

Frequency of histopathologically positive lymph nodes at level V in neck dissection of T3 and T4 oral squamous cell carcinoma

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ABSTRACT

Objective: To determine the frequency of histopathologically positive lymph nodes at level V in neck dissection of T3 and T4 oral squamous cell carcinoma.

Material and Methods: This prospective descriptive cross-sectional hospital-based study was conducted in the Department of ENT, head and neck surgery of Dow medical college, Dr. Ruth K.M Pfau Civil Hospital Karachi from 1st February to 30th August, 2021 A total of one hundred and fourteen (114) histopathologically proven cases of T3 and T4 oral squamous cell carcinoma were included in the study via non-probability consecutive sampling technique. The collected data was entered in SPSS version 26.0 for data analysis. Frequencies and percentages were calculated for qualitative variable, whereas, mean $\pm$ SD for quantitative variables.

Results: Postoperative analysis revealed positive neck nodes in 91 patients (79.8%), with metastasis observed at level I in 59 (51.8%), level II in 26 (22.8%), level III in 5 (4.4%), and level IV in 1 (0.9%) patient; none had level V involvement. Stratification by age, gender, tumor site, and cancer stage showed significant differences only for age and stage of the primary lesion.

Conclusion: The findings of this study suggest that, oral SCC with T3–T4 lesions does not require level V neck dissection. However, given the small sample size, more research with a greater number of patients is necessary to develop future standards for the extent of neck node clearance in oral cancer

Keyword: Level V neck dissection, Lymph nodes metastases, Oral squamous cell carcinoma

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INTRODUCTION

Oral cancer is the sixth most common cancer in the world, globally accounting for 377,713 new cases and 177,757 deaths in 2020, representing an increase in new cases from 2018 [1]. It is estimated that more than 90% of all oral cancer are oral squamous cell carcinoma (OSCC) [2]. In the last few decades it has been suggested that the incidence of oral cancer in all age groups may be rising worldwide [3]. The highest rates of oral cancer in people of all ages occur in developing countries such as south and south-east Asia where oral cancer is often the first or

second most common site for malignancy [4]. There are several causes of squamous cell oral carcinoma and oncogenes are activated as a result of mutation of the DNA. South Asian regions chewing betel, pan and chalia is known to be a strong risk factor for developing oral cancer [5].

In patients with OSCC, clinical evidence of lymph node metastasis (LNM) is observed in about 40%, while rates of occult metastasis vary between 15 and 34% [6]. Moreover, LNM is an important prognostic factor for a patient with OSCC, for the reason that the 5-year survival rate can decrease to below 20% when cervical metastasis occurs [7].

Currently, neck dissection is a standard treatment for the majority of oral squamous cell carcinoma (OSCC) patients. However, the procedure can lead to a series of complications, these include restricted movement of the neck and shoulders, nerve damage, and bleeding

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complications, significantly reducing patient quality of life and even affecting the antitumor immune response in patients undergoing immunotherapy [8]. The extent of cervical lymph node removal is dependent on the clinical and imaging classification of cervical metastasis, the "T" stage, and the localization of the primary tumor. Lymph node metastases are seen as the most important prognostic factor [6]. Further, it has been studied that Oral cancer metastases are rarely found in the posterior triangle (level V). Dissection of level-V lymph node is not only linked to lengthier anesthesia and surgical duration, but also postoperative shoulder dysfunction as well as injury to the spinal accessory nerve [9]. Even if the nerve is unaffected; shoulder dysfunction develops as a result of traction caused by the ischemic nerve injury. Extra capsular spread, lymph node size >3cm, lymph node fixed with mandible, skin, or neighbouring structure, matted lymph node, and numerous LN involvement are all potential risk factors for level V lymph node metastasis [10]. Therefore, in the era of precision surgery, gaining a deeper understanding of the patterns of lymph node metastasis (LNM) in OSCC is crucial as this would help in preventing the unnecessary dissection.

MATERIAL AND METHODS

This prospective descriptive cross sectional was carried out over a period of six months from 1st February to 30th August, 2021 in the head and neck surgery department of Dr. Ruth K.M Pfau Civil Hospital, Karachi after taking the approval of synopsis from IBRD (IRB-1931/DUHS/Approval/2021/212 dated 18th January 2021). A total of one hundred and fourteen biopsy proven patients of T3 and T4 oral squamous cell carcinoma of either gender and had age between 20-60 years and were fit for general anesthesia were included via non-probability consecutive sampling technique after taking the written consent of the patients.

Patients in whom neck dissection was already done, patients who had received prior radiotherapy or chemotherapy and patients suffering with recurrent lesion were excluded

from the study. The sample size was calculated using Open EPI version 6, on the basis of 8 % prevalence of oral squamous cell carcinoma in oral cavity, taken 95% confidence interval, margin of error 5%, then calculated sample was 114 [1].

After taking the demographic characteristics of the patients along with other related to clinical, lab, radiological imaging and operational procedures, each patient underwent for the resection of primary lesion along with comprehensive neck dissection. The specimen of tumor with neck dissection was marked according to anatomical levels of nodes in operation theatre and sent for histopathology in separate containers. The status of nodal involvement was recorded in the proforma after receiving the histopathology report. The collected data was entered in SPSS version 27.0 for analysis purposes. Frequencies and percentages were calculated for each qualitative variable like gender, stage of primary lesion, level of neck nodes. For quantitative variables like age, duration of disease, mean with standard deviation was computed. Stratification was done with respect to age, gender, primary site of lesion and cancer stage. Post-stratification, chi-square test was applied to compare the frequency of histopathologically positive lymph nodes at level V in neck dissection of T3 and T4 oral squamous cell carcinoma among different strata's. P-value ≤ 0.05 was considered as significant.

RESULTS

A total of 114 histopathologically proven T3 and T4 oral squamous cell carcinoma patients were selected for the study in which 95(83.3%) were males and 19(16.7%) were females. Most of the patients had age between 40-50 years followed by 50-60 years i.e. 32 (28.1%) and 23(20.2%) had age between 20-40 years. The buccal mucosa is the primary site of cancer in 64 (56.1%) of patients followed by tongue in 26(22.8%) of patients, Lip in 13(11.4%) patients and alveolus in 7(6.1%) patients. 28(24.6%) cases were highly differentiated, 66(57.9%) cases were moderately differentiated and

20(17.5%) cases were poorly differentiated. On histopathological examination, free margins were found in 82(71.9%) patients, close margins were found in 32(28.1%) patients. Further, the invasion depth greater than 4mm were found in 96 (84.2%) patients while less than or equal to 4mm were found in 18(15.8%) patients. 41(36.0%) patients had tumor size greater than 4cm (T3) while 73(64.0%) cases invaded the adjacent structures (T4), as shown table-I.

Clinically, involvement of Lymph nodes at the level I and II found in 114(100%) each, whereas, level III lymph node involvement in 25 (21.9%) cases, level IV lymph node involvement in 4 (3.5%) cases, whereas only 1(0.87%) showed level V lymph node involvement, as shown in table-II.

On consideration of post-operative investigations, positive neck nodes found in 91 (79.8%) patients, in which level I lymph node metastasis were reported in 59(51.75%) patients, level II lymph node metastasis were

reported in 26(22.80%) patients, level III lymph node metastasis was reported in 5(4.38%) patients and level IV lymph node metastasis was reported only in 1(0.87) patients, none of the patient had involvement of level V lymph node, as shown in table-III.

The stage-wise involvement was also stratified with respect to age, gender, primary site of tumor involved and stage of cancer. The statistically significant difference was found with respect to age and stage of primary lesion. The level-I (40.6%) found mostly in patients with age group >40-50 years, whereas, level-II (56%), III (80%) & IV (100%) found in patients with age group >50-60 years. With respect to gender, level-I (54.2%) and level-II (64%) found more in male, whereas, level-III (60%) and level-IV (100%) found more in female. Level-I (86.4%), level-II (96%) and level-III (80%) highly found in Buccal mucosa, whereas, level-IV found 100% in palate. As far as cancer state, all levels were highly found in T3, as shown in table-IV.

Table I. Demographic characteristic of histopathological proven T3 and T4 patients (n=114).

Characteristics	n (%)
Age	
20-40	23 (20.0%)
>40-50	59 (51.8%)
>50-60	32 (28.1%)
Gender	
Female	19 (16.7%)
Male	95 (83.3%)
Site of primary oral cancer	
Buccal mucosa	64 (56.1%)
Tongue	26 (22.8%)
Lip	13 (11.4%)
Alveolus	7 (6.1%)
Palate	3 (2.6%)
Floor of mouth	1 (0.87%)
Cancer stage	
T3	41 (36%)
T4	73 (64%)
Differential degree on histopathology	
Highly	28 (24.6%)
Moderate	66 (57.9%)
Poorly	20 (17.5%)
Margin status	
Free	82 (71.9%)
Close	32 (28.1%)
Invasion Depth	
>4mm	96 (84.2%)
Less than or equal to 4mm	18 (15.8%)

Table-II: Frequency of involvement of Lymph node on clinical assessment in histopathological proven patients of T3 and T4 Squamous cell carcinoma (n=114).

Clinical involvement of Lymph node	n (%)
Level I	114 (100%)
Level II	114(100%)
Level III	25 (21.92%)
Level IV	4 (3.50%)
Level V	1 (0.87%)

Table-III: Frequency of positive neck nodes and level wise involvement of lymph nodes in histopathological proven patients of T3 and T4 oral squamous cell carcinoma (n=114).

Postoperative cervical node metastasis	n	%
Positive neck nodes	91	79.8%
Level I	59	51.75
Level II	26	22.80
Level III	5	4.38
Level IV	1	0.87
Level V	-	-

Table-IV. Frequency of level V lymph nodes involvement in histopathologically proven patients of T3 and T4 oral squamous cell carcinoma with respect to demographic data (n=114).

Demographic data	Involvement of Lymph Node Metastasis				P-value
	Level-I (n=59)	Level-II (n=25)	Level-III (n=5)	Level-IV (n=1)	
Age (years)					
20-40	02 (3.38%)	02(8%)	00	00	<0.001
> 40-50	24(40.6%)	09 (36%)	01 (20%)	00	
>50 -60	33(55.9%)	14 (56%)	04 (80%)	01 (100%)	
Gender					
Male	32 (54.2%)	16 (64%)	02 (40%)	00	0.474
Female	27 (45.7%)	09 (36%)	03 (60%)	01 (100%)	
Stage of primary lesion					
Buccal mucosa	51 (86.4%)	24 (96%)	04 (80%)	00	< 0.001
Tongue	04 (6.7%)	00	00	00	
Lip	02 (3.3%)	01 (2%)	00	00	
Alveolus	01 (1.69%)	00	00	00	
Palate	01 (1.69%)	01 (2%)	01 (20%)	01 (100%)	
Floor of mouth	00	00	00	00	
Cancer stage					
T3	37 (62.7%)	23 (92%)	5 (100%)	1 (100%)	0.037
T4	22 (37.2%)	03 (8%)	00	00	

DISCUSSION

The current study was designed to investigate the involvement of level V lymph nodes in histopathologically verified patients with T3 and T4 oral squamous cell carcinoma.

According to certain research, males are more commonly afflicted by OSCC than females, presumably because males are more likely to engage in activities such as tobacco smoking and alcohol use than females [11]. Another study found that males (75 percent) were more likely than females (25 percent) to be impacted by the OSCC, and that males consumed more

alcohol and smoked more cigarettes than females. Our study found that 95 percent of men and 19 percent of women were affected by oral squamous cell carcinoma, which was consistent with the findings of the previous studies. It had a male slant to it. This can be explained by the fact that men are more likely to smoke and drink alcohol [12].

The OSCC can affect any portion of the oral cavity's mucosa epithelium, but in Western countries, the tongue is the most commonly afflicted part (20% -40%), followed by the base

of the mouth (15% -20%), and these two sites account for around half of all OSCCs [11]. Another study indicated that in 30 percent of patients, tongue cancer was discovered, followed by the base of the mouth (19 percent) [13]. It's possible that the lower side of the tongue and the floor of the mouth have thin non-keratinized epithelium that allows carcinogens, primarily tobacco smoke and alcohol, to infiltrate. As a result, carcinogens interact with the progenitor cell present in the epithelium's basal cell layer, causing malignancy to develop. As a result, it's clear that OSCC [14] affects the ventral side of the tongue and the base of the mouth the most. Our findings contradicted the findings of the above-mentioned studies, revealing that buccal mucosal surfaces are the most common sites of cancer in 64 (56.1%) of patients, followed by the tongue in 26 (22.8%) of patients, which is in contrast to the findings of a recent study [15], which found that the tongue was the most frequently affected site of primary cancer (53.2%). This was also in agreement with other studies, which found that the tongue was the most usually impacted site [16,17], indicating that tobacco and betel nut usage thins the non-keratinized epithelium of the buccal mucosa and tongue, allowing carcinogens to easily infiltrate into underlying tissues.

In terms of age, the majority of OSCC patients are over 45 years old at the time of diagnosis, with only 6% being under 45 [18]. On the contrary, one study found that about one-third of patients were under the age of 41 years, a figure that is significantly higher than other international [19, 20] and regional [21] investigations. In our study, 59 (51.8%) of patients with oral squamous cell carcinoma were between the ages of 40 and 50 years, followed by 32 (28.1%) of patients who were between the ages of 50 and 60 years.

In current study, level I lymph node metastasis was reported in 59 (51.75%) patients, level II lymph node metastasis was reported in 26 (22.80%) patients, level III lymph node metastasis was reported in 5 (4.38%) patients, level IV lymph node metastasis was reported in only 1 (0.87%) patient, however, in none of the

patient had level-V lymph node metastasis. The frequency of LNM is consistent with the 'cascade theory', which indicates that OSCC LNM should first appear in proximate levels I, II, and III lymph nodes, with fewer metastases in level IV and V [20]. In a prospective study of 583 neck dissections, the order of the frequency of LNM from highest to lowest was level I, level II, level III, level IV, level V in tongue site, which was consistent with the results of this study [18]. Similar type of study was conducted by Marfani MS, et al reported the involvement of level-I lymph node in 24.4% cases of OSCC, level-II in 8.1%, level-III & IV in 4.8% each, and level-V did not found in any of the case [21]. Akhtar S et al reported that level III was seen in 2 patients (6%), Level IV involvement was seen in 4 patients (13%) and none of the patient had level-V involvement [22]. Moreover, the order of the frequency of LNM from highest to lowest was level I, level II, level III, level V, level IV in buccal mucosa site, which was highly similar to the results of Sangeet *et al.*'s study [23]. This reflected the potential influence of primary site on frequency of LNM at different neck levels. This finding is similar to the results of Gouri *et al.*'s study, as the order of the frequency of LNM from highest to lowest was level I, level II, level III from all primary site and the frequency of LNM in level IV, and level V were significantly lower than that in level I, level II, and level III from all primary sites [24]. This was also consistent with the findings of Woolgar's study [25]. Nevertheless, this finding required further research. Notably, this study did not take the frequency of LNM in sublevels such as IIb into account, which may be influenced by different primary sites seriously. Clinicians should exercise caution when adopting this conclusion and rigorously evaluate it.

More clinical studies are required in the future to further the advancement of precision surgery. Numerous questions remain unresolved. For example, creating a customized surgical plan for patients who have undergone immunotherapy and those who have undergone other therapies, such as radiation. To fully understand the

patterns of LNM at various neck levels from various OSCC, more research is necessary.

LIMITATION

Single center study and use of non-probability consecutive sampling technique may minimize the generalizability of the findings.

CONCLUSION

In conclusion, the findings of this study suggest that the frequency of LNM was 51.78% in level I, 22.8% in level II, 4.38% in level III, 0.87% in level IV and level V was not found in none of the patient. Every patient with head and neck cancer underwent a neck dissection as part of our regimen. Based on the results, we advise that, in clinically NO necks, at least a selective neck dissection be carried done since it provides definitive staging and results in little morbidity. Certain areas of the oral cavity and higher stages can benefit from a thorough approach to the neck. However, further research needs to be conducted to figure out the LNM status of patients who have received immunotherapy and further modified the extent of neck dissection.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Qurat Ul Ain: Substantial contributions to study design, acquisition of data, manuscript drafting or reviewing it critical for important intellectual content, final approval, accountable for all aspects of publication.

Omair Ahmed: Substantial contributions to acquisition of data, manuscript drafting, reviewing it critical for important intellectual content, final approval, accountable for all aspects of publication.

Irfan Ahmed Shaikh: Substantial contributions to analysis and interpretation of data, critical review, final approval, accountable for all aspects of publication.

Atif Hafeez Saddiqui: Substantial contributions to study design, critical review, final approval, accountable for all aspects of publication.

Muhammad Shuja Farrukh: Critical review, proofreading, final approval, accountable for all aspects of publication.

Sadaf Zia: Substantial contributions to acquisition of data, final approval, accountable for all aspects of publication.

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