

Outcomes of Squamous Cell Carcinoma Oropharynx in Elderly Patients Treated with External Beam Radiation Therapy - A Retrospective Study from Tertiary Care Cancer Center - India

Kaluvoya Ramanaiah

Department of Radiation Oncology, Cancer Institute (WIA), Adyar Chennai, Tamil Nadu, India.

Sadanand S

Department of Radiation Oncology, Cancer Institute (WIA), Adyar Chennai, Tamil Nadu, India.

Gautam V V

Department of Radiation Oncology, Cancer Institute (WIA), Adyar Chennai, Tamil Nadu, India.

Mukesh B

Department of Radiation Oncology, Cancer Institute (WIA), Adyar Chennai, Tamil Nadu, India.

Sai Pranav M

Department of Radiation Oncology, Cancer Institute (WIA), Adyar Chennai, Tamil Nadu, India.

Arunkumar M,N

Department of Radiation Oncology, Cancer Institute (WIA), Adyar Chennai, Tamil Nadu, India.

Background: Majority of Elderly patients with oro-pharyngeal Squamous cell (OPSCC) are treated with External beam Radiation Therapy(EBRT) alone, the benefit of chemotherapy after 70years is doubtful, we aim to analyze outcomes and morbidity in elderly OPSCC treated with EBRT.

Methods: Retrospective study, all patients with Oropharyngeal squamous cell carcinoma histology, more than or equal 70 years of age, having performance status Eastern Cooperative Oncology Group (ECOG) 0-2, All stages other than metastatic disease, who were registered and treated with Radical radiation therapy alone at our institute from January 2015 to December 2018 were included. Having ECOG performance status 3-4, Patients treated with brachytherapy, or concurrent chemoradiation, synchronous primaries, re-irradiation are excluded from this study. Entire cohort of 30 patients (25 male, 5 female) were treated with EBRT, who received total dose 50Gy to 66Gy were included for analysis.

Results: 90% of cases (27/30) were locally advanced (Stage III & IV), At median follow up duration of 18months (range 1 to 81 months), at 3, 4, and 5 years OS was 36.7% (95% Confidence interval (CI) = 19.4% - 54%), 23.3% (95% CI = 8.2% - 38.4%) and 19.4% (95% CI = 5.1 - 33.7%) respectively.

Conclusion: compared to young, elderly OPSCC has poor outcomes, this subset may do as well as young people if treated with multi modality treatment with proper selection. By addressing the risk factors , using preventive measures, early detection , and ensuring access to the adequate health care facilities are pivotal in reducing the burden of cancer. Poor representations of this subset of population in clinical trails, facing challenges treating with multi modality approach may be one of the reason for poor outcomes compared to the young patients, needs prospective trails specifically focusing on this group of patients should be performed.

Introduction

Majority of Elderly patients with oro-pharyngeal Squamous cell Carcinoma (OPSCC) are treated with External beam Radiation Therapy (EBRT) alone, few of this subset even in good general condition will deny the systemic therapy, also the effect of adding chemotherapy after 70 years of age has doubtful benefit, we aim to analyze response rate and morbidity in elderly patients with OPSCC, treated with EBRT alone.

Materials and Methods

Retrospective study, all patients with Oropharyngeal squamous cell carcinoma histology, more than or equal 70 years of age, having performance status Eastern Cooperative Oncology Group (ECOG) 0-2, All stages other than metastatic disease, who were registered and treated with Radical radiation therapy alone at our institute from January 2015 to December 2018 were included. Having ECOG performance status 3-4, Patients treated with Brachytherapy, or Concurrent chemoradiation, having synchronous primaries, re-irradiation are excluded from this study.

Between 2015 January to 2018 December, 48 cases were registered, out of 48 patients (43 were male 5 were female), one patient has ECOG performance status 4, advised best supportive care, 5/48 treated with concurrent chemoradiation (given weekly carboplatin) were not included for analysis, 5/48 patients denied radiation after planning, 1/48 patients received Brachytherapy, 3/48 patients has metastatic disease, 2/48 cases defaulted after starting radiation who were received less than 30Gy of radiation.

Entire cohort of 30 patients (25 male, 5 female patients) were treated with EBRT, in the range of 50Gy - 66Gy were included for analysis. Once looking at sub site presentation, base of tongue was commonest site 46.66% (14/30), followed by tonsil 36.66% (11/30), Vallecula 10% (3/30) and soft palate 6.66% (2/30). Commonest presentation was locally advanced stage having 90% of cases (27/30), (Stage III patients 33.33% (10/30), stage IV patients 56.66% (17/30). Smoke form of tobacco usage was the commonest habit 66.66% (20/30) patients. Diabetes is the commonest comorbidity among the entire cohort 33.33% (10/30), squamous cell carcinoma grade II histology was seen in (46.66%) 14/30 patients and grade 3 was seen in 40% of cases 12/30 patients, (all of these details mentioned in Table 1).

Total number of cases	30
Male	25 (83.33%)
Female	5 (16.67%)
Sub site wise case distribution	
Base of tongue	14 (46.67%)
Tonsil	11 (36.7%)
Vallecula	3 (10%)
Soft palate	2 (6.67%)
T N M stage (AJCC 7th)	
T1N1M0	1
T1N2M0	1
T1N3bM0	1
T2N0M0	3
T2N1M0	3
T2N2M0	2
T3N0M0	4
T3N1M0	2
T3N2M0	7
T3N3aM0	1

T4aN0M0	3
T4a N1M0	2
Stage grouping	
Stage II	3
Stage III	10
Stage IVa	15
Stage IVb	2
Histology grade	
Squamous cell carcinoma grade I	4
Squamous cell carcinoma grade II	14
Squamous cell carcinoma grade III	12
Comorbidities	
DM alone	3
DM/HTN	4
DM/HTN/IHD	2
HTN alone	2
CKD	1
DM/IHD	1
Habits	
Smoking	8
Smoking / Alcohol	8
Smoking /alcohol/chewing	2
Smoking/chewing	2
Chewing	4

Table 1. Baseline Characters of Study Population.

All patients were admitted before treatment, and was advised nasogastric tube placement for nutrition purpose, 53.33% of (16/30) patients had before starting of radiation, 46.66% (14/30) of patients had between 30Gy to 40Gy of delivery Radiation, due to pharyngeal mucositis.

Among 30cases 7/30 patients were treated with 2D conventional therapy, 22/30 patients treated with 3D conformal therapy (3DCRT), 1patient received Intensity Modulated Radiation Therapy (IMRT), (technique details mentioned in Table 2), Radiation dose delivery details mentioned in (Table 3), dose delivered at 2Gy per fraction in weekly 5days.

Technique	Total number of cases
2D Conventional	7
3D conformal	22
IMRT	1

Table 2. Radiation Technique Details.

Radiation dose	Number of patients
50Gy	3
60Gy	9
66Gy	18

Table 3. Radiation Dose Details.

Toxicity profile as per Common Terminology Criteria for Adverse Events (CTCAE version 4.0) documented,SPSS version 29.0 software was used for data analysis.Overall survival (OS) was obtained using Kaplan Meier survival curve.

Results

90% of cases (27/30) were locally advanced (Stage III & IV), as per AJCC 7th TNM staging. Smoke form of tobacco usage was the commonest habit, 66.66% (20/30) patients were smokers, Diabetes is the common comorbidity 33.33% (10/30). The average time to complete Radiation was between 43 to 58 days in patients who received 60Gy to 66Gy. 60 % (18/30) patients completed planned total dose of Radiation. 30% (9/30) patients denied Radiation after 60Gy, 10% (3/30) patients denied radiation after 50Gy.

At median follow up duration of 18months (range 1 to 81 months) , at 3, 4, and 5 years OS was 36.7% (95% Confidence interval (CI) = 19.4% - 54%), 23.3%(95% CI = 8.2% - 38.4%) and 19.4% (95% CI = 5.1 - 33.7%) respectively (Figure 1).

Figure 1. Kaplan Meier Survival Curve Overall Survival Duration of Entire Cohort.

Toxicity Grade 3 mucositis was observed in (46.66%) 14/30 patients, rest and all developed grade II mucositis.

Grade 2 skin reaction was seen in 16/30 (54.44%) patients, no patient had developed Grade 4 mucositis and Grade 3 to 4 skin reaction and no neutropenia were observed as per CTCAE version 4.0 (Table 4).

Toxicity	Number of patients
Mucositis	
Grade 2	16/30
Grade 3	14/30
Skin Reaction	
Grade 1	25/30
Grade 2	5/30

Table 4. Radiation Induced Toxicity.

Discussion

Data on outcomes of oro-pharyngeal carcinomas more than 70 years of age was less. As per GLOBOCAN 2020 [1] summit almost 1 in 4 patients having oropharyngeal carcinoma was in more than 70years, as per age standardized rate for 100000 population. And also GLOBOCON 2020 states that worldwide 98412 new oropharyngeal carcinomas for all age group reported including both sexes (79045 men, 19365 women), looking at in more than 70 years of age worldwide 22335 cases including both sexes reported (men 16659, women 1169). In India totally 20617 oropharyngeal cancers reported (men 17175, women 3442), in this group above 70 years of age is having 5295 cases for both sexes, (men 4126, women 1169). In Tamil nadu totally 1178 cases has been reported for all ages, (men 1108, women 150), among these cases 238 cases were more than 70years (men 212, women 26). In Chennai it was reported that totally 87 cases for all ages with 87 men and 10 women, looking at the age group more than 70 years, 22 cases in both sexes with 20 men and 2 women patients has been reported. Data for patients with more than 70 years alone was less, and most of the time considering the chemotherapy along with radiation was difficult, and literature also concluded that adding chemotherapy above 70 years of age the benefit was less [2]. Poorer prognosis is due to multiple factors, possibly including the effects of aging, which make elderly patients more susceptible to the pathogenesis of OPSCC [3].

Developed countries has prolonged life expectancy, which results in increasing number of patients

in older than 75 years who have cancer [4, 5]. However majority of elderly patients decline systemic therapy and were treated with EBRT alone. The landmark Meta-analysis of Chemotherapy in Head and Neck Cancer (MACH-NC) study regarding the role of concomitant chemotherapy in head and neck cancer detected a significant survival benefit for the addition of chemotherapy to definitive radiotherapy in patients with non metastatic HNSCC; however, the benefit was found to be decreasing with higher patient age and to be lost in patients aged 70 years or older [2]. Increasing age after 65 is associated with worsening overall survival and Disease specific survival in OPSCC. In our study we found that refusal of treatment after 50Gy of EBRT in 3/30patients, 9/30 patients after 60Gy. Poorer prognosis is due to multiple factors, possibly including the effects of aging, which make elderly patients more susceptible to the pathogenesis of OPSCC [6].

Literature wise data involved showing the all age group of population, data on outcomes OPSCC was not separately mentioned for people more than 70years. When compared with study done by DE Felice F (4), only 15 cases with locally advanced disease treated with Intensity Modulated Radiation Therapy (IMRT) were included in the study, where five-year overall survival was documented 63.6%, in our study 5year overall survival only 19.4%, another study, done by Jerome Sarini MD - A Long term retrospective review of 273 cases (more than 74years with HNSCC were included) [7], concluded that elderly patients did not seem to have significant difference in outcome when compared to the young population, in this study entire cohort overall survival at 5 years was 23.8% vs 36.4% compared to young, in our study the 5 year overall survival (19.4%) is comparable with existing data. Literature wise data was not available for dropouts of the patients who were on treatment, in our study we observed significant number of patients denying the radiation. 30% (9/30) of study population denied radiation after 60Gy, 10% (3/30) of study population denied radiation after 50Gy, due to various reasons. even though they were fit enough to continue treatment.

Uni variate analysis showed locally advanced stage, and smoking were associated with poor outcomes.

Status of Human papilloma virus infection was not assessed, was the limitation of this study.

In conclusion, there is rapidly increasing prevalence of OPSCC in elderly patients. By addressing the risk factors, using preventive measures, early detection, and ensuring access to the adequate health care facilities are pivotal in reducing the burden of cancer. Overall survival is less comparing to the young patients, this subset may do as well as young people if treated with multi modality treatment with proper selection, same thing need to be studied in prospective randomized clinical trails. Patients and caregivers need to be properly counseled to avoid radiation in between the treatment. Poor representations of this subset of population in clinical trails, facing challenges treating with multi modality approach may be one of the reason for poor outcomes compared to the young patients, needs prospective trails specifically focusing on this group of patients should be performed.

Acknowledgments

Statement of Transparency and Principals:

- Author declares no conflict of interest
- Study was approved by Research Ethic Committee of author affiliated Institute.
- Study's data is available upon a reasonable request.
- All authors have contributed to implementation of this research.

References

References

1. GLOBOCAN 2020: New Global Cancer Data.
2. Lacas B, Carmel A, Landais C, Wong SJ, Licitra L, Tobias JS, Burtneess B, et al. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 107 randomized trials and 19,805 patients, on behalf of MACH-NC Group. *Radiotherapy and Oncology: Journal of the European Society for Therapeutic Radiology and Oncology*. 2021; 156^{[DOI](#)}
3. DE Felice F, Galdieri A, Abate G, Bulzonetti N, Musio D, Tombolini V. Definitive Intensity-modulated Radiation Therapy in Elderly Patients with Locally Advanced Oropharyngeal Cancer. *In Vivo (Athens, Greece)*. 2017; 31(3)^{[DOI](#)}
4. Lesur ARios M. Evolution of elderly patients for fitness to receive treatment. *Oncol Pract*.1998;2:9-11, *Google scholar*. 1998; 2:9-11.
5. Hirano M., Mori K.. Management of cancer in the elderly: therapeutic dilemmas. *Otolaryngology--Head and Neck Surgery: Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*. 1998; 118(1)^{[DOI](#)}
6. Ryan Camilon P, Stokes WA, Nguyen SA, Lentsch EJ. The prognostic significance of age in oropharyngeal squamous cell carcinoma. *Oral Oncology*. 2014; 50(5)^{[DOI](#)}
7. Jerome Sarini MD, Charles Fournier, Jean- Louis Lefebvre MD, et al.