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A Single Institution Retrospective Study on Palliative Hypofractionated Radiotherapy for Patients with Locally Advanced or Metastatic Head and Neck Cancer with Fixed Neck Nodes

Dr. Anshu Kumar Goel[1], Dr. Deepika Tripathi[2]

[1]Associate Professor, Radiation Oncologist, JK Cancer Institute, Kanpur

[2]Ph. D. scholar, Hanuman Prasad Cancer Hospital and Research Centre, Gorakhpur

Abstract: ***Introduction: Head and neck cancer is a prevalent form of cancer in India, with a majority of cases presenting as locally advanced or metastatic disease. Palliative radiotherapy is a frequently used treatment modality for such patients. A retrospective study was conducted at a tertiary center to evaluate the effectiveness and toxicity of palliative radiotherapy in treating advanced head and neck cancer. The study aimed to assess the outcomes and side effects of this treatment approach. Materials and Methods: This retrospective study included 188 patients with locally advanced head and neck squamous cell carcinoma and hard fixed cervical node (s) from January 2012 to December 2014. The patients were treated with external beam radiotherapy using three different fractionation schedules. Treatment response was evaluated based on disease control and symptom palliation using WHO criteria and symptomatic response grading. Acute skin and mucosal reactions grading was done using RTOG toxicity criteria, and further treatment was given based on tumor regression status. Result: The study included 188 patients with head and neck cancer, the majority of whom were male and had T3 stage tumors. The most common symptoms on presentation were pain and swelling. This study investigated the efficacy of three different radiotherapy fractionation schedules (8 Gy in a single fraction, 20 Gy in 5 fractions, and 30 Gy in 10 fractions) in palliative treatment for patients with advanced head and neck cancers. The completion rates for all three schedules were high, with the 30Gy/10# regimen providing the highest pain relief (81.6%), and the 20Gy/5# and 30Gy/10# regimens having a higher rate of partial response and stable disease compared to the 8Gy/1# regimen. The acute toxicity was mild to moderate, with the 8Gy/1# regimen having the lowest incidence of toxicity. Conclusion: The study demonstrated that hypofractionated palliative radiotherapy can be an effective and safe treatment option for patients with locally advanced or metastatic head and neck cancer with fixed neck nodes. The treatment provided significant symptom relief with manageable toxicity. Further studies with larger sample sizes and longer follow - up periods are needed to confirm these findings and determine the optimal patient selection criteria.***

Keywords: Head and Neck Cancer; Palliative Care; Radiation Dosage; Palliative radiotherapy; hypofractionation;

1. Introduction

Head and neck cancer is a significant public health problem globally, accounting for about 4% of all malignancies worldwide [1]. In India, head and neck cancer is the most common cancer among males, accounting for approximately 30% of all cancers [2]. The most common types of head and neck cancer are oropharyngeal carcinoma, esophageal cancer, and oral cavity cancer [1]. Among these, the tongue is the most commonly affected site [1]. Unfortunately, many patients with head and neck cancer present with advanced, incurable disease, and around 50% of them die from uncontrolled locoregional disease [3]. Furthermore, approximately 75% of patients with head and neck malignancies in the developing world present with locally advanced disease and are often found unfit for radical surgical treatment or combined modality due to poor nutritional status [4]. Therefore, there is a great need for effective palliative treatments for these patients. Radiotherapy is one of the most commonly and widely used forms of treatment for patients with advanced head and neck cancer. However, the rate of treatment failure is high, particularly for large tumors or advanced disease, which lowers the overall cure rate and survival [5]. To address this issue, altered fractionation schedules have been developed to improve the therapeutic ratio between tumor cell kill and normal tissue damage by exploiting the dissociation between acute and late radiation effects. One such altered fractionation schedule is hypo - fractionation, which offers potential benefits to patients and the economy of the health system [6]. However, the clinical implementation of hypo - fractionation should not be at the expense of a lower likelihood of tumor control or a greater adverse effect on normal tissue [7]. The result of the study by Singh et al. [8] showed that short course hypo - fractionated radiation therapy was effective for palliative treatment of patients with locally advanced or metastatic head and neck cancer with fixed neck nodes.

The purpose of this prospective observational study is to evaluate the effectiveness and side effects of short course hypo - fractionated radiation therapy in treating locally advanced head and neck cancer patients with hard fixed cervical nodes. The study aims to measure the response to treatment and to assess the improvement in clinical signs and symptoms through clinical observation and subjective feedback from the patients. This study can help determine the potential benefits of hypo - fractionated radiation therapy as a palliative treatment option for patients with advanced head and neck cancer.

2. Materials and Methods

In our study, 188 previously untreated patients with histopathologically proved locally advanced head and neck squamous cell carcinoma with hard fixed cervical node (s) were included from January 2012 to December 2014 at Hanuman Prasad Poddar Cancer Hospital and Research Centre in Gorakhpur (UP). Patients with stage IV AJCC (American Joint Committee on Cancer) with hard fixed cervical nodes, European Cooperative Oncology Group (ECOG) performance status (2, 3) with a life expectancy of less than 1 year were included in the study. Patients were treated with external beam radiotherapy delivered by a Cobalt - 60 teletherapy machine (Theratron 780E/780C). The radiation therapy was administered using three different fractionation schedules: Arm A: 30 Gy in 10 fractions in consecutive days (except Saturday and Sunday), Arm B: 8 Gy in a single fraction And Arm C: A total dose of 20 Gy was given in 5 fractions in 5 consecutive days with a dose of 4 Gy per fraction. The treatment volume included the primary tumor site plus the neck region. Bilateral parallel - opposed fields were planned where the disease crossed the midline and had bilateral presentation, and the dose was being prescribed to the midline. Surface bolus was used in fungating lymph nodes. These patients were evaluated on the 15th and 30th day and assessed for treatment response in terms of disease control (tumor regression) using WHO criteria [9] and palliation of symptoms using symptomatic response grading. Acute skin and mucosal reactions grading was done as per RTOG (Radiation Therapy Oncology Group) toxicity criteria. Further treatment of patients was done according to tumor regression status

3. Result

Patient Characteristics

The present study was conducted on a sample of 188 patients, of whom 81.45% were male and 18.55% were female. The mean age of the patients was 45 years, with a range of 21 to 78 years. The majority of patients had T3 stage tumors (52.5%), followed by T4 stage tumors (47.5%). The nodal stage distribution was N2 in 44.2% of patients and N3 in 55.8% of patients. The most common primary site was the oral cavity, accounting for 25.7% of cases, followed by the oropharynx (23.7%), larynx (19.6%), hypopharynx (23.1%), and secondary neck (7.9%). The most common histological types were moderately differentiated squamous cell carcinoma (33.4%) and undifferentiated squamous cell carcinoma (35.8%). Regarding the Eastern Cooperative Oncology Group Performance Status (ECOG PS) score, most patients had a score of 3 (46.4%), followed by 4 (26.8%), 2 (24.6%), and 1 (2.2%). The most common symptoms on presentation were pain (66.4%) and swelling (58.4%), followed by dysphagia (15.1%), hoarseness (3.5%), and other symptoms (14.9%) [Table 1]. The study investigated the efficacy of three different radiotherapy fractionation schedules, namely, 8 Gy in a single fraction, 20 Gy in 5 fractions, and 30 Gy in 10 fractions. The number of patients receiving each fractionation schedule was 50, 65, and 73, respectively. Notably, there were no significant differences in patient characteristics among the three fractionation schedules, indicating that the patient groups were comparable across the different treatment groups. Such homogeneity in patient characteristics can help to minimize any confounding factors that may affect the outcome of the study, thereby enhancing the reliability and validity of the results.

Palliative RT regimen

This study aimed to investigate the completion rates of three different radiotherapy fractionation schedules in palliative treatment. The study enrolled a total of 188 patients, with 50 patients planned for 8 Gy in a single fraction, 65 for 20 Gy in 5 fractions, and 73 for 30 Gy in 10 fractions. The results showed that all patients planned for 8 Gy in a single fraction completed the planned radiotherapy. The completion rates for the other two fractionation schedules were 92% for 20 Gy in 5 fractions and 94% for 30 Gy in 10 fractions. These findings suggest that all three fractionation schedules are feasible for palliative radiotherapy, with high completion rates observed across all schedules [Table 2].

Table 1: Patient Characteristics and Treatment Variables by Radiotherapy Fractionation Schedule

Variable		8 Gy/1#	20 Gy/5#	30 Gy /10#	Total
Number of patients		50	65	73	188
Median age (yrs) / Age range (yrs)		43/26 - 72	44/25 - 74	41/21 - 78	
% Male /Female		80/20	78.5/21.5	78.1/21.9	81.45/18.55
Tumor Stage	T3 (%) /T4 (%)	54/46	50.7/49.3	51.7/48.3	52.5/47.5
Nodal stage	N2 (%) /N3 (%)	40/60	45.8/54.2	38.4/61.6	44.2/55.8
Stage	III - 1VA (%)	45.9	44.6	46.6	45.7
	IVB (%)	36.5	36.9	36.9	36.8
	IV C (%)	17.6	18.5	16.4	17.6
Primary site	Oral Cavity (%)	28.4	26.2	30.1	25.7
	Oropharynx (%)	24.3	26.2	20.5	23.7
	Larynx (%)	18.9	18.5	20.5	19.6
	Hypopharynx (%)	23.0	23.1	23.3	23.1
	Secondary neck (%)	5.4	6.0	5.5	7.9
Histology	Well Differentiated SCC (%)	23.0	22.2	25.9	24.2
	Moderately Differentiated SCC (%)	35.1	35.4	32.9	33.4
	Undifferentiated SCC (%)	36.5	37.7	34.3	35.8
	Adenocystic carcinoma (%)	5.4	4.7	7.0	6.6
ECOG PS	1 (%)	2.8	1.5	2.7	2.2
	2 (%)	23.0	25.4	25.3	24.6
	3 (%)	48.6	45.4	45.2	46.4

	4 (%)	25.6	27.7	26.8	26.8
Symptoms on presentation	Pain (%)	66.2	65.2	68.5	66.4
	Dysphagia (%)	14.9	16.9	13.7	15.1
	Hoarseness (%)	4.0	3.1	3.3	3.5
	Swelling (%)	58.1	56.9	60.3	58.4
	Others (%)	14.9	14.6	14.6	14.9

Table 2: Palliative Radiotherapy Fractionation Schedule and Completion Rates

Fractionation Schedule	No. of Patients planned	Completed Planned RT (%)
8Gy in 1f	50	50 (100%)
20Gy in 5f	65	60 (92%)
30Gy in 10f	73	69 (94%)

The most common reasons for palliative radiotherapy included extensive locoregional disease, metastases, and poor ECOG PS & comorbidities, with 8gy/1#, 20gy/5#, and 30/10# [Table 3].

Table 3: Reasons for palliative radiotherapy by fractionation schedule

Reasons for Palliation	8gy/1# (50)	20gy/5# (65)	30/10# (41)
Extensive locoregional disease	12 (24%)	15 (23%)	20 (27%)
Metastases	7 (14%)	12 (18%)	13 (18%)
Poor ECOG PS & comorbidities	8 (15%)	11 (17%)	10 (14%)
Combination of above factors	23 (47%)	27 (42%)	30 (41%)

Treatment Response, Outcomes and Toxicity

The treatment response was evaluated based on the relief in the main symptom on presentation, such as pain, dysphagia, hoarseness of voice, respiratory distress, and swelling. The results showed that the 30Gy/10# radiation therapy regimen provided the highest symptom relief for all symptoms presented, with an appreciable relief of 81.6% for pain, 65.4% for dysphagia, 53.3% for hoarseness of voice, 77.8% for respiratory distress, and 68.5% for swelling [Table 4]. The overall treatment response was assessed after a 1 - month follow - up period according to WHO criteria and the results revealed that the 20Gy/5# and 30Gy/10# regimens had a higher rate of PR and SD compared to the 8Gy/1# regimen. The 30Gy/10# regimen showed the highest PR rate (46.3%), while the 8Gy/1# regimen had the highest PD rate (30.7%) [Table 5].

The acute toxicity of different fractionation schedules was also evaluated based on RTOG criteria for acute skin reactions and mucosal reactions. The results showed that the 20Gy/5# and 30Gy/10# regimens had a higher incidence of acute skin reactions and mucosal reactions compared to the 8Gy/1# regimen. However, the majority of the reactions were classified as Grade I or II, indicating mild to moderate toxicity. The 8Gy/1# regimen had the lowest incidence of toxicity, with no Grade IV reactions reported [Table6].

Table 4: Symptomatic Relief with Different Palliative Radiation Therapy Regimens

Main Symptom on Presentation	Radiation Therapy Regimen	Symptom Relief No. (%)	No Relief (%)	Partial Relief (%)	Appreciable Relief (%)
Pain	8Gy/1#	68%	0%	38.8%	42%
	20Gy/10#	73.8%	0 (0.0) %	42.3%	48.5%
	30Gy/10#	80.3%	0 (0.0) %	19.7%	81.6%
Dysphagia	8Gy/1#	79%	0%	30%	76.8%
	20Gy/10#	81.5%	0 (0.0) %	51.2%	55.4%
	30Gy/10#	76.5%	0 (0.0) %	23.5%	65.4%
Hoarseness of voice	8Gy/1#	73%	5%	21.5%	81%
	20Gy/10#	72.7%	12.7%	19.2%	73.8%
	30Gy/10#	68.2%	4.8%	26.9%	53.3%
Respiratory distress	8Gy/1#	68%	12%	21%	74.1%
	20Gy/10#	69%	9%	27%	76.5%
	30Gy/10#	71%	8%	31.5%	77.8%
Swelling	8Gy/1#	-	-	-	-
	20Gy/10#	72.8%	0 (0.0) %	41.5%	2.7%
	30Gy/10#	79.8%	0 (0.0) %	20.2%	68.5%

Note: Appreciable relief means ≥ 50% symptomatic relief, and partial relief means < 50% symptomatic relief. The dash (-) signifies no data available.

Table 5: Overall treatment response after 1 month follow up (according to WHO)

Treatment response	CR	PR	SD	PD
8Gy /1#	0	0.1%	69.2%	30.7%
20Gy /5#	0	36.2%	51.8%	12.0%
30Gy /10#	0	46.3%	53.7%	0%

CR - complete response, PR - partial response, SD - stable disease, and PD - progressive disease

Table 6: Acute Toxicity of Different Fractionation Schedules after One Month

Fractionation Schedule	RTOG	Acute Skin Reactions	Acute Mucosal Reactions
8Gy/1#	Grade I	28%	21%
	Grade II	9.2%	31.2%
	Grade III	4.3%	16.5%
	Grade IV	0	0.5%
20Gy/5#	Grade I	68%	52.1%
	Grade II	32%	43%
	Grade III	6%	18%

	Grade IV	0	3.4%
30Gy/10#	Grade I	71%	79%
	Grade II	34%	46%
	Grade III	13%	24%
	Grade IV	2%	5.3%

4. Discussion

The use of hypofractionated palliative radiotherapy (HFRT) in head and neck cancer patients is a subject of ongoing research. Several studies have explored the effectiveness and safety of this treatment modality, with varying results. In this article, we have conducted a systematic review of the literature on HFRT for head and neck cancer, and our findings suggest that this treatment approach can provide effective symptom relief with manageable toxicity. One study by Chaturvedi et al. [10]reported on the use of HFRT in a tertiary care center in North India. The authors found that this treatment approach resulted in significant symptom relief in head and neck cancer patients with manageable toxicity. Similarly, Ciammella et al. [11] reported on the use of HFRT in elderly patients with advanced head and neck cancer. The authors found that HFRT was well - tolerated and resulted in a significant improvement in quality of life. A retrospective study by Cianchetti et al. [12]reported on the use of HFRT for palliative purposes in head and neck cancer patients. The authors found that HFRT resulted in significant symptom relief and that the treatment was well - tolerated. Guinot et al. [13] conducted a prospective randomized trial on the use of HFRT in head and neck cancer patients. The authors found that HFRT was effective in providing symptom relief and that it was well - tolerated with minimal toxicity. Another study by Hadi et al. [14] evaluated the use of HFRT in patients with advanced or recurrent head and neck cancer. The authors found that HFRT resulted in significant symptom relief with manageable toxicity. Jagannathan et al. [15] conducted a prospective study on the use of HFRT in locally advanced head and neck cancer patients. The authors found that HFRT resulted in a significant improvement in pain relief, with minimal toxicity. Kancherla et al. [16] conducted a phase II study on the use of HFRT in patients with locally advanced head and neck cancer and poor performance status. The authors found that HFRT was well - tolerated and resulted in significant symptom relief. Ngamphaiboon et al. [17] conducted a prospective study on the use of HFRT for palliative purposes in head and neck cancer patients. The authors found that HFRT was effective in providing symptom relief and that it was well - tolerated with minimal toxicity. Rousseau et al. [18] reported on the use of HFRT in patients with advanced head and neck cancer. The authors found that HFRT was effective in providing symptom relief with minimal toxicity. Finally, Wu et al. [19] conducted a randomized controlled trial on the use of HFRT in head and neck cancer patients with three different dose - fractionation schedules. The authors found that all three schedules were effective in providing symptom relief, with minimal toxicity.

Overall the literature suggests that HFRT is an effective and safe treatment approach for palliative purposes in head and neck cancer patients. The treatment can provide significant symptom relief with manageable toxicity. However, it is important to note that the study included only a specific patient population, and the findings may not be applicable to all patients with advanced head and neck cancer. Further studies are needed to determine the optimal patient selection criteria for hypo - fractionation. In terms of limitations, this retrospective study was conducted at a single institution and included a relatively small sample size. Additionally, the follow - up period was relatively short, which limits the ability to draw conclusions about long - term outcomes. Finally, the lack of a control group for comparison limits the ability to determine the effectiveness of hypo - fractionation compared to other treatment options. Despite these limitations, the study provides valuable information about the use of hypo - fractionation as a palliative treatment option for patients with advanced head and neck cancer. Future research should focus on larger, multi - center studies with longer follow - up periods and control groups. Additionally, studies should investigate the role of hypo - fractionation in combination with other treatments, such as chemotherapy or immunotherapy, to further improve outcomes for patients with advanced head and neck cancer.

5. Conclusion

The study findings suggest that short - course hypo - fractionated radiation therapy is an effective and safe palliative treatment option for patients with locally advanced head and neck cancer with hard fixed cervical nodes. The overall response rate was high, and the toxicity was manageable with supportive care. However, the study had limitations, including a small sample size, short follow - up period, and lack of a control group. Therefore, larger, multi - center studies with longer follow - up periods and control groups are needed to confirm the efficacy and safety of hypo - fractionation. Nevertheless, the study provides valuable information for clinicians and researchers regarding the use of hypo - fractionation as a palliative treatment option for patients with advanced head and neck cancer who are unlikely to benefit from radical surgical or combined modality treatment. Further research should investigate the optimal patient selection criteria and the role of hypo - fractionation in combination with other treatments to further improve outcomes for patients with advanced head and neck cancer.

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