ORIGINAL ARTICLE

Evaluation of Lymph Node Ratio in Oral Squamous Cell Carcinoma and its Association with Pathological Prognostic Parameters: A 5-Year Retrospective Study

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ABSTRACT

Aims & Objectives: To evaluate the lymph node ratio (LNR) in resection specimens of oral squamous cell carcinoma (OSCC) with radical neck dissection and to associate it with various pathological prognostic parameters. **Materials and Methods:** A retrospective observational study conducted over a period of 5 years (December 2018 to December 2023) on 62 OSCC patients who underwent resection of primary tumour with radical neck dissection at a tertiary care center. A detailed histopathological evaluation of hematoxylin and eosin stained slides from tumor and lymph nodes was done. LNR is defined as the ratio of positive lymph nodes and the total number of lymph nodes dissected. LNR was calculated and categorised into two groups: <0.068 (low) and ≥0.068 (high) and was statistically analyzed for association with pathological prognostic parameters. **Result:** The mean age of presentation was 55 years with a male-to-female ratio of 5:6. Most patients presented with advanced-stage IV disease, moderately differentiated tumor, and a mean tumor size of 4 cm. Significant associations were found ($p < 0.05$) between LNR and pT stage, pN stage, TNM stage, and perineural invasion, while no significant association was observed with pathological grade or lymphovascular invasion. Low LNR associated with low nodal stages (N1), whereas high LNR was associated with higher nodal stages (N3). **Conclusion:** LNR is a significant prognostic marker in node-positive OSCC patients and can aid in tailoring adjuvant treatment strategies after curative resection. Its routine evaluation can enhance risk stratification and treatment planning in OSCC management.

KEY WORDS: Lymph node ratio, Oral squamous cell carcinoma, TNM stage, Pathological prognostic markers, Prognosis

Introduction

Head and neck cancer ranks as the sixth most prevalent cancer globally[1, 8]. Oral squamous cell carcinoma (OSCC) constitutes about 90% of all malignancies occurring in the oral cavity, with a global incidence exceeding 350,000 cases, with the highest incidence in India[2, 3]. Despite treatment advances, survival rates remain poor due to cervical lymph node metastasis, the most critical prognostic factor[4].

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Lymph node ratio (LNR) is defined as the ratio of the number of positive lymph nodes to the total number of lymph nodes dissected , offers improved prognostic accuracy[1, 5-7, 9-12].

The aim of this study was to assess LNR in OSCC resection specimens and its association with pathological markers like pathological T stage (pT), pathological N stage (pN), tumor stage, tumor grade, perineural invasion, and lymphovascular invasion, as there is paucity of such studies in India[13].

Materials And Methods

This retrospective observational study was conducted over a period of 5 years (December 2018 to December 2023) on 62 patients with OSCC who underwent resection of primary tumour with radical neck dissection, received in the Department of Pathology, at a tertiary care centre. The study was conducted in accordance with the ethical standards given in the 1975 Declaration of Helsinki, as revised in 2000.

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A detailed histopathological evaluation of hematoxylin and eosin stained slides from tumor and lymph nodes was done. LNR was calculated as the number of pathologically positive lymph nodes divided by the total number of lymph nodes dissected. A validated LNR cut-off of 0.068 reported by Sano D et al., was used, as their study involved a comparable sample size. LNR was analysed and categorised into two groups [<0.068 (low) and ≥0.068 (high)]. LNR was associated with pathological prognostic parameters like pathological T stage (pT), pathological N stage (pN), tumor stage, tumor grade, perineural invasion and lymphovascular invasion. Pathological staging was performed according to the American Joint Committee on Cancer (8th edition -2017).

Inclusion Criteria:

All patients aged 18 years or older with OSCC who underwent primary tumor resection and radical neck dissection.

Exclusion Criteria:

Patients with previous neck dissection, prior radiation therapy or chemotherapy, unresectable primary lesion, or multiple primary lesions were excluded from this study. Cases where only biopsy or limited surgery without neck lymph node dissection were excluded from the study.

Statistical Analysis:

Data was entered into Microsoft Excel data sheet and was analyzed using Statistical Package for Social Sciences [SPSS] windows 22 version (IBM SPSS Statistics, Somers NY, USA) software. Categorical data was represented in the form of frequencies and proportions.

Continuous data was represented as mean and standard deviation. Associations between LNR and categorical prognostic parameters were assessed using the Chi-square test or Fisher's exact test, as appropriate. Correlations were performed with Pearson Correlation coefficient. MS Excel and MS word were used to obtain various types of graphs.

A p-value <0.05 was considered statistically significant after assuming all the rules of statistical tests.

Result

The study included 62 cases of OSCC in patients who underwent primary tumour resection along with radical neck dissection. The median age of the patient was 55 years, ranging between 21 to 80 years. The majority of the cohort consisted of female patients (34/62, 55%), with a male:female ratio of 5:6 [Table. 1].

Based on the tumor size majority of patients were diagnosed with pT2 disease (20/62, 32%), with mean tumor size of 4 cm. Cervical node metastasis was predominantly classified as pN2 stage (23/62 , 37%). All patients are presented with stage III or stage IV disease, the majority being stage IV. Most patients were diagnosed with moderately differentiated grade (80.3%) of OSCC. Among the 62 cases , 20 (32%) exhibited lymphovascular invasion and 39 (63%) demonstrated perineural invasion. The tumor characteristics are detailed in [Table. 2].

Table 1: Age and Gender distribution among the study population

Variables	Category	Number of patients	Percentage (%)
Age groups (in years)	≥ 40	54	13
	<40	8	87
Gender	Female	34	55
	Male	28	45

Table 2: Distribution of tumor characteristics among the study population

Variable	Category	Number of Patients	Percentage (%)
Pathological T Stage	T1	4	6
	T2	20	32
	T3	19	31
	T4	19	31
Pathological N Stage	N1	22	35
	N2	23	37
	N3	17	27
TNM Stage	III	14	23
	IV	16	26
	IVA	20	32
	IVB	12	19
Perineural Invasion	Absent	42	68
	Present	20	32
Lymphovascular Invasion	Absent	23	37
	Present	39	63

The median number of lymph nodes examined was 24, with a range of 6 to 48. The number of positive lymph nodes identified in any specimen ranged from 1 to 9. In

most specimens (42 out of 62, 68%), fewer than three positive lymph nodes were identified [Table. 3]. LNR was categorised into 2 groups [<0.068 (low)and ≥ 0.068(high)]. The majority of cases exhibited high LNR (35/62, 56%) [Table. 4].

Table 3: Distribution of total positive lymph nodes isolated among the study population

Total Positive Lymph Nodes Isolated	Number of Patients	Percentage (%)
<3	42	68
≥3	20	32
Total	62	100

Table 4: Distribution of lymph node ratio among the study population

Lymph node ratio (LNR)	Number of patients	Percentage (%)
<0.068	27	44
≥ 0.068	35	56
Total	62	100

Statistical analysis revealed significant association between the LNR and several pathological parameters [Table. 5], including pT stage (p=0.040), pN stage (p <0.001), TNM stage (p=0.006) and perineural invasion (p=0.035). Notably, low LNR was associated with lower nodal involvement (N1 stage), whereas high LNR was associated with higher nodal involvement (N3 stage). However, no significant association was observed between LNR and pathological grade or lymphovascular invasion.

Table 5: Association between Lymph node ratio and pathological parameters

Variable	Category	Low LNR <0.068	High LNR ≥ 0.068	Total	P value
Pathological T stage	T1	3(7%)	1(5%)	4	P=0.04
	T2	11(26%)	9(45%)	20	
	T3	13(31%)	6(30%)	19	
	T4	15(36%)	4(20%)	19	
	Total	42(100%)	20(100%)	62	
Pathological N Stage	N1	22(52%)	0(0%)	22	P= <0.001
	N2	14(33%)	9(47%)	23	
	N3	6(14%)	11(53%)	17	
	Total	42(100%)	20(100%)	62	
Tumor Stage	III	14(33%)	0(0%)	14	P=0.00
	IV	28(67%)	20(100%)	48	
	Total	42(100%)	20(100%)	62	
Perineural invasion	Absent	32(76%)	8(42%)	42	P=0.03
	Present	10(24%)	12(58%)	20	
	Total	42(100%)	20(100%)	62	

Discussion

The presence of lymph node metastasis in OSCC is known to be the most important prognostic factor and is associated with poor outcome[14]. Identification of metastatic positive lymph nodes is based on quality of neck dissection as well as on the sampling procedure. Limited lymph node dissection or retrieval may result in pathological understaging[15]. Occurrence of positive lymph node is considered in current TNM classification, but no further differentiation is made if more than one lymph node is affected. In this regard , an alternative lymph node staging system is of utmost importance. LNR has gained importance as an important prognostic factor for several types of tumors, including OSCC[17].

High incidence rates of OSCC were observed among women in southern India, largely due to the widespread habit of tobacco chewing, which is deeply rooted in the cultural practices of this region. This trend is reflected in our study, where women constituted 55% of the cohort, indicating a female predominance that contrasts with global patterns, where OSCC is more commonly seen in men. The unique lifestyle factors in southern India, including the habitual use of betel quid and other smokeless tobacco products, are likely major contributors to this disparity, highlighting the regional variations in risk factors for OSCC[18].

LNR can be obtained from a simple calculation using pathological records. This may help determine appropriate postoperative treatment for OSCC patients , as many studies with cancer from other solid malignancies such as breast cancer, colon cancer and gastric cancer have shown the prognostic significance of LNR in terms of survival[19, 20].

In our study, the cutoff for LNR was set at 0.068, consistent with the methodology described by Sano D et al., and divided in two groups: low (LNR <0.068) and high (LNR ≥0.068)[13]. Notably, different studies have

used varying cutoff limits and criteria for LNR classification, highlighting the absence of a universal standard. For instance, Chen KW et al. categorised LNR into three groups: high (LNR > 0.17), medium (LNR 0.06–0.17), and low (LNR < 0.06)[16]. Similarly, Spoerl S et al. adopted a simpler approach, classifying LNR into two groups: low (<0.05) and high (>0.05)[10]. These variations in cut-off likely arise from differences in study populations, the extent of neck dissection and lymph node yield, statistical approaches used for cut-off determination, disease stage distribution, and geographic population. This highlights the variability in LNR cutoff thresholds across studies which underscores the need for standardized criteria , to enhance the comparability and prognostic utility of LNR [Table. 6].

Table 6: Comparison of data with various studies

	Age	Gender	Range of positive lymph nodes excised	Lymph Node ratio (cut-off)	Association
Present study N-62	55	F>M	1-9	0.068	pT,pN,TNM,LVI
Sano D *et al.* n=63	63	M>F	1-23	0.068	pT,pN
Spoerl S *et al.* n=290	60	M>F	1-41	0.055	pT,pN
Chen KW *et al.* n= 117	51	M>F	1-15	0.10	—

Sano D *et al*. conducted a study involving 63 OSCC patients, with a median age of 63 years and a male-dominant cohort (M > F). Their findings demonstrated significant associations with pT and pN stages. The range of positive lymph nodes excised (1–23) was broader than in our study, potentially reflecting differences in surgical or pathological practices. Notably, the study reported a strong correlation between the number of positive lymph nodes and LNR value (r = 0.953), with higher LNR values indicating greater tumor spread. The authors concluded that LNR serves as a valuable prognostic parameter, strongly associated with pT and pN stages. However, unlike our study, their findings did not extend to associations with TNM staging or lymphovascular invasion (LVI). These differences highlight the variability in study designs and the scope of LNR's prognostic utility [Table. 7][13].

Table 7: Comparison of Lymph node ratio with Sano D *et al*. and present study

Lymph node ratio (LNR)	Sano D *et al.*	Present study
<0.068	37(58%)	27(44%)
≥ 0.068	26(41%)	35(56%)
Number of cases	63	62

Spoerl S *et al*. investigated the prognostic value of LNR in OSCC in a study involving 717 patients. Significant associations were observed between LNR and the extent of neck dissection, as well as pT and pN stages. A subset analysis, with a median age of 60 years and a male-predominant cohort, with a broader range of positive lymph nodes excised (1-41). While strong associations with pT and pN stages were noted, no associations with TNM staging or lymphovascular invasion (LVI) were found. The study concluded that LNR is an independent prognostic factor for OSCC, emphasising its importance in stratifying prognosis and the need for standardized cutoff values[10].

Chen KW *et al*. conducted a study on 117 OSCC patients with a median age of 51 years, predominantly male (M > F), to evaluate the prognostic value of LNR. The range of positive lymph nodes excised was 1–15. The study concluded that LNR is an important prognostic factor for node-positive OSCC patients[16].

While our findings align with those of Sano D *et al*. and Spoerl S *et al*. in terms of associations with pT and pN stages, the broader associations with TNM stage and LVI in our study suggest that LNR may serve as a more comprehensive prognostic marker when standardized cutoff values are applied. This variability highlights the need for consensus on LNR thresholds and evaluation criteria to enhance its prognostic utility and comparability across studies. This study was limited by its single-center design and relatively small sample size. Potential variations in neck dissection technique and lymph node retrieval could influence LNR calculation. Follow-up survival data were not analyzed, preventing direct prognostic validation in terms of disease-free or overall survival.

Conclusion

This study highlights the significant association between Lymph Node Ratio (LNR) and various clinical parameters in OSCC, including higher T stage, N stage, advanced TNM stage, and the presence of perineural invasion. By adopting LNR as a prognostic index, treatment strategies could be tailored more effectively. For patients with high LNR, intensifying treatment through the addition of chemotherapy to adjuvant radiotherapy or other advanced approaches may be beneficial. Conversely,

lower-risk patients (N1–N2, low LNR) may avoid overtreatment and achieve optimal outcomes with less aggressive therapy. Therefore, we propose that LNR serves as a valuable prognostic marker for guiding treatment decisions in node-positive OSCC patients.

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