

# Analysis of Tumor Buds & Worst Pattern of Invasion as Emerging Factor in Determining Lymph Node Metastasis in Oral Squamous Cell Carcinoma

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## ABSTRACT

**Introduction:** Lymph node metastasis is associated with poor prognosis in oral squamous cell carcinoma. So, it's important to identify most influencing histological parameter in association with lymph node metastasis.

**Aim of Study:** The aim of this study is to analyze various histological parameter including tumor buds and worst pattern of invasion to check its association with lymph node metastasis positive cases.

**Materials & Methods:** The study done on 100 oral squamous cell carcinoma patients. The various histopathological parameters like Nuclear Pleomorphism, Number of mitosis, Lymphoplasmacytic inflammation along with tumor buds and WPOI analyzed to check association with node metastasis. The data was tabulated and Fischer's exact & chi square test applied to calculate p value.

**Result:** Invasive tumor buds more than 5 and worst pattern of invasion (WPOI) were strongly associated with positive lymph node metastasis cases. The p value for both has been lowest among all other parameter.

**Conclusion:** The tumor buds and Pattern of invasion are most important emerging influencing factor having strong association with nodal metastasis and thus high risk patient can be identified in biopsy specimen.

**Keywords:** Tumor Buds, Oral Squamous Cell Carcinoma, Histopathological Parameters, Worst Pattern Of Invasion

## Introduction

The early detection of oral squamous cell carcinoma doesn't always mean good prognosis of patient. It has been reported that 20-40% cases of oral squamous cell carcinoma have occult metastasis during presentation to hospital.<sup>1,2</sup> The chances of long term survival increased up to 40-50% after surgery in lymph node metastasis free patient as compare to lymph node metastasis positive cases.<sup>3</sup> The prognostic survival is high in node metastasis negative case with treatment as compare to node metastasis positive cases. Hence, Lymph node involvement is very important prognosticator in oral Squamous cell carcinoma cases.<sup>4,5,6,7</sup> So, it's important to identify most influencing histological parameter in association with lymph node metastasis. Hence, prognosis of patient can be predicted with more accuracy and multimodality treatment including radiotherapy can be planned if we can predict high risk patient for lymph node metastasis. The aim of this study is to analyze various histological parameter including tumor buds and worst pattern of invasion to check its association with lymph node metastasis positive cases.

## Materials & Methods

This study has been conducted in retrospective manner on 100 oral squamous cell carcinoma cases during time period

from 2013-2019 in tertiary care hospital. All cases were diagnosed by histopathological examination only. The oral squamous cell carcinoma cases include buccal mucosa, lip, palate and tongue region growth in our study.

Among all these 100 cases, the 40 cases were having lymph node metastasis that was diagnosed by CT scan or histopathological study of radical neck dissection specimen of that patients.

We have studied Nuclear pleomorphism, Number of mitosis, Lympho plasmacytic inflammation, Lymphovascular invasion, Tumor buds and worst pattern of invasion (WPOI) like histopathological parameter in detail to check it's association with lymph node metastasis and to identify high risk patients. The nuclear pleomorphism was reported as mild degree pleomorphism and moderate to severe degree pleomorphism. The number of mitosis divided into >5 mitosis per high power field and <5 mitosis per high power field. The lymphovascular invasion and lympho plasmacytic inflammation were reported as present or absence of it. The tumor buds were analyzed as >5 invasive tumor buds or <5 invasive tumor buds in underlying stroma. The >5 invasive tumor buds in stroma related to poor prognosis in oral squamous cells carcinoma patient.<sup>8</sup>

The new emerging parameter is tumor buds that indicating loss of cell cohesion and active invasive movement of squamous cancer cells. The tumor bud is defined as single cancer cell or <5 cancer cells group in stroma.<sup>9</sup>The worst pattern of invasion reported as low risk type in tumor with large cohesive invasion, pushing border or finger like growth in stroma. The worst pattern of invasion is reported as high risk type in tumor with small tumor island of <15 cells or if satellite tumor located at least 1 mm away from main tumor.<sup>10</sup>

The nuclear pleomorphism and lymphovascular invasion were studied in 40x objective lense. The number of mitosis, Worst pattern of invasion , lymphoplasmacytic inflammation and tumor buds were studied in 20x objective lens. All the mentioned histopathological parameters were analyzed by 2 pathologists both of us are authors. The association of all above mentioned parameters with

positive lymph node metastasis were checked by plotting data in table and p value were calculated for each parameter using Fischer's exact and chi-square test.

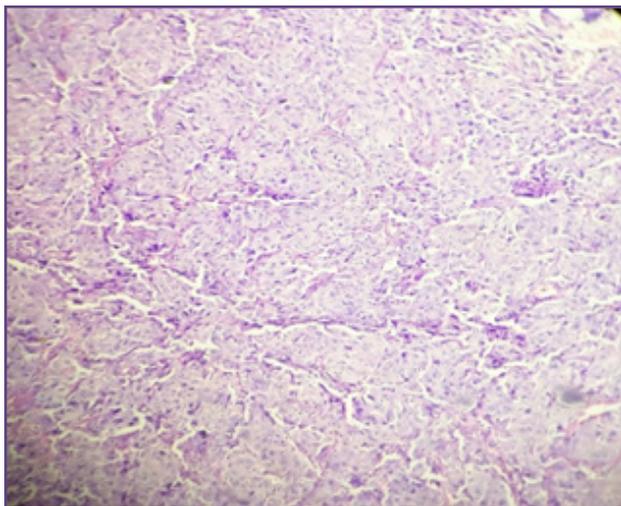
## Results

The mean age of occurrence of oral squamous cell carcinoma in both male and female was 38 years. 80% patient were male and buccal mucosa was most common site for oral squamous cell carcinoma in our study.

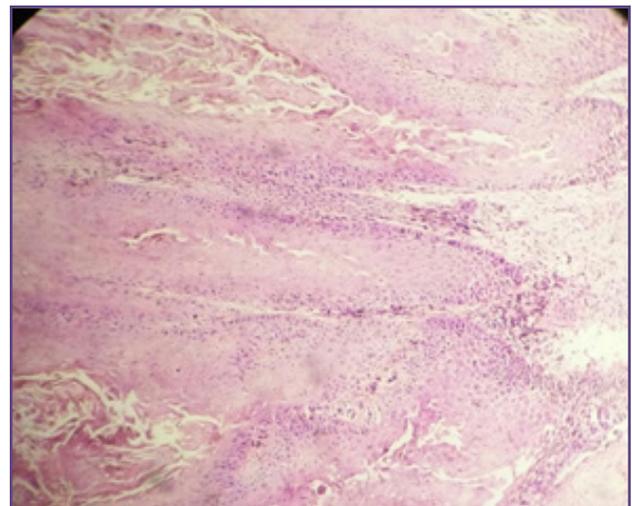
The result of P values for each parameter has been mentioned in table 1. The invasive tumor buds > 5 and High risk worst pattern of invasion (WPOI) were strongly associated with positive lymph node metastasis. The p value for both has been lowest among all other parameter. So >5 invasive tumor buds and high risk pattern of invasion has been considered to be associated with prediction of bad prognosis and such patient can be considered high risk type.

**Table 1: The Analysis of Various Histopathological Parameter with Their Stastical Association to Lymph Node Positive Cases.**

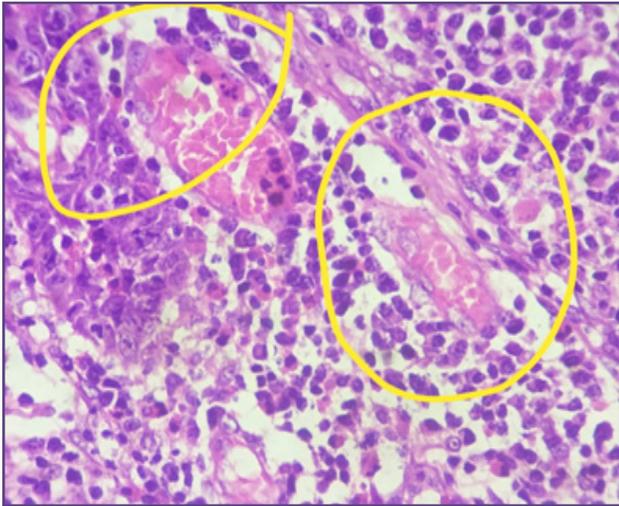
Histopathological Parameters	Subcategorization Description	Lymph Node Metastasis Positive Cases	Lymph Node Metastasis Negative Cases	P Value
1.Nuclear Pleomorphism	Mild	18	82	0.4795
	Moderate To Severe	22	78	
2.Number Of Mitosis	>5 Per Hpf	26	74	0.0339
	<5 Per Hpf	14	86	
3.Lymphovascular Invasion	Present	30	70	0.0004
	Absent	10	90	
4.Lympho Plasmacytic Inflammation	Present	18	82	0.4795
	Absent	22	78	
5.Tumor Buds	>5 Invasive Tumor Buds	36	64	<0.0001
	<5 Invasive Tumor Buds	04	96	
6.Worst Pattern Of Invasion Wpoi	High Risk Type	38	62	<0.0001
	Low Risk Type	02	98	



**Fig. 01: >5 Invasive Tumor Buds and Wpoi High Risk Type.**



**Fig. 2 :<5 Invasive Tumor Buds And Wpoi Low Risk Type.**



**Fig. 3: Lymphovascular Invasion By Tumor Cells.**

### Discussion

Prediction of lymph node metastasis is always been important factor for prognosis and treatment of squamous cell carcinoma.<sup>11</sup> In our study, mitosis, lymphovascular invasion, tumor buds and worst pattern of invasion factors were associated significantly to lymph node metastasis (p value <0.05). Tumor buds and assessing pattern of invasion (WPOI) having strongest correlation to lymph node metastasis (p value <0.0001) and hence most important parameter among all.

Almanghush A et al.<sup>8</sup> concluded that Tumour budding is a simple and reliable prognostic marker for OSCC. Evaluation of tumour budding could facilitate personalised management of OSCC. Our observation consist with his study in terms of considering tumour buds as prognostic predictor. Khwaja et al.<sup>12</sup> concluded that the factors that are basically quantified were not able to show association, rather PI was identified as the most influencing parameter of all. Debajyoti Chatterjee et al.<sup>13</sup> conducted study on 126 cases of OSCC, of which 48 showed LN metastasis. Histological grade, WPOI, tumor budding ( $\geq 3/\times 40$  field), LVE, and PNI were significantly associated with risk of LN metastasis. On multivariate analysis, WPOI and tumor budding were 2 most significant factors. Among the early-stage tumors with available follow up (n = 48), DOI, WPOI, tumor budding, and LVE were associated with a shorter overall survival, although it was not statistically significant. He concluded, WPOI and tumor budding are important risk factors for predicting LN metastasis in all stages of OSCC and associated with a poorer outcome in early-stage tumors. These are easy and reliable prognostic factors and should be included in the histopathological reporting guidelines.<sup>13</sup> Tadaaki Kirita et al.<sup>14</sup> in their review article

stated that Distant metastasis and poor prognosis were significantly more common in the higher budding group. In their review, they focused on the studies related to tumor budding in several cancers including oral squamous cell carcinoma (OSCC) and showed the association among the intensity of tumor budding, risk of lymph node metastasis, and poor prognosis in OSCC is strongly supported by many studies. Moreover, arguments for the assessment of tumor budding, scoring system, stains to mark budding, specimens, and the association with epithelial mesenchymal transition (EMT) were recommended. Kailiu Wu et al.<sup>15</sup> in their cohort study, 141 TSCC patients enrolled for the analysis of the clinicopathological features, cervical lymph node relapse and TSCC prognosis. In multivariate analysis, they identified the trabes growth pattern in the invasive front and depth of invasion larger than 4 mm as risk factors for cervical lymph node relapse.

### Conclusion

In our study >5 invading tumor buds and high risk worst pattern of invasion considered most emerging important factor showing statistical significant association with lymph node metastasis as compare to other parameter. Hence, tumor buds and worst pattern of invasion are recommended to report in every oral squamous cell carcinoma cases to predict lymph node metastasis & to plan multimodality treatment by oncologist.

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