

## Squamous cell carcinoma of oral cavity and oropharynx: A retrospective analysis of nodal involvement and survival

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### Abstract

**Introduction:** The magnitude of head and neck cancers in the Indian subcontinent is very high. Involvement of neck nodes is indicative of higher stage and subsequent adverse prognosis when compared with node negative disease. The frequency of such spread is high, approximately 20% for head and neck squamous cell carcinomas (SCC). The purpose of this study was to analyse the pattern of nodal involvement in patients presenting with SCC of oral cavity and oropharynx and its correlation with survival.

**Materials and Methods:** Forty cases of carcinoma of oral cavity and oropharynx were analysed retrospectively. Data were collected and reviewed from the patient's case files. Patients were analysed for age and sex distribution, tumour staging, metastasis and overall survival.

**Results:** The majority of cases were T4 lesions (n=18, 45%), followed by T2 lesions (n=14, 35%) and T3 lesions (n=8, 20%). 65% patients (n=26) had positive neck nodes, with/without adverse pathologic features mandating post-operative radiotherapy, while 35% patients had nodes negative neck. The mean overall survival of the node negative was 15 months (range 01 – 65 months) and was significantly more (p value 0.0028) than that of node positive patients 9months (range 01-40 months). A statistically significant difference in survival was seen between the nodes negative patients than those with  $\geq 3$  positive neck nodes. (p=0.03)

**Conclusion:** Involvement of neck nodes in cases of carcinoma of oral cavity and oropharynx is an indicator of poor prognosis. The number of pathologically positive neck nodes can be used as a predictor of treatment outcome.

### Introduction

Carcinoma of head and neck (H&N), comprising 6% of all malignancies, is the sixth most common type of cancer in the world.<sup>1</sup> Overall, approximately 58% of all the H&N cancers around the world occur in Asia, especially in India.<sup>2</sup> Betel quid chewing, consumption of tobacco and alcohol are associated risk factors. There are significant differences in pathology, clinical presentation, outcomes and survival of these between Western and Asian populations.<sup>3</sup> Surgery or radiotherapy (RT) as single modality is recommended for the treatment of early stage oral cavity and oropharyngeal squamous cell carcinoma, whereas adjuvant radiotherapy with/without chemotherapy is suitable for locally advanced and metastatic tumours.<sup>4</sup> However with surgery or radiotherapy, main cause of death has been ascribed to the failure of local control.<sup>3</sup>

There are approximately 300 lymph nodes (LN) in H&N, comprising one-third of the total nodes of the body. Metastasis to cervical nodes has a major impact on the

prognosis in patients of SCC of oral cavity and oropharynx, frequency of which is greater than 20% for most cases.<sup>5</sup>

This study was conducted to correlate the incidence of cervical LN metastasis in carcinoma of oral cavity and oropharynx and compare the survival outcome with the pathologically node negative patients.

### Materials and Methods

Forty patients of oral cavity and oropharyngeal carcinoma, treated with adjuvant RT (postoperative RT, PORT) were analysed in the study. Patients in this study were advised PORT based on the histopathological findings that indicated adjuvant therapy. Histopathological report was used to determine the nodal involvement and staging. Patients were classified into three groups as [A] no nodal involvement, [B] Up to three LN positive and [C]  $\geq 3$  LN involved. All patients received adjuvant RT face and neck region using cobalt -60 gamma rays with standard treatment portals to a total mean dose of 60 Gray (range 54-62 Gray) at 2 Gray/fraction and spinal cord shielding at a dose of 46 Gray.

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All appropriate steps were taken during the planning and implementation of treatment protocol. Hospital records were analysed to evaluate the post treatment status and the follow up duration of patients. Overall survival was calculated from the duration between the dates of diagnosis to the last recorded follow up and was calculated in months. Online Graph Pad software was used for statistical analysis. P value was calculated using unpaired for t test and a value of  $p < 0.05$  was considered significant.

## Results

Forty patients of carcinoma of oral cavity and oropharynx were evaluated retrospectively. Of these, 70% were males ( $n = 28$ ) and 30% were females ( $n = 12$ ). The male: female ratio was 2.33:1. The mean age of the patients was 43 years (range 25-70 years). According to T classification, cases in descending order were T4 ( $n=18$ , 45%) followed by T2 ( $n=14$ , 35%) and T3 ( $n= 8$ , 20%) with no T1 lesions.

PORT was not only given to those patients with positive neck nodes (65%) but also to those with negative neck node involvement but having other adverse pathologic risk features (35%).

The total number of positive LN was 80 (minimum 01 to maximum 10). Between T status and metastatic node, cross tabulation showed the following incidence of LN metastasis. (Table 1)

**Table 1**

Stage	N	No. of positive nodes	%	Total no. of nodes
T4	18	36	85.71	42
T3	8	20	74.07	27
T2	14	8	72.72	11
T1	0	0	0	0

The mean overall survival of the entire group was 13.8 months (range 01-65 months), 15 months for node negative patients (Group A) ( $n=14$ ) and 9 months for node positive cases (Group B&C) (range 01-40 months). On statistical analysis, this value was found to be significant ( $p=0.0028$ ). Survival between groups B and C showed no statistically significant difference ( $p=0.1217$ ). Statistically insignificant difference was also seen between Group A and B ( $p=0.1108$ ) but was significant between A and C ( $p=0.0356$ ).

## Discussion

Oral cancer is the sixth most common cancer in the world. This amounts to 575,000 new cases and 200,000 deaths each year.<sup>6</sup> These numbers reflect the intensity of this disease as a major health problem worldwide with its particular relevance in certain parts of Europe and South-Eastern Asia such as India, Pakistan and Bangladesh.<sup>7</sup> Most of these cases remain asymptomatic and are usually detected on routine examination. These lesions then enlarge which might cause mechanical obstruction or they may ulcerate causing pain. This limits the oral intake ultimately causing poor nourishment and dehydration. Bleeding, facial

weakness, dysphagia, odynophagia and trismus are associated symptoms with these carcinomas.<sup>5</sup> A meticulous history helps in deciding the further course of treatment either in the form of surgery or RT. Generally the patients present with history of betel nut chewing and alcohol use. The incidence of neck nodes metastasis in oral SCC is reported to be 34% to 50%.<sup>3</sup> Cervical nodal positivity is the most influential and independent indicator of loco regional recurrence and overall survival rate, hence an appropriate management of the neck nodes in these cancers become extremely important.

Retrospective analysis of forty patients during this study showed male: female ratio of 2.33:1 ( $M=28$ ,  $F=12$ ). A male preponderance of cases was consistent with literature.<sup>8</sup> This data was also supported by the evidence that age – standardized incidence of oral cancers is highest in the world among males.<sup>10</sup> However, gender does not contribute much to the survival of the patients. Among the forty patients in our study, mean age was 43years, which was similar to that trend mentioned in the literature.<sup>3</sup>

Among all the sub sites of oral cavity, buccal mucosa is the most common presenting site in India. The major causative agent for the lesions is use of chewable tobacco. However, unlike previous studies where T3 was more than T2, in our study the incidence of T2 lesions exceeded that of T3.

Involvement of cervical LN can occur even in early stages of disease (incidence reported to be between 27-40%) which is not in accordance with the results of our study.<sup>9,10</sup>

Metastasis to cervical LN is an important and poor prognostic factor for H&N SCC.<sup>11</sup> In the present study 65% patients presented with positive cervical LN, which is in accordance with those of DeConde et al<sup>12</sup> who reported 54% of neck nodal positivity. The possible explanation for this is the differences in the tumour differentiation, tobacco chewing habits and geographical distributions.

Stage at presentation, status of surgical margin, and extra capsular spread of neck nodes are the most important prognostic factors in these patients.<sup>13</sup> In our results, statistically significant difference in survival was found between pathologically node negative and node positive disease group. ( $p=0.0356$ ). Patients with nodal disease and extra capsular spread had inferior outcome as compared with those who are node negative.<sup>14</sup>

Tumour spread to the LN is influenced by the primary site of disease, thickness of tumor, double DNA aneuploidy and poor differentiation in histology. Also, peri-neural invasion, infiltrating-type invasive front, and low E-cadherin contribute to same.<sup>14</sup>

The study conducted by Shibuya et al<sup>15</sup> had reported that head and neck SCC having multiple neck metastasis ( $>10$ ) had a poorer prognosis when compared to node negative cases. These observations support our results which also demonstrates a poor survival in the group of  $>3LN$ .

The majority of oral cavity and oropharyngeal SCC are initially treated with surgical management.<sup>14</sup> Resection of the primary tumour and dissection of neck nodal chains is

the protocol. The survival has increased from 40% to 70% with the use adjuvant RT.<sup>16</sup> Neck dissection is electively done when the risk of cervical involvement is >15-20%. It is a therapeutic as well as staging procedure which assists in defining the neck nodal status and determines the need for adjuvant therapy.<sup>14</sup> Patients with extra capsular spread require aggressive adjuvant therapy.<sup>17</sup> RT is an essential component of the management of early –stage and locally advanced cancer of oral cavity and oropharynx, either alone or in combination with surgery with or without chemotherapy.<sup>18</sup>

With advancement in the knowledge and on-going research work, better prognostic factors have been emerging for H&N SCC. One of these is LN ratio (positive LN/total LN) which has gained much repute as an independent prognostic factor for overall survival of the patients with H&N SCC.<sup>19,20</sup>

The study by Mamalle et al<sup>21</sup> differs in opinion with that of our study. In their study, the number of positive LN was found to be a superior predictor of outcome for H&N cancer patients. Other studies<sup>22,23</sup> have documented a significant likelihood of finding neck LN metastasis with increase in the total number of dissected LN. The criteria of evaluating total number of LN to be pathologically positive is superior as compared to the previous ones and has been further supported in recent various studies.<sup>19,24-26</sup> The results of our study are in accordance with these studies that demonstrates a poor outcome in patients with >3 positive LN.

Our study is retrospective. Its limitation is in the form of dependence of dissection of lymph node on the disease and physician's LN criteria that might affect the resection outcome. At the same time, the advantage of this study is its homogeneity in the form of treatment and RT dosing which was almost consistent for all patients. We recommend further studies to confirm our hypothesis.

## Conclusion

H&N SCC is a major public health problem presenting mainly in advanced stages and treated primarily with surgery and RT. Neck nodal positivity serves as a major indicator of treatment outcome.

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