

Implementation of Radiotherapy and Overcoming the Treatment Breaks in COVID-19 Crisis

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ABSTRACT

Introduction: Tackling of; the patients who had defaulted for radiation therapy due to implementation of lockdown following COVID-19 outbreak, new patients presenting to out-patient department(OPD) and continuing Radiotherapy treatment without postponing during this health crisis is challenging. Study objective was to evaluate the outcomes of hypofractionated radiation therapy in the COVID-19 era and to provide guidance on measures for preparedness in the Department of Radiation Oncology to continue the treatment and tackling treatment breaks.

Material and Methods: Patients reporting to the OPD, patients who defaulted for treatment during lockdown phase and newly diagnosed patients awaiting treatment were included in the study. Hypofractionated schedules were used for treatment to reduce the overall treatment time and duration of hospital stay

Results: Clinical response evaluation was done at the end of 1 month by RECIST criteria. In Head and neck cancer patients 60%, 26% and 13.3% of the patients showed Complete Response (CR), Partial response (PR) and Progressive disease respectively in primary disease and 46%, 40%, 13.3% of the patients showed CR, PR and progressive disease respectively in nodal disease. Among Cervical cancer patients: 75% and 25% of the patients showed CR and PR respectively. All Breast cancer patient were disease free at the time of assessment.

Conclusion: Hypofractionated radiotherapy schedules to be used wherever feasible reducing the overall treatment time and the exposure of Cancer patients to COVID-19 and viral transmission can be mitigated with best clinical practice of sanitization, wearing masks, Face shield, PPE and Social distancing.

Keywords: Radiotherapy, Hypofractionation, COVID-19, Overall treatment time, Cancer treatment.

discontinuing radiation therapy and the patients who were scheduled for radiation therapy could not come for the treatment during the strict 1st and 2nd phase of lockdown. Here, the measures taken for the treatment breaks, initiation of treatment, tackling new patients presenting to out-patient department during this health crisis created by COVID-19 is listed.

Novel Corona virus is new pathogen known to mankind and the complete knowledge of disease course affecting the humans is limited. The health care measures taken in combating this disease has always fell short as the COVID-19 cases are ever increasing in India. Radiotherapy treatment of the cancer patients is always challenging in COVID-19 period. The CFR (Case fatality rate) was 8% in elderly aged 70-79 years and 14.8% for aged more than 80years.³ In India, majority of the people are in the age group of 20-60 years and 11.57 lakh people have the Cancer.⁴ with CFR of COVID-19 in Cancer patients is 5.6% versus 2.6% in General Public.⁵ Cancer patients are at highest risk of Corona infection as they have Immuno-compromised state and present with severe symptoms if infected. About 50% of patients reporting to Oncology Centre need Radiotherapy and it is delivered by daily fractionation risking the patients, health care workers and patient's caregivers for COVID-19. 200-300 patients

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INTRODUCTION

Corona virus was first detected in the city of Wuhan in China on December 1st, 2019.¹ Thereafter, it led to a pandemic disease affecting 216 countries of the world with more than 6,140,934 infected cases and 373,548 deaths worldwide and 190,535 confirmed cases and 5394 deaths in India as on 02.06.2020.² In India, first case was reported on 30th January 2020. To control the spread of infection, gearing up of Health care facilities and to postpone the peak burden of the disease, lockdown was implemented in India from 25th March 2020 to 3rd May 2020 (1st and 2nd phase) and from 4th May 2020 to 31st May 2020 (3rd and 4th phase). Most of the patients on radiation therapy had to return back to their native places

receive treatment every day in Radiotherapy machines. High patient turnover with their attenders in Waiting rooms, holding areas is expected. The routine uses of Accessories like Base plates, Arm positioning handles, Leg rest, Breath hold devices, Thermoplastic immobilizations and other accessories can become a source of Infection as they are used routinely for every patient during Radiotherapy delivery.

MATERIAL AND METHODS

Patients reporting to the Department of Radiation Oncology for Radiotherapy in this health crisis, Patients who defaulted for treatment during lockdown phase and newly diagnosed patients were included in the study after taking written informed consent. To compensate for the treatment breaks-Gap correction was done for the loss of days and suitable Hypofractionated regimes was selected keeping the EQD2, BED doses in mind case wise. All the necessary precautionary measures were taken at registration, evaluation of patient, Radiotherapy planning and treatment delivery points to avert COVID-19. Patient and disease characteristics are depicted in Table:1.

Measures taken to control the spread of Infection: A

Screening/Holding area was created at the entrance of the Hospital, temperature was measured, verifying history of contact with COVID-19 cases, travel history to high risk area, ruling out COVID-19 symptoms, COVID-19 RTPCR test was made mandatory to all the patients before starting the Radiotherapy. Patients were triaged and prioritized based on disease burden and necessary measures were taken for starting treatment, keeping the minimum exposure possible to avoid COVID-19. Hands free Alcohol based hand sanitizers was provided at registration, Out Patient Department (OPD) counters to all the patients and caregivers. Wearing masks was made mandatory for all patients and health care professionals according to guidelines from Health bodies. Personal Protective Equipment(PPE) was made mandatory for Technicians delivering radiation therapy. Strict social distancing was practiced at OPD, Radiation Treatment delivery machines and patient holding areas.

Radiation Therapy: Majority of the cases reporting to Radiotherapy department were Head and Neck cancer cases in Males and Cervix, Breast cancers in females contributing about 80% of cases. 20% of cases were cancer from other sites and Palliative cases.

1. Head and Neck Cancer:

Patients with break in treatment:

- 1) For Patients who had completed more than 50% of the planned dose, Total planned BED and delivered BED was calculated. Remaining BED was delivered by short course hypofractionated radiation therapy (3-4Gy/Fr) by 14 Gy/4Fr or 15Gy/5Fr or 20Gy/5Fr.
- 2) For Patients who had received less than 50% of prescribed dose, the remaining dose was calculated after gap correction and treatment given in short course regimes or conventional fractionation assessing the Performance status.

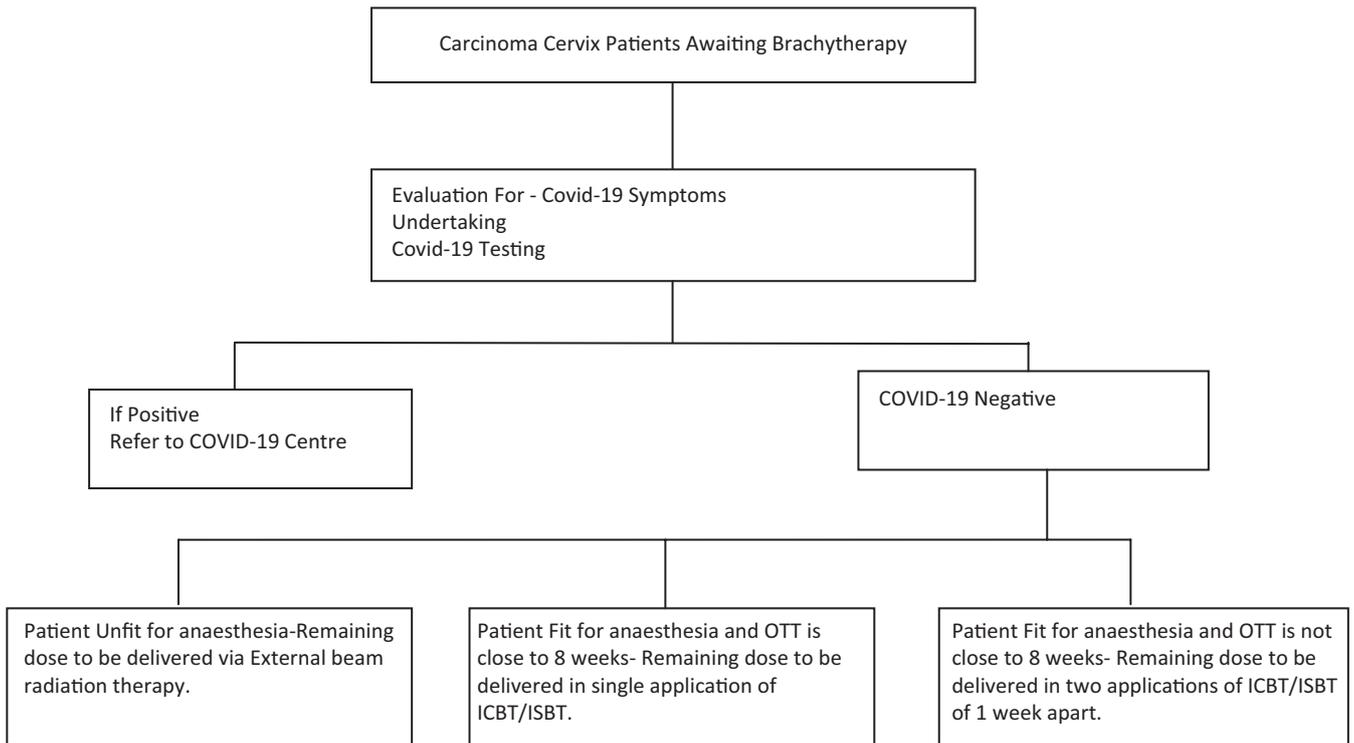
- 3) For Patients who had received less than 50% of prescribed dose and who presented with progressive disease due to which the intent of treatment was changed to palliation were treated with hypofractionated radiation therapy of 20Gy/5Fr or 30Gy/10Fr.
2. Cervical Cancer (locally advanced disease): Treated with hypofractionated radiation therapy 30Gy/10Fr (EQD2=38Gy) followed by 10Gy/2Fr. So that total External Beam Radiotherapy is completed in 16 days. Patients with advanced disease or with metastasis were treated by Palliative Radiotherapy.
3. Breast Cancer: All patients received hypofractionated radiotherapy of 40Gy/15Fr. Now in view of FAST-FORWARD trail results, the new regimen of 26Gy/5Fr can also be considered.

RESULTS

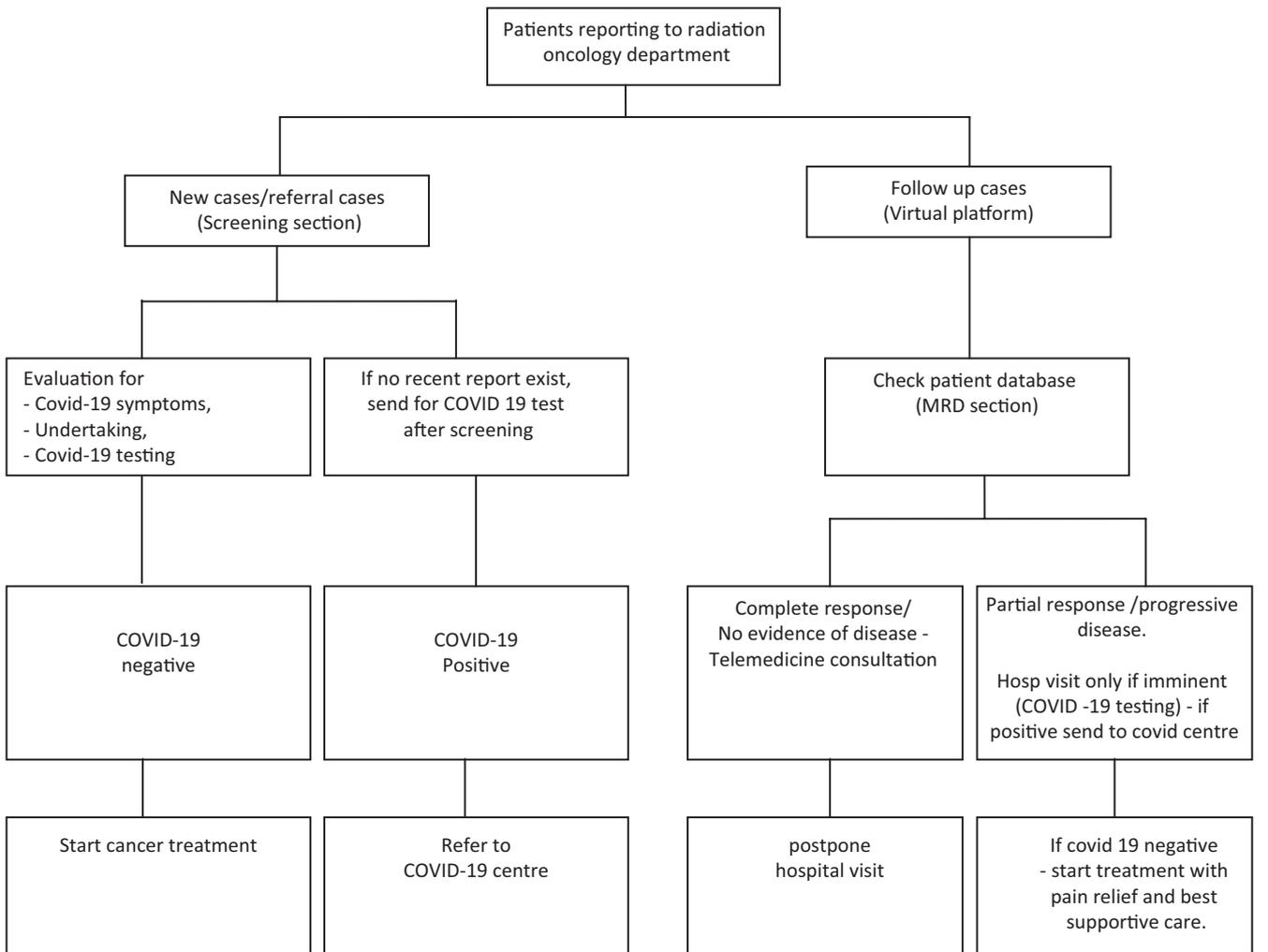
69.3% of the patients were in the age group of less than 50 years and 30.7% of the patients were more than 50 years of age. 57.69% and 42.31% of the patients were male and female patients respectively (Table- 1). Clinical response evaluation was done at the end of 1 month by RECIST criteria. In Head and neck cancer patients 60%, 26% and 13.3% of the patients showed Complete response, Partial response and Progressive disease respectively in primary disease site and 46%, 40%, 13.3% of the patients showed complete response, Partial response and progressive disease respectively in nodal disease area (Table- 2). Overall, out of 15 head and neck cancer patients 7 had Complete Response, 6 Had Partial Response and 2 had Progressive Disease at the

Variable	Finding
Age (years)	
<40	10
40-50	8
50-60	5
>60	3
SEX	
Male	15
Female	11
Primary site	
Head and neck cancer	
Buccal Mucosa(post op) (stage III/IV)	3
Tongue (Ant 2/3) (Stage III)	2
Base of Tongue (Stage III)	2
Vocal Cord (Stage I)	2
Hypopharynx	
Stage III	4
Stage IV	2
Cervical Cancer	
Stage IIB	4
Stage IIIA	2
Stage IIIB	1
Stage IVA	1
Breast (post op)	3

Table-1: Patient characteristics.



Flowchart-1: Flow chart for carcinoma cervix patients with covid-19 risk awaiting brachytherapy



Flowchart-2: Flow chart of cancer patient with covid-19 risk

Site	Stage	Response Evaluation	
		Primary	Node
Buccal Mucosa (post op)	PT3N1M0	CR	CR
	pT4aN2bM0	CR	CR
	pT3N2bM0	CR	CR
Tongue (Ant 2/3)	T2N2aM0	CR	CR
	T3N1M0	CR	CR
Base of Tongue	T3N1M0	CR	PR
	T3N2aM0	CR	PR
Vocal Cord	T1N0M0	CR	CR
	T1N0M0	CR	CR
Hypopharynx	T3N1M0	PR	PR
	T3N2aM0	PR	PR
	T2N1M0	PR	PR
	T3N0M0	PR	PR
	T4aN2cM0	PD	PD
	T3N2cM0	PD	PD
Cervical cancer	IIB (4)	CR	
	IIIA (2)	CR	
	IIIB (1)	PR	
	IVA (1)	PR	
Breast cancer (post op)	pT2N1M0	CR	
	pT3N0M0	CR	
	pT3N1M0	CR	

CR - Complete response, PR - Partial response, PD- Progressive disease

Table-2: Clinical Response assessment.

visits to telephonic or video consultation or short message service(SMS) for weekly review or monthly review and postponing follow-ups to restrict the patient’s exposure to Corona viral infection.

The Workforce management on rotation basis keeping a Reserve team as backup is necessary in case, there are Positive cases detected in the center and if Health care workers are to be Quarantined. Remote working can be permitted for the Radiation Physics team by utilizing the Central Treatment Planning System, which can cater to remote treatment machines. This also minimizes the Health Workers of exposure to COVID-19.

Head and Neck Cancer: Head and neck cancers should be on high priority of treatment list, the treatment can be postponed upto 1-2 weeks and patients planned on radical radiation therapy and adjuvant radiation therapy for involved margins should be given preference over patients requiring adjuvant radiation therapy for minor risk factors. Patients can be considered for hypofractionated regimen with fraction size of 2.4-3 Gy/Fr and 40Gy/16Fr followed by 14Gy/4Fr can also be considered.⁶

Breast Cancer: Radiotherapy can be omitted in patients aged over 65 years (or younger age with relevant co-morbidities) with invasive breast cancer that are upto 30 mm with clear margins, grade 1,2. Oestrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2) negative and

Site	Overall response		
	Complete response	Partial response	Progressive disease
Head and neck cancer	46.60%	40%	13.30%
Cervical cancer	75%	25%	
Breast cancer(post op)	100%		

Table-3: Overall Response

time of clinical response assessment. Among Cervical cancer patients (post external beam radiation therapy all patients received brachytherapy in single application with low dose rate or High dose rate technique): 75% and 25% of the patients showed Complete and Partial response respectively. All Breast cancer patients were disease free at the time of assessment (Table-3).

DISCUSSION

With the present health emergency of novel COVID 19 and as per the situation analyzed till date, everyone has to come to terms of accepting the fact that COVID-19 is going to stay with us all for a very long time. As more than 50% of patients diagnosed with Cancer will need to undergo radiation therapy as a part of their radical, adjuvant or palliative treatment regimens, further postponing the treatment might lead to disease progression and curable disease might become incurable disease. Hence the preparedness to deal with current situation of COVID-19 and continuing the radiotherapy with all the precautions is the need of the hour. Different plan of action can be taken to control the spread of infection. Consultation can be changed from personal

node negative who are planned for treatment with endocrine therapy.⁷ As per FAST and FAST-FORWARD trial patients with all patients requiring radiotherapy with node negative tumours that do not require a boost can be considered for 28-30 Gy in once weekly fractions over 5 weeks or 26 Gy in 5 daily fractions over 1 week⁸⁻¹⁰, and all other patients can be treated with moderate hypofractionated regimen of 40Gy/15Fr.¹¹⁻¹⁴

Esophageal Malignancy: In operable cases, if neoadjuvant chemoradiation therapy is preferred, 40 Gy in 15 fractions (walsh regimen)¹⁵ can be considered along with concurrent chemotherapy.¹⁶ In Inoperable esophageal malignancy 40 Gy in 15 fractions can be considered. This should be followed by 2 cycles of chemotherapy (Fluorouracil and Cisplatin) as per RTOG 85-01.¹⁷⁻¹⁸ In Patients requiring palliative radiation therapy 30 Gy in 10 fractions can be used to minimise hospital visit, shorter course such as 6-8 Gy in one fraction for bleeding or pain and 20Gy/5Fr for dysphagia can also be considered.^{19,20}

Rectal Cancer: In locally advanced rectal cancers, based

on expert consensus statement on the management of rectal cancer during the COVID-19 pandemic long course (50Gy/25Fr) neoadjuvant chemoradiation therapy or short course radiation therapy (25Gy/5Fr) can be considered, but short course radiation therapy with delay to surgery is preferred.^{21,22} Surgery can be delayed upto 12 weeks with reassessment at 8 weeks.^{20,21}

Anal Canal Cancer: Since the patient with anal canal cancer can be cured with chemo radiation therapy deviation from standard approach is not recommended.²⁵

Gynaecological Malignancy: Patients can be considered for Hypofractionated radiotherapy of 30 Gy/10Fr and further consolidated to radical dose after a week. Brachytherapy may be performed and completed by single application only with LDR and HDR techniques under local/regional anaesthesia. Major Institutions have also provided Guidelines for prioritising the Cancer cases and Radiotherapy delivery without delaying in this COVID-19 era. It will help in generating an individualised Institution policy based on available resources and patient load.^{26,27} The departmental protocol for managing patients in OPD and for patients awaiting brachytherapy is given in Flowchart- 1 and 2.

CONCLUSIONS

Radiotherapy is an integral part of multidisciplinary treatment approach in cancer patients, consisting of a large health work force of Radiation oncologists, Radiation physicists, Dosimetrists, Radiotherapy technologists, Nurses and supporting staff. Radiation treatment delivery in this COVID-19 crisis is challenging and mitigating the viral transmission is the need of the hour with best clinical practice of sanitization, personal protection by wearing Masks, Face shield, PPE and maintaining Social distance. Hypofractionated radiotherapy schedules keeping the EQD2, BED doses in mind is to be used wherever feasible reducing the overall treatment time and the exposure of cancer patients to COVID-19, until a cure is found to treat this dreadful disease in the near future.

The most updated recent guidelines from the Local Health bodies, Government Administration must be followed to tackle this novel disease. Like Radiotherapy, following ALARA principle for COVID-19 also holds good. As Low as Reasonably Achievable in reducing the exposure of cancer patients to COVID-19 must be the priority. Maximal safe cancer care and flattening the pandemic curve is the key to reduce the case fatality rate in this cohort of Cancer patients.

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