Cervical Lymph Node Evaluation in Oral Squamous Cell Carcinoma Patients Using Ultrasound-Guided Fine-Needle Aspiration Cytology – A Descriptive Diagnostic Evaluation Study in a Tertiary Care Center

Abstract

Background: Oral cancer is the most frequent type of cancer of the head and neck area, with squamous cell carcinoma (SCC) being the most common single entity. Worldwide, oral cancer accounts for 2%–4% of all cancer cases, the prevalence being highest in India. Lymph node metastases occur in about 40% of patients with oral cancer. Clinically, their manifestations are hidden in rates of 15% to 34%. More accurate imaging techniques can reduce the risk of undiagnosed metastasis. Ultrasonography has gained wide acceptance as a diagnostic aid in the evaluation of reactive and metastatic lymph nodes. The present study is an attempt to assess the earliest evaluation of the cervical lymph nodes by ultrasound-guided fine-needle aspiration cytology (FNAC). **Methodology:** A descriptive diagnostic evaluation study was carried out to find out the sensitivity and specificity of ultrasound-guided FNAC in detecting metastasis to cervical lymph nodes from oral SCC in the Department of Oral Medicine and Radiology, Government Dental College, Thiruvananthapuram, in collaboration with the Department of Imageology, Regional Cancer Centre, Thiruvananthapuram during the time period from July 2015 to September 2016. **Results:** A total of 112 patients with histologically proven oral SCC having palpable lymph nodes were evaluated clinically and ultrasonographically. In this study, sensitivity and specificity of >90% were obtained for ultrasonographic criteria such as the long axis to short axis ratio <2, the absence of hilum, heterogeneous architecture, and altered vascularity in the evaluation of metastatic lymph nodes. The diagnostic yield in the detection of metastatic lymph nodes was much higher in the ultrasonographic examination. **Conclusion:** Ultrasound-guided FNAC offers an opportunity to enhance patient prognosis through early detection and a specific diagnosis (92.5%) when compared to clinical examination (78.6%) in the current study.

Keywords: *Biopsy, cervical lymph nodes, hilum, metastases, ultrasonography, ultrasound-guided fine-needle aspiration cytology*

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Introduction

Oral cancer is the most frequent type of cancer of the head and neck area, with squamous cell carcinoma (SCC) being the most common single entity.[1] Worldwide, oral cancer accounts for 2%–4% of all cancer cases, the prevalence being highest in India.[1] In some regions, the prevalence of oral cancer is higher, reaching upto10% of all cancers in Pakistan, and around 45% in India.[1] Regardless of the primary tumor, the presence of a metastatic node reduces the 5-year survival rate by 50%, and the presence of another metastatic node on the contralateral side further reduces the survival rate to 25%.[2]

Lymph node metastatic tumors occur in about 40% of patients with oral lymph node metastatic tumors that occur in about 40% of patients with oral cancer.[1] Clinically, their manifestations are hidden in rates of 15% to 34%.[1] The overall rate of metastatic lymph node was 77.9% in a recent study conducted in Chennai.[3] Level I is the most common site of nodal metastasis.[4] Clinical palpation has got a sensitivity of 79.5% and accuracy of 60%–86% in detecting cervical lymph node metastasis.[3] Ultrasonography (USG) is the most reliable diagnostic tool for soft-tissue evaluation. It achieves sensitivity and specificity of 97.1% and 93%, respectively, in detecting lymph node metastasis.[5]

Ultrasound-guided fine-needle aspiration cytology (FNAC) localizes the lesion better. The reported sensitivity and

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specificity of ultrasound-guided FNAC for detecting lymph node metastases ranges from 63%–97% to 74%–100%, respectively, compared to conventional FNAC.[3] The present study is an attempt to assess the earliest evaluation of cervical lymph nodes by ultrasound-guided FNAC.

Objectives

1. To describe the ultrasonographic features of reactive and malignant cervical lymph nodes in patients with oral SCC
2. To assess the most decisive diagnostic ultrasonographic criteria for reactive and malignant cervical lymph nodes of oral SCC patients against USG-FNAC/biopsy
3. To evaluate the diagnostic yield of clinical examination/ultrasonographic/USG-FNAC procedures in cervical lymph nodes of patients with oral SCC.

Methodology

This descriptive diagnostic evaluation study was carried out in the Department of Oral Medicine and Radiology, Government Dental College, Thiruvananthapuram, from July 2015 to September 2016 in collaboration with the Department of Imageology, Regional Cancer Centre, Thiruvananthapuram. The study included 112 patients with histologically proven oral SCC, with clinically palpable lymph nodes. The cases were collected at random with no preference given to the age, sex, or any other criteria. Clinical examination of these patients was done, and lymph nodes were grouped as follows.

- Group 1: Clinically palpable enlarged tender/nontender lymph nodes with an absence of fixity–These lymph nodes were considered as reactive lymph nodes. There were a total of 78 lymph nodes in this group
- Group 2: Clinically palpable enlarged tender/nontender lymph nodes, with fixityThese lymph nodes were considered as metastatic. There were 54 lymph nodes in this group.

The study was conducted after obtaining clearance from the institutional ethical committee. Informed consent was obtained from all the patients satisfying all the inclusion and exclusion criteria. All the procedures were in accordance with the Declaration of Helsinki. Written and verbal consent were obtained by the patients before the start of the study in accordance with the declaration of Helsinki.

All cases indicated for ultrasound examination were evaluated clinically after taking proper informed consent. Ultrasonographic evaluation was performed following a systematic scanning protocol. Sonograms were obtained with high-resolution real-time LOGIQUE C5 ultrasound scanner with 7–12 MHz transducers. Ultrasound findings were documented with special reference to shape, size, border, internal architecture, vascularity, and echogenicity, etc., Colour Doppler was used for all cases. As lymph nodes are encountered during the examination, their site is noted as per the classification given by the American Joint Committee on Cancer. The investigator and the sonologist evaluated the cases independently.

Characteristic sonographic features of malignant lymph nodes noted include altered shape (round), increased short-axis diameter, peripheral vascularity, extra-capsular spread manifesting as irregular boundary echo, and cystic or calcific internal foci. Reactive lymph nodes, sonographically satisfied criteria such as oval shape, retained echogenic hilum, smooth-walled boundary echo, normal hilar vascularity, maximum short-axis diameter <8 mm.[6] Based on these criteria, a provisional diagnosis was suggested after the ultrasound examination.

The patients were recruited to the regional cancer center, Thiruvananthapuram, for USG-FNAC. Cervical regions of these patients were scanned by the experienced radiologist separately in the Cancer Centre. Ultrasound-guided FNAC of the largest lymph node done under the standard aseptic protocol. A 22/23G needle fitted on a 10 ml disposable syringe was used for aspiration with full aseptic precaution. We used the Angled approach for USG-FNAC. Samples undergone cytopathological evaluation and were graded as follows:
- Group 1: Positive – Evidence of reactive inflammatory cell
- Group 2: Positive – With evident dysplastic features.

The cytological diagnosis was considered as the gold standard for reactive lymph nodes. In all oral cancer patients, FNAC was suggestive of either metastatic or reactive lymph node involvement. For all USG-FNAC positive cases, modified neck dissection was done at the regional cancer centre as a part of treatment, and suspected metastatic lymph nodes were sent for biopsy. A comparative study was done between the clinical features, USG, cytological features, and histopathology of the cervical lymph node.

Statistical analysis

For the diagnostic evaluation of clinical examination, ultrasound, USG-FNAC results expressed as sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios. Diagnostic accuracy was calculated. A $P < 0.05$ was considered as statistically significant. SPSS version 22 was used for the statistical analysis.

Results

The age of the patients included in the study ranged from 36 to 80, with a mean age of 59 [Figure 1]. 56.4 cases were below 40 years old, 18 cases were 40–49 years old, 33 cases were 50–59 years old, 35 cases were 60–69 years old, and 22 cases were above 70 years old. Male predominance was there in all age groups. Of the 112 cases, eighty patients were males and 32 were females. Most predominant sites

of cases were on the tongue [Figure 2]. Majority of the lymph nodes were palpated at Level 1b region (100 cases). Two cases were palpated at Level 1a region and ten cases were palpated at Level II region.

After ultrasonographic examination, based on the ultrasonographic criteria previously mentioned [Tables 1 and 2] 56 cases were diagnosed as reactive and the other 56 cases diagnosed as malignant [Table 3]. Ultrasound-guided FNAC results showed that 54 lymph nodes were reactive, and 58 lymph nodes were malignant. Of the 54 cases diagnosed as metastatic by USG-FNAC, biopsy yielded the same diagnosis in all cases. The summary shown in Table 2. Ultrasonographic images of malignant and reactive lymph nodes are shown in Figure 3 and 4 respectively.

Discussion

USG enables the visualization of the fine detail of the superficial structures of the oral and maxillofacial tissues without the use of ionizing radiation. Recent studies have shown that there is a tendency to overdiagnose nodes as metastatic in patients with oral cancer and have suggested that all clinically palpable cervical lymph nodes in oral cancer patients cannot be assumed to be metastatic. There should be a reevaluation of the clinical criteria for suspicion of cervical lymph nodes in patients with oral cancer.[7]

Rate of occult metastasis to cervical lymph nodes as detected by USG found to be 25.6% (20 of 78 lymph nodes) in this study, which is comparable to previous studies by Dangore-Khasbage *et al*.[7] In the current study of 58 reactive lymph nodes, 32 lymph nodes were having maximum short axis size >8 mm (55.17%), 26 lymph nodes had a size <8 mm (44.82%). Of 54 malignant lymph nodes, only 1 lymph node was <8 mm (1.8%). In this study, 94.4% of metastatic cervical lymph nodes had L/S ratio <2, when compared to reactive nodes. The present

Table 1: Clinical examination versus ultrasonography-fine needle aspiration cytology examination

	USG-FNAC result		Total
	Malignant	**Reactive**	
Clinically positive	32	2	34
Clinically negative	22	56	78
Total	54	58	112

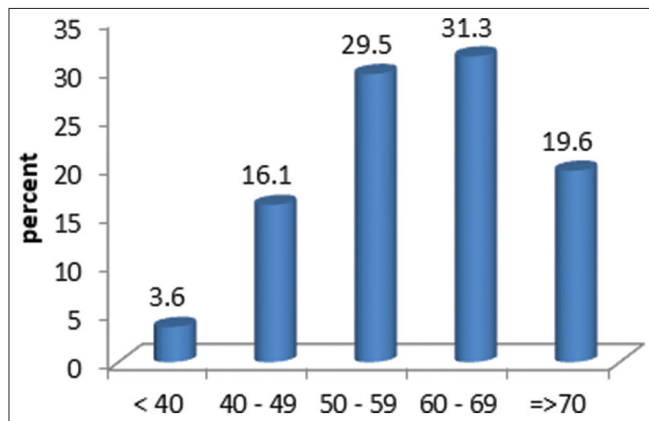USG: Ultrasonography; FNAC: Fine needle aspiration cytology

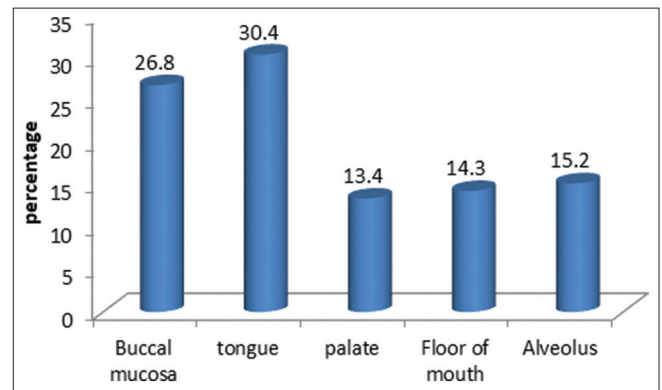Figure 1: Percentage distribution of age groups in the study sample (*n* = 112)

Figure 2: Distribution of sites of oral cancer according to present study
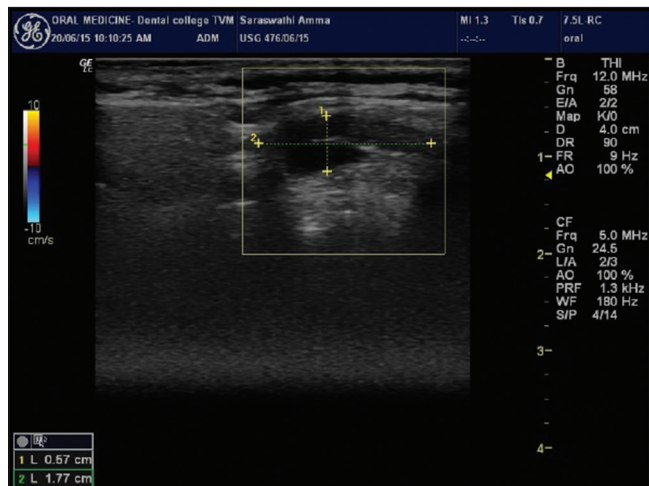

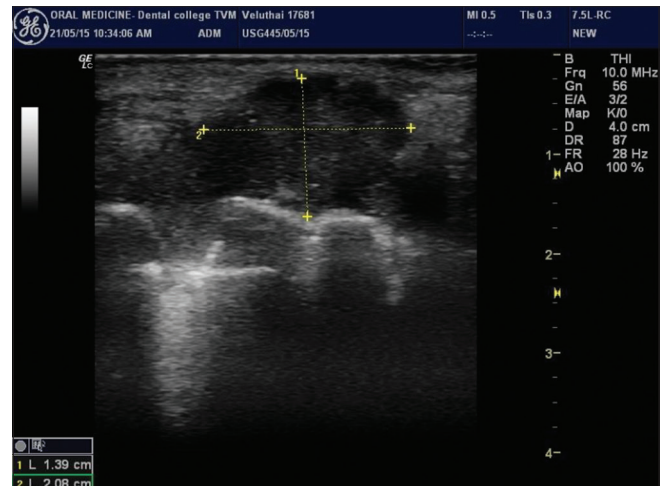Figure 3: Ultrasonography image of malignant lymph node

Figure 4: Reactive lymph node

Table 2: Performance indicator values of ultrasonographic features

Ultrasonographic criteria	Malignant (*n*=54)	Reactive (*n*=58)	Total	Sensitivity	Specificity	PPV	NPV	Accuracy	Likely hood ratio
Ultrasound size >8 mm	53	32	85	98.1	44.8	62.4	37.03	70.5	1.77
Long axis to short axis ratio <2	51	2	53	94.4	96.6	96.2	94.9	95.5	27.4
Round shape	44	5	49	81.5	91.4	89.8	84.12	86.6	9.45
Sharp nodal borders	34	2	36	63	96.5	94.4	73.7	80.4	18.3
Hilum absent	51	6	57	94.4	89.7	89.5	94.5	92.0	9.12
Internal hyper echogenicity	47	7	54	87.0	87.9	87.0	87.9	87.5	7.21
Presence of internal foci	29	1	30	53.7	98.3	96.7	69.5	76.8	31.1
Posterior wall echo enhancement	32	1	33	59.3	98.2	96.9	72.15	79.5	34.3
Vascularity-peripheral and mixed	51	4	55	94.4	93.1	92.7	94.73	93.8	13.69

NPV: Negative predictive values; PPV: Positive predictive values

Table 3: Ultrasonography versus ultrasonography-fine needle aspiration cytology examination

USG result	USG-FNAC result		Total
	Malignant	Reactive	
USG positive	51	5	56
USG negative	3	53	56
Total	54	58	107

USG: Ultrasonography; FNAC: Fine needle aspiration cytology

study has shown that 62.9% of nodal borders of metastatic cervical lymph nodes were sharp, whereas only 3.4% of reactive lymph nodes were with sharp borders. Sharp borders in malignancy are due to the infiltrating tumor cells which replace normal lymphoid tissues, and it causes an increasing acoustic impedance difference between lymph nodes and surrounding tissues whereas unsharp borders in malignant nodes indicate invasion into adjacent structures. However in reactive lymph nodes because of edema or active inflammation of the surrounding tissues, they will have unsharp borders.[8] This result is comparable to other studies where malignant nodes 52% showed sharp border, reactive (68%) showed unsharp border.[7]

Vassallo *et al*. reported that the echogenic hilus corresponds to the abundance of collecting sinuses and provides acoustic interfaces to reflect a portion of the ultrasonic wave making the hilus echogenic.[9] In this study, 94% of metastatic cervical lymph nodes revealed the absence of hilar echo when compared to reactive cervical lymph nodes where hilar echo was seen in 88.7% of the samples. Hence, the absence of hilum, is statistically significant in detecting malignant lymph nodes (*P* value <0.001). Hilum may be present in the early stage of involvement in which medullary sinuses have not been sufficiently disrupted to eradicate it. The findings in the present study can be attributed to the fact that the majority of the malignant cases were in an advanced stage.[6]

Hyperechogenicity is a useful sign to identify metastatic nodes as stated by Ying and Ahuja.[10] Considering the internal echogenicity, the present study confirmed that 88.9% of the metastatic cervical lymph nodes showed

a hyperechoic pattern of echogenicity, whereas normal and reactive nodes revealed 86.8% hypoechoic pattern of echogenicity. Yusha also found that interechogenic pattern was hyperechoic in 86% and 2% of metastatic and reactive cervical lymph nodes, respectively.[11]

According to Ahuja *et al*, Cystic necrosis is commonly found in metastatic nodes from squamous cell carcinomas and papillary carcinoma of the thyroid.[10] In the current study, the intranodal necrosis was found in 53.8% of metastatic cervical lymph nodes. 98.1% of reactive cervical lymph node showed no intraoral foci. Hence, this ultrasonographic criteria is also highly statistically significant.(*P* < 0.001).Previous studies also reported similar findings.[12] In the current study, 59.3% of metastatic lymph nodes showed posterior wall echo enhancement. This may be because of cystic necrosis in metastatic lymph nodes.

In the current study, 92.5% of reactive lymph nodes showed hilar vascularity. Although the reactive nodes tend to have hilar vascularity or to be apparently avascular, peripheral and mixed (nodes showing both hilar and peripheral vascularity) patterns have also been found (2%–3% and 6%–8%, respectively). This is comparable to Giovagnorio *et al*. study, where they reported that hilar vascularity or apparent avascularity are common in reactive lymph nodes.[13] Dragoni *et al*. studies found that 45-100% of reactive lymph nodes showed hilar vascularity & 19-35% were apparently vascular.[14]

In the current study, criteria showed highest specificities, were internal foci (98.3%), posterior echo enhancement (98.3%) L/S ratio, nodal margins (96.6% each), and vascularity (93.1%). The positive predictive value was highest for internal foci, posterior wall echo enhancement, and L/S ratio. Nodal margin showed the highest likelihood ratio. This is comparable to previous studies.[13]

Three cases of metastatic lymph nodes were misdiagnosed by USG in this study as reactive. Two of these cases were misinterpreted due to peripheral vascularity. One misdiagnosed case was having the presence of echogenic

hilum. Five cases of reactive lymph nodes were misdiagnosed in ultrasound as malignant. Two cases were misdiagnosed based on the sonographic findings, including partial presence of echogenic hilum. Another case of benign lymphadenopathy considered as malignant by ultrasound due to altered internal echogenicity.

Performance indicator values in the evaluation of lymph nodes clearly suggest that USG diagnosis has a definite edge over clinical diagnosis. USG definitely improved the ability to accurately diagnose metastatic lymph nodes in oral SCC. USG-FNAC showed 100% sensitivity in detecting metastatic lymph nodes. Ultrasound-guided FNAC should be considered as a safe skip from a biopsy in diagnosing metastatic lymph nodes in oral carcinoma patients.

Merits of the study

- The early changes of lymph nodes in oral SCC reporting to a tertiary care setting were assessed
- Ultrasonographic patterns of reactive and malignant lymph nodes were evaluated, and an image database was initiated for further reference
- Occult metastasis can be assessed in a clinically no neck.(TNM staging stages 1, stage II, and stage III cases)
- Oral medicine specialists, as sonologist can develop and explore the discipline of head-and-neck USG for the betterment of diagnosis in the field of dentistry
- The utility of USG as a diagnostic and opportunistic screening tool could be assessed.

Limitations of the study

- This study was conducted only in a group of patients with oral SCC reported to a tertiary care setting
- Only the USG-FNAC positive group of patients underwent biopsy
- The sample size calculated was, for a descriptive diagnostic evaluation study, as per the primary objective. Hence, further prospective studies with an adequate sample size for subgroup analysis may be attempted.

Implications

- Diagnostic parameters of cervical lymph nodes evaluated in the study can be utilized for the staging of oral malignancy
- Considering the positive results of the current study, head-and-neck ultrasound should be recommended for all oral premalignancy patients for the nodal evaluation and periodic review.

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Conflicts of interest

There are no conflicts of interest.

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