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ORIGINAL ARTICLE

Critical Evaluation of Role of Ultrasonography and Computed Tomography in Guiding Surgical Management of Clinically Negative Neck (CN0) in Carcinoma Oral Cavity

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ABSTRACT

Aim: Carcinoma oral cavity ranks third in the incidence of freshly detected cancers among both the genders. The most impactful prognostic factor in carcinoma oral cavity is the presence of cervical lymph node metastasis. Clinically node negative neck harbors occult metastasis in 06 to 46% of cases. The gold standard currently of managing cN0 neck is Supra Omohyoid neck dissection (SOHND). However, various imaging modalities are challenging the gold standard. The present NCCN guidelines incorporate clinical palpation, USG Neck and contrast-enhanced computed tomography (CECT) in evaluating the nodal status of such patients. This study has critically evaluated, whether USG/CECT is sufficient in the clinically node-negative neck (cN0), in patients with an early stage carcinoma oral cavity or do we need to add other investigations in evaluating the nodal status.

Materials and methods: A single-center prospective study of 51 patients of early stage carcinoma oral cavity with cNo neck underwent evaluation of the neck by ultrasonography (USG) and CECT in a tertiary care center. All patients subsequently underwent SOHND and the results were compared.

Results: Fifty-eight neck sides were dissected (44 unilateral, 7 bilateral), involving a total of 885 lymph nodes (mean, 15.26 lymph nodes per neck side). Histopathologic analysis revealed occult lymph node metastases in 10 of 51 patients (19.6%) which equated to 10 of 58 neck sides (17.24%). The sensitivity and specificity of USG was 40% and 97.8% respectively with a diagnostic accuracy of 87.9%. CECT neck was found to be a better diagnostic modality with a sensitivity of 90% and specificity of 87.5%.

Conclusions: Contrast-enhanced computed tomography (CECT) is a better modality than USG and clinical palpation. However, we recommend further studies with other modalities like PET–CT, and lymphangoscinitigraphy.

Keywords: Carcinoma oral cavity, Node-negative neck, Single-center prospective study, Supra-omohyoid neck dissection.

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INTRODUCTION

Squamous cell carcinoma (SCC) of the oral cavity is one of the commonest malignancies affecting a significant cohort of the population in India. It is the third most frequently occurring cancer in India amongst both men and women.[1]

The most impactful prognostic factor in SCC oral cavity is the presence of cervical lymph node metastasis. Metastatic involvement of the cervical lymph nodes hampers the overall survival rates by approximately 50%.[2] Several studies have depicted a clear correlation between increasing T stage (increasing depth) to an increased risk of cervical metastasis.[3,4] Ten to 30% of early-stage carcinoma oral cavity (T1-T2 lesions) are associated with a risk of regional lymph node metastasis.[5] These regional cervical lymph node metastases can be clinically evident (cN1-3) or occult (cNo).

Even after multiple modalities of detecting the status of cervical lymph nodes, the proportion of occult metastatic disease remains significant.[6,7] Therefore, surgical staging with selective neck dissection in the form of supraomohyoid neck dissection (SOHND) and histopathological examination of neck dissection specimen is the recommended staging procedure for cN0 neck in early stage carcinoma oral cavity cases.[8]

Proponents of selective neck dissection argue that the morbidity of surgical staging outweighs the risk of being confronted with advanced neck disease later. They also cite reduced relapse rates and better survival rates.[8-10] Supraomohyoid neck dissection (SOHND) and histopathological examination of neck dissection specimen although being the gold standard is also subjective to the pathologist's expertise. Five to 8% of lymph node metastasis is missed even with standard sectioning and hematoxylin and eosin staining of SOHND specimen.

Thus management of clinically node-negative neck (cNo), in patients with early-stage, carcinoma oral cavity continues to remain a topic of great interest, a debatable issue spanning five decades. With these considerations, recent studies on management of cNo neck in carcinoma

oral cavity have focussed on newer diagnostic strategies-Sentinel lymph node biopsy (SLNB). Recent literature has highlighted several problems in relying on SLNB, like skip metastases, missed level I sentinel lymph nodes in oral carcinoma. The supremacy of SLNB over SOHND remains yet to be proven.

The role of a noninvasive imaging modality like USG and CECT to guide management of cNo neck in carcinoma oral cavity continues to interest a vast section of surgical oncologists. In a study by Lindberg and Shah 6 to 46% of patients with Head and neck cancer will harbor occult disease in their necks. The critical determinant of the utility of an imaging modality for oral cavity carcinoma is its ability to detect the presence or absence of metastatic neck disease.

This study has critically evaluated the accuracy of clinical palpation, USG and CECT Neck with an aim to determine the need for additional investigations in the management of neck in case of Carcinoma oral cavity.

MATERIALS AND METHODS

A prospective cross-sectional study was conducted in a Tertiary care center from May 2016 to Apr 2018. A total of 51 patients with histologically proven, early stage (cT1-T2) carcinoma of the oral cavity, clinically node-negative neck (cN0), who underwent USG and CECT neck before undergoing staging in the form of Supra-omohyoid neck dissection were included. The criteria used to define a node as metastatic in USG were nodes with diameter >10 mm, central hypoechogenicity, distorted hilum, the presence of necrosis with irregular margin and roundness index >2. The criteria used to define a node as metastatic on CECT are minimal axial diameter > 10mm, L/S ratio <2, central hypodensity and peripheral rim enhancement, a conglomeration of at least 3 lymph nodes, extranodal tumor extension.

Surgical staging of a neck in the form of elective neck dissection (SOHND) was done along with surgical management of primary. In case of enlarged or suspicious nodes found during surgery, SOHND specimen was subjected to frozen section evaluation and SOHND was extended to therapeutic neck dissection (MRND) when frozen section evaluation was positive for metastatic deposits. Histopathologic analysis was performed by dedicated on co-pathologists, using standard hematoxylin-eosin (H and E) staining. Lymph nodes were cut in half and microscopic analysis of 4- to 5-mm-thick sections was performed. The pathologist was unaware of radiological findings.

Preoperative evaluation of neck with USG and CECT was analyzed subsequently and compared to intraoperative findings and postoperative histopathological evaluation of neck dissection specimen. Statistical software SPSS, (Version 22, SPSS Inc. Chicago, USA) was used to calculate outcomes such as sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy. A p-value of less than 0.05 was taken as significant.

RESULTS

Patient's age ranged from 32 to 82 years, and mean age was 54.69 years. There was a male preponderance (80%) in our study. One patient had low-grade adenocarcinoma of buccal mucosa, and rest 50 patients had squamous cell carcinoma of the oral cavity (SCCOC). When patients were segregated as per primary subsite of the oral cavity, the tongue was the most common subsite (52.9%), followed by buccal mucosa (29.41%).

Out of 51 patients, 31 belonged to the pT1 stage and 20 to pT2. In all patients frozen section evaluation (FSE) of the SOHND specimen was performed. A total of 58 neck dissections were performed–44 Unilateral and 07 Bilateral. 45 necks (77.6 %) were negative, and 13 (22.4%) were positive. In the 13 necks with a positive FSE of the SOHND-specimen, the SOHND was extended to a therapeutic comprehensive neck dissection. Ten out of 13 necks positive on FSE turned out to be true-positive and 3 turned out to be false positive on final histopathological examination (HPE) of the neck specimen.

Histopathologic analysis revealed occult lymph node metastases in 10 of 51 patients (19.6%) which equated to 10 of 58 neck sides (17.24%). A number of occult cervical lymph node metastases was greater in pT2 tumors (25%) compared to pT1 tumors (16.13%). Overall the subsite tongue had the highest number occult metastases 6 out of 10 total occult metastases detected. With regards patients with occult metastases, subsite- lip had the highest percentage (25% in total), followed by the tongue (22.22%).

In the clinically negative neck, USG reported 05 neck sides out of 58 sides as positive and 53 neck sides as negative for occult metastases. Out of the 05 neck sides reported positive by USG, 04 sides actually harbored metastases to the neck nodes (Table 1). Out of the 53 neck sides reported negative by USG, 06 side actually harbored metastases to the neck nodes (false negative). The sensitivity of USG in detecting occult lymph node metastases was 40%.

Similarly, out of the 05 neck sides reported positive by USG, 01 side actually did not harbor metastases to the

Table 1: True positive (TP) and false negative(FN) rates for N0 neck

USG N status/	*pN+*	*%*	*Sensitivity*
USG + (n=05)	4 (TP)	80	40%
USG - (n=53)	6 (FN)	11.2	

Table 2: False positive(FP) and True negative(TN) rates for N0 neck

USG N status/	*pN0*	*%*	*Specificity*
USG + (n=05)	1 (FP)	20	97.8%
USG - (n=53)	47 (TN)	88.8	

neck nodes (Table 2). Out of the 53 neck sides reported negative by USG, 47 sides actually did not harbor metastases to the neck nodes (true negative). Specificity of USG in detecting occult lymph node metastases was 97.9%. Overall, USG correctly characterized the occult lymph node metastasis status (TP +TN) in 51 of 58 neck sides, yielding an accuracy of 87.93% (Table 3).

In the clinically negative neck, CECT reported 15 neck sides out of 58 sides as positive and 43 neck sides as negative for occult metastases. Out of the 15 neck sides reported positive by CECT, 9 sides actually harbored metastases to the neck nodes (Table 4). Out of the 43 neck sides reported negative by CECT, 1 side actually harbored metastases to the neck nodes (false negative). The sensitivity of CECT in detecting occult lymph node metastases was 90%.

Similarly, out of the 15 neck sides reported positive by CECT, 6 sides actually did not harbor metastases to the neck nodes (Table 5). Out of the 43 neck sides reported negative by CECT, 42 sides actually did not harbor metastases to the neck nodes (true negative). Specificity of CECT in detecting occult lymph node metastases was 87.5%.

Overall, CECT correctly characterized the occult lymph node metastasis status (TP +TN) in 51 of 58 neck sides, yielding an accuracy of 87.93% (Table 6).

DISCUSSION

Regional lymph node (N) staging is critical for prognosticating patients with carcinoma oral cavity. Clinical N staging in carcinoma oral cavity begins with palpation of neck; however, it can miss 20 to 28% of lymph node metastases. Therefore imaging has become the cornerstone of staging.

Table 3: Outcomes of USG staging of N0 neck in T1/T2 carcinoma oral cavity

Outcome	*%*	*Confidence Interval*
Sensitivity (Sn)	40	12.16 – 73.76
Specificity (Sp)	97.8	88.93 – 99.95
Positive predictive value (PPV)	80	28.36 – 99.49
Negative predictive value (NPV)	88.8	76.97 – 95.73
Diagnostic Accuracy	87.93	

Table 4: True positive (TP) and false negative (FN) rates for N0 neck

CECT N status/	*pN+*	*%*	*Sensitivity*
CECT + (n = 15)	9 (TP)	60	90%
CECT - (n = 43)	1 (FN)	2.32	

Table 5: False positive (FP) and True negative (TN) rates for N0 neck.

CECT N status/	*pN0*	*%*	*Specificity*
CECT + (n = 15)	6 (FP)	40	87.5%
CECT - (n = 43)	42 (TN)	97.67	

Table 6: Outcomes of CECT staging of N0 neck in T1/T2 carcinoma oral cavity

Outcome	*%*	*Confidence Interval*
Sensitivity (Sn)	90	55.5 to 99.75
Specificity (Sp)	87.5	74.5 to 95.27
Positive predictive value (PPV)	60	40.83 to 76.53
Negative predictive value (NPV)	97.67	86.71 to 99.63
Positive Likelihood ratio (LR+)	7.2	3.31 to 15.65
Negative Likelihood ratio (LR-)	0.11	0.02 to 0.74
Diagnostic Accuracy	87.93	

Imaging modalities such as USG, MRI, and CECT detect regional lymph node metastases by size and structural changes. However, studies which subjected patients classified as cN0 by these modalities to subsequent surgical staging showed that the average error rate of assessing the presence of cervical lymph node metastasis by CT ranged from 7.5 to 28% and it was 16% for MRI. Therefore even with state-of-the-art staging modalities, there is always the risk of missing occult metastases in regional lymph nodes.

Mean age of the patient population was 54.69 years. Males were predominant. When patients were segregated as per primary subsite of the oral cavity, the tongue was the most common subsite (52.9%), followed by buccal mucosa (29.41%). The majority (60.78%) were pT1 primary tumors. These epidemiological findings are consistent with those by D'Cruz et al. in their large randomized control trial on 500 clinically node-negative carcinoma oral cavity patients done in India.

Our studies revealed an incidence rate of 17.24% for occult cervical lymph node metastases. This number is similar to those reported by other studies which have reported prevalence rates ranging from 15 to 50%2].2 depending on the sub-site and stage of the primary tumor. Since this study included patients in the early stage only (T1/T2), the incidence figure is near the lower limit of the range.

The sensitivity and specificity of CECT was 90% and 87.5% respectively. The diagnostic accuracy in our study is 87.93%. When compared to the literature, our results were comparable with previous studies. The anatomic precision offered by CECT is better, especially in patients where USG neck is less accurate (short and thick necks, deeply situated lymph nodes).

Despite its limitations, USG neck remains the first investigation to evaluate neck. The added benefit it offers is the quick evaluation of neck in a high patient load center. USG achieved a specificity and sensitivity of 97.8 and 40% respectively. Due to its low PPV, USG has less accuracy in detection of nodes. However, it remains an excellent modality to detect true negatives.

In conclusion, the Chi-square analysis shows that all of the preoperative evaluation modalities (palpation, CECT, and USG) yield results that are significantly lower as compared to histopathological results. This means that SOHND remains unchallenged and continues to be the standard of care in the management of cN0 neck.

There are already studies being carried out to evaluate the role of newer modalities like PET-CT in the evaluation of neck. However, no consensus has been reached in recommending it as per NCCN Guidelines.

CONCLUSION

This study was undertaken to critically evaluate the value of USG and CECT neck in preoperative staging workup of in early stage carcinoma oral cavity patients. In our study, even after combining recommended imaging modalities with palpation for the purpose of cN0 staging, the occult lymph node metastases detection rate was 17.24%. It highlights the fact that there is still scope for improvement in clinical N staging so that occult metastatic rate can be brought down below the threshold for elective neck treatment. Hence, we conclude that CECT is a better modality than USG and clinical palpation. However, we recommend further studies with other modalities like PET–CT, and lymphangioscintigraphy.

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