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STUDY OF LYMPH NODE RATIO AS INDEPENDENT PROGNOSTIC FACTOR FOR DISEASE FREE SURVIVAL IN BUCCAL MUCOSA AND ORAL TONGUE CANCER PATIENTS

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ABSTRACT

Lymph node density or lymph node ratio (LNR), equals the ratio of positive lymph nodes to the total number of excised lymph nodes. This ratio attempts to compensate for the potential bias of the sampling method by utilizing two information components: The disease regional spread (number of positive nodes) and the surgical treatment (total number of nodes removed during surgery). In this study, we aimed to validate the utility of LND as a prognostic tool in patients with OSCC. To evaluate and establish lymph node ratio as an independent prognostic factor in operated cases of buccal mucosa and oral tongue cancer and to plan for appropriate adjuvant therapy, so no patient undergoes under treatment. A total of 30 cases of buccal mucosa & tongue malignancies meeting the inclusion criteria were admitted and operated in various units of surgical oncology department during this period.They were analysed using a detailed proforma. All patients were followed-up for 2 years and data collected. In concordance with different national & international studies accepting LNR as a important & significant prognostic factor in DFS & OS in buccal mucosa & oral tongue patients, this study finds LNR>0.08 as a significant prognostic marker. **Categories**: surgical oncology, radiation oncology, pathology.

KEYWORDS: Lymph node ratio, disease free survival, neck dissection.

INTRODUCTION

With an estimated 3,00,000 new cases and 1,28,000 deaths per year, squamous cell carcinoma of the oral cavity (OSCC) is among the most common malignant tumors and a significant source of morbidity. In AJCC system of tumor classification, the presence of lymph node metastases has been associated with poor outcome. However, nodal stage by itself was not shown to reliably predict prognosis. As limited lymph node dissection may result in pathological under staging, lymph node density (LND) has emerged as an independent prognostic factor for carcinoma of the bladder as well as for OSCC. Lymph node density or lymph node ratio (LNR), equals the ratio of positive lymph nodes to the total number of excised lymph nodes. This ratio attempts to compensate for the potential bias of the sampling method by utilizing two information components:

1. The disease regional spread (number of positive nodes) and
2. The surgical treatment (total number of nodes removed during surgery). In this study, we aimed to validate the utility of LND as a prognostic tool in patients with OSCC.

Well over three-fourths of all head and neck cancers can be attributed to tobacco and alcohol use. Tobacco is the most important factor and over 90 per cent of patients have a history of smoking. Tobacco contains over 30 known carcinogens, such as polycyclic aromatic hydrocarbons and nitrosamines. Drainage in tumors of buccal mucosa and tongue is in the neck nodes. There are approximately 150 lymph nodes on either side of the neck. The normal range in size is from 3mm to 3 cm, but most nodes are less than a centimetre. Nodal stations in neck are divided into seven stations marked by roman letters I to VII. TNM stating of tumor involves tumor size & local spread, nodal involvement (staged based on size of node) and metastatic spread. Different types of neck dissection are done such as radical neck dissection, modified neck dissection I,II,III and supra-omohyoid neck dissection.

MATERIAL AND METHODS

This prospective study is done over a period of two and a half years, of patients operated for oral cavity cancers in our hospital. Evaluation of disease free survival period in relation to lymph node ratio is done. Pre-op evaluation is done by clinical examination, imaging study and biopsy. Evaluation of post-op histopathological report is done to

calculate lymph node ratio. Follow up of patient for disease free survival is done over the study duration.

Inclusion Crieteria
Patients included are those with diagnosis of squamous cell carcinoma of oral cavity. Patients operated in our hospital with/without adjuvant radiotherapy or chemo-radiotherapy.

Exclusion Criteria
Patients having diagnosis other than squamous cell carcinoma. Patients operated outside. Patients having distant metastasis before neck dissection.

A total of 30 cases of buccal mucosa & tongue malignancies meeting the inclusion criteria were admitted and operated in various units of surgical oncology department during this period.They were analysed using a detailed proforma. All patients were followed-up for 2 years and data collected. Patients were informed of the study in detail and an informed consent was obtained from patients.

RESULTS

This study was done in 30 patients operated for ca buccal mucosa & ca tongue with thorough study of final histopathology report, relating lymph node positivity as compared to total lymph node harvest with disease free survival & overall survival. The OS was calculated from the date of surgery to the date of death from any cause or last follow-up. The DFS was measured from the date of surgery to the date of any evidence of local recurrence.

Analysis is done describing various different parameters of study such as- age, sex, site, NACT, type of ND, HPE staging, patients with positive lymph nodes, LNR, adjuvant treatment, DFS & OS.

1. SITE- two different sites of lesion where examined; buccal mucosa & tongue. There where 20 patients of ca buccal mucosa & 10 patients of ca tongue.

Site	No of Patients	Percentage
Buccal Mucosa	20	66%
Tongue	10	34%

2. Types of neck dissection - RND, MND I,II & SOHND where performed, with MNDII being the most commonly done variant.

Type of Neck Dissection	No of Patient	Percentage
RND	3	10%
MND I	6	20%
MND II	18	60%
SOHND	3	10%

3. Nodal Staging- According to TNM system it is classified as N0,NI,N2a,N2b,N2c,N3.

Nodal Stage	No of patients	Percentage
N0	15	50%
N1	6	20%
N2a	1	4%
N2b	8	26%
N2c	0	0
N3	0	0

4. LNR - as per definition it is ratio of total node positive for metastasis out of total nodes dissected. In this study we found 15 patients out of total 30 patients with node positivity, having different LNR, ranging from 0.02 to 0.5.

Range of LNR	No of patients	Percentage
<0.05	6	40%
0.05-0.1	5	34%
0.1-0.2	2	13%
>0.2	2	13%
Total	15	100%

5. Recurrence /DFS - out of total 30 patients 12 patients developed recurrence over the study period. two patients lost to follow up early (<2months).

DFS	No of patients	Percentage
Recurrence	12	40%
Lost to follow up	2	7%
No complains	16	53%
TOTAL	30	100%

6. Ratio of node negative patients developing recuurence - 6 out of 15 node negative patients developed recurrence.

Recurrence	No of patients	Percentage
Present	6	40%
Absent	9	60%
Total	15	100%

7. Ratio of node positive patients developing recuurence - 6 out of 15 node negative patients developed recurrence.

Recurrence	No of patients	Percentage
Present	6	40%
Absent	9	60%
Total	15	100%

8. Significant LNR- Out of all 15 node positive patients 6 patients have recurrence of disease resulting in shortened disease free survival. A noticeable observation is presence of LNR >0.08 in all the 6 patients.

9. Out of 15 lymph node positive patients 7 patients have LNR>0.08 & 8patients have LNR<0.08. among these 7 patients 6 patients developed recurrence indicating a high propensity (86%) of developing recurrence.

10. None of node positive patient having LNR<0.08 developed recurrence over study duration.

DISCUSSION

In this study of 30 patients all were treated with surgery. Among 30, 20(66%) patients were diagnosed as ca buccal mucosa & rest 10(34%) patients were having ca tongue. Out of all operated patients 9(30%) received Neo-Adjuvant treatment in form of either CT or CT+RT. Rest 21(70%) patients were operated afferently.

Surgery performed for patients having ca buccal mucosa was composite resction, which included local wide excision of lesion along with appropriate margins and mandibular resection as per need for safe oncological margins together with neck dissection. For patients having ca tongue, local wide excision of tongue with adequate margin along with neck dissection was done.

Different types of neck dissection were performed, appropriate according to the pre-op clinical staging of patient. MNDII is the most commonly performed (60%) neck dissection.

Histopathological staging is done after studying post-op HPE report, which categorized disease into 4 stages. on analysis it was found that 40%(12) of patients presented with early stage disease (stage I+II) were as 60%(18) patients presented with advanced stage(stage III+IV) disease. Nodal positivity makes disease stage III and above.

Nodal positivity was present in 50%(15) of patients, among which 20%(6) were N1, 4%(1) were N2a, 26%(8) were N2b, rest 50%(15) patients were N0.

Out of 15 node positive patients 5 have extra capsular extension. And among these 5 patients 1 lost to follow up early(<2months), from the rest 4 patients 2(50%) patients developed recurrence within 1yr despite of adjuvant treatments. this indicates poor prognosis & prediliction for recurrence in patients having extra capsular extension.

Patients with early stage disease having adverse prognostic features and all patients of advance stage disease (T3,T4,N+) where subjected to post-op adjuvant treatment. Total 22(74%) patients received adjuvant treatment, 6(20%) patients received CT+RT were as rest 16(54%) patients received post-op RT.

Recurrence was present in 40% (6) out of total 15 node positive patients, as well as in 40% (6) of total 15 node negative patients. total 12 patients out of studied 30 patients developed recurrence over the study period. Two patients lost to follow up early(<2months). Most of the recurrence occurred within 1 year of follow-up.

Lymph node ratio was calculated in node positive patients, which is ratio of number of nodes positive for metastasis to total number of nodes retrieved in neck dissection specimen. In this study range of LNR was from 0.02 to 0.5. It is observed that patients having high LNR have shortened DFS, having early recurrence. one patient having LNR 0.5 and other patient having LNR 0.21 developed recurrence within 2 months of follow up.

After analysis of recurrence in all 15 node positive patients and correlating LNR values with recurrence & DFS, statistical significance of LNR>0.08 and its association with recurrence has been established.

It was observed that out of 15 node positive patients 7 patients were having LNR>0.08 and rest 8 patients were having LNR<0.08. All 6 out of 15 node positive patients presenting with recurrence have LNR>0.08. It was also observed that 6(86%) out of 7 patients having LNR>0.08 developed recurrence in study period despite of adjuvant treatment. This indicates poor prognosis in patients having LNR>0.08.

So on the basis of this study results LNR can be recommended as a prognostic indicator for predicting DFS in ca buccal mucosa & ca tongue patients.

As 40%(6) out of 15 node negative patients also developed recurrence, it suggest that nodal positivity is not the only sole factor determining DFS & OS. Multivariate factors affect DFS & OS in patients treated for ca buccal mucosa and ca tongue. Factors of important concern are- Tumor T stage, Nodal invasion, Extra Capsular Spread, Margin clearance, pre-op neoadjuvant or post-op adjuvant treatment administered as well as patients response to these treatment.

This study is being done over a limited time period, in a single centre, on small number of patients(30), so to adopt LNR as a prognostic marker in treatment of ca buccal mucosa and ca tongue patients, it is recommended to perform or correlate with a large number of patient study over a longer duration of time.

CONCLUSION

Different disease related factors affect DFS & OS in buccal & oral tongue cancer patients. These are as follows:
The prognostic factors for lymph node metastasis in early lesions of buccal mucosa& oral tongue are (in order of significance)-Poorly differentiated tumor, Lymphatic permeation, Depth of disease - 4 mm or more, Endophytic (infiltrative) disease, Muscle invasion, Young age at presentation, Male sex.

The different prognostic factors on final histopathological report affecting DFS & OS are:
Tumor T stage, Nodal invasion, Extra Capsular Spread, Margin clearance, Perineural invasion, lymphovascular permeation, pre-op neoadjuvant or post-op adjuvant treatment administered as well as patients response to these treatment.

In concordance with different national & international studies accepting LNR as a important & significant prognostic factor in DFS & OS in buccal mucosa & oral tongue patients, this study finds LNR>0.08 as a significant prognostic marker.

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