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Concurrent Chemo-radiotherapy Versus Radiotherapy alone in Patients with Head and Neck Cancer: A Prospective Hospital-based Study

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Abstract
Background:*The prognosis and multimodal therapeutic options for patients with head and neck cancer vary depending on epidemiologic factors, anatomical location, and staging of the disease. The study aimedto evaluate the contribution of concurrent chemoradiation therapy (CCRT) and radiotherapy alone in previously untreated patients with unresectable head and neck cancer.*
Methods: *This prospective observational study was conducted at the department of radiotherapy in the Sylhet MAG Osmani Medical College, Sylhet from January 2021 to December 2021. The study was carried out with a total of 36 previously untreated patients with unresectable head and neck cancer. A convenient sample selection method was done for the selection of the participants. Available data were analyzed through SPSS software.*
Result: *The majority of the participants were over 50 years of age, with 33.33% belonging to the age group of 51-60 years, 22.22% belonging to the age group of 61-70 years, and 8.33% being over the age of 70 years. According to the clinical diagnosis, 13 participants (36.11%) had carcinoma (Ca). larynx, 30.56% had Ca. pyriform fossa, either on right, left, or full fossa form, 19.44% had Ca. on the base of tongue (BOT), 5.56% had Ca. posterior cricoid cartilage, and right side metastatic neck, Ca. post pharyngeal wall and right glottis growth were observed in 2.78% of patients each. Among the total 36 patients, 66.67% were given concurrent chemo-radiation therapy (CCRT), and 33.33% had normal radiotherapy. The primary site of lesion was the laryngopharynx for 50% of the CCRT group and 75% of the radiotherapy group. The oral cavity and other sites of lesions had a higher prevalence among the CCRT group compared to the radiotherapy group. Overall survival (Kaplan-Meire Estimations) in patients treated with RT alone or CCRT. Five years of survival is increased from 44% to 80% (log-rank test, $p<0.0003$) by additional chemotherapy along with radiotherapy (CCRT). Kaplan-Meier estimates show a plateau after 3 years.*
Conclusion:*Benefits of RT alone and CCRT might be outweighed by the risk of side effects and risk of toxicity–induced treatment strategy and survival of the patients. The benefit of CCRT is still controversial. Thus further research is needed to identify a suitable candidate who might be benefitted from CCRT*
Keywords: *Concurrent Chemo-radiotherapy (CCRT), Radiotherapy (RT), Carcinoma of Head and Neck Region.*

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I. Introduction

Head and neck cancer is the seventh most common type of cancer. The overall prognosis of head and neck cancer patients is poor. Newer treatment modalities like adjuvant chemotherapy, concurrent chemoradiotherapy, and induction chemotherapy are being studied to achieve control of the local tumor and decrease dissemination, and thereby have an impact on overall patient survival [1,2]. It has been seen that concurrent chemoradiotherapy (CCRT) is a standard-of-care method for the treatment of advanced loco-regional head and neck cancers, non-surgically [4]. When CCRT is compared to radiotherapy alone, meta-analyses show an improved 5-year survival by approximately 8% [6]. CCRT results in the highest laryngectomy-free survival rate, optimum loco-regional control rate, and minimum distant metastasis rate compared to radiotherapy alone [7]. The most significant risk factors include smoking and alcohol consumption. It is seen that those who smoke are ten times at greater risk to develop head and neck malignancies [5]. With there being greater advantages,

CCRT increases toxicity when compared to radiotherapy alone. The increased incidence of these acute toxicities like nausea, vomiting, and long-term toxicities in terms of taste impairment, weight changes, etc. leads to some perplexity about whether CCRT is a better option compared to radiotherapy alone [6]. It should be kept in mind that toxicities might exert a detrimental effect on local control. Toxicity related to treatment is one of the causes of interruption of treatment, which results in delayed treatment overall [7].This study was done to evaluate the overall survival of patients with head and neck cancer receiving CCRT or radiotherapy alone, and also to find out certain basic physiological and histological features of the malignancies.More research is still pivotal to establish biomarkers that would enable a modified, compliant use of the available treatment regimens.The study aimedto evaluate the contribution of concurrent chemoradiation therapy (CCRT) and radiotherapy alone in previously untreated patients with unresectable head and neck cancer.

II. Methods

This prospective observational study was conducted at the department of radiotherapy in the Sylhet MAG Osmani Medical College, Sylhet from January 2021 to December 2021. The study was carried out with a total of 36 previously untreated patients with unresectable head and neck cancer.A convenient sample selection method was done for the selection of the participants. The participants were informed regarding the purpose of the study and all possible risks and written consent was obtained. Ethical approval was also obtained from the ethical review committee of the study hospital. All patients underwent repeated clinical examinations during therapy given (CCRT and RT alone) for the identification of response and acute toxic reactions. Twenty-four patients received CCRT and twelve patients were given RT alone. All necessary history and data were collected through a questionnaire that was prepared previously, and medical information was also collected. After data collection was done, available data were analyzed through SPSS software. Survival analysis was performed by Kaplan-Meire estimate.

Inclusion Criteria

- Patients with newly diagnosed cancers ofthe head and neck regions
- Patients aged 30 and above
- Patients who are willing

Exclusion Criteria

- Critically ill patient
- Relapse case
- Patients with recurrent disease

Data analysis:

The study coordinators performed random checks to verify data collection processes. Completed data forms were reviewed, edited, and processed for computer data entry. Frequencies and percentages were used to analyze statistical significance. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0.

III. Results

Male prevalence was observed among the participants of the present study, with 86.11% male and 13.89% female participants. The majority of the participants were over 50 years of age, with 33.33% belonging to the age group of 51-60 years, 22.22% belonging to the age group of 61-70 years, and 8.33% being over the age of 70 years. Occupation-wise, the businessman had the highest prevalence at 41.67%, with 5.56% housewives, and 2.78% govt. employees and 36.11% being unemployed (Table 1). According to the clinical diagnosis, 13 participants (36.11%) had Ca. larynx, 30.56% had Ca. pyriform fossa, either on right, left, or full fossa form, 19.44% had Ca. at the base of tongue (BOT), 5.56% had Ca. posterior cricoid cartilage, and right side metastatic neck, Ca. post pharyngeal wall and right glottis growth were observed in 2.78% of patients each (Table 2). Among the total 36 patients, 66.67% were given concurrent chemo-radiation therapy (CCRT), and 33.33% had normal radiotherapy (Figure 1). Nausea and vomiting had a very high prevalence in both therapy groups, but vomiting had a slightly higher prevalence among the CCRT group (62.50% vs 41.67%) while nausea had a slightly higher prevalence among the radiotherapy group (Table 3). The primary site of lesion was the laryngopharynx for 50% of the CCRT group and 75% of the radiotherapy group. The oral cavity and other sites of lesions had a higher prevalence among the CCRT group compared to the radiotherapy group (Table 4). TNM classification showed that T2 was the most prevalent among T patients, observed in 100% of the radiotherapy group and 91.67% of the CCRT group. Grade II tumor was observed in 95.83% of the CCRT group patients and 91.67% of the radiotherapy group patients (Table 5).

Table 1: Basic characteristics of the participants (N=36)

Characteristics	N	%
Gender		
Male	31	86.11%
Female	5	13.89%
Age groups		
31-40	5	13.89%
41-50	8	22.22%
51-60	12	33.33%
61-70	8	22.22%
>70	3	8.33%
Occupation		
Businessman	15	41.67%
Housewife	2	5.56%
Govt. Job	1	2.78%
Others	5	13.89%
Unemployed	13	36.11%
History of		
alcohol abuse	3	8.33%
Smoking	25	69.44%

Table 2: Distribution of the participants by clinical diagnosis (N=36)

Clinical Diagnosis	N	%
Ca. Larynx	13	36.11%
Ca. Pyriform Fossa	11	30.56%
Ca. BOT	7	19.44%
Ca. Posterior Cricoid Cartilage	2	5.56%
Right Side metastatic neck (Node of unknown Primary)	1	2.78%
Ca. Post Pharyngeal wall	1	2.78%
Right Glottic Growth	1	2.78%

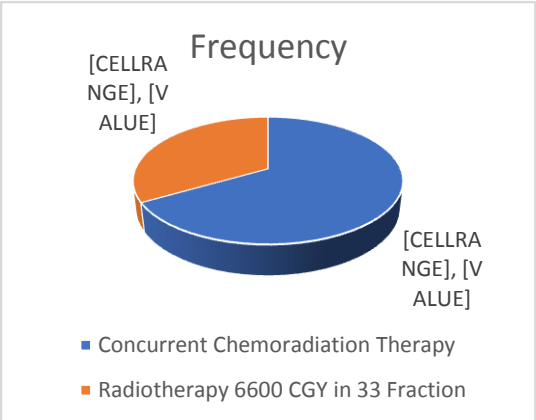

Figure 1: Distribution of the participants by therapy given (N=36)

Table 3: Distribution of the participants by type of therapy and clinical features (N=36)

Clinical Features	CCRT Group n= 24	Radiotherapy Group n= 12
Nausea	21 (87.50%)	11 (91.67%)
Vomiting	15 (62.50%)	5 (41.67%)
Skin Rash	13	2 (16.67%)

	(54.17%)	
Myalgia	9 (37.50%)	2 (16.67%)
Hoarse voice	13 (54.17%)	9 (75.00%)
Dysphagia	5 (20.83%)	1 (8.33%)

Table 4: Distribution of the participants by type of therapy and primary site of lesion (N=36)

Primary Site of Lesion	**CCRT Group n= 24**	**Radiotherapy Group n= 12**
Oral Cavity	3 (12.50%)	1 (8.33%)
Laryngopharynx	12 (50.00%)	9 (75.00%)
Others	9 (37.50%)	2 (16.67%)

Table 5: Distribution of the participants by type of therapy and TNM classifications (N=36)

TNM Classification	**CCRT Group n= 24**	**Radiotherapy Group n= 12**
T Classification		
T1	1 (4.17%)	0 (0.00%)
T2	22 (91.67%)	12 (100.00%)
T3	1 (4.17%)	0 (0.00%)
Tumor Grade		
Grade II	23 (95.83%)	11 (91.67%)
Grade III	1 (4.16%)	1 (8.33%)

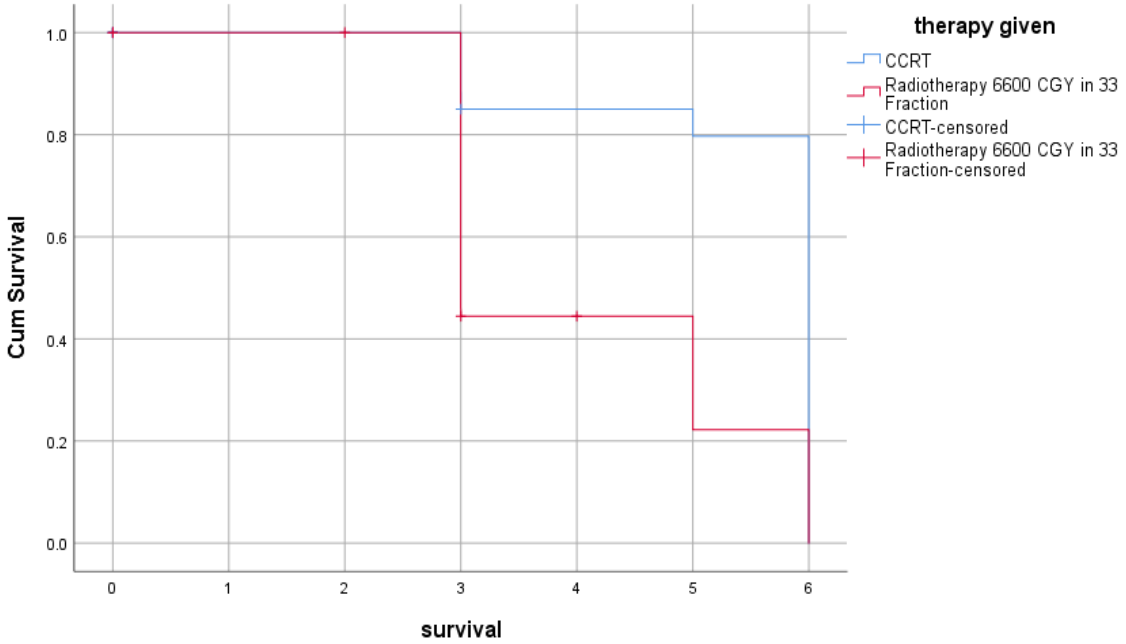

Fig 2: Overall survival (Kaplan-Meire Estimations) in patients treated with RT alone or CCRT. Fiveyears survival is increased from 44% to 80% (log-rank test, $p<0.0003$) by additional chemotherapy along with radiotherapy (CCRT). Kaplan-Meier estimates show a plateau after 3 years.

IV. Discussion

For the treatment of early stages cancer patients, radiotherapy is generally the primary treatment method. But, control of different forms of carcinoma with radiotherapy alone can often be unsatisfactory [8].To improve the prognosis of such cases, a combination of chemotherapy and radiotherapy can have potential positive benefits. Few recent studies with NPC patients demonstrated the benefits of using concurrent chemoradiotherapy (CCRT) over using only radiotherapy, including increased overall survival rates [9,10]. The present study was an open-label study to observe the effects of CCRT and radiotherapy among patients having head and neck cancer. Among the total 36 participants, 24 had received CCRT treatment, while the remaining 12 had received radiotherapy 6600 CGY in 33 fractions. The present study observed a higher prevalence of male participants (86.11%) compared to females. This high male prevalence was supported by the findings of other studies [11]. The majority of the participants were over 50 years of age, and many were businessmen, while 36.11% were unemployed.According to the clinical diagnosis, 13 participants (36.11%) had Ca. larynx, 30.56% had Ca. pyriform fossa, either on the right, left, or full fossa form, 19.44% had Ca. at the base of tongue (BOT), 5.56% had Ca. posterior cricoid cartilage and 2.78% of patients each had right side metastatic neck, Ca. post pharyngeal wall, and right glottis growth.It was further observed that nausea had a slightly higher prevalence among the radiotherapy group compared to CCRT, while vomiting was observed in a higher frequency among the CCRT group. Other symptoms like skin rash and myalgia had a much higher prevalence among CCRT group patients, and hoarse voice was observed in a much higher percentage of radiotherapy group patients. The primary site of lesion was the laryngopharynx for 75% of the radiotherapy group and half of the CCRT group participants. Oral cavity and other lesion sites were observed more in the CCRT group. The role of CCRT in elderly patients remained unclear due to poor physiologic function, presence of comorbidities, advanced age, and/or patients' preference [12]. Advance stage disease and older patients are not candidates for surgical resection [13]. CCRT might be the treatment of choice instead of surgical resection [14-16]. Studies found that the addition of chemotherapy along with conventional fractionation RT was associated with significantly better median survival and five-year survival than RT alone [17,18]. Xu *et. al.* (2014) demonstrated that patients aged more than 70 years treated with CCRT had improved survival rates compared with RT alone with the overall and progression-free survival in the CCRT group versus the RT group were 17 months versus eight months and 14 months versus five months respectively [19]. Zhang *et. al.* (2014) also indicated that the3-year overall survival was 36.1% for CCRT in comparison with 28.5% following RT alone [20]. Studiesauthenticated that CCRT had significant survival benefit compared to RT alone with similar efficacy whether chemotherapy was administered as single or double agents. Although the disparity of increased toxicities of CCRT was found in several studies [21-23]. Toxicities are nearly equivalent to RT alone [24].

V. Conclusion

The present study suggests that the overall survival was increased after adding chemotherapy along with radiotherapy. The benefits of RT alone and CCRT might be outweighed by the risk of side effects and risk of toxicity–induced treatment strategy as well. Age, selection factor of performance status, and presence of comorbidities would hamper the benefit ofa combined treatment approach. The benefit of CCRT is still controversial. Thus further research is needed to identify a suitable candidate who might be benefitted from CCRT [25].

VI. Recommendation

Formulating Specific guidelines for the treatment of malignant patients is of great need.To get robust data, multicenter studies should be carried out to better the understanding ofpolicymakers to interpret the demonstrable scenario.

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