-institution cohorts, limited toxicity data, and a short follow-up. An overlap of a small

fraction of patients with similar characteristics among the two groups is possible because of the adjacent timelines that might have compromised the demonstration of statistically significant difference in survival. In addition, most follow-up data in this study were collected over telephonic conversation as patients were reluctant to travel amid the pandemic. Despite these limitations, our study is the first study, to our knowledge, to report the outcome of patients with HNSCC treated with radiotherapy during the COVID-19 pandemic from an LMIC.

In conclusion, our study elucidates the adverse impact of the COVID-19 pandemic and the resultant curfew on cancer care. We have demonstrated that radiotherapy for HNSCC can be delivered safely without major acute adverse effects. Despite a significant increase in treatment breaks, early outcome data also suggest 1-year PFS and OS are comparable with that of the pre-COVID-19 times; however, a longer follow-up is needed before drawing any conclusions. A global preparedness initiative is warranted with the emerging outbreaks worldwide, even in vaccinated populations because of newer variants. Therefore, a nation-specific pragmatic consensus guideline is essential for providing optimal cancer care during the pandemic.

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DATA SHARING STATEMENT

Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians ([Open Payments](#)).

No potential conflicts of interest were reported.

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