Primary Tumour Characteristics Poorly Correlate with Extracapsular Spread and Cervical Sublevel IIb Metastasis in Patients with Oral Squamous Cell Carcinoma and Clinically N0 Neck: A Retrospective Study

Akhilesh Kumar Singh, Rathindra Nath Bera, Janani Anandkumar, Aswathi Krishnan, Ravina Rajpoot
Faculty of Dental Sciences, Unit of Oral and Maxillofacial Surgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Abstract

Introduction: Nodal metastasis reduces the survival by 50% in head-and-neck squamous cell carcinomas. The presence of nodal extension/ extracapsular spread (ECS) further reduces survival. Current literature favors a selective level IIb sparing neck dissection in clinically N0 neck. Studies have evaluated the role of primary tumour size, number of lymph nodes, and depth of invasion (DOI) with the occurrence of extranodal extension (ENE). Patients and Methods: Patients were retrospectively reviewed who presented with oral cavity carcinomas and clinically N0 neck. Relationship was sought between tumour site, size, histological grading, DOI, and the occurrence of level IIb metastasis and ECS. A P < 0.05 was considered statistically significant. Results: The relationship showed insignificant correlation with P values (0.6643, 0.6704, 0.6779, and 0.6779) between site, size, grading, DOI, and level IIb and ENE. Discussion: Previous studies have shown DOI >5 mm and lymph node size 15 mm and multiple lymph nodes predict ECS. DOI and primary site with more than 20% for occult metastasis predicts elective neck treatment. However, in our study, no correlation was found between primary tumour characteristics and ECS or level IIb metastasis. Elective neck dissection is the standard surgical protocol from both diagnostic and therapeutic viewpoints. The only criterion for level IIb dissection is concomitant presence of level IIa involvement intraoperatively. Since ENE can occur early in the disease process, elective neck dissection remains the standard of care.

Keywords: Extracapsular spread, extranodal extension, neck metastasis, oral squamous cell carcinomas, primary tumour

Introduction

India is reported to have the highest number of oral cancer cases in the world and the number is increasing, 90%-95% of these are oral squamous cell carcinomas (OSCCs).[1] Tobacco, alcohol, diet and nutrition, viruses, radiation, ethnicity, familial and genetic predisposition, oral thrush, immunosuppression, use of mouthwash, syphilis, dental factors, occupational risks, etc., are some of the etiologic factors.[2] The American Joint Committee on Cancer (AJCC) and International Union for Cancer Control initially developed the staging for oral cancer. At present, the 8th edition of the manual is in use. The depth of invasion (DOI) being incorporated in the new edition is the distance from the basement membrane relative to an area of intact mucosa to the area of greatest invasion and a distinct entity from tumour thickness. The extranodal extension (ENE)/ extracapsular spread (ECS) is the spread of tumour beyond the lymph node into the perinodal areas.[3] DOI is a strong predictor for lymph node metastasis and prognosis. Kligerman et al. considered 4 mm as a guide for elective neck dissection, with a range from 2 to 10 mm.[4] Surgery still remains the first
option of treatment for oral cancers. Although early-stage OSCC can often be cured with surgery, metastasis to cervical lymph nodes reduces the prognosis. Nodal metastasis is the single most important prognostic factor affecting the quality of life in patients with OSCC. The prognostic significance of ENE of tumour in cervical lymph nodes has been documented. In patients with cervical metastasis, the presence of ENE further reduces the survival, larger the node, more likely the presence of ENE. The poor prognosis in patients with ENE has led to an effort to improve the treatment results through adjuvant therapy. It has been found that radiation therapy after radical neck dissection has improved the results in patients. ENE is associated with an increased risk of recurrence and death. The current universal guidelines for OSCC treatment strongly recommend that patients with ENE receive adjuvant chemoradiotherapy to reduce the risk of treatment failure.

Selective neck dissection (I-III) is currently the most common surgical procedure to treat clinically N0 neck and detect occult metastasis in OSCC. Dissection of cervical sublevel IIb (submuscular recess) is anatomically challenging and is associated with a high risk of damaging the spinal accessory nerve. In N0 neck, the overall metastasis to IIb is 6% for all supraomohyoid neck dissection (SOHNDs) and 18% for positive SOHND. Isolated metastasis to IIb is rare, and hence, cervical level IIb can be spared in clinically N0 neck. Furthermore, metastasis to level IIb is associated with metastasis to level IIa and level III. Hence, dissection of level IIb is to be carried out only when multilevel cervical metastasis exists intraoperatively or IIa metastasis is present in clinically N0 neck. ECS can occur even in clinically N0 neck with rates ranging from 24% to 49%. Imaging techniques for staging clinically N0 neck show similar accuracy with all modalities. Hence, an elective neck dissection is currently the most definitive procedure from both diagnostic and therapeutic viewpoints. Studies have shown that DOI, size, and number of metastatic nodes predict early ECS in OSCC.

Objectives
The following study would evaluate the role of primary tumour characteristics in the incidence of ECS and cervical level IIb metastasis. In this current retrospective review, we would assess the predictability of site, size, histological grading, and DOI of primary tumour for the occurrence of early ECS in OSCC and to predict whether the same also influences cervical metastasis to sublevel IIb. Considering null hypothesis, we assume that primary tumour characteristics do not influence the outcomes evaluated in our study.

Patients and Methods

Study design and setting
A retrospective single-arm study of patient records was made from January 2012 to December 2020. Patient records from the Oral and Maxillofacial Surgery department were searched for data in accordance with the eligibility criteria. Ethical clearance was obtained from the Institute’s Review Board (No. Dean/2020/EC/2135). The following study is conducted in accordance with the Strobe Statement (strobe-statement.org). The study is in accordance with the Declaration of Helsinki.

Participants

Inclusion criteria
1. Patients who presented with biopsy-proven oral squamous cell carcinoma and a clinically N0 neck were selected for the study
2. Patients who were treated with surgery as the primary modality
3. Records with adequate data on primary tumour characteristics; site, size, grading, DOI
4. Adequate data on cervical metastasis, lymph nodes involved, tumour, node, metastasis (TNM) staging, and adjuvant treatments rendered.

Exclusion criteria
Patients with a positive node, patients who received neoadjuvant treatments, and patients lost to follow-up were excluded from the study.

Treatment and evaluation

Data from preoperative workups were obtained. For the initial staging, physical examination, biopsy, and imaging (computed tomography [CT] and/or magnetic resonance imaging [MRI] and orthopantomogram) were done to assess the primary tumour, and CT/MRI/ultrasonography with or without FNAC was done to evaluate and stage the neck. The clinical stage was determined according to the AJCC TNM 8th edition. DOI was recorded according to the final histopathological reports. The preoperative CT images were visually inspected and interpreted by a consultant radiologist with clinical experience in head-and-neck radiology who was blinded to clinical outcomes. The greatest diameter of metastatic lymph nodes was measured on the axial, coronal, and sagittal CT images of each patient and recorded. Every metastatic node was evaluated in terms of ENE by preoperative contrast-enhanced CT scans. Lymph nodes were considered metastatic if central necrosis or inhomogeneous enhancement was present, if their shortest axial diameter was >1 cm, long/short axis ratio <2, or if there was a cluster of 3 or more lymph nodes of borderline size. The treatment of choice for each patient was decided by the tumour board of our institution, which consisted of maxillofacial surgeons, medical and radiation oncologists, oral pathologists, and oral radiologists. Standard surgical procedures were carried out on the patients, and adjuvant therapy (radiotherapy/chemoradiation) was given according to the final histopathological reports. Elective neck dissection was routinely performed on all patients with postoperative radiotherapy or chemoradiation as dictated by the final histological reports. Radiotherapy was added to the treatment when postoperative histological reports showed one or more of the following features; advanced T and N stage, multiple lymph nodes, positive margins, lymphovascular involvement, perineural spread, or extranodal.
involvement. Adjuvant chemoradiotherapy was given when final histopathological reports showed evidence of a positive margin or ENE. All patients underwent a thorough physical examination at every follow-up visit for a minimum of 1 year. Patients who had recurrence were planned either for salvage treatment or palliative treatment depending upon the stage. The site and size of the primary tumour, histologic grading, and DOI were the predictor variables. The primary outcome variables were metastasis to sublevel IIb and occurrence of ENE. The secondary outcome variables assessed were chances of occult metastasis, adjuvant therapies, complications related to surgery, and postoperative therapies.

**Statistical analysis**
The statistical analysis was performed using IBM SPSS software, version 20.0 (IBM, Armonk, NY, USA). ANOVA statistics was used to appraise the relationship between the predictor and primary outcome variables. A $P < 0.05$ was considered statistically significant.

**RESULTS**
A total of 120 patient records were initially accessed who presented with biopsy-proven OSCC. 90 patient records were finally considered for evaluation on the basis of inclusion and exclusion criteria. The mean age of presentation was $55.48 \pm 4.43$ years. The male:female ratio was 1:0.06. Tables 1-3 shows the distribution of study subjects according to primary site of tumour, size, histological grading, DOI, and lymph node metastasis.

A total of 53 patients (58.88%) had pathological node-negative neck (pN0), and 37 (41.1%) patients had a pathological node-positive neck. A total of 73 patients presented with advanced stage disease (T3/T4) on presentation [Table 1].

Majority of the tumours are moderately differentiated. All the tumours of the upper alveolus were well differentiated [Table 2].

Cervical level Ib had the majority of occult metastasis; followed by IIa, III, and IIb. There was no case of isolated metastasis to level IIb or III [Table 3].

Most of the patients were in the T3 stage, and the most common site for occult metastasis was level Ib. Two patients had cervical level Ib involvement and one of them also had ENE. Wide local excision with SOHND was the most common surgical procedure. Marginal mandibulectomy, segmental mandibulectomy, coronoidectomy, and upper alvelectomy were the other treatments rendered. For oral tongue carcinomas, a selective neck dissection I–IV was done. Contralateral SOHND was done for three cases for oral tongue cancers [Supplemental Table 1].

A total of 2 patients had level IIb metastasis and 1 had ECS. Oral tongue tumour was the only primary site associated with both these outcomes. However, the association was not significant [Table 4].

Advanced stage tumours (T4a) were insignificantly associated with both cervical level IIb metastasis and ECS [Table 5].

Only DOI >10 mm was associated with cervical level IIb metastasis and ENE but again the relationship was insignificant [Table 7].

In our study, a total of 41.1% of patients had occult metastasis with floor of mouth being the highest (66.66%) followed by oral tongue (60%), lower alveolus (38.1%), buccal mucosa (37.14%), retromolar trigone and posterior gingivobuccal sulcus (33.33%), and no occult metastasis with upper alveolus tumours. A total of 9 patients received adjuvant RT and one received adjuvant chemoradiotherapy. Fifty percent of the patients had temporary shoulder immobility. None of the patients had shoulder immobility beyond 6 months. Two patients with oral tongue carcinoma developed osteoradionecrosis which was managed by debridement and decortication. A total of 10 patients had wound dehiscence which was managed conservatively. Surgical margins were negative in 88 patients (>5 mm) and close in 2 patients (1–5 mm).

**Table 1: Distribution of study subjects according to tumour, node, metastasis staging**

| Primary site                      | cTNM | pTNM |
|----------------------------------|------|------|
|                                  | T1N0M0 | T2N0M0 | T3N0M0 | T4aN0M0 | T3N1M0 | T3N2bM0 | T4aN1M0 | T4aN2bM0 | T4aN3bM0 | NO |
| BM                               | 4     | 10    | 14     | 7       | 6       | 0       | 4       | 3       | 0       | 22  |
| Oral tongue                      | 0     | 3     | 9      | 3       | 5       | 1       | 0       | 2       | 1       | 6   |
| Lower alveolus                   | 0     | 0     | 11     | 10      | 0       | 0       | 6       | 2       | 0       | 13  |
| FOM                              | 0     | 0     | 4      | 2       | 0       | 0       | 2       | 2       | 0       | 2   |
| Upper alveolus                   | 0     | 0     | 4      | 0       | 0       | 0       | 0       | 0       | 0       | 4   |
| RMT and posterior GB sulcus      | 0     | 0     | 2      | 7       | 0       | 0       | 2       | 1       | 0       | 6   |

Differentiation

| Well                             | 4     | 10    | 8      | 0       | 0       | 0       | 0       | 0       | 0       | 22  |
| Moderately                       | 0     | 3     | 36     | 19      | 13      | 1       | 11      | 2       | 0       | 31  |
| Poorly                           | 0     | 0     | 0      | 10      | 0       | 0       | 3       | 6       | 1       | 0   |

BM=Buccal mucosa; FOM=Floor of mouth; RMT=Retromolar trigone; cTNM=Clinical tumour, node, metastasis; pTNM=Pathological tumour, node, metastasis; GB=Gingivobuccal
Singh, et al.: Influence of primary tumour characteristics on ECS and level IIb metastasis

**Table 2: Distribution of study subjects according to histologic grading of primary tumour**

| Primary site         | Well differentiated | Moderately differentiated | Poorly differentiated |
|----------------------|--------------------|---------------------------|----------------------|
| BM                   | 15                 | 17                        | 3                    |
| Oral tongue          | 0                  | 12                        | 3                    |
| Lower alveolus       | 2                  | 18                        | 0                    |
| FOM                  | 0                  | 4                         | 2                    |
| Upper alveolus       | 4                  | 0                         | 0                    |
| RMT and post-GB sulcus| 0               | 7                         | 2                    |

BM=Buccal mucosa; FOM=Floor of mouth; RMT=Retromolar trigone; GB=Gingivobuccal

**Table 3: Distribution of study subjects according to pathological lymph node involvement and depth of invasion**

| Primary site         | Lymph node | DOI (mm) |
|----------------------|------------|----------|
|                      | IB         | IIA       | IIB       | III       | <5 | 5-10 | >10 |
| BM                   | 13         | 3         | 0         | 0         | 4  | 28   | 3   |
| Oral tongue          | 9          | 4         | 2         | 3         | 5  | 7    | 10  |
| Lower alveolus       | 8          | 2         | 0         | 0         | 7  | 14   | 0   |
| FOM                  | 4          | 0         | 0         | 0         | 0  | 5    | 1   |
| Upper alveolus       | 0          | 0         | 0         | 0         | 3  | 1    |     |
| RMT and post-GB sulcus| 2         | 2         | 0         | 1         | 0  | 9    | 0   |

Differentiation

- Well: 0 0 0
- Moderately: 26 3 0
- Poor: 10 7 2

BM=Buccal mucosa; FOM=Floor of mouth; RMT=Retromolar trigone; GB=Gingivobuccal; DOI=Depth of invasion

**Table 4: Relationship of primary tumour site with cervical sublevel IIb metastasis and extranodal extension**

| Primary site         | Level 2b | ENE  | P     |
|----------------------|----------|------|-------|
| BM                   | 0        | 0    |       |
| Oral tongue          | 2        | 1    | 0.6643|
| Lower alveolus       | 0        | 0    |       |
| FOM                  | 0        | 0    |       |
| Upper alveolus       | 0        | 0    |       |
| RMT and post-GB sulcus| 0      | 0    |       |

BM=Buccal mucosa; FOM=Floor of mouth; RMT=Retromolar trigone; GB=Gingivobuccal, ENE=Extranodal extension

**DISCUSSION**

**Key results**

The association between primary site, size, histological grading, DOI of tumour, and the occurrence of cervical sublevel IIb metastasis and ENE was insignificant. Nevertheless, OSCC of the oral tongue was the only primary site associated with cervical sublevel IIb metastasis (13.33%) and ENE (6.66%). Advanced stage tumours (T4) and poorly differentiated tumours are more likely to be associated with ENE and IIb metastasis. A DOI >10 mm insignificantly increases the chance of ENE and IIb metastasis. Oral tongue and buccal mucosa carcinomas are more likely to present as poorly differentiated tumours. Oral tongue carcinomas showed the highest chances of level III metastasis (20%) followed by RMT (11.11%).

**Limitations**

One of the demerits of our study is the sample size. The large confidence intervals of sensitivity and specificity are mainly due to the low power of this study. Histopathological examination was not performed with serial slices. Due to the retrospective analysis, this fact could not be changed.

**Interpretation**

The single most important prognostic factor in predicting local and distant failure as well as survival is metastases to the regional lymph nodes. Nodal metastasis reduces the survival rate by 50%. While there are currently no established methods of assessing tumour thickness preoperatively, various options are histology, intraoral ultrasonography, MRI, cone-beam CT, and CT.[25-27] DOI is considered as one of the decisive factors in performing an elective neck dissection in the clinically N0 neck. Several studies have showed that DOI >4 mm is associated not only with treatment failures but also with increased incidence of nodal metastasis.[25-27] An elective neck dissection is warranted when DOI is >4 mm and/or there are more than 20% chances of occult metastasis.[28,29] Similar results were noticed by O-Charoenrat et al.,[30] and DOI (>5 mm) was the only factor affecting occult nodal metastasis. DOI and ENE both impact survival in OSCC.[4,31] A study by Woolgar showed that cervical lymph node IIb and extranodal involvement were found in carcinoma of tongue, and the level of significance was found to be insignificant.[32] Suton et al. also had similar results, and the primary tumour characteristics did not influence ECS occurrence.[10] The study by Mair et al.[16] showed that lymph node size >15 mm, multiple neck nodes, and DOI >5 mm were significantly associated with ECS. Several studies have reported a great variation in the incidence of ECS. Our study showed that although poorly differentiated tumours, oral tongue carcinomas, advanced stage, and DOI >10 mm are more likely to have ECS, the relationship was insignificant. As already discussed lymph node status, in particular, the lymph node size might influence ECS occurrence. However, this factor was not considered in our study.

Mair et al.[16] discussed that no current diagnostic modality is accurate enough to diagnose occult nodal metastasis and ECS preoperatively and hence lays the importance of END (elective neck dissection). ECS can be present even in lymph nodes smaller than 5 mm, thus favoring END.

Lim et al.[33] carried out a study to determine whether level IIb lymph nodes can be saved in elective SOHND as a treatment for patients with squamous cell carcinoma of the oral cavity. It was found that no instance of isolated metastasis to level IIb lymph nodes was reported without involvement of other nodes in the SOHND specimens.
In our study, there was no instance of isolated metastasis to cervical level IIb. Two patients who had metastasis to level IIb also had concomitant metastasis to IIa and III. Similar results were also showed by Krauss et al. Literature shows that the overall metastasis to level IIb is 5%–6% in all neck dissections and around 18% in neck dissections with occult metastasis. In our study, the overall incidence of level IIb involvement was 2.22% and 5.4% among positive neck dissections. The lower incidence levels may be due to a smaller sample size. A study by Roy et al. showed that primary site may not be the contributing factor toward cervical level IIb involvement. However, certain other features such as poor grading, lymphovascular and perineural invasion, and positive margins may influence level IIb metastasis. Our study also had poorly differentiated more commonly associated with level IIb metastasis. Nevertheless, the association was insignificant. The current literature favors a level IIb sparing neck dissection in the clinically N0 neck based on the background that level IIb metastasis is unlikely in the absence of level IIa and III involvements. Further preserving level IIb also reduces the morbidity associated with impairment of shoulder movements.

### Table 5: Relationship of primary tumour size with cervical sublevel IIb metastasis and extranodal extension

| Staging       | Level 2b | ENE | P     |
|---------------|----------|-----|-------|
| T1N0M0        | 0        | 0   | 0.6704|
| T2N0M0        | 0        | 0   |       |
| T3N0M0        | 0        | 0   |       |
| T4aN0M0       | 2        | 1   |       |

ENE=Extranodal extension

### Table 6: Relationship of primary tumour histological grading with cervical sublevel IIb metastasis and extranodal extension

| Differentiation | Level 2b | ENE | P     |
|-----------------|----------|-----|-------|
| Well            | 0        | 0   | 0.6779|
| Moderately      | 0        | 0   |       |
| Poor            | 2        | 1   |       |

ENE=Extranodal extension

### Table 7: Relationship of primary tumour depth of invasion with cervical sublevel IIb metastasis and extranodal extension

| DOI (mm) | Level 2b | ENE | P     |
|----------|----------|-----|-------|
| <5       | 0        | 0   | 0.6779|
| 5-10     | 0        | 0   |       |
| >10      | 2        | 1   |       |

ENE=Extranodal extension; DOI=Depth of invasion

In our study, there was no instance of isolated metastasis to cervical level IIb. Two patients who had metastasis to level IIb also had concomitant metastasis to IIa and III. Similar results were also showed by Krauss et al. Literature shows that the overall metastasis to level IIb is 5%–6% in all neck dissections and around 18% in neck dissections with occult metastasis. In our study, the overall incidence of level IIb involvement was 2.22% and 5.4% among positive neck dissections. The lower incidence levels may be due to a smaller sample size. A study by Roy et al. showed that primary site may not be the contributing factor toward cervical level IIb involvement. However, certain other features such as poor grading, lymphovascular and perineural invasion, and positive margins may influence level IIb metastasis. Our study also had poorly differentiated more commonly associated with level IIb metastasis. Nevertheless, the association was insignificant. The current literature favors a level IIb sparing neck dissection in the clinically N0 neck based on the background that level IIb metastasis is unlikely in the absence of level IIa and III involvements. Further preserving level IIb also reduces the morbidity associated with impairment of shoulder movements.

### Conclusion

Our study aimed at evaluating the primary tumour factors which might predict early cervical sublevel IIb metastasis and ENE. Our study failed to find any significant correlation between the primary tumour factors and ECS and IIb metastasis. The current imaging techniques offer similar and limited accuracy in the diagnosis of occult metastasis making END the most ideal therapeutic and diagnostic decision. Since no primary tumour characteristic could predictably foresee cervical sublevel IIb metastasis, elective neck dissection and intraoperative presence of IIa metastasis would dictate the necessity for IIb dissection. However, a DOI >10 mm, oral tongue cancers, poorly differentiated tumours, and stage (T4a) are more likely for IIb metastasis and ENE.

### Clinical relevance

#### Rationale

The current imaging modalities offer similar diagnostic accuracy in staging neck. Principal findings: primary tumour factors are poorly correlated with ENE and IIb metastasis. Oral tongue cancers, aggressive histological pattern, invasive tumours, and high-stage tumours may insignificantly increase the risk for early ECS and cervical metastasis.

#### Practical implications and future research

END is most valuable standard of care in OSCC both from diagnostic and therapeutic viewpoint. Further studies, especially prospective studies and clinical trials, need to be conducted to determine the effects of primary tumour on ECS and cervical IIb metastasis.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### References

1. Gupta B, Ariyawardana A, Johnson NW. Oral cancer in India continues in epidemic proportions: Evidence base and policy initiatives. Int Dent J 2013;63:12-25.
2. Kumar M, Nanavati R, Modi TG, Dobariya C. Oral cancer: Etiology and risk factors: A review. J Cancer Res Ther 2016;12:458-63.
3. Mupparapu M, Shanti RM. Evaluation and staging of oral cancer. Dent Clin North Am 2018;62:47-58.
4. Tam S, Amit M, Zafereo M, Bell D, Weber RS. Depth of invasion as a predictor of nodal disease and survival in patients with oral tongue squamous cell carcinoma. Head Neck 2019;41:177-84.
5. Rogers SN, Brown JS, Woolgar JA, Lowe D, Magennis P, Shaw RJ, et al. Survival following primary surgery for oral cancer. Oral Oncol 2009;45:201-11.
6. Joo YH, Cho JK, Koo BS, Kwon M, Kwon SK, Kwon SY, et al. Guidelines for the surgical management of oral cancer: Korean society of thyroid-head and neck surgery. Clin Exp Otorhinolaryngol 2019;12:107-44.
7. Kuan EC, Mallen-St Clair J, Badran KW, St John MA. How does depth of invasion influence the decision to do a neck dissection in clinically N0 oral cavity cancer? Laryngoscope. 2016;126:547-8. Doi: 10.1002/lary.25707.
8. Arain AA, Rajput MS, Ansari SA, Mahmood Z, Ahmad AN, Dogar MR, et al. Occult nodal metastasis in oral cavity cancers. Cureus 2020;12:e11640.
9. Chheda YP, Pillai SK, Parikh DG, Dipayan N, Shah SV, Alaknanda G. A prospective study of level IIb nodal metastasis (supraretrospinal) in clinically N0 oral squamous cell carcinoma in Indian population. Indian...
Singh, et al.: Influence of primary tumour characteristics on ECS and level IIb metastasis

J Surg Oncol 2017;8:105-8.
10. Suton P, Salaric I, Granic M, Mueller D, Lukic I. Prognostic significance of extracapsular spread of lymph node metastasis from oral squamous cell carcinoma in the clinically negative neck. Int J Oral Maxillofac Surg 2017;46:669-75.

11. Wenzel S, Sagowski C, Kehrl W, Metternich FU. The prognostic impact of metastatic pattern of lymph nodes in patients with oral and oropharyngeal squamous cell carcinomas. Eur Arch Otorhinolaryngol 2004;261:270-5.

12. Koo Y, Zhao T, Huang S, Liu J, Duan W, Wang Y, et al. Cervical level IIb metastases in squamous cell carcinoma of the oral cavity: A systematic review and meta-analysis. Onco Targets Ther 2017;10:4475-83.

13. Kraus DH, Rosenberg DB, Davidson BJ, Shaha AR, Spiro RH, Strong EW, et al. Supraspinal accessory lymph node metastases in supraomohyoid neck dissection. Am J Surg 1996;172:646-9.

14. Talmi YP, Hoffman HT, Horowitz Z, McCulloch TM, Funk GF, Graham SM, et al. Patterns of metastases to the upper jugular lymph nodes (the “submuscular recess”). Head Neck 1998;20:682-6.

15. Ord RA, LubeK J. Management of the neck in oral cavity cancer. In: Kuriakose MA, editors. Contemporary Oral Oncology Diagnosis and Management. Switzerland: Springer International Publishing; 2017. p. 189-210.

16. Mair MD, Shetty R, Nair D, Mathur Y, Nair S, Deshmukh A, et al. Depth of invasion, size and number of metastatic nodes predicts extracapsular spread in early oral cancers with occult metastases. Oral Oncol 2018;81:95-9.

17. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenhouwrecke JP, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg 2014;12:1495-9.

18. Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK, et al., editors. AJCC Cancer Staging Manual. 8th ed. New York: Springer International Publishing, American Joint Committee on Cancer; 2017.

19. Huang SH, O’Sullivan B. Overview of the 8th Edition TNM classification for head and neck cancer. Curr Treat Options Oncol 2017;18:40.

20. Sunny L, Yeole BB, Hakama M, Shiri R, Sastry PS, Mathews S, et al. Oral cancers in Mumbai, India: A fifteen years perspective with respect to incidence trend and cumulative risk. Asian Pac J Cancer Prev 2004;5:294-300.

21. Ravikanth R, MR evaluation of tongue carcinoma in the assessment of depth of invasion with histopathological correlation: A single center experience. Indian J Radiol Imaging 2020;30:126-38.

22. Baba A, Ojiri H, Ogane S, Hashimoto K, Inoue T, Takagiwa M, et al. Usefulness of contrast-enhanced CT in the evaluation of depth of invasion in oral tongue squamous cell carcinoma: Comparison with MRI. Oral Radiol 2021;37:86-94.

23. Iida Y, Kamijo T, Kusakuka K, Omae K, Nishiya Y, Hamaguchi N, et al. Depth of invasion in superficial oral tongue carcinoma quantified using intraoral ultrasonography. Laryngoscope 2018;128:2778-82.

24. Chakraborty PS, Das AK, Vatsayan A, Rahman T, Das R, Medhi SK, et al. Metastatic involvement of level IIb nodal station in oral squamous cell carcinoma: A clinicopathological study. Nat J Maxillofac Surg 2019;10:8-12.

25. Hosokawa S, Mochizuki D, Takahashi G, Okamura J, Imai A, Ishikawa R, et al. Relevance of level IIb neck dissection in patients with head and neck squamous cell carcinomas. World J Surg 2019;43:3059-64.

26. de Bree R, Takes RP, Shah JP, Hamoir M, Kowalski LP, Robbins KT, et al. Elective neck dissection in oral squamous cell carcinoma: Past, present and future. Oral Oncol 2019;90:87-93.

27. Fakih AR, Rao RS, Borges AM, Patel AR. Elective versus therapeutic neck dissection in early carcinoma of the oral tongue. Am J Surg 1989;158:309-13.

28. Kligerman J, Lima RA, Soares JR, Prado L, Dias FL, Freitas EQ, et al. Supraomohyoid neck dissection in the treatment of T1/T2 squamous cell carcinoma of oral cavity. Am J Surg 1994;168:391-4.

29. Weiss MH, Harrison LB, Isaacs RS. Use of decision analysis in planning a management strategy for the stage N0 neck. Arch Otolaryngol Head Neck Surg 1994;120:699-702.

30.  O-cho reen no rnat P, Pillai G, Patel S, Fisher C, Archer D, Eccles S, et al. Tumour thickness predicts cervical nodal metastases and survival in early oral tongue cancer. Oral Oncol 2003;39:386-90.

31. Yamada SI, Otsuru M, Yanamoto S, Hasegawa T, Aizawa H, Kamata T, et al. Progression level of extracapsular spread and tumor budding for cervical lymph node metastasis of OSCC. Clin Oral Investeg 2018;22:1311-8.

32. Woolgar JA. The topography of cervical lymph node metastases revisited: The histological findings in 526 sides of neck dissection from 439 previously untreated patients. Int J Oral Maxillofac Surg 2007;36:219-25.

33. Lim YC, Song MH, Kim SC, Kim KM, Choi EC. Preserving level IIb lymph nodes in elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma. Arch Otolaryngol Head Neck Surg 2004;130:1088-91.

34. Roy P, Mallick I, Arun I, Zameer L, Dey D, Singh A, et al. Nodal yield and topography of nodal metastases from oral cavity squamous cell carcinoma – An audit of 1004 cases undergoing primary surgical resection. Oral Oncol 2021;113:105115.

35. Pandey M, Karthikeyan S, Joshi D, Kumar M, Shukla M. Results of a randomized controlled trial of level IIb preserving neck dissection in clinically node-negative squamous carcinoma of the oral cavity. World J Surg Oncol 2018;16:219.
**Supplemental Table 1: Distribution of study subjects according to treatments received**

| Primary site                  | BM | Oral tongue | Lower alveolus | FOM | Upper alveolus | RMT and post-GB sulcus | Well | Moderately | Poorly |
|-------------------------------|----|-------------|----------------|-----|----------------|------------------------|------|------------|--------|
| WLE + SOHND                  | 28 | 0           | 0              | 0   | 3              | 0                      | 18  | 13         | 0      |
| WLE + SM + SOHND (1-4)       | 7  | 0           | 8              | 0   | 0              | 0                      | 0   | 0          | 0      |
| WLE + SM + SND (1-4) + C/L SOHND | 0  | 0           | 12             | 3   | 0              | 0                      | 0   | 0          | 0      |
| WLE + MM + SM + B/L SOHND    | 0  | 0           | 0              | 4   | 4              | 0                      | 0   | 0          | 0      |
| WLE + CLASS 3 maxillectomy + SOHND | 0  | 0           | 0              | 0   | 0              | 0                      | 0   | 0          | 0      |
| WLE + MM + CND + SOHND       | 0  | 0           | 0              | 0   | 0              | 0                      | 0   | 0          | 0      |
| WLE + SM + CND + SOHND       | 0  | 0           | 0              | 0   | 0              | 0                      | 0   | 0          | 0      |

BM=Buccal mucosa; FOM=Floor of mouth; RMT=Retromolar trigone; GB=Gingivobuccal; SOHND=Supraomohyoid neck dissection; WLE=Wide local excision, SM=Segmental mandibulectomy; SND=Selective neck dissection; CND=Comprehensive neck dissection; MM=Marginal mandibulectomy