

## Assessment of the Diagnostic Accuracy of Clinical and Recent Radiological Modalities in Detecting Metastatic Lymph nodes in Oral Carcinoma: Study at a Tertiary Care Center

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### Abstract

**Background:** Recent advances in imaging methods, including Ultrasonography (USG), Color Doppler, and Contrast Enhanced Computed Tomography (CECT), have made it accurate to identify cervical lymph nodes that have metastatic oral cancer.

**Objective:** To compare the popular clinico-imaging diagnostic modalities with the gold Standard histopathological examination and assess their effectiveness in identifying lymph node metastases in Oral Squamous Cell Carcinoma (SCC).

**Methods:** A prospective study with twenty oral SCC patients was conducted. They were evaluated for metastatic cervical lymph nodes preoperatively using clinical palpation, and they were afterwards submitted for CECT, Gray scale USG, and Color Doppler studies. Histopathologic analysis of the lymph nodes obtained after neck dissection, later confirmed for the presence of malignant metastases. The obtained data was gathered, documented, and subjected to appropriate tests for analysis. The CECT, Gray scale USG, Color Doppler, and clinical palpation tests were all unable to identify non-cancerous nodes. Clinical palpation was 100% sensitive, CECT was 100% sensitive, grey scale USG was 80% sensitive, and colour Doppler was 80% sensitive. Clinical palpation had a 64% specificity, as did CECT and Gray scale USG. With these diagnostic methods, there are more opportunities for both false positive and false negative cases. When compared to histological findings, the diagnostic accuracy of clinical palpation, CECT, grey scale USG, and colour doppler was not significant. Therefore, in order to determine the treatment strategy, the test for the presence of cancer in the oral cavity region must be accompanied by a conclusive histological confirmation.

**Keywords:** cervical lymph node, positive lymph node, oral cancer, metastasis, ultrasound, and colour doppler.

## Introduction

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In economically developed countries as well as developing countries, cancer is the second largest cause of death. Oral cavity, larynx, hypopharynx, and oropharynx are all sites of squamous cell carcinoma (OSCC). According to the incidence rate, it is listed as the sixth most common cancer in the world [1].

The primary prognostic factor for OSCC is cervical lymph node metastases [2]. The primary tumor's level of aggressiveness is reflected in the rate of metastasis. According to the literature, a single metastatic lymph node in either the ipsilateral or contralateral side depicts the reduction in life of 50% and 75% respectively is-five-year survival rate [3]. For patients to have a better outcome and prognosis, the detection of positive cervical lymph nodes is crucial [4]. Predicting the existence of metastatic lymph nodes in a neck with clinically negative nodes is particularly challenging. This one reason was the driving force behind the widespread use of preventive (elective) neck treatments like radiation or neck dissection [5,6]. However, there is debate regarding how best to treat OSCC patients whose necks have clinically negative nodes.

Patients that are clinically node negative may anchor occult metastases, which if undiscovered could result in treatment failure. These patients typically receive an elective neck procedure, such as radiation, neck dissection, or even both. It has been shown that elective neck dissection increases the 5-year disease-free survival rate to 86% from 55% when "watchful waiting" is used. It also significantly decreased regional recurrence-related mortality to 3% and decreased the regional recurrence rate to 9% [2].

The disadvantage of elective neck dissection is that the most patients do not have metastases, meaning that unneeded therapy could result in increased expenses and morbidity. The likelihood of nodal metastases can be used to guide treatment decisions. Small metastatic nodes or occasionally moderate-sized nodes may be excluded during clinical palpation, particularly in obese patients, while big inflammatory nodes may be misdiagnosed. [4]. The key elements that determine the accuracy of clinical palpation are the examiner's clinical background and the physical characteristics of the neck following prior therapy, whether surgical or irradiative. About 20–40% of patients with early-stage mouth cancer have concealed cervical lymph node metastases, which are essentially imperceptible to the touch [7]. It is a well-documented fact that there is a difference in clinically node negative neck and its post-investigation positivity. Thus, one must review clinical lymph node exam sensitivity before sending the patient for radiological investigation.

Contrast-enhanced Computed Tomography (CECT), which aids in the identification of tumour size, infiltration of the vasculature, and demonstration of cervical metastatic lymph nodes, is well-established in the pre-therapeutic staging of head and neck tumours [5].

According to certain studies, USG can distinguish between metastatic and non-metastatic nodes in the neck more effectively than CT. This is because it can more clearly differentiate whether the internal structure of the node has changed [6].

The accuracy of detecting cervical lymph nodes with metastatic disease has increased thanks to recent advancements in imaging modalities like ultrasonography and CECT. Clinically node negative patients are now managed in a contentious manner because elective neck dissection is essentially done blindly, regardless of the lymph nodes' actual condition. However, the danger of postponing a neck dissection in a node negative patient is difficult to assess because no diagnostic technique can identify a patient as really node negative or free of metastatic lymph nodes. Therefore, the development of a valid scientific recommendation for when to proceed with and perform neck dissection, as well as to what extent, requires a confirmed diagnostic criterion [4]. Doppler ultrasound imaging results are promising but yet preliminary, according to recent studies. Although CECT has long been a popular diagnostic tool, there are too many problems to overlook. Many studies have discounted clinical palpation, yet it remains the primary method for determining whether a patient has nodes or not [5].

### Aim & Objective

The goal of the study was to assess the effectiveness of clinical palpation CECT, USG and Color Doppler diagnostic methods in identifying lymph node metastases and compare them to the gold standard histological investigation.

## Materials and Methods

The study was conducted from December 2018 to March 2019, among patients reported in the department of Oral and Maxillofacial Surgery and 20 patients who had been diagnosed with oral squamous cell carcinoma participated in the study. A practical sampling technique was used.

The following criteria were used for the recruitment of the participants.

### Inclusion criteria

- 1) Patients above the age of 18 years
- 2) Patients requiring neck dissection
- 3) Patients who sign an informed consent form in writing.

### Exclusion criteria

- 1) Patients who have had their neck lymph nodes surgically treated in the past.
- 2) Patients who have had a history of head and neck radiation.
- 3) Patients who have previously undergone chemotherapy.
- 4) Recurring oral cancer cases.
- 5) Patients who have any other types of lymphadenopathy, such as tuberculosis, lymphoma, etc., currently or in the past.
- 6) Patients who decline to give an informed written consent.
- 7) Data from level four nodes was not used in cases needing level four neck dissection.

### Data Collection Method

Preoperatively all patients were evaluated for presence of cervical metastasis by using clinical palpation, CECT, USG and Color Doppler. Patients were monitored postoperatively, and histopathologic analysis of lymph nodes retrieved following neck dissection was subjected to confirm the presence or absence of metastasis. The results were compared and assessed against the histopathology confirmation to determine their diagnostic accuracy. The four preoperative diagnostic techniques and their criteria for detecting metastatic nodes are as follows.

1. Clinical palpation (CP): In this investigation, the criteria for determining metastasis were nodes with firm consistency, fixity to underlying and/or overlying tissues, and size >3cm [6,8]. According to research by Haberal et al, metastatic nodes are solid and anchored to the surrounding structures [6,9]. Although the lymph node's size is not a reliable indicator, Snow et al discovered that lymph nodes less than 3 cm have a considerably higher probability of extracapsular dissemination [10].

2. Contrast-enhanced computed tomography (CECT): The rounder form of the lymph node, an L/S ratio (L-long axis/S- short axis of lymph node, normal L/S ratio is 2 indicating oval shape) of less than 1.5, the presence of cortical or rim enhancement, or heterogeneous medullary contrast enhancement were all understood to be indicators of metastasis using CECT. A review of CECT criteria suggests that a metastatic lymph node can be considered as positive if it shows change in size >1 cm, a change in architecture showing rim or cortical enhancement, and heterogenous medullary contrast enhancement [9]. Yuasa et al discovered that a metastatic lymph node is more spherical in shape as it appears on CECT [11,12].

3. Ultrasonography in grayscale (grayscale USG): Grayscale USG criteria for metastatic identification included nodes with a round shape (> 1.5 L/S ratio), the absence of hilar echo, and the presence of internal echo. To locate a metastatic lymph node, an L5-13 linear transducer with a 3.5 cm depth of penetration and a 15 Hz frequency was used. According to Robin, the clinical lines were drawn on the patients' necks. While analysing the detected lymph nodes' ultrasonographical features in each level, the transducer probe was positioned inside those bounds. The UltraIQ, Cablon Medical Software, was used to determine size [13]. Sumi and colleagues found that lymph nodes larger than 1 cm, circular in shape (> 1.5 L/S axis ratio), lacking an echogenic hilum, and having a clear internal echo are more likely to have metastases [14].

4. Color Doppler Ultrasonography (CD): After employing grayscale USG, the Doppler function of the ultrasound system was turned on, and each lymph node in each level (level I, II, and III) had its Doppler characteristics recorded. Resistivity Index > 0.7 and Pulsatility Index > 1.4 were used as criteria for Doppler USG metastatic detection. According to a study by Dudea et al., metastasis is most likely to exist in lymph nodes with a Resistivity Index >0.7 and Pulsatility Index >1.4 [15].

Following the documentation of data obtained, the scheduled surgery was carried out, and the dissected specimen was labeled according to the levels of lymph nodes and sent for histological confirmation of the metastasis.

Histologically, a lymph node with tumor cell infiltration with or without extracapsular spread, lympho-vascular invasion and perineural invasion was classified as a positive node. For the purpose of staging and grading the histopathological analysis followed the most recent AJCC TNM criteria. [16].

Following data collection, statistical analysis was conducted to compare the four investigations (CP, CECT, grayscale USG, CD) and determine which of these diagnostic tools was most valid in assessing the condition of the cervical lymph nodes and providing preoperative information about cervical lymph node invasion in OSCC.

Data entered in Microsoft Excel 2013 was appropriately cleaned and tallied. SPSS 22.0 (IBM) software was used to conduct the necessary statistical analysis on the data. Calculations were made for sensitivity, specificity, and diagnostic accuracy. Chi square test was applied to obtain the value of significance.

## Results

Among 20 participants 10 were male and 10 were female. Patients ranged in age from 43 to 60 years old. Pre-operatively if all four (CP, CECT, grayscale USG, CD) diagnostic modality does not revealed a positive lymph node it was considered as node negative neck. On the other hand, if any of the diagnostic modality showed a positive lymph node it was labeled as node positive neck. The comparison of the four diagnostic modalities was done using histopathological confirmation as the gold standard. In order to compare various diagnostic modalities their accuracy, sensitivity, and specificity were taken into account.

The overall comparison of the number of positive and negative cases in relation to histopathological results is shown in Table number 1. The predictive values of tests against the histopathological findings are shown in Table number 2.

	True positive	True negative	False positive	False negative
Clinical Palpation	4	16	9	0
CECT	4	16	9	0
Gray Scale USG	4	16	9	1
Colour Doppler USG	4	16	9	1

**Table 1:** Overall comparison of number of positive and negative cases with respect to histopathological findings of dissected cervical lymph nodes.

	Clinical Palpation	CECT	Gray Scale USG	Color Doppler USG
Sensitivity	100	100	80	80
Specificity	64	64	64	64
Positive predictive value	30.76	30.76	30.76	30.76
Negative predictive value	100	100	94.11	94.11
Accuracy	68.96	68.96	66.77	66.77

**Table 2:** Overall predictive values of the different tests in comparison with the histopathological findings of dissected cervical lymph nodes

The calculated sensitivity of Clinical palpation was 100%, CECT was 100%, Gray scale USG was 80% and Color Doppler was 80% respectively.

While Specificity of Clinical palpation was 64%, CECT was 64%, Gray scale USG was 64% and Color Doppler was 64%.

Clinical palpation had a positive predictive value of 30.76%, as did CECT, Gray scale USG and Color Doppler.

Clinical palpation, CECT, Gray scale USG, and Color Doppler all had negative predictive values of 100%, 100%, 94.11%, and 94.11% respectively.

When identifying positive neck nodes, the clinical palpation technique and CECT Neck were found to have the highest diagnostic accuracy when compared to Gray scale USG and Color Doppler. However, none of the four diagnostic techniques were able to recognize a difference that was significantly different from histopathological findings.

## Discussion

Numerous studies are being done to determine the best methods for predicting the lymph node metastasis status prior to surgery. With the depth of the lesion, the probability of cervical lymph node metastasis increases. Faisal et al. demonstrated that nodal metastasis increases from 23% to 53% with an increase in lesion depth from 1–5 mm to >10 mm [17]. Numerous studies have examined the depth of invasion as a reliable indicator of the rising frequency of cervical metastases [18,19]. Since the higher probability of cervical nodal metastasis is directly correlated with the depth of the tumour; this observation justifies the inclusion of depth of tumour in the T staging of the current AJCC TNM classification [20].

The palpation method of neck examination is operator dependant and accuracy may be related to the experience [21]. It is clear from recent studies and earlier studies that clinical palpation is a poor, unreliable tool for identifying metastatic nodes [6]. The results of a research by Stewart A. et al. on 40 neck dissections, 20 of which had histologically N- and 20 of which had N+ necks, showed no appreciable difference between clinical examination and CECT scan accuracy in identifying both positive and negative cervical nodes. But a positive node identified by a CT scan and a clinical assessment was unquestionably real. However, a third of the cervical nodes that tested negative were misdiagnosed [2]. This favors the findings of our study. On the other hand, Wooglar JA came to the conclusion that only patients with large metastatic deposits could reliably be diagnosed with metastases by inspection under anesthesia and CT [22].

Hohlweg-Majert B performed research on 45 patients with HNSCC and concluded that ultrasound can be used safely for lymph node staging because the true positive rate of sonographically discovered malignant lymph nodes was much greater than that of CECT. For the purpose of checking lymph nodes for possible head and neck cancer, ultrasound is a trustworthy and useful instrument [5].

Geetha NT investigated 10 patients for the neck node metastasis, and they employed clinical palpation, CECT, ultrasounds, and FNACs with ultrasound guidance to look for cervical metastatic lymph nodes. All methods were equally effective, although the Ultrasound FNAC is the most reliable method for determining lymph node metastases [23]. In our investigation, cervical lymph node detection by clinical palpation and CECT is found to be equally sensitive and precise.

Chang DB used Doppler flow wave analysis and colour Doppler sonography to assess the cervical lymph nodes of 48 diagnosed cases of HNSCC. According to histological analysis, 16 lymph nodes were benign and 32 were cancerous. As a result, they came to the conclusion that colour Doppler sonography is not very useful clinically in identifying benign from malignant lymph nodes [24]. Dangore SB used colour Doppler ultrasonography on 100 patients with clinically obvious cervical lymphadenopathy. Histopathology had revealed that 143 of the lymph nodes were clinically positive, but they had also discovered that colour Doppler had assisted in the search of an additional 25 lymph nodes that had also been histologically demonstrated to be positive. They concluded that colour Doppler had a greater specificity than clinical examination and that colour doppler USG also had a higher accuracy [25]. These results were at odds with those of our study. Dong Gyu Na revealed that malignant lymphadenopathy is particular for high resistivity and pulsatile index values [26]. In addition, Koichi Y et al. found that hilar blood flow data obtained by Doppler sonography considerably increases diagnostic accuracy for finding metastatic nodes in head and neck cancer [27]. Gray scale colour doppler USG in our investigation demonstrated 80% sensitivity and low specificity, indicating that its utility in distinguishing benign from malignant lymph nodes is limited.

In our investigation, there was no discernible difference between the methods of clinical palpation, CECT, grey scale USG, and colour doppler for identifying positive lymph nodes. However, compared to histology, the number of metastatic lymph nodes detected by the aforementioned 4 diagnostic modalities was significantly much lower.

Our study's findings are consistent with those of Haberal I et al., who draw the conclusion that no pre-treatment study can accurately predict the need for histopathological confirmation and also the staging of the neck because all pretreatment evaluation methods differ significantly from the histopathologic results [9].

However, in situations with squamous cell carcinoma of the head and neck region, assessment of a clinically negative node neck (N0) is necessary to establish whether the neck has to be treated. In order to evaluate the precision of PET/CT scan with that of USG and CECT Neck in determining clinically N0 neck in squamous cell carcinoma of the upper aerodigestive tract, Chavan et al. did a study. There were 51 neck dissections performed on the 49 patients. The USG, CECT, and PET-CT were shown to have sensitivity values of 4.76%, 23.80%, and 71.43%, respectively, and specificity values of 93.33%, 93.33%, and 96.67%. For USG, CECT, and PET-CT, the positive predictive value (PPV) was calculated to be 33.33%, 71%, and 93.5%, respectively, whereas the negative predictive value (NPV) was 58.33%, 63.63%, and 82.85%. They came to the conclusion that FDG-PET-CT is more accurate than either USG or CECT in staging the neck in N0 HNSCC, but it is not accurate enough to change the present therapy paradigm [28].

As a result, there are various radiographic methods for detecting neck metastases. For CECT, the sensitivity and specificity values vary from 40% to 68% and 75% to 85%, respectively; for ultrasonography, they are 50% to 58% and 75% to 82%; for magnetic resonance imaging, they are 55% to 80% and 82% to 92%; and for positive emission tomography, they are 57% to 79% and 82% to 96%. Therefore, cervical metastases cannot be confirmed by a single radiologic modality [29]. Clinical palpation and CECT both exhibited 100% sensitivity and 64% specificity in our investigation. However, both the colour Doppler and grayscale USG exhibited identical specificities of 64% and 80%, respectively. Our study was found to have higher sensitivity, specificity, positive predictive value, and negative predictive value for all four diagnostic modalities than the studies mentioned above. Interestingly combining 2 modalities for assessing neck node metastasis produce better outcome in determining presence or absence of positive node.

All four diagnostic modalities of the pre-operative evaluation methods are significantly different from the post operative histopathological results, suggests that none of the pre-treatment modality was able to accurately assess the metastatic nature of lymph nodes. Grayscale and Doppler USG were less sensitive in identifying true positive nodes than clinical palpation and CECT. This is because it is highly dependent on the skill and experience of USG operator in the field of oncology. It is therefore necessary to conduct a more thorough study using a larger sample size and additional research techniques.

## Conclusion

The sensitivity and diagnostic precision of the clinical palpation, CECT, USG, and Color Doppler tests are not significantly different from one another. Therefore, preoperative non-invasive clinical and radiological approaches are not entirely reliable for identifying metastatic lymph nodes. With these diagnostic methods, there is more potential for both false positive and false negative cases. This is mostly due to the high prevalence of undetected metastases in early oral SCC cases. To overcome this issue combining 2 modalities leads to an improved outcome. As none of the four tests considerably outperformed the histopathological findings in terms of providing accurate test results, therefore the preoperative tests for oral SCC metastatic confirmation must be accompanied by a conclusive histological confirmation in order to decide on further treatment.

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