Orginal Artical

Detection of Cervical Lymphnode Metastasis in Oral Squamous Cell Carcinoma by Ultrasonogram Guided Fine Needle Aspiration Cytology (FNAC) and Comparison with Computed Tomographic (CT) Findings

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Abstract

Background: *Several imaging methods are using for investigating the presence and extent of nodal metastasis including Computerized Tomography, Magnetic Resonance Imaging, Radionuclide scintigraphy, Positron Emission Tomography and Ultrasound Guided FNAC. To find out the over all accuracy of detection of metastatic lymph nodes by two available and cost effective methods (Ultrasound Guided FNAC and CT scan) will help to make an effective treatment protocol.* **Objectives:** *This study opted to compare the relative sensitivity and specificity of Ultrasound Guided FNAC and CT scan in the detection of lymph node metastasis in oral squamous cell carcinoma.* **Materials & Methods:** *37 patients were included with oral squamous cell carcinoma and both Ultrasound Guided FNAC and CT scan were done in all these patients. Later, following surgical excision, histopathology reports of the patient's neck nodes were collected.* **Results:** *CT scan of the neck nodes revealed 26 of the subjects having nodal metastasis; there was 1 (2.7%) false positive node and 1 (2.7%) false negative nodes. Sensitivity of CT scan test was found 96.15 % and specificity was found 90.9%. Positive predictive value and negative predictive value was found 96.15% and 90.9% respectively, and the accuracy was found 94.59%, Ultrasound Guided FNAC detected 25 (67.6%) metastatic lymph node. Among those 1 (2.7%) was false positive and 2 (5.4%) were false negative. It showed 92.3% sensitivity and 90.9% specificity. Positive predictive value and negative predictive value of the test were 96.0% and 83.3% respectively and accuracy was 91.89%.* **Conclusion:** *Ultrasound Guided FNAC was found comparable to CT scan in the evaluation the node metastasis. Both the two tests showed high sensitivity, specificity and overall accuracy.*

Key words: *Oral squamous cell carcinoma; Ultrasound Guided FNAC; CT scan; Metastasis*

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Introduction

Lymphatic metastasis is the most important mechanism in the spread of head and neck squamous cell carcinomas. Lymph node metastasis is regarded as independent predictor of adverse prognosis, influencing disease free and overall survival in patient with oral squamous cell carcinoma[1]. Determination of the cervical lymph node status is essential to plan treatment as well as to predict the prognosis. Assessment of the cervical lymph node for possible metastasis is difficult in patients with oral squamous cell carcinoma. Palpation of the lymph node is not quite reliable method for the assessment of neck node metastases and gives a large percentage of false negative result which has significant implication on patient's treatment and survival. False negative metastases in palpation method may toll between 20-40% and similarly they can also yield large false positive findings[2,3]. The risk of an undetected metastasis is related to the method with which the lymph nodes are evaluated. Among accurate detection technique with high sensitivity and specificity and low false positive and negative is warranted to treatment disease like cancer, to reduce the risk of undetected lymph node with metastases[4,5]. Studies have proposed several imaging methods for investigating the presence and extent of nodal metastasis including Computerized Tomography (CT) scan, Magnetic Resonance Imaging, Radionuclide scintigraphy, and Positron Emission Tomography and Ultrasound Guided FNAC.

Comparative analysis from the published evidence suggests that, CT scan and magnetic resonance imaging are generally considered superior to palpation. The overall accuracy of detection of metastatic lymph nodes varies between 69 - 82 percent with palpation, and with the use of CT scan or MRI the percentage can be raised to 78-93 percent[6,7].

Similarly, Ultrasonography can detect a large number of non-palpable lymph nodes. If FNAC is added to Ultrasonography for detection of neck nodes, it serves several purposes together, satisfies surgeon with a histo-pathological clue, and raises the accuracy level. Brekel even suggests an increment to nearly 100 percent over the accuracy of Ultrasonography alone in the detection of lymphnode metastasis[6,7].

Materials and Methods

A Cross sectional study was carried out at the Department of Oral Maxillofacial Surgery, Bangabandhu Sheikh Mujib Medical University and Dhaka, Dental College and Hospital, Dhaka from 1 January'2007 to 31 December'2008. Total 37 patients of Oral Squamous Cell Carcinoma were included in the study purposively who met the inclusion criteria that were patients with Oral Squamous Cell carcinoma confirmed by histopathology and patient with Oral Squamous Cell Carcinoma with or without palpable cervical lymph node. Cases were excluded according to some criteria like: Non-invasive squamous cell carcinoma (exophytic lesion); clinically suspected oral squamous cell carcinoma patient, histopathology after excisional biopsy revealed no malignancy; patient with advanced and inoperable oral squamous cell/carcinoma; patients declared as inoperable for systemic illness; previously treated with chemo or radiotherapy; patients who have not consented to participate in the study.

Neck was evaluated by clinical examination; CT scan and Ultrasound Guided FNAC were performed to detect lymph node and its status. Histopathology of the neck nodes was done following excision biopsy. A standard data sheet and structured tool were used for collection and compilation of data for processing and analysis. The data presented on scale were expressed as frequency and corresponding percentage, while the quantitative data were presented as mean and standard deviation from the mean. Association between two variables was done using Pearson Chi-square test. For all analysis, level of significance was set at 0.05 and p-value <0.05 was considered significant. Validity of Ultrasound Guided FNAC and CT scan were assessed based on sensitivity analysis. Sensitivity, specificity, positive predictive value, Negative predictive value and accuracy were calculated according to standard formula from contingency table. Accuracy of the two tests was compared through generation of Z statistics.

Results

Out of 37 subjects, 9.9% were aged less than 40 years, 52% were aged between 41 - 50 years 25.4% were aged between 51-60 years only 12.7% were aged above 60 years. Average age of the subjects were 50.22 ± 8.3 years. Among the subjects, 59.5% were male and 40.5% female. Majority of the study subjects (60.3%) had lesion in mandible,17.5% had maxillary lesion, and 9.5% had lesion over cheek and only 6.3% in tongue and floor of the mouth. According to the site of involvement majority (51.4%) had right sided lymph nodes with 81.1% lymph nodes are mobile, 6.5% lymph

nodes non-tender and 75.7% were firm in consistency. Among them 70.3% were metastatic and 29.7% were reactive. Similarly scan diagnosed 70.3% nodes as metastatic and 29.7% as reactive. Similarly, Ultrasound Guided FNAC diagnosed 67.6% nodes as metastatic and 32.4% as reactive.

Sensitivity of CT scan test was found to be 96.15 % and specificity was found 90.91%. 'Predictive value for a positive test' and 'Predictive value for a negative test' was found 96.15 % and 90.91% respectively. In this analysis accuracy was found 94.59%, which translates into ability of CT scan test to provide correct diagnosis in 95% cases. (Table - I)

Table - I

CT Scan	Accuracy statistics
Sensitivity	96.15%
Specificity	90.91%
Positive predictive value	96.15%
Negative predictive value	90.91 %
Accuracy	94.59%

USG guided FNAC as a method of diagnostic aid showed 92.31 % sensitivity and 90.91% specificity. Positive predictive value and negative predictive value of the test are 96.0 % and 83.3 % respectively. In this analysis accuracy was 91.89%. (Table - II)

Table - II

USG guided FNAC	Accuracy statistics
Sens itivity	92.31 %
Specificity	90.91 %
Positive predictive value	96.00 %
Negative predictive value	83.33 %
Accuracy	91.89%

Comparison of sensitivity and specificity of CT and USG guided FNAC in detecting lymph node metastasis in oral squamous cell carcinoma was illustrated in Table - III and Figure 1. The Sensitivity (P>.05), Specificity (P>.05), PPV (P>.05), NPV (P>.05) and Accuracy (P>.05) of both the two methods were found statistically indifferent in comparison to gold standard (Histopathology).

Comparison	CT	USG/FNAC	Z statistic	P Value
Sensitivity	0.9615	0.9231	0.460	0.648
Specificity	0.9091	0.9091	0.599	0.549
PPV	0.9615	0.9600	0.596	0.551
NPV	0.9091	0.8333	0.466	0.641
Accuracy	0.9459	0.9189	0.770	0.441

Table III: Comparison of sensitivity and specificity of CT and USG guided FNAC
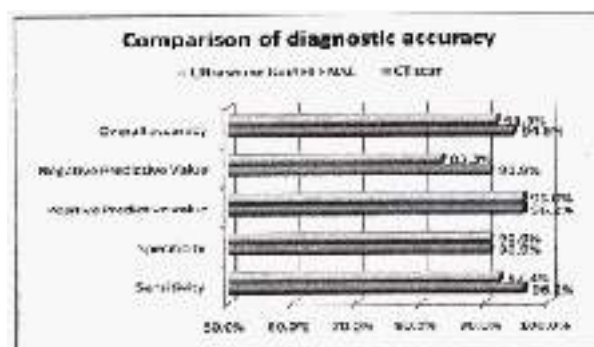
Figure 1: Comparison of diagnostic accuracy of CT scan and USG guided FNAC in detecting Lymph node metastasis in oral squamous cell carcinoma comparison of diagnostic accuracy

Discussion

Oral squamous cell carcinoma presents with advanced lesions with variable involvement of neck nodes. The status of the cervical nodes is the single most important prognostic indicator of survival for patients with oral cancer[8] since the development of nodal metastases halves the 5-year survival rate[9]. In this context it is imperative to diagnose nodal involvement in planning any therapeutic modality. However, two recent studies have demonstrated that clinical examination of the neck is imprecise because there was a false negative rate of between 27% and 34%, and a false positive rate of between 31% and 40%[10,11]. The importance of identifying and eliminating nodal disease was recognized as early as late 19 century[12].

Kalin[13]estimated a five-year survival rate of 75% for neck nodes, which fell to 49% if one node was involved and 13% if multiple nodes were involved. Study by Ross

had also reported almost similar survival. Hence, there is therefore a need for precise evaluation with relatively non-invasive diagnosis to accurately predict cervical nodal involvement in oral squamous cell carcinoma[14]. Various diagnostic techniques, both invasive and non-invasive, have been employed to enhance the early detection of metastasis[15,17]. they included ultrasonography alone, CT scan, MRI, PET scan and lymphoscintigraphy. However published literature mostly provides evidence in favor of the usefulness of ultrasonography and CT scan. Not many evidences are reported whether they match up to the desired levels of sensitivity and specificities with the post-operative histopathology. Preoperative imaging may not improve the accuracy of clinical examination as many occult nodal metastases are only detectable by thorough post-resection histological examination[11].

The study attempted to evaluate the relative sensitivity and specificity of Ultrasound Guided FNAC and CT scan in detection of lymph node metastasis in oral squamous cell carcinoma with reference to post-operative lymph node histopathology. The ultimate goal is to determine a best diagnostic aid for pre-surgical diagnosis of cervical lymph node metastases in the setting of limited resources.

Out of 37 patients, 26 (70.3%) were diagnosed as metastatic and 11 (29.7%) were diagnosed as reactive in histopathology (table-Ia).

Tables:

Table I (a, b & c): Diagnostic accuracy of CT scan in detection of Lymph node metastasis.

Table I a:

	Excision Histopathology		Total
CT scan finding	Metastatic	Reactive	
Metastatic	25 (96.2%)	1 (9.1%)	26 (70.3%)
Reactive	1 (4.5%)	10 (90.9%)	11 (29.7%
Total	26 (100.0%)	11(100.0%)	37 (100.0%)

CT scan of the neck node revealed 25 of the subjects having nodal metastasis; there was one (2.7%) false positive node (a reactive inflammatory node) and one (2.7 %) false negative nodes (table-Ib) which results in Sensitivity of 96.15% and specificity of 90.91%.

Table I b:

	Number of patient & percentage	Positive or negative
CT scan (+) ve Histopathology (+) ve	25 (67.6%)	True positive
CT scan (-)ve Histopathology (-) ve	10 (27.0%)	True negative
CT scan (+)ve Histopathology (-) ve	01 (2.7%)	False positive
CT scan (-)ve Histopathology (+) ve	01 (2.7%)	False negative

Based on study data CT scan was found to be able to detect around 96% of the positive cases correctly and able to detect around 91% of the reactive cases correctly. Both sensitivity and Specificity of the test in the current study is found to be little high. 'Predictive value for a positive test' and 'predictive value for a negative test' is found to be 96.15% and 90.91% respectively, which suggests CT scan as a precise test for the detection of both metastatic and reactive cases (table-Ic).

Table I c:

CT Scan	Accuracy statistics
Sensitivity	96.15%
Specificity	90.91%
Positive predictive value	96.15%
Negative predictive value	90.91 %
Accuracy	94.59%

However, its accuracy in detecting the positive cases is more than the negative cases. In the analysis accuracy was found 94.59%, which translates into the ability of CT scan test to provide correct diagnosis in 95% occasions. Comparative analysis from the published evidence suggests that, CT scan and magnetic resonance imaging are generally considered superior to palpation[6,7]. The two imaging techniques can reduce up to two thirds of necks that remain occult at palpation. The overall accuracy of detection of metastatic lymph nodes varies between 69 - 82 percent with palpation, and with the use of CT scan or MRI the percentage can be raised to 78-93 percent[7,18]. The most important drawback of the study that CT scan of metastatic node may mimic a benign node, Metastasis may occur in the period between CT scan and surgery. Histopathologic diagnosis is therefore necessary for the final diagnosis before treatment by surgery or radiotherapy. So, FNAC must need to be done before critical decision of the different type of radical neck dissection. In the present study, Ultrasound Guided FNAC detected 25 (67.6%)

metastatic lymph node (table-IIa).

Table II (a)

USG guided FNAC of the lymph node	Excision Histopathology		Total
	Metastatic	Reactive	
Metastatic	24 (92.3%)	1 (9.1%)	25 (67.6%)
Reactive	2 (7.7%)	10 (90.9%)	12 (32.4%)
Total	26 (100.0%)	11(100.0%)	37(100.0%)

Among those 1 (2.7 %) were false positive (reactive inflammatory node) and among the negative cases 2 (5.4%) were false negative. (Table II b)

Table II (b)

	Number of patient & percentage	Positive or negative
USG guided FNAC (+) ve Histopathology (+) ve	24 (64.9%)	True positive
USG guided FNAC (-) ve Histopathology (-) ve	10 (27.0%)	True negative
USG guided FNAC (+) ve Histopathology (-) ve	01 (2.7%)	False positive
USG guided FNAC (-) ve Histopatlhology (+) ve	02 (5.4%)	False negative

Ultrasound Guided FNAC were found to detect 92.3% of the positive cases correctly and 90.9% of the reactive cases correctly. Both sensitivity and specificity of the test was found to be quite high, 'Predictive value for a positive test' and 'predictive value for a negative test' was found 96.0% and 83.3% respectively, which suggests FNAC as a precise test for the detection of both metastatic and reactive cases. In the analysis accuracy was found 91.9%, which translates into ability of FNAC test to provide correct diagnosis in 92 % occasions (table-IIc).

Table II (c)

USG guided FNAC	Accuracy statistics
Sens itivity	92.31 %
Specificity	90.91 %
Positive predictive value	96.00 %
Negative predictive value	83.33 %
Accuracy	91.89%

Study by Seetharam[19] et al. assessed the possibility of using fine needle aspiration cytology as a primary diagnostic test in oral squamous cell carcinoma. A cytological and histopathological, correlation was undertaken to determine the proportion of cancers that can be accurately diagnosed by FNAC and its ability to identify differentiation grading of squamous cell carcinomas. According to their study finding, in oral squamous cell carcinomas 92.85% of true positive and 5rf 7.14% of false negative results were obtained. The overall positive correlation was 86.66%. They recommended FNAC as a reliable diagnostic test for oral squamous cell carcinoma.

Direct comparison between the two methods did not reach statistical significance. The Sensitivity, Specificity, PPV and NPV of both the two methods were found statistically indifferent in comparison to gold standard (Histopathology). The overall accuracy of CT scan or Ultrasound Guided FNAC were also similar. It should be noted that Ultrasonography of the neck is highly operator-dependent and learning curve exists for even an experienced ultrasonographer. In CT scan the technological improvement to some extent safeguards against some of the error. However evidence suggests that, in expert hands techniques like FNAC with ultrasonography may have high accuracy.

Finally, cervical node metastasis in oral cancer is an indicator of advanced disease. It is therefore, important to evaluate neck node involvement as a predictor of progression and treatment planning. In the existing economic condition in Bangladesh, even the use of CT scan can be prohibitive. Ultrasonography alone being not very accurate is a financially reasonable tool to detect neck nodes. However addition of FNAC with Ultrasonography increases the accuracy of the procedure. The limitation of clinical evaluation can significantly be overcome by CT scan and or Ultrasound Guided FNAC. Fine Needle Aspiration Cytology not only confirms the presence of metastatic disease, but also gives clues regarding the nature and origin of the primary tumor.

Ultrasound Guided FNAC and CT scan were comparable in our study in evaluating the neck node in patients with oral cancer. Although the sample size of the current study was relatively small, our findings were consistent with studies having larger sample size evaluating the diagnostic techniques[6,20,21]. Ultrasound-

FNA of the neck has been well tolerated by patients in previous studies [6,20,21] and, similar to our experience, no serious complications have occurred. Ultrasound, FNAC also has the potential advantage of being less costly than CT. Although our study did not involve a formal cost analysis, the projected cost of Ultrasound Guided FNAC to evaluate our whole patient group were less overall than the cost of CT.

Conclusion

In our study finding, Ultrasound Guided FNAC was found comparable to CT scan in the evaluation of the neck node metastasis. Both the tests showed high sensitivity, specificity and overall accuracy. The choice as to which modality to employ for imaging the neck nodes depends on a number of factors, including the location and clinical extent of the primary tumor. Besides, costing is also a factor in the resource limited country setting. Although the cost analysis was not done in the current study, based on anecdotal evidence. Ultrasound Guided FNAC can be recommended as a cheaper and most feasible alternative to the CT scan in the evaluation of the neck node metastasis.

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