DOI:10.31557/APJCC.2024.9.3.417

RESEARCH ARTICLE

Assessment of Pattern of Cervical Lymph Node Metastasis in Squamous Cell Carcinoma of Oral Cavity

Haripriya Chakravarthy, Sudheesh Manoharan, Santhosh Kumar N, Dileep Damodaran, Shafeek Shamsudeen, Lavanya S

MVR Cancer Centre and Research Institute, India.

Abstract

Objective: Cervical lymph node involvement is crucial for prognostic factor for oral squamous cell carcinomas, and understanding nodal metastasis pattern is essential for optimal neck dissection, oncological control, and minimizing morbidity. This study reviews nodal involvement and skip metastasis in 316 oral SCC patients to determine the extent of neck dissection. Methods: The retrospective study analysed 316 patients with oral cancer diagnosed between 2017 and 2020, including those with primary oral cavity cancer who underwent neck dissection. A comprehensive assessment of patient data was used to determine the extent and size of the lesion and lymph node involvement. Preoperative staging was confirmed using various imaging techniques, including OPG, CT MRI, and biopsies. Histological examination results were used to categorize carcinomas based on differentiation levels and to identify nodal involvement patterns. Results: The most common subsite for 316 patients was the tongue (62%), followed by the buccal mucosa (19%), lower alveolus (10.2%), hard palate (3.2%), retro molar trigone (2.8%), floor of the mouth (1.6%), upper alveolus (0.9%), and lower lip (0.3%). Nodal metastasis were more common in Levels II and Ib, with less involvement in Level III and beyond. Tumour with a DOI greater than 10 mm showed higher nodal metastasis frequency, with an increased occurrence in Levels IA, IB, II, III, and IV. Conclusion: Nodal metastasis in oral cancer are common in Levels II and Ib, with variations based on subsite. Alveolus and buccal mucosa malignancies involve fewer lymph nodes beyond Level III, while tongue malignancies show greater involvement in lower levels Level IV involvement is more frequent with greater DOI, and skip metastasis are rare.

Keywords: Squamous cell carcinoma- lymph node- tumor- metastasis

Asian Pac J Cancer Care, 9 (3), 417-423

Submission Date: 09/25/2023 Acceptance Date: 3/27/2024

Introduction

Oral squamous cell carcinoma (OSCC) frequently metastasizes to cervical lymph nodes. The regional spread of the disease is present in over 40% of patients with oral cancers at the time of clinical presentation.

Tumour dissemination in oral cancer from the primary tumor site to the cervical lymph node happens predictably and sequentially. The nodal staging of the tumour determines the treatment strategy and survival outcomes. It has been reported that the chance of survival for five years is reduced by 50% in the presence of a positive metastatic lymph node. Additionally, the survival rate is further decreased by 50% in the presence of extra-nodal extension (ENE). The guidelines suggest the need

for adjuvant therapies in patients with cervical nodal metastasis to improve survival and reduce the chances of

Traditional radical neck dissection was switched to a functional neck dissection with the emergence of evidence regarding the biology of cancer metastasis over the years. Lindberg et al. [1] in 1972 showed that levels I, II, and III were more susceptible to nodal metastasis from primary oral squamous cell carcinoma. A recent study by D'Cruz et al [2]. in 2015, showed that an elective neck dissection has better survival than a therapeutic neck dissection in oral cancers. It is the topic of debate on the extent of an elective neck dissection considering the T stage, subsite

Corresponding Author:

Dr. Haripriya Chakravarthy MVR Cancer Centre and Research Institute, India. Email: dr.haripriyachari@gmail.com

417

and nodal metastasis.

As the nodal metastasis is more sequential, with a potential for skip metastasis to Level IV and V nodes, on the basis of primary tumour site, patterns of involvement can be predicted and utilised to guide the range of selective neck dissection.

The present study aims to evaluate the pattern of lymph node metastasis from different subsites in oral cancer to help achieve optimal oncological treatment and minimize morbidity associated with extensive neck dissection.

Materials and Methods

A retrospective study was conducted on 316 individuals who underwent neck dissection for primary OSCC. The patient database at the hospital was used for collecting patients' surgico-pathological information. Over a course of two years (from 2020 to 2022) a thorough analysis was conducted on the clinical profile data, which included demographics, clinical and histological characteristics, and treatment profile. The study had been approved by the hospital's regional Ethical Review Board and adhered to the Declaration of Helsinki on medical ethics and protocol. The research included 320 individuals (male and female) over the age of 18 who underwent surgery for an oral cavity squamous cell carcinoma that was confirmed by biopsy between June 2017 and June 2020. All necessary measures were implemented to ensure complete confidentiality of the patient's information. The exclusion criteria were: (a) patients with a prior history of other head and neck malignancy; (b) Individuals who have previously undergone any kind of treatment both surgical and non-surgical for any head and neck malignancies. (c) the history of neoadjuvant therapy (chemotherapy or chemotherapy with radiation), (d) the existence of metachronous malignancy. Four subjects were eliminated due to incomplete/inconclusive data. Thus 316 subjects fulfilling all the inclusion criteria were included in the

Age, sex, tumour location, clinical and pathological staging were taken into consideration when analysing the cases. The eight anatomical areas of the oral cavity the buccal mucosa, hard palate, floor of mouth, lower lip, retromolar trigone, and upper/lower alveolus were used to analyse the cases. A thorough assessment was conducted to ascertain the extent and size of the lesion (T), as well as the involvement of the lymph nodes (N). The confirmation of preoperative staging was achieved by the use of orthopantomography (OPGs), computed tomography scans, magnetic resonance imaging of the head and neck area, and lesion biopsies. According to Broder's categorization of carcinomas according to their level of differentiation, each case was assigned a histological grade (well, moderately well, and poorly differentiated carcinomas). To look for patterns of nodal involvement, data from the histological examination were further examined. Comprehensive neck dissections were conducted on all clinically node-positive patients, whereas selective neck dissections (level I-III/IV) were carried out on node-negative patients. The presence of metastasis at

a lower level in the absence of metastasis at the proximal levels was defined as skip metastasis. Rates of skip metastasis was evaluated at levels III, IV, and V.

Data were analysed using SPSS 14 for Windows software (SPSS, IBM, Armonk, NY). The Chi-Square test of independence was done to find the association between nodal metastasis and subsite, indicating the influence of subsite of the tumor on the likelihood of nodal metastasis, and also to find the association between the pathological T stage, DOI and the levels of ipsilateral lymph node metastasis.

Results

A total of 316 patients diagnosed with primary OSCC between June 2017 and June 2020 were included in the study. Among them, 237 patients (75%) were male, and 79 patients (25%) were female. The patients' ages ranged from 23 to 87 years, with an average age of 58.15 years. The majority of the patients, accounting for 72% of the cohort, were above the age of 50. The age group above 60 years comprised 45.9 % of the total, while the age group of 40-60 years represented 44.6% of the patients. A smaller proportion of patients, only 9.5% were below 40 years (Table 1). On average, men had a mean age of 57.41 years, while women had a mean age of 60.39 years.

Table 1. Distribution of Patients Based on Age and Sex

Variables	n (%)
Age (in years)	
Less than 40	30 (9.5)
40-60	141 (44.6)
Above 60	145(45.9)
Sex	
Female	79 (25)
Male	237 (75)

Table 2. Distribution of the Patients Based on Tumor Diagnosis, Sub Site and Side

Diagnosis	n (%)
Well differentiated	159 (50.3)
Moderately differentiated	135 (42.7)
Poorly differentiated	22 (7.0)
Sub site of Tumor	
Buccal Mucosa	60 (19.0)
Floor of Mouth	5 (1.6)
Hard palate	10 (3.2)
Lower lip	1 (0.3)
Retromolar trigone	9 (2.8)
Upper alveolus	3 (0.9)
Lower alveolus	32 (10.1)
Affected Side	
Left	152 (48.1)
Midline	3 (0.9)
Right	161 (50.9)

Table 3. Distribution of Patients Based on Level Wise Patterns of Lymph Node Involvement

	n (%)
Ia	14 (12.1)
Ib	60 (51.7)
II	73 (62.9)
III	34 (29.3)
IV	12 (10.3)
V	4 (3.4)
ECS	37 (31.9)

ECS- Extracapsular spread

Histopathologically, the majority of cases were well-differentiated squamous cell carcinomas, accounting for 159 cases (50%). Moderately differentiated squamous cell carcinomas constituted 135 cases (43%), while poorly differentiated squamous cell carcinomas were observed in 22 cases (7%) (Table 2). Among the 316 patients, the most common subsite of oral squamous cell carcinoma was the tongue, observed in 196 patients (62%). Buccal mucosa was the second most common subsite, found in 60 patients (19%), followed by the lower alveolus in 32 patients (10.2%). Other subsites included the hard palate in 10 patients (3.2%), retro molar trigone in 9 patients (2.8%), floor of the mouth in 5 patients (1.6%), upper alveolus in 3 patients (0.9%), and lower lip in one patient (0.3%) (Table 2).

Based on the data analysis, the results focus on the relationship between subsite, pT stage and DOI and levels of lymph node involvement in oral squamous cell carcinomas. (Table 3)

Subsite vs. Levels of Lymph Node Involvement (Table 4).

Among the 116 node-positive cases, Level Ia exhibited 12.1% involvement, with 57% of these cases originating from the tongue, 21.5% from buccal mucosa, and 21.5% from the lower alveolus. In Level Ib, 51.7% of positive nodes were observed, with 41.7% from the tongue, 31.7% from buccal mucosa, 18.33% from the lower alveolus, 5% from the retromolar trigone, and 1.66% each from the hard palate and lip. Level II had the highest involvement at 62.9%, with 70% from the tongue, 14% from buccal mucosa, 7% from the lower alveolus, 3% from the retromolar trigone, and 4% each from the hard palate, floor of the mouth, and upper alveolus. In Level III,

29.3% of positive nodes were observed, with 79% from the tongue, 9% each from buccal mucosa and lower alveolus, and 3% from the floor of the mouth. Levels IV and V exhibited 10.3% and 3.4% involvement, respectively, with predominantly tongue involvement.

These results indicate a strong correlation between the location of the primary tumor and the extent of lymph node involvement in oral squamous cell carcinomas. The Chi-square test confirmed a significant association between nodal metastasis levels and tumor subsite, as evidenced by the calculated chi-square value (11.9428) exceeding the critical chi-square value (3.84) with a p-value less than 0.005.

Pathologically, the distribution of the tumor stages was as follows: 76 patients (24.1%) were classified as T1, 118 patients (37.3%) were T2, 58 patients (18.4%) were T3, 55 patients (17.4%) were T4a, and 9 patients (2.8%) were diagnosed with T4b (Table 5).

Levels vs Pathological T stage: (Table 6)

Among the 14 Level Ia positive nodes, there were none in T1, 3 (21%) in T2, 3 (21%) in T3, 6 (43%) in T4a, and 2 (14%) in T4b. Out of the 60 Level Ib nodes, one (1.66%) was in T1, 20 (33.33%) were in T2, 16 (26.67%) were in T3, 16 (26.67%) were in T4a, and 7 (11.67%) were in T4b. Within the 73 Level II nodes, one (1.4%) was in T1, 25 (34.2%) were in T2, 25 (34.2%) were in T3, 17 (23.28%) were in T4a, and 5 (6.9%) were in T4b, and they tested positive. Among the 34 positive nodes in Level III, only one (2.94%) was in T1, 17 (50%) were in T2, 7 (20.5%) were in T3, 7 (20.5%) were in T4a, and 2 (5.88%) were in T4b. Within the 12 positive nodes in Level IV, one (8.33%) was in T1, 3 (25%) were in T2, 4 (33.33%) were in T3, and 2 (16.67%) each were in stages T4a and T4b, respectively. Among the 4 positive nodes in Level V, two (50%) were in T2, while one (25%) each were in T3 and T4b. Since the calculated chi-square value (41.023) is greater than the critical chi-square value (31.4104), this indicates that there is a significant association between the pathological T stage.

The data analysis revealed the frequency distribution of nodal metastasis levels in relation to the Depth of Invasion (DOI) categories. For tumors with a DOI of less than or equal to 5mm, the occurrence of metastasis was observed in Level IB in 3 cases, and in Level II and Level III in 1 case each. However, there were no occurrences of metastasis in Level IA, Level IV, or Level V for this DOI category. When the DOI was in the range of >5mm to <= 10mm,

Table 4. Distribution of Patients Based on Association between Level of Lymph Node Involvement and Subsite

Subsite	Ipsilateral level Ia	Ipsilateral level Ib	Ipsilateral level II	Ipsilateral level III	Ipsilateral level IV	Ipsilateral level V
	n=14 (%)	n=60 (%)	n=73 (%)	n=34 (%)	n=12 (%)	n=4 (%)
Buccal Mucosa	3 (0.9)	19 (6.0)	10 (3.2)	3 (0.9)	1 (0.3)	0
Floor of Mouth	0	0	1 (0.3)	1 (0.3)	0	0
Hard Palate	0	1 (0.3)	3 (0.9)	0	0	0
Lower Alveolus	3 (0.9)	11 (3.5)	5 (1.6)	3 (0.9)	2 (0.6)	1 (0.3)
Lower Lip	0	1 (0.3)	0	0	0	0
Retromolar Trigone	0	3 (0.9)	2 (0.6)	0	0	0
Tongue	8 (2.5)	25 (7.9)	51 (16.1)	27 (8.5)	9 (2.8)	3 (0.9)
Upper Alveolus	0	0	1 (0.3)	0	0	0

Table 5. Distribution of Patients Based on Clinical and Pathological Staging of SCC.

Type of staging		n (%)
Clinical Staging		
cT	T1	100 (31.6)
	T2	110 (34.8)
	T3	35 (11.1)
	T4a	62 (19.6)
	T4b	9 (2.8)
cN	N0	233 (73.7)
	N1	60 (19.0)
	N2b	17 (5.4)
	N2c	1 (0.3)
	N3b	5 (1.6)
Pathological Staging		
pT	T1	76 (24.1)
	T2	118 (37.3)
	T3	58 (18.4)
	T4a	55 (17.4)
	T4b	9 (2.8)
pN	N0	200 (63.3)
	N1	37 (11.7)
	N2a	6 (1.9)
	N2b	42 (13.3)
	N2c	2 (0.6)
	N3b	29 (9.2)

cT- clinical primary tumor; cN- clinical nodal involvement; pT- pathological primary tumor, pN- pathological nodal involvement

the distribution of metastasis levels showed higher frequencies. Specifically, Level IA had 6 occurrences, Level IB had 16 occurrences, Level II had 17 occurrences, Level III had 7 occurrences, Level IV had 3 occurrences, and Level V had 2 occurrences. For tumors with a DOI greater than 10mm, the frequency of nodal metastasis was even higher, with Level IA having 8 occurrences, Level IB having 23 occurrences, Level II having 24 occurrences, Level III having 8 occurrences, Level IV having 2 occurrences, and Level V having 1 occurrence. These findings highlight the association between tumor DOI and the likelihood of nodal metastasis, with higher DOI values demonstrating a stronger correlation with nodal involvement and the levels of ipsilateral lymph node metastasis (Table 7).

To interpret the chi-square test result, we compare

the calculated chi-square value (75.12) with the critical chi-square value (18.307). If the calculated chi-square value is greater than the critical chi-square value, and conclude that there is a significant association between DOI and nodal metastasis levels.

Out of 316 patients, 200 (63.3%) patients were node-negative, and 116 (36.7%) were node positive in final histopathology. Out of 116 clinically positive neck cases, 64 were true positives and 19 were false positives. True negatives were 181, and false negatives were 52. The sensitivity, specificity, positive prognostic value, negative prognostic value, and reliability of the clinical examination were 55.17%, 90.5%, 77.11%, 77.68%, 77.53% respectively. Among the 233 clinically node-negative cases, 52 were pathologically node-positive, indicating a 22% incidence of occult metastasis (Table 8).

Skip metastasis were observed in 6.89% of the 116 node-positive patients, with Level III alone being affected in 8 cases (6.89%), and Level IV alone in only one patient (0.86%). In 8.6% of patients, metastasis were found to involve both Level II and III exclusively. Additionally, 1.72% of patients had metastasis affecting both Level Ib and Level IV, while one patient (0.86%) exhibited metastasis in Level II and Level IV without involving Level III. Similarly, another patient (0.86%) had metastasis involving Level III and IV exclusively. Overall, only one patient (0.86%) showed skip metastasis in Level IV out of the 116 node-positive cases, while no skip metastasis were observed in Level V.

Out of the total 316 patients, 233 (74%) underwent elective neck dissections and were initially diagnosed as node-negative. Among these, selective neck dissection of levels I-III was performed in 128 patients (54.27%), while levels I-IV were dissected in 56 patients (24.7%). Modified neck dissection was conducted in 38 patients (16.23%), and bilateral neck dissection was performed in 11 patients (4.7%). On the other hand, 83 patients (26%) presented with clinically node-positive necks and subsequently underwent therapeutic neck dissection (Table 9).

Discussion

Since Lindberg's [1] report in 1972 on the involvement and anatomical distribution of lymph node metastasis in squamous cell carcinomas of the upper aerodigestive tract, several papers have been published, including Sharpe et al [3], Shah et al [4], and Woolgar et al [5], studying the pattern of cervical lymph node metastasis in head and neck

Table 6. Distribution of Patients Based on Association between Level of Lymph Node Involvement and pT (Pathological Primary Tumor)

pT	Ipsilateral level Ia	Ipsilateral level Ib	Ipsilateral level II	Ipsilateral level III	Ipsilateral level IV	Ipsilateral level V	Total
	n=14 (%)	n=60 (%)	n=73 (%)	n=34 (%)	n=12 (%)	n=4 (%)	
T1	0	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)	0	4
T2	3 (0.9)	20 (6.3)	25 (7.9)	17 (5.4)	3 (0.9)	2 (0.6)	70
T3	3 (0.9)	16 (5.1)	25 (7.9)	7 (2.2)	4 (1.3)	1 (0.3)	56
T4A	6 (1.9)	16 (5.1)	17 (5.4)	7 (2.2)	2 (0.6)	0	48
T4B	2 (0.6)	7 (2.2)	5 (1.6)	2 (0.6)	2 (0.6)	1 (0.3)	19

Table 7. Association between Level of Lymph Node Involvement and Depth of Invasion (DOI)

	Level Ia	Level Ib	Level II	Level III	Level IV	Level V
DOI <= 5mm	0	3	1	1	0	0
DOI > 5mm,	6	16	17	7	3	2
<= 10mm						
DOI > 10mm	8	23	24	8	2	1

Table 8. Sensitivity and Specificity of Clinical Neck Examination

cN		p	N		Total
		Dis	ease		
	Present	n	Absent	n	
Positive	True Positive	a= 64	False Positive	c= 19	a+c=83
Negative	False Negative	b= 52	True Negative	d= 181	b+d=233
Total	a+b= 116		c+d=159		
Statistic	Sensitivity	Specificity	PPV	NPV	Accuracy
	55.17%	90.50%	77.11%	77.68%	77.53%

cN- Clinical Nodal involvement; pN- pathological Nodal involvement; PPV- Positive predictive value; NPV- Negative predictive value

malignancies, establishing data to support an appropriate surgical approach to neck dissection.

The most significant independent prognostic marker is cervical lymph node metastasis, which reduces the likelihood of survival by 50%. As a result, surgical interventions of the neck nodes via neck dissection are critical for maximizing loco-regional control and overall survival. As a result, neck dissection is critical in surgical intervention of oral cavity malignancies, not only as part of the primary intervention but also in defining the role of adjuvant therapy. The degree of dissection in elective neck dissections in both node-negative and node-positive necks is debatable. Over the last few decades, as our understanding of the incidence and pattern of nodal metastasis has grown, the amount of neck dissections has decreased from a radical neck dissection to a functional neck dissection.

The inclusion of Levels IV and V in the elective neck dissection is debatable due to reports of skip nodal metastasis from oral cancer cases, particularly tongue tumors, as well as the morbidity involved with the dissection of these levels.

The goal of our study was to examine the patterns of metastasis in cervical lymph nodes in patients with oral cancer and to optimize the extent of neck dissection to achieve oncological control while causing

Table 9. Distribution of Patients Based on Mode of Treatment as Per Nodal Involvement

Treatment	n (%)	
Node-negative		
Selective neck dissection levels I-III	128 (54.27)	
Selective neck dissection levels I-IV	56 (24.7)	
Modified neck dissection	38 (16.23)	
Bilateral neck dissection	11 (4.7)	
Node-positive		
Therapeutic neck dissection	83 (26.0)	

the least amount of morbidity.

Level II showed the highest number of positive nodes (73 out of 116 cases), followed by Level III (34 cases). Level Ia and Level V had the lowest number of positive nodes (14 and 4 cases, respectively).

In our study, we observed a distinct pattern of cervical lymph node metastasis across various subsites of the oral cavity. Specifically, for cases involving the tongue, a significant proportion of nodal metastasis were observed in Level II (70%) and Level III (37%), with Level Ib also showing notable involvement (35%). Conversely, for cases involving the buccal mucosa and lower alveolus, the predominant sites for metastasis were Level Ib (82.6%) and Level II (43.5%). It's noteworthy that metastasis to levels beyond Level III were relatively infrequent in subsites other than the tongue. Similar findings were reported by Patil et al [6] in their study, where pathologically, Level II (56.3%) emerged as the most frequently affected lymph node station among oral cancer patients, aligning closely with the trends observed in our present study. This shared observation suggests that the high incidence of Level II nodal metastasis may be attributed to the prevalence of tongue cases in both studies, supporting a consistent pattern across the research.

These findings align with Nithya et al [7], who reported that in their series, Level II was the most commonly affected site, representing 63.6% of cases. Similarly, in the Pantvaidya et al [7] study, they found that tongue cancers often metastasized to Level IIA and Level III, while buccal mucosa cancers primarily spread to levels IB and IIA. Notably, Level III lymph nodes exhibited a high incidence of metastasis particularly in cases of tongue cancers (22.1%). Our study results corroborate these findings, demonstrating consistency with previous research.

Adding to this, Deo et al [8] reported nodal involvement rates of 17.26%, 8.79%, and 5.32% for levels III, IV, and V, respectively, which further underscores the variability in nodal metastasis patterns across different subsites within

the oral cavity.

Occult metastasis were observed in 22% of node-negative patients, indicating the importance of thorough examination and assessment even in clinically node-negative cases. When comparing our findings with those of other studies, it's notable that Patil et al [6] reported a similar rate of occult metastasis, in 22% of their patients. In contrast, Sharma et al [9] found a lower prevalence only 15.4% of occult metastasis.

In our study, out of 116 clinically positive necks, 64 were true positives, yielding a sensitivity of 55.17%. However, the specificity was high at 90.5%. In contrast, Deo et al [8] reported a higher sensitivity of 83.51% but a lower specificity of 30.05% in their clinical observations. Furthermore, in Patil et al [6], they reported a sensitivity of 76.8% and a specificity of 81.8% for clinical examination.

The most important discussion is skip metastasis, based on the Byers et al [10] study in 1997, especially in tongue cases, which has led to the argument of clearance of Level IV and inadequacy of selective neck dissection of Levels I-III. There has been much discussion in the literature regarding extending Selective neck dissection to include Level IV also. Shah et al [6] documented 3.5% metastasis to level IV in the clinically node negative patients with oral SCC. The studies by Woolgar et al [5] and the prospective study by Pantvaidya et al [11] stated that the incidence of skip metastasis to Levels IV and V is very less (<5%). In Deo et al [8] study, skip metastasis at level III was seen in 5% cases, at level IV in 2% cases, and at level V only in 0.5% cases. Nithya et al [7] study showed that level IV involvement was seen in 15.2 % patients. Isolated level IV involvement in the absence of involvement of one of the higher levels (I, II or III) was not documented in any patient and clinically node-negative cases never showed level IV involvement.

In our study, there was only one (0.86%) case out of 116 node positive cases at Level IV alone, and zero cases in isolated Level V. Therefore, our research findings align with the previously mentioned studies, indicating that the occurrence of skip metastasis in oral cancers is infrequent. This observation underscores the significance of focusing on Level IV when discussing neck dissection, as Levels I to III constitute the minimum elective neck dissection required for oncological adequacy while minimizing surgical morbidity.

Several studies have explored the relationship between tumor depth of invasion (DOI) and the presence of occult neck node metastasis in oral squamous cell carcinoma. Muhammad et al [12] in 2021 emphasized the significance of DOI as a predictive factor for neck metastasis, revealing that patients with a DOI greater than 5 mm were 1.41 times more likely to exhibit neck metastasis compared to those with a DOI of 5 mm or less. This suggests the importance of elective neck dissection in cases where the DOI exceeds 5 mm. In Tarun Kumar et al [13] study from 2013, the role of neck observation in carcinoma of the tongue was discussed. They found that positive nodal disease was rare when the tumor depth was less than 5 mm. They recommended that in cases where observation of the neck is considered, preoperative

ultrasonography of the tongue should be performed, and tumors exceeding 5 mm in DOI should be considered for extended supraomohyoid neck dissection, with the exclusion of Level V involvement in N0 and N1 necks.

Our study further corroborates these findings. For tumors with a DOI of 5 mm or less, nodal metastasis was observed predominantly in Level IB, with only occasional occurrences in Level II and Level III, and no instances in Level IA, Level IV, or Level V. However, as the DOI increased beyond 5 mm, the incidence of metastasis across various nodal levels notably increased. Specifically, tumors with a DOI greater than 10 mm exhibited a higher frequency of nodal metastasis, with an increased occurrence in Levels IA, IB, II, III, and IV. These results underscore the strong correlation between DOI and levels of nodal involvement, highlighting the importance of extended supra omohyoid neck dissection in DOI greater than 5mm.

The strengths of our study lie in the collection of prospective and meticulously maintained electronic data, as well as a substantial sample size. However, it's important to acknowledge the limitations of our research. It should be noted that our study primarily adopts a retrospective approach. Additionally, we lacked data regarding the specific pattern of lymph node metastasis in relation to nodal recurrences or disease-free survival, which could have provided valuable insights to support our objective of assessing the adequacy of neck dissections and ensuring oncological safety.

In conclusion, our study revealed a consistent distribution of positive lymph nodes across various neck levels in oral cancer cases. Level II emerged as the most frequently affected site, followed by Level Ib, Level III, Level Ia, Level IV, and Level V, which exhibited the least involvement. Tongue tumors displayed a distinct metastatic pattern favoring Levels II and III, with Level Ib also showing significant involvement. Likewise, cases involving buccal mucosa, lower alveolus, and the retromolar trigone predominantly exhibited nodal metastasis in Level Ib and Level II.

Notably, Levels I to III contained a substantial 89% of all positive nodes, suggesting that a selective neck dissection strategy focused on clearing these levels could provide an effective oncological procedure with minimal morbidity. Skip metastasis to Level IV and V were exceptionally rare, regardless of the subsite involved.

Furthermore, considering the prognostic value of tumor depth of invasion (DOI) in predicting neck metastasis, it is imperative to factor DOI into the assessment of neck dissection extent. However, to substantiate the adequacy of neck dissection extent and its impact on patient outcomes, further research, and larger randomized control trials are warranted. Future studies should also delve into the correlation between nodal recurrence patterns, especially in Levels IV and V, and disease-free survival.

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

- 1. Lindberg R. Distribution of cervical lymph node metastasis from squamous cell carcinoma of the upper respiratory and digestive tracts. Cancer. 1972 06;29(6):1446-1449. https://doi.org/10.1002/1097-0142(197206)29:6<1446::aid-cncr2820290604>3.0.co;2-c
- D'Cruz AK, Vaish R, Kapre N, Dandekar M, Gupta S, Hawaldar R, Agarwal JP, et al. Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer. The New England Journal of Medicine. 2015 08 06;373(6):521-529. https://doi.org/10.1056/NEJMoa1506007
- 3. Sharpe DT. The pattern of lymph node metastasis in intra-oral squamous cell carcinoma. British Journal of Plastic Surgery. 1981 01;34(1):97-101. https://doi.org/10.1016/0007-1226(81)90110-7
- 4. Shah JP. Patterns of cervical lymph node metastasis from squamous carcinomas of the upper aerodigestive tract. American Journal of Surgery. 1990 Oct;160(4):405-409. https://doi.org/10.1016/s0002-9610(05)80554-9
- Woolgar JA, Scott J. Prediction of cervical lymph node metastasis in squamous cell carcinoma of the tongue/floor of mouth. Head & Neck. 1995;17(6):463-472. https://doi. org/10.1002/hed.2880170603
- Patil LS, Arjun MA, Hanumanthappa BN. Clinicopathological correlation of pattern of cervical lymph node metastasis in oral cavity cancers. International Journal of Surgery. 2019;3(1):337-44.
- Nithya CS, Pandey M, Naik BR, Ahamed IM. Patterns of cervical metastasis from carcinoma of the oral tongue. World Journal of Surgical Oncology. 2003 07 03;1(1):10. https:// doi.org/10.1186/1477-7819-1-10
- Deo S, Singh V, Mokkapati PR, Shukla NK, Dwivedi SN, Sharma A, Biswas A. Clinical Spectrum, Pattern, and Level-Wise Nodal Involvement Among Oral Squamous Cell Carcinoma Patients - Audit of 945 Oral Cancer Patient Data. Indian Journal of Surgical Oncology. 2020 03;11(1):86-91. https://doi.org/10.1007/s13193-019-01011-7
- Sharma A, Kim J, Paeng J. Clinical analysis of neck node metastasis in oral cavity cancer. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2018 Dec;44(6):282-288. https://doi.org/10.5125/ jkaoms.2018.44.6.282
- 10. Byers RM, Weber RS, Andrews T, McGill D, Kare R, Wolf P. Frequency and therapeutic implications of "skip metastasis" in the neck from squamous carcinoma of the oral tongue. Head & Neck. 1997 01;19(1):14-19. https://doi.org/10.1002/(sici)1097-0347(199701)19:1<14::aid-hed3>3.0.co;2-y
- Pantvaidya GH, Pal P, Vaidya AD, Pai PS, D'Cruz AK. Prospective study of 583 neck dissections in oral cancers: implications for clinical practice. Head & Neck. 2014 Oct;36(10):1503-1507. https://doi.org/10.1002/hed.23494
- Muhammad AY, Dhanani R, Salman S, Shaikh Z, Ghaloo SK, Ikram M. Depth of Invasion as a Predictor of Cervical Nodal Metastasis of Oral Tongue Squamous Cell Carcinoma: Findings From a Tertiary Care Center in Pakistan. Cureus. 2021 Oct;13(10):e18976. https://doi.org/10.7759/cureus.18976
- 13. Kumar T, Patel MD. Pattern of lymphatic metastasis in

relation to the depth of tumor in oral tongue cancers: a clinico pathological correlation. Indian Journal of Otolaryngology and Head and Neck Surgery: Official Publication of the Association of Otolaryngologists of India. 2013 07;65(Suppl 1):59-63. https://doi.org/10.1007/s12070-012-0504-y



This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.