

Retrospective Study of Palliative Radiotherapy in Locally Advanced and Metastatic Head and Neck Carcinoma: A Single Institution Study

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ABSTRACT

Introduction

The most common cancer of India is head and neck, and about 70% of them present in locally advanced or metastatic disease. Palliative radiotherapy is one of the commonly used treatments in such cases. A retrospective study on the outcomes and toxicity of palliative radiotherapy is studied at a tertiary centre.

Materials and Methods

In this study, 74 patients who underwent palliative radiotherapy at the tertiary centre between Nov 2017 and Oct 2019 were retrospectively analysed. The frequency of different presenting symptoms, radiotherapy regimens, their outcome in form of symptomatic relief and disease status along with toxicity was studied and analysed through the available records.

Results

We identified 74 eligible patients. The median age was 48 years (range, 26–82). Oropharyngeal primary cancer was the most common primary site. The Eastern Cooperative Oncology Group performance status was 3 or more in 74.4% patients. The radiation regimen used were ranged from 8Gy in single fraction, 20Gy in 4 fractions, 20Gy in 5 fractions, 30Gy in 10 fractions and 60Gy in 30 fractions. 93.2% of them completed their treatment. Pain and swelling were the most common presenting symptoms and 90.6% of them had more than 50% relief, while 46.5% had complete or partial response to the treatment.

Conclusion

Palliative radiotherapy to the head and neck provides some symptomatic benefit in most patients, there are multiple dose fractionation regimens currently being used for palliative radiation treatment, and consideration should be given to higher dose palliative RT regimens in patients having good performance status to maximize locoregional control and minimize late toxicity, patient with poor performance status will benefit from a hypofractionated palliative radiation treatment.

Keywords

Head and Neck Cancer; Palliative Care; Radiation Dosage

Head and neck cancer being the most common cancer in India with approx 66% of them are non metastatic locally advanced and 4.4% have metastasis at the time of diagnosis,¹ and many of them are not the candidate for definitive treatment due to advanced disease, comorbidities or poor performance status. The primary aim of treatment shifts from curative to palliative intent to alleviate the symptoms and sufferings of the patients. Palliative radiotherapy is one of the most commonly and widely used form

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of treatment for such patients. The treatment plan of radiotherapy, which includes the target volumes, dose and fractionation, is often influenced by patient related factors such as age, comorbidities and performance status, along with the radiation oncologist decision in relation to anatomic site and treatment goal.

With this knowledge in background, we did a retrospective study on outcomes and toxicity of palliative radiotherapy in head and neck cancer for cancer related distressing symptoms at a tertiary cancer centre in north western India which caters the patient of Rajasthan, Madhya Pradesh and Uttar Pradesh.

Materials and Methods

The records of Radiotherapy from Nov 2017 to Oct 2019 were searched to find out untreated head and neck cancer patient of skin, mucosal or salivary gland origin (excluding lymphomas, sarcomas, and thyroid malignancies) who underwent palliative Radiotherapy at Department of Radiation Oncology of our institute. Radiotherapy was considered palliative, if it was mentioned palliative with reasons like medically inoperable, fixed, and unresectable disease; very advanced locoregional disease, poor performance status, comorbidities, short life expectancy, and metastatic disease by treating radiation oncologist while starting treatment. Recurrent as well as 2nd head and neck carcinoma were excluded from the study. Any patient who has received chemotherapy in form of concurrent, neo-adjuvant or adjuvant within 4 weeks of Radiotherapy were excluded from the study. Patient receiving only single modality of treatment in form of Radiotherapy were only included in the study. Once the inclusion criteria were fulfilled and exclusion criteria were checked, records were reviewed to collect the demographic information, histopathology, site and stage as per AJCC TNM staging system for head-and-neck malignancies - 8th edition.² The performance status was recorded using ECOG performance scale³ along with any comorbidity as per the records.

All the patients were treated in Cobalt 60 teletherapy units, and the gross tumour volume based on clinical and ENT examination (including the primary tumour and/or involved nodes) with 2 cm margin was irradiated. single

fraction was delivered on consecutive working days (5days/week) as per the regimen used.

The primary endpoint was the palliative response, 4 weeks after the completion of the radiotherapy. Percentage symptom relief was quantified by the patient using a rupee scale.⁴ Treatment response was assessed using the WHO Criteria.⁵ Acute skin and mucosal reactions grading was done as per the Radiation Therapy Oncology Group toxicity criteria.⁶ Further treatment of patients was done according to tumour regression status.

Results

Patient characteristics

74 patients were identified who met inclusion criteria and underwent palliative radiotherapy at Department of Radiation Oncology of our institute during Nov 2017 to Oct 2019 period. These 74 patients represent 16% of all HNC patients who underwent RT at our institution during the study period. The patient characteristics are listed in Table I. Of these 74 patients 62.2% were male and 37.8% were females and the mean age of presentation was 48yrs. 17.6% of them were having metastatic disease at presentation i.e. stage IVC, 36.5% were having stage IVB and 45.9% were having stage III-IVA. Most patients had a histopathology of squamous cell carcinoma of which 23% were well and 35.1% were moderately differentiated. Adenocystic carcinoma was found in 5.4% and rest 36.5% were having undifferentiated carcinoma. Oral cavity was found to be the most common site of primary disease constituting 28.4% of the total patients, followed by oropharynx (24.3%), hypopharynx (23%) and larynx (18.9%). 5.4% patients had unknown primary with secondary neck metastasis. The two most common presenting features were pain (66.2%) and swelling (58.1%), followed by dysphagia (14.9%), hoarseness (4%) and other symptoms like bleeding, fungation etc (14.9%). 25.6% had ECOG performance scale scoring of 4, 48.6% had score of 3 while around 26% had score of 2 and 1.

Palliative RT regimen

Palliative radiotherapy only was advised in 23% of the patients because of extensive loco-regional disease,

Table I: Patient characteristics (n = 74)

CHARACTERISTIC	VALUE
Age	
Mean age	48 yrs
Range	26-82 yrs
Gender	
Male	46 (62.2%)
Female	28(37.8%)
Stage	
III-IVA	34(45.9%)
IVB	27(36.5%)
IV C	13(17.6%)
Primary site	
Oral Cavity	21(28.4%)
Oropharynx	18(24.3%)
Larynx	14(18.9%)
Hypo pharynx	17(23%)
Secondary neck	4(5.4%)
Histology	
Well Differentiated Squamous Cell Carcinoma	17(23%)
Moderately Differentiated Squamous Cell Carcinoma	26(35.1%)
Undifferentiated Squamous Cell Carcinoma	27 (36.5%)
Adenocystic carcinoma	4(5.4%)
ECOG PS	
1	02(2.8%)
2	17(23%)
3	36(48.6%)
4	19(25.6%)

Table I: Patient characteristics (n = 74) (Contd.)

CHARACTERISTIC	VALUE
Symptoms on presentation	
Pain	49(66.2%)
Dysphagia	11(14.9%)
Hoarseness	3(4%)
Swelling	43(58.1%)
Others (bleeding, fungation, etc.)	11(14.9%)

13.5% received only due to metastasis at presentation, whereas 17.6% received due to only poor performance status and comorbidities. Majority of them (45.9%) received palliative radiotherapy for combination of more than one factors mentioned above (Table II).

The palliative radiotherapy regimen used were different in subset of patients depending upon their age, comorbidities and performance status, along with the radiation oncologist decision in relation to anatomic site and treatment goal (Table III). The different palliative radiotherapy fractionation used were 8Gy in single fraction (5.4%), 20Gy in 4 (9.4%) or 5 (13.5%) fraction, 30Gy In 10 fractions (46%) and 60Gy in 30 fractions (25.7%). Radiotherapy could be completed in 69 out of 74 (93.2%) as planned. Two patients left treatment in between due to worsening ECOG PS, one of them succumbed to death and 2 left due to toxicity and tumour progression.

Treatment response and outcomes

Majority of the head and neck cancer patients undergoing palliative had relief in their symptoms at the end of 4 weeks (Table IV). The two most common presenting complain were pain and swelling. 93.9% of the patients

Table II: Reason for palliation

Extensive locoregional disease	17 (23%)
Metastases	10(13.5%)
Poor ECOG PS & comorbidities	13(17.6%)
Combination of above factors	34(45.9%)

Table III: Most common radiotherapy regimens used

FRACTIONATION	NO OF PATIENTS PLANNED	COMPLETED PLANNED RT (%)
8Gy in 1f	4	4(100%)
20Gy in 4f	7	6(85.7%)
20Gy in 5f	10	9(90%)
30Gy in 10f	34	34(100%)
60Gy in 30f	19	16(84.2%)

Table IV: Symptom relief after radiotherapy

SYMPTOMS	≤50%	50-75%	≥75%
Pain	3(6%)	36(73.5%)	10(20.4%)
Dysphagia	1(9.1%)	7(63.6%)	3(27.3%)
Hoarseness	2(66.7%)	1(33.3%)	0
Swelling	4(9.3%)	22(51.1%)	17(39.5%)
Others (bleeding, fungation, etc.)	1(9.1%)	6(54.5%)	3(27.3%)

Table V: Treatment response (WHO)

FRACTIONATION	CR	PR	SD	PD	TOTAL
8Gy in 1f	0	0	2 (50%)	2 (50%)	4
20Gy in 4f	0	1(17%)	4 (66%)	1(17%)	6
20Gy in 5f	0	3(30%)	6(60%)	1(10%)	10
30Gy in 10f	0	15(44%)	19(56%)	0	34
60Gy in 30f	1(5%)	12 (63%)	6 (32%)	0	19
Total	1 (1.4%)	31 (46.5%)	36 (50.7%)	4 (5.4%)	

CR: Complete Response, PR: Partial Response, SD: Stable Disease, PD: Progressive Disease

having pain and 90.6% of the patients having swelling as presenting complain got more than 50% relieve in their symptom. 90.9% patients got relief in their dysphagia. Symptomatic relief was achieved in only 33.3% of the patients having hoarseness of voice at the end of 4 weeks. Patients having symptoms like bleeding and fungation got relived in majority of the patients.

Regardless of symptomatic relief, only 46.5% patient had complete or partial regression of tumour. 50.7% had stable disease whereas 5.4 % had progressive disease (Table V). One of the patients died during the treatment.

As per RTOG guidelines, only 2.7% had grade 3, none had grade 4 acute skin toxicity, where as 19% had grade 3 and 1.4% had grade 4 acute mucosal toxicity (Table VI).

Discussion

The present study helped to understand the pattern of presentation, treatment plans and outcomes in patients undergoing palliative radiotherapy at a tertiary centre of northwest India. The analysis showed that majority

Table VI: Acute toxicity

RTOG	ACUTE SKIN REACTIONS	ACUTE MUCOSAL REACTIONS
Grade I	17(23%)	14(18.9%)
Grade II	5(6.8%)	12(16.2%)
Grade III	2(2.7%)	14(19%)
Grade IV	0	1(1.4%)

of the patients presented with pain and swelling with a poor ECOG performance scale. Different variety of fractionation and dose were used, giving a clear picture of heterogeneity of the patient's symptoms, the goals of palliation and individualisation of treatment decisions.

The prognosis is poor when only best supportive care is used in patients having incurable head and neck cancer, such patients have median survival of 3.8 months only.⁷ The primary goal of treatment in patient having incurable disease is to palliate and give symptomatic relief to the patients and to improve quality of life. As per NCCN guidelines "The goal of palliative care is to anticipate, prevent, and reduce suffering; promote adaptive coping; and support the best possible quality of life for patients/families/caregivers, regardless of the stage of the disease or the need for other therapies".⁸

The prognostic factors associated with palliative radiotherapy in head and neck cancer has not been exclusively studied. The prognostic value of dose and fractionation had been studied and investigated in different dose-fractionated regimens.

Mohanti et al. offered a short course of palliative radiotherapy of 20 Gy in 5 fractions over 1 week and had achieved symptom relief for pain, dysphagia, hoarseness, cough and otalgia in 47%-59% of the patients.⁹

Agarwal et al. shared their single institution experience with hypofractionated radiotherapy for palliation in incurable head and neck cancer. Pain and dysphagia were the most common complaints which were relieved by more than 50% in 74% of patients. Eleven patients (10%) had complete response (CR) and 80 (73%) patients had complete and partial response (PR) with acceptable acute reactions.¹⁰

At University of Florida, Erkal et al. retrospectively

reviewed squamous cell carcinomas metastatic to cervical lymph nodes from an unknown head and neck mucosal site who received palliative radiotherapy.¹¹ Patients with relatively good performance status received 30Gy in 10 fractions (3Gy/daily) in once-daily fractions, and patients with poorer performance status received two 10Gy fractions one week apart. 87% of them had either complete or partial response and 57% of them had continued response at 1-year post-treatment. Similarly, Fortin et al. used 25Gy in 5 fractions to palliate the incurable head and neck cancer patients and found this regime to improve the quality of life and PFS in these patients with benefit in overall survival also.¹²

"Christie's" regimen, 16 fractions of 3.125 Gy for palliative radiotherapy was retrospectively studied and reviewed at Netherlands reported 45% complete response and 28% partial response, 6% had stable disease, and 21% progressed during or directly after completion of treatment. The overall inference was an excellent palliation, excellent symptom control with acceptable toxicity profile with "Christie's" regimen.¹³

Stevens et al. also did a retrospective study to find out survival benefit along with symptomatic improvement and quality of life in patients undergoing palliative radiotherapy in incurable head and neck cancer. The most common primary site among these patients was oropharyngeal carcinoma. The median fraction used for these palliative radiotherapy was 20 (range, 1-40) and the median dose was 50 Gy (range, 2-70)(14). It was found that the median survival time was 5.2 months. The radiation dose was found to be an independent predictor of both overall survival and treatment response in multivariate analysis^{14,15}.

The above studies and many more studies have supported the use of palliative radiotherapy in the

inoperable head and neck cancer patients, but there is no consensus guideline for appropriate fractionation regimen of palliative radiotherapy. The ranges of regimens used are of short range hypofractionated radiotherapy to prolong conventional radiotherapy. Many regimens had used cyclical palliative radiotherapy to escalate the dose of palliative radiotherapy, taken into consideration about the toxicity, which indirectly have an impact on quality of life of these patients. Most published series have shown comparable outcomes in respect to survival, symptomatic improvement and quality of life irrespective of dose and fractionation used.^{9,10,12,14,16,17}

Radiation oncologist individualises treatment decision according to the assessment of the patient's symptoms, disease burden, comorbidities, performance status, weight loss, and anemia etc., also taking into the personal consideration of the patient. Therefore the fractionation scheme used becomes a surrogate for such factors. Still, the radiation dose remains the independent predictor of the outcome after known variables are taken into account.

The present study has some limitations, the major one is its retrospective design as information is derived from documentation of follow up, from which precise response and outcome cannot be defined as what can be achieved from prospective studies. Acute toxicity and palliative response was not assessed by standardised methods as other factors also plays a role in their standing like medications, social factors, alternative treatment etc.. Late toxicity and survival outcome was not recorded.

Conclusion

The present study along with other published series, has demonstrated that Radiation Oncologist should assess incurable head and neck cancer patient's performance status, their symptoms, quality of life and goals very carefully. These issues can be improved by palliative radiotherapy and should be offered as a treatment option. Palliative radiotherapy to the head and neck provides some symptomatic benefit in most patients, there are multiple- dose fractionation regimens currently being used for palliative radiation treatment, and

consideration should be given to higher dose palliative RT regimens in patients having good performance status to maximize locoregional control and minimize late toxicity, patient with poor performance status will benefit from a hypofractionated palliative radiation treatment. Additional prospective research is required to better define the subset of incurable head and neck patients who would benefit from different fractionation regimens for palliation.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation (please name) and with the Helsinki Declaration of 1975, as revised in 2008.

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