

Frequency of Skip Metastasis to the Cervical Lymph Nodes in Oral Squamous Cell Carcinoma

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ABSTRACT

Background: Oral Squamous Cell Carcinoma (OSCC) commonly spreads across regional lymph nodes. Presence or lack of metastasis to the cervical lymph nodes is an essential prognostic factor. The regional metastatic pattern to the cervical lymph nodes is defined as the orderly involvement of the successive anatomical lymph node levels. When the sequential order of involvement is lost and metastases are found at a lower level without involving the first echelon nodes or groups of intermediate nodes, then it is called skip metastases. Knowledge of Skip metastases will allow patients to prevent from receiving under and overt therapy. Current treatment of oral squamous cell carcinoma is primary resection followed by elective/therapeutic neck dissection. Regarding neck dissection, there is a dilemma that up to which level should be performed. Some prefer up to level III and some prefer up to level IV based on evidence of skip metastasis to level IV. This study conducted to find out the frequency of skip metastasis and its pattern according to the site, size and grading of primary oral squamous cell carcinoma.

Materials and methods: This was a cross sectional study performed in between August 2018 to September 2019 among 58 patients having histologically proven oral squamous cell carcinoma of tongue, buccal mucosa and retro molar trigone undergoing elective and therapeutic neck dissection. Cervical lymph nodes along with fibro-fatty tissue from patients underwent neck dissection except super selective neck dissection were fixed with 10% formalin in separate containers. The containers were marked with nodal level and sent to pathology department for histopathological examination.

Results: Out of 58 patients, 32 (55.2%) had cervical nodal metastasis on postoperative histopathology report, 26 (44.8%) patients had no nodal metastasis and 7 (12.1%) developed skip metastasis. Oral squamous cell carcinoma of tongue was found to be the most frequent site to develop skip metastasis to the cervical lymph node. Also, skip metastases were relatively higher in greater tumour grading and T-stages.

Conclusion: Chances of skip metastasis should be considered during treatment planning, especially for oral squamous cell carcinoma of the tongue. For the majority of cases with NO neck, elective neck dissection up to level III should be performed. In case of carcinoma of Tongue, high-grade tumour and advanced T-stages, elective neck dissection should be performed up to level IV.

Key words: Cervical lymph nodes; Neck dissection; Oral squamous cell carcinoma; Skip metastasis.

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Introduction

In 18th century, it was considered impossible to remove the metastatic cancer cell entirely after the spread of cancer to cervical lymph nodes. Although Warren identified an operation for removing metastatic neck nodes in 1847 and later Butlin recommended that the nodes be removed by means of a Köcher incision.¹⁻³ A systematic operative procedure for removal of cervical lymphatic nodes, and the first description of Radical Neck Dissection (RND) based on anatomical principles, was described by George Crile Sr., in 1906.⁴ Hayes Martin (the father of modern head and neck cancer surgery) and his associates standardized the technique of RND.⁵ The RND is still considered by some to be the 'gold standard' treatment for neck nodes. However, modifications of the procedure are accepted and are being performed with increasing frequency. Suarez proposed that muscles, vessels and nerves could be pre-served without adversely affecting regional

control and described 'functional neck dissection'. With increasing knowledge of tumor biology, the next stage in the surgery of metastatic neck disease was the promotion of the functional neck dissection by Bocca.^{6,7} A standard RND has no role in the management of patients with N0 neck status. A SND, or rarely a MRND, would be required. A recent study has shown comparable recurrence rates for RND compared with SND bears no statistically significant difference.⁸

Selective neck dissection is defined as cervical lymphadenectomy in which with the preservation of one or more of the lymph node groups are routinely removed in the radical neck dissection. For oral cavity carcinomas as well as oropharyngeal carcinomas, selective neck dissection is generally advocated for N0 disease and cautiously for N1 (Low bulk N+) disease.⁹ Discussion remains however which nodal levels should be removed, focusing especially on level IV. In a widely quoted paper from 1997, Byers et al the incidence of skip metastases in patients with cancer of the oral cavity is discussed.¹⁰ They showed a high risk for skip metastases in up to 15.8% of patients with a carcinoma of the oral cavity. Based on Byers et al skip metastases' is defined as a disease which bypasses levels I and II and goes directly to level III, level IV or both and or Level V.¹⁰ This study was conducted to determine the frequency of skip metastasis to the cervical lymph nodes confirmed by histopathological examination of resected lymph nodes specimen obtained from neck dissection of oral squamous cell carcinoma patients.

Materials and methods

This was a cross sectional study conducted in the Departments of Oral and Maxillofacial Surgery, Bangabandhu Sheikh Mujib Medical University, (BSMMU) Dhaka from August 2018 to September 2019. A total of 58 patients with oral squamous cell carcinoma diagnosed histopathologically underwent elective/therapeutic neck dissection were selected for the study based on inclusion and exclusion criteria. All patients included are T1-T4 stage OSCC patient. Due to the late presentation of the most patient in BSMMU. It was not possible to include any T1 OSCC patient. Written consent from all the patients and ethical clearance for the entire research procedure was obtained from appropriate authority.

Detailed history was taken, clinical examination was done for each patient and recorded in predesigned data entry sheet. Informed consent was obtained with signature of each patient after being informed about the study. On the day of surgery, after neck dissection cervical lymph nodes along with fibro-fatty tissue were

fixed with 10% formalin in separate containers according to nodal level. The containers were marked with nodal level and sent for histopathological examination. In the department of Pathology, lymph nodes were identified and serial sectioning of the lymph nodes were performed, routine histopathological examination was done by pre informed pathologist. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 24 (IBM Corporation, Armonk, NY, USA). Continuous variables were described as mean \pm SD and qualitative or categorical variables were described as frequencies and proportion, compared by Chi-square test. The histopathological results served as a reference to evaluate the sensitivity, specificity, and accuracy with a significance level of $p \leq 0.01$. The data was presented in the form of tables, figures and graphs, as necessary.

Results

The age range of the patient was 30 to 80 years. The mean age of the patients was $58.1 \pm 11.8.3$ years. 15 (26.9%) patients aged below 50 years, 16 (27.6%) patients were in 51-60 years group and 27 (45.6 %) patients were above 60 years. Both male and female patient were included in this study. Out of 58 subjects, 25 (43.1%) were female and the rest 33 (56.9%) were male patients. Male: female ratio was 1:1.3.

Table I Patient distribution according to site of the primary lesion (n=58)

Site	Frequency	Percent (%)
Buccal mucosa	27	46.6
Retro molar area	9	15.5
Tongue and FOM	22	37.9
Total	58	100.0

Among 58 patients, 27 (46.6%) patient had OSCC at buccal mucosa, 9 (15.5%) patients had at retro molar area, 22 (37.9%) had at tongue.

Table II Grading of the patients by tumour size (n=58)

Size	Frequency	Percent (%)
T2	12	20.7
T3	17	29.3
T4	29	50.0
Total	58	100.0

Table II shows 12 (20.7%) patients were T2 grade, 17 (29.3%) patients were T3 in tumour size and 29 (50.0%) patients were T4 category.

Table III Skip metastasis according to size of primary tumour (n=58)

Size	Skip metastasis		Total (%)
	Yes	No	
T2	0(0.0%)	12(20.7%)	12(20.7)
T3	2(3.4%)	15(25.9%)	17(29.3)
T4	5(8.6%)	24(41.4%)	29(50.0)
Total	7(12.1%)	51(87.9%)	58(100.0)

Table III shows the skip nodal metastasis in relation to the size of the primary oral squamous cell carcinoma.

In this study, out of 58 patients, 7 (12.1%), the patient had skip metastasis to the cervical lymph node. Among them T2 patient had no skip metastasis, 2 (3.4 %) T3 patient has skip metastasis and T4 category patients had skip metastasis.

Table IV Skip metastasis according to site of primary lesion

Site	Skip metastasis		Total
	Yes	No	
Buccal mucosa	1(3.70%)	26(44.8%)	27(46.6%)
Retro molar area	0(0.0%)	9(10.0%)	9(15.5%)
Tongue	6(27.27%)	16(82.73%)	22(37.9%)
Total	7(12.1%)	51(87.9%)	58(100.0%)

In this study, out of 58 patient 26 (44.8%), the patient has no cervical nodal metastasis and 32(55.2) patient cervical nodal metastasis. Out of 58(n) patient 7 (12.1%), the patient had skip metastasis to the cervical lymph node and 51(87.9) patient had no skip metastasis to the cervical lymph nodes. Considering the site of primary OSCC, those with OSCC of buccal mucosa had 1(1.7%) those with OSCC of retro molar trigon had 0(0.0%) and those with OSCC of tongue had 6(10%) skip metastasis. Table 5.4 shows the skip metastasis to the cervical lymph nodes in relation to the site of primary OSCC.

Table V Skip metastasis according to histological grades of primary tumour

Grading	Skip metastasis		Total
	Yes	No	
Grade 1	0 (0.0%)	8 (13.8%)	8 (13.8%)
Grade 2	1 (1.7%)	10 (17.2%)	11 (19.0%)
Grade 3	2 (3.4%)	14 (24.1%)	16 (27.6%)
Grade 4	4 (6.9%)	19 (32.8%)	23 (39.7%)
Total	7(12.1%)	51 (87.9%)	58(100.0%)

In relation to Grading of OSCC, skip metastasis to the cervical lymph nodes occurred mostly in grade-4 which is 4 (6.9%). In grade-3 patients 2 (3.4%) and in grade-2 patients 1 (1.7%) skip cervical nodal metastasis occurred but in grade -1 patients no skip metastasis was found. (Table V)

Table VI Frequency of skip metastasis in different lymph node level

Level	Number	Percentage (%)
Regular progression from upper levels (I-II) to lower levels (IV-V)	25	43.10
Skipping to level (III)	2	3.40
Skipping to levels (III-IV)	0	0.00
Skipping to level (IV)	5	8.60
Total	32	55.17

In this study 25(43.1%) patients had regular sequential progression, skipping direct to level III was found in 2 (3.4%), skipping direct to level III & IV was found in 0 (0.0%), skipping direct to level IV was found in 5 (8.6%). Total number of skip metastasis was 7 (12.1%) in whole study population (Table VI).

Among 58 study cases 32 (55.2%) had cervical nodal metastasis on postoperative histopathology report and 26 (44.8%) patients had no nodal metastasis. 7 (12.1%) developed skip metastasis of total sample and 21.8% of nodal positive samples. Pearson Chi-Square test reveals that $\chi^2=3.14$ and p-value is 0.011.

Discussion

Early-stage oral cancer (T1 and T2) is managed with radiation or surgery to the primary site. However, because of greater frequency of occult nodal metastases in clinically N0 patients, it is now well accepted that elective neck dissection should be undertaken in addition to primary site resection. But there is some controversy regarding the elective neck dissection that up to which level should be performed. This controversy aroused due to some author found that in some cases, metastasis to the cervical lymph node can involve lower neck nodes without preceding nodes and this phenomenon is termed as skip metastasis. In this study, we included patients undergoing neck dissection along with the resection of the primary tumour. The results of this study showed a frequency (12.1%) of skip metastasis in the neck.

Out of 58 patients, 7 (12.1%) patient had skip metastasis and 51(87.9%) patients had no skip metastasis to the cervical lymph nodes. In this study skipping direct to level III was found in 2(3.4%) cases and skipping direct to level IV was found in 5 (8.6%) cases. According to Lodder et al skip metastases to level III or IV occurred in 14 cases out of 226 neck dissections conducted for oral cavity cancer, accounting for about 6% of the total cases¹¹. Only ten skip metastases were confirmed at level III, accounting for around 4% of all cases. As a result, four necks developed level IV metastases.

In their investigation, Dias et al found a 2.0 % incidence of skip metastases.¹² They looked at 339 individuals with T1–T2 N0 M0 squamous cell cancer of the tongue and floor of the mouth who had never been treated before. A total of 0.9 % of patients had stage IV skip metastases that would have been overlooked by a selective neck dissection. Current study did not show any skip metastasis in T2 primary tumors. This may be due to small number of T2 cases in current study or may be due to the fact that skip metastasis in early stages is not higher than T3 and T4 disease.

270 untreated individuals with oral tongue squamous cell carcinoma were examined by Byers et al. 15.8% of all patients had skip metastases to level III or IV, however this number includes two patients who had level IIb metastases. They came to the conclusion that all patients with oral tongue squamous cell carcinoma should have elective neck dissection at levels I–IV.¹⁰ According to the Woolgar study, 21 out of 25 cases of lateral tongue cancer had unilateral metastases, with two cases had skip metastasis directly to level IV and one case had skip metastasis from level II to IV.¹³ Current study found 6(10.3%) skip metastasis in oral squamous cell carcinoma of the tongue.

Considering the site of primary OSCC, buccal mucosa group had 1(1.7%) skip metastasis total study population. This one patient had T4 stage, Histopathological grade 4 and skipped to level III. However, Pandey et al. performed a retrospective examination of 100 consecutive neck dissections for cancer of the buccal mucosa to examine the pattern of lymphatic dissemination.¹⁴ Pathological investigation revealed that only 36 individuals had lymph node metastases. The majority of them were only found in levels I and II. There was no evidence of skip metastases in any of the patients. There was no involvement of level V nodes in any of the patients, however one patient revealed involvement of level IV nodes.

In retromolar area group of 9 (15.5%) patients 3 (5.16%) had cervical nodal metastasis but none had skip metastasis and no other author reported skip metastasis from the retromolar area. This may be due to a small group of 9 patients. This should be further evaluated with a large group of study populations.

Current study found greater propensity to skip metastasis in higher grade tumors. Skip metastasis to the cervical lymph nodes occurred in 4 (6.9%) patients who had a grade-4 lesion. 2 (3.4%) skip metastases occurred in grade-3 lesions, 1(1.7%) skip metastasis occurred in grade-2 lesion. There was no skip metastasis in grade -1 patients.

Limitation

This is a single centre study with a limited number of samples. Hence sufficient representation may not be depicted.

Conclusion

The results of this study indicate that the skip metastasis occurs mostly in oral squamous cell carcinoma of the tongue, carcinoma with advanced stage and higher grade and has the propensity to involve level III and IV cervical lymph nodes. Skipping also occurs in oral squamous cell carcinoma of buccal mucosa, but a lower rate. In oral squamous cell carcinoma of the retro molar trigone, no skip metastasis was found.

Recommendation

Further studies are recommended involving a larger number of participants in multicentre to represent valid scenarios.

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Disclosure

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