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Research Article

STUDY OF ASSOCIATION OF STAGE WITH RESPONSE IN A PATIENT RECEIVING CONCURRENT CHEMO RADIOTHERAPY WITH 3 WEEKLY DOCETAXEL 45 MG/MT^2 AND CISPLATIN 60 MG/MT^2 IN LOCALLY ADVANCED TONGUE CARCINOMA

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Abstract

Background: Head and neck carcinoma is a heterogeneous disease, encompassing a variety of tumors that originate in the lip, oral cavity, hypopharynx, oropharynx Naso-pharynx, or larynx.

Objective: to Study of association of Stage with Response in a patient receiving concurrent chemo radiotherapy with 3 weekly Docetaxel 45mg/mt^2 and Cisplatin 60 mg/mt^2 in Locally Advanced Tongue Carcinoma.

Methods: The present was conducted in department of Radiation Oncology, Pt. JNM medical college and Regional cancer center (RCC) of Dr. BRAM Hospital Raipur. This study was approved by ethical and scientific committee Pt.JNM medical college Raipur. It was prospective study which was conducted during July 2020 to September 2022.

Results: In our study, 71% were diagnosed at stage IVA, 19.35% at stage III and only 9.68% at stage IVB. In our study, all 44 patients had completed 1 month followup, out of which 10 patients (22.72%) had achieved CR, 12 patients (27.27%) had achieved PR, 18 patients (40.90%) had SD and only 4 patients (9.90%) had progressed. 18 patients had completed 3 month follow up, out of which 4 patients (9.09 %) had achieved CR, 4 patients (9.09 %) had achieved PR, 8 patients had SD (18.18%) and only 2 patients had (4.54%) PD. 6 patients had completed 6 month followup, out of which 4 patients (9.09%) had achieved

CR, 0 patients had achieved PR, 2 patient (4.5%) had SD and none had PD.

Conclusion: As our study is not powered enough to comment overall survival and disease-free survival and further study is needed with large sample size and longer follow up.

Keywords: Stage, Response, concurrent chemo radiotherapy Locally Advanced Tongue Carcinoma

INTRODUCTION

The projected number of patients with cancer in India is 1,392,179 for the year 2020, and the common 5 leading sites are breast, lung, mouth, cervix uteri and tongue. The majority of the patients with cancer were diagnosed at the locally advanced stage forehead and neck (66.6%).[1]Head and neck Squamous cell carcinoma (HNSCC) accounts for 90% of all malignant disease in the head and neck region of the body.[2] Global contribution of head and neck cancer patients is 57.5% by India.

Radiotherapy and Surgery are the only curative treatments for oral cavity cancers. Although chemotherapy alone is not curative, it enhances the effects of radiotherapy and is routinely used as part of combined modality treatment in patients with stage III or IV disease in concurrent setting and neoadjuvant setting in some sub-sites. Radiation therapy has long played an integral role in the management of locally advanced oral cavity cancers for organ preservation and to improve tumor control. Over the years, the delivery of radiation therapy has improved with innovations that have reduced toxicity without compromising loco-regional control. Because loco-regional recurrence is the most common pattern of failure in these patients, improvement in outcomes focuses on local disease control.

Radiotherapy for head and neck cancer can be challenging due to complex anatomy of head and neck region with these tumor often located in close proximity to critical structures which can limit the radiation dose. In addition, these tumors often display an aggressive phenotype and often grow rapidly due to rich lymphatic supply in head and neck region, therefore present at locally advanced stage.

Randomized trials have demonstrated that IMRT/VMAT for HNC patients provides better outcomes regarding salivary toxicity when compared to conventional three-dimensional techniques. Volumetric modulated arc therapy (VMAT) is a novel radiation technique, which can achieve highly conformal dose distributions with improved target volume coverage and sparing of normal tissues compared with conventional radiotherapy techniques. VMAT also has the potential to offer additional advantages, such as improvement in treatment delivery

efficiency as a result of reduction in treatment delivery time and reduction in monitorunit (MU) usage with subsequent reduction in integral radiation dose to the rest of the body.

We are doing an analytical study in locally advanced tongue carcinoma patients treated using VMAT technique in our institute. In our study, we have assessed response using clinical examination sign, symptoms, MRI face and neck. Then we assessed the dose received by target tissue and organ at risk with acute and late toxicities and response in term of Locoregional control.

Concurrent chemo radiotherapy with sequential integrated boost for locally advanced head neck cancer is well tolerated and results in treatment outcomes comparable to simultaneous integrated boost. Rates of acute grade 3 and 4 dysphagia and dermatitis were significantly higher in SIB as compare to with Sequential integrated boost.[3]

MATERIAL AND METHODS

The present study was conducted in department of Radiation Oncology, Pt. JNM medical college and Regional cancer center (RCC) of Dr.BRAM Hospital Raipur. This study was approved by ethical and scientific committee Pt.JNM medical college Raipur. It was prospective study which was conducted during July 2020 to September 2022.

INCLUSION CRITERIA

1. Age 20 to 60 years
2. Biopsy proven Tongue Carcinoma
3. WHO Performance Status 0, 1, 2
4. Normal Blood Profile (Blood profile to be corrected)
5. Locally advanced stage (Stage III to IV B).

EXCLUSION CRITERIA

1. Patients with co morbidities, ex:

   Chronic renal failure

   Profound hearing loss diagnosed in PTA

2. Patient with Metastatic disease
3. Patients who received prior treatment
4. WHO performance status >2

METHODOLOGY

Informed written consent have been taken from every patient.

Detail history was recorded for each patient pertaining to the onset and duration of present complaint.

Physical examination was done on all patients including general, local and systemic examination.

All the routine investigations including CBC, RFT, LFT, VIRALMARKER, X-ray chest PA View, ECG, CECT MRI face and neck Dental Prophylaxis, PTA was done on all the cases.

All Patients have been simulated with appropriate immobilization according to the standard protocol

Planning CT scans will be acquired with 3mm axial images from glabella to tracheal bifurcation and images will be transferred to contouring station.

These images are transferred to Eclipse treatment planning system (TPS) Varian work station.

TV and OARs will be contoured as per standard protocol.

GTV represents gross visible tumor and/or enlarged lymph nodes identified clinically or on CT.

CTV includes regions at high risk of microscopic disease and a 0.5-2cm margin on GTV was given.

A symmetric PTV margin of 2-5 mm will be used to account for daily setup errors. Planning target volume (PTV) high risk, PTV inter mediate risk & PTV low risk drawn (non adaptive plan) during CT based contouring and planning procedure accounts for organ motion and set-up uncertainties.

Dose prescription of 66 Gy to PTV high risk, 60 Gy to PTV intermediate and 50 Gy to PTV low.

Treatment planning have been perform using VARIAN (eclipse V.S13.6.23) treatment planning system.

Phasic VMAT plans will be generated, evaluated and approved for each patient u sing Treatment Planning System.

All treatments will be delivered by using Varian linear accelerator. Original treatment plan will be implemented

Treatment will be delivered once daily, 5 days/week, over 7 weeks. Dose to PTV and OARs was calculated.

Clinically observed changes in patient‘s anatomy will be identified during the course of treatment.

Concurrent Docetaxel 45mg/mt^{2}and Cisplatin 60mg/m^2 on 3 weekly regimen for Day1 and Day22 would be administered.

Treatment toxicities during course of radiation and after radiation have been compared using QUANTEC data and RTOG, CTC version 5.0 respectively.

Follow up was done at 1st, 3rd&6thmonths. Patients were evaluated for local response and toxicities.

RESULTS

In our study maximum percentage of patient (87.10%) were male as compared to female (12.9%)**.** Patients evaluated belonged to the age group between 30-60 years. Majority of the patients (35.5%) are of 30-39 and 40-49 years each, followed by patients (16.13%) are of 50-59 years, while minority of the patients

(12.9%) are of 60years.In our study, majority of the patients belonged to urban background (67.74%) and the rest (32.26%) belonged to rural background. In our study majority of the patients (67.74%) are from urban area and out of which the most common area is Raipur 19.35%.

In our study out of 62 patients, the occupation which is most common is farmer (43.38%) followed by labourer (38.71%). In our study, maximum patients had a socioeconomic status of V.

All the patients in my study had a performance status of ECOG (Eastern Cooperative Oncology Group) grade 0 or 1.

Table 1: Performance status of ECOG

ECOG	Number	Percentage (%)
0	54	87.10%
1	8	12.90%
TOTAL	**62**	**100%**

In our study, maximum patients (64.51%) had habit of smoking followed by patients (61.29%) smokeless tobacco and the least common is sepsis found in 3.22%.
Also beetle nut chewing sharp tooth are also the important risk factor for tongue carcinoma which is present in patients (6.45% each).

The synergistic effect on the carcinogenic potency of tobacco in oral cancer by alcohol consumption is well documented that is patients (35.48%) alcohol plus smoke and patients (38.7%) with alcohol plus smokeless present.

In our study, majority of the patients (59.83%) had proliferative type of growth.

STAGE WISE DISTRIBUTION

In our study, 71% were diagnosed at stage IVA, 19.35% at stage III and only 9.68% at stage IVB.

Table 2: **Stage wise distribution**

Stage	Number	%
III	12	19.35%
IVA	44	71.00%
IVB	6	9.68%
TOTAL	62	100%

RESPONSE ASSESSMENT

OVERALL RESPONSE ASSESSMENT (ASPER RECISTCRITERIA)

In our study, all 44 patients had completed 1 month followup, out of which 10 patients (22.72%) had achieved CR,12 patients (27.27%) had achieved PR,18patients (40.90%) had SD and only 4 patients (9.90%) had progressed.

18 patients had completed 3 month follow up, out of which 4 patients (9.09 %) had achieved CR, 4 patients (9.09 %) had achieved PR, 8 patients had SD (18.18%) and only 2 patients had (4.54%) PD.

6 patients had completed 6 month followup, out of which 4 patients (9.09%) had Achieved CR, 0 patients had achieved PR, 2 patient (4.5%) had SD and none had PD.

Table 1: **Overall response assessment**

MONTH	CR		PR		SD		PD		TOTAL
1 MONTH	10	22.72%	12	27.27%	18	40.90%	4	9.90%	44
3 MONTHS	4	9.09%	4	9.09%	8	18.18%	2	4.54%	18
6 MONTHS	4	6.45%	0	0%	2	3.22%	0	0%	6

STAGE WISE RESPONSE

1 MONTH ASSESSMENT

Out of 4 patients in this study,10 patients were diagnosed at stage III, 32 were diagnosed at stage IVA and 4 were diagnosed at stage IVB.

Out of 10 patients diagnosed at stage III, 4 patients (9.09%) had CR, 2 patient (4.54%) had PR, 4 patients (9.09%) had SD and none had PD. Out of 32 patients diagnosed at stage IVA, 6 patients (13.63%) had CR, 10 patients (22.72%) had PR, 12 patients (27.27%) had SD and 4 patients (9.09%) had PD. Only 2 patients (4.54%) diagnosed

at stage IVB which had SD.

Table 2 – 1 Month Assessment

Stage	1 MONTH									
	CR		PR		SD		PD		TOTAL	
III	4	9.09%	2	4.54%	4	9.09%	0	0%	10	22.72%
IVA	6	13.63%	10	22.72%	12	27.27%	4	9.09%	32	72.72%
IVB	0	0%	0	0%	2	4.54%	0	0%	2	4.54%

3 MONTHS ASSESSMENT

Out of 18 patients in this study, 6 patients were diagnosed at stage III, 10 were diagnosed at stage IVA and 2 were diagnosed at stage IVB.

Out of 6 patients diagnosed at stage III, none had CR and SD, 4 patients (9.09%) had PR, 2 patients (4.54%) had SD. out of 10 patients diagnosed at stage IVA, 4 patients (9.09%) had CR, none had PR and PD, 6 patients (13.6%) had SD. Only 2 patients (4.54%) diagnosed at stage IVB which had SD.

Table 3–**3 MONTHS ASSESSMENT**

STAGE	3 MONTHS							
	CR		PR		SD		PD	
III	0	0%	4	9.09%	0	0%	2	4.54%
IVA	4	9.09%	0	0%	6	13.60%	0	0%
IVB	0	0%	0	0%	2	4.54%	0	0%
TOTAL	4	9.09%	4	9.09%	6	13.6%	2	4.54%

6 MONTHS ASSESSMENT

Out of all patients in this study, 6 patients were diagnosed at stage III, 10 were

diagnosed at stage IVA and 2 were diagnosed at stage IVB.

Out of 6 patients diagnosed at stage III, 2 patients (4.54%) had CR and 2 patients (4.54%) SD, none had PR and PD. Only 2 patients (4.54%) diagnosed at stage IVA which CR. None of the patient had stage IVB.

Table 4–**6 MONTH ASSESSMENT**

STAGE	6 MONTHS									
	CR		PR		SD		PD		TOTAL	
III	2	4.54%	0	0%	2	4.54%	0	0%	4	9.09%
IVA	2	4.54%	0	0%	0	0%	0	0%	2	9.09%
IVB	0	0%	0	0%	0	0%	0	0%	0	0%

DISCUSSION

Surgical resection, radiation, chemotherapy or combined modality approaches are classical treatment options that have been employed for the patients with cancer of oral cavity. The choice of treatment modality, either singlyorin combination, depends on the stage and size of the tumor and relevant patient factors such as toxicity, performance status, comorbid disease, and convenience. The overall health and functional status of the patient are important determinants for patients with advanced lesions of the oral cavity, a combined modality approach is generally recommended.[4,5,6]

Routinely radiotherapy is given with conventional fractionation 60-70 Gyin 30-35#in 6-7 weeks. This requires along treatment duration, poor compliance and treatment results. We did an analytical study in 62 cases of stage III to IVB Tongue Cancerat Pt. JNM medical college and associated regional cancer center Dr.BRAM Hospital Raipur CG in the department of radiotherapy for assessing effectiveness and toxicity profile. The study included all the patient of Tongue carcinoma treated with voloumated arc therapy 2 Gy perfraction, 5 fraction in a week for 7 weeks with concurrent chemotherapy docetaxe l45 mg/mt^2 and Cisplatin 60 mg/mt^2 at day 1 & day 22. During radiation therapy patient have been assessed for acute toxicity weekly than after completion of chemo-radiotherapy patient

were assessed for tumor response on 1 month, 3 months and 6 months and latetoxicity every month.

In our study gender wise male patients represent 87.1% of case where as female patients represent 12.9% with male to female ratio is 6.75:1, male patients are more prone to Tongue carcinoma than female.

According to **Sato K, Hayashi Y, Watanabe K, Yoshimi R, Hibi H** male:female ratio 4:1.[7]

According to **S.Warnakula suriya et al** it might be due to the increased consumption of tobacco and tobacco related products in males.[8]According to study by **A.M. Eliassen et al** head and neck Squamous cell carcinoma (HNSCC) Is typically considered to be a disease that predominantly affects older males, with a male:female ratio of approximately 4:1 which is more as compare to our study. Long term alcohol and tobacco use have been identified as the traditional risk factors for this disease.[9]

In our study age wise distribution in our study, patient belong to age group between 30 to 60 years, Majority of the patients (35.5%) are of 30-39 and 40-49 years each, youngest patient was 30 years and eldest was 60 years old. A study by Malik A, MishraA, GargA,ShettyR, MairM, ChakrabartiS, et al majority of patients between 40 to 50 years.

According to **SEER Data: (**Surveillance, Epidemiology and End Results) An increasing incidence of oral tongue carcinoma in young white individual age between 18 to 44.[10]

STAGE WISE

In our study,71% were diagnosed at stage IVA,19.35% at stage III and only 9.68% at stage IVB. In Chhattisgarh state patients came to us with locally advanced stage. It is due to illiteracy, poverty, lack of awareness, lack of health facility. Study by **Kailash Chandra Pandey et al** found that oral cavity cancer cases with stage I0%, stage II6%, stage III6%, stage IVA 44% and stage IVB 44%. [11]

Study by **Jagrutia patel et al** in their study reported that in oral cavity cancers 27% in stage I and 14% in stage II, 11% in stage III, 39% diagnosed in stage IVA and 3% in stage IVB.[12]

According to Singh MP, MisraS, RathanaswamySP, GuptaS, TewariBN, BhattML, KumarV. Clinical max percentage that is 55.3% were from IVA followed by 28.2% were III, 8% were IVB

CORRELATION OFRESPONSEWITH STAGE

Out of 44 patients in this study, 10 patients were diagnosed at stage III, 32 were diagnosed at

stage IVA and 4 were diagnosed at stage IVB.

Out of 10 patients diagnosed at stage III, 4 patients (9.09%) had CR, 2 patient (4.54%) had PR, 4 patients (9.09%) had SD and none had PD. Out of 32 patients diagnosed at stage IVA, 6 patients (13.63%) had CR, 10 patients (22.72%) had PR, 12 patients (27.27%) had SD and 4 patients (9.09%) had PD. Only 2 patients (4.54%) diagnosed at stage IVB which had SD

In a study by Foster CC, Melotek JM, Brisson RJ, Seiwert TY, Cohen EE, Stenson KM, BlairEA, Portugal L, GooiZ, Agrawal N,Vokes EE(90). Done in USA

140 patients with locally-advanced OC-SCC were treated with definitive CRT. Of these, 75.7% had T3/T4 disease, 68.6% had ≥N2 nodal disease, and 91.4% had stage IV disease. **Most common primary sites were oral tongue** (47.9%) and floor of mouth (24.3%). Median follow-up was 5.7 years. Five-year OS, PFS, LRC, and DC were63.2%, 58.7%, 78.6%, and 87.2%, respectively. Rates of ORN and long-term feeding tube dependence were 20.7% and10.0%, respectively. Differences in LRC ($P = 0.90$), DC($P = 0.24$), PFS($P = 0.38$),OS($P = 0.10$), or ORN($P = 0.38$)were not significant across treatment decades.

In a study, HosniA, ChiuK, Huang SH, Xu W, Huang J, BayleyA, Bratman SV, Cho J, Giuliani M, Kim J, O'Sullivan done in Canada**.** [13]

CONCLUSION

It is concluded that due to pandemic (Covid19) I got a smaller number of cases and wasn't able to follow up because of strict lock down. This was the root cause for my limited number of cases and toxicities was the barrier to dose escalation by External Beam Radiotherapy in Tongue Carcinoma. As our study is not powered enough to comment overall survival and disease-free survival and further study is needed with large sample size and longer follow up.

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