Section: Miscellaneous

Original Research Article

OUTCOME OF PERI-OPERATIVE ACCURATE DETECTION OF METASTATIC CERVICAL LYMPH NODES IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Received : 05/01/2024
Received in revised form : 23/02/2024
Accepted : 09/03/2024

Keywords:
Head and neck squamous cell carcinoma, Lymph node metastasis, Selective neck dissection, Comprehensive neck dissection, Ultrasonography.

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DOI: 10.47009/jamp.2025.7.1.17

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (1); 80-85

Abstract

Background: HNSCC is a prevalent malignancy in India, due to smokeless tobacco use. Accurate nodal assessment is critical for prognosis and treatment, and selective neck dissection is recommended for cN0 and specific nodal conditions to minimise morbidity. This study aimed to detect clinical-radiological lymph nodal involvement and compare it with that of the final postoperative histopathological examination. **Materials and Methods:** This prospective observational study included 61 patients admitted to Government Royapettah Hospital between March 2020 and March 2021. All patients underwent a thorough preoperative nodal assessment with USG and FNAC, including repeat USG-guided FNAC for cytologically negative palpable nodes. Cytologically positive cases underwent comprehensive neck dissection, whereas cytologically negative cases underwent elective neck dissection with intraoperative SLNB using methylene blue dye, converting to MRND-1 if SLNB was positive. **Result:** Of the 61 patients, 13 were cytology-positive and underwent CND, and 7 were treated with composite resection and PMMC flap. Among the 48 cytology-negative patients, 28 underwent SLNB with frozen section, detecting metastasis in 7 patients who were converted to CND, while 21 underwent SND. The final HPE revealed six false-negative cases (three treated with CND, three with SLNB, and SND). Combined USG and FNAC improved the sensitivity (72%) and maintained 100% specificity and PPV. Contrast CT and MRI showed lower accuracies than USG and FNAC. Adjuvant RT was administered to all node-positive patients. **Conclusion:** Preoperative USG and FNAC are cost-effective and reliable tools for detecting metastatic lymph nodes, with FNAC offering 100% specificity and PPV. Perioperative SLNB enhances accuracy and reduces the need for CND and its associated complications.

INTRODUCTION

Head and Neck Squamous Cell Carcinoma (HNSCC) is the sixteenth most common cancer worldwide. Approximately 600,000 new cases are diagnosed annually. Among developing countries, India tops owing to increased oral smokeless tobacco usage. The incidence of HNSCC is more than 30 per 100,000 people in India.[1] HNSCC more commonly affects men in the 50-60 age group, with a recent surge in the incidence among younger individuals.[2] More than 90% of tumours arising in the head and neck are squamous carcinomas.[3] The principal curative treatment modalities for locally or locoregionally confined HNSCC are neck surgery, radiation, and systemic therapy. Surgery is a commonly used treatment modality for oral cavity cancers, while radiation therapy is more commonly given for pharyngeal and laryngeal cancers.[3]

One of the most important prognostic factors in head and neck cancer is the presence or absence, level, and size of metastatic neck nodes. In HNSCC, intratumoral and peritumoral lymphangiogenesis have been associated with lymph node metastases.[4-6] Regional lymph node metastasis is an important prognostic factor in oral cavity cancers. Nodal involvement significantly decreases survival when compared with those who are disease-free.[7] The term, "occult nodal disease" refers to the presence of metastatic disease in the neck nodes that cannot be clinically or radiologically identified. Accurate preoperative detection of nodal

ISSN (O): 2687-5365; ISSN (P): 2753-6556

involvement is impertinent to decide about the type of neck dissection.[8] However, if the probability of neck metastases is minimal or nil, neck dissection merely acts as an overtreatment, where the morbidity of the neck procedure only presents a reduction in quality of life and functional deficits.[9]

Surgery has changed from radical neck dissection to modified and selective neck dissection. This protects functions, especially the accessory nerve, which if removed will usually give rise to stiffness and pain in the shoulder.[1] SND is recommended for the cN0 neck, for selected clinically positive necks (mobile, 1- 3-cm lymph nodes), and for removing residual disease after RT when there has been excellent regression of N2 or N3 disease.[10,11] MRND is a sufficient treatment for the ipsilateral neck in patients with N0 or N1 disease without ECE.

Aim

1. To prove selective neck dissection (SND) is a viable alternative to comprehensive neck dissection (CND) (avoiding complications related to CND) by accurate preoperative assertion of lymph node status by USG and FNAC before assigning nodal status.
2. To prove that the addition of SLNB in the CN0 neck provides a further advantage in favouring SND and avoiding CND.

MATERIALS AND METHODS

This prospective observational study included 61 patients admitted to the surgical oncology department of Government Royapettah Hospital, Kilpauk Medical College, for a period of one year from March 2020 to March 2021. This study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

The patient's neck was addressed using comprehensive or selective neck dissection for oral cavity head and neck squamous cell carcinomas.

Exclusion Criteria

Patients with non-squamous histology, prior h/o radiation, chemotherapy/radiotherapy upfront, presence of synchronous or second primary tumour, and cancers other than oral cavity cancers were excluded.

Methods

All the patients included in our study were preoperatively examined for nodal metastasis. The nodal status of all patients was characterized using USG. Irrespective of the USG examination, FNAC was performed. Palpable node FNAC was performed in minor OT, and if cytology was negative, repeat FNAC was performed under USG guidance. All cytologically positive patients underwent comprehensive neck dissection. In patients whose primary defect was reconstructed with a pectoralis major myocutaneous (PMMC) flap, CND(MRND-1) was performed.

All the patients with negative cytological results were treated with elective neck dissection. Preoperative sentinel lymph node biopsy (SLNB) was performed using methylene blue dye. If SLNB yielded positive results, the procedure was converted to a modified radical neck dissection. SLNB was negative, and neck dissection was concluded with SND. All neck dissection specimens along with primary submitted for histopathology. The final histopathological examination of nodal status was taken as the gold standard and compared with various modalities for accurate detection.

Statistical analysis: The data are presented as frequencies and percentages. Cross tabs were created to determine sensitivity and specificity. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Corp., Armonk, NY, USA).

RESULTS

The mean age of the patients was 51.65 years. Among the 61 patients, 45 (73.8%) were male and 16 (26.2%) were female.

The primary subsite of malignancy was classified, and the majority were lesions in the tongue 35 (57.4%), followed by the buccal mucosa and alveolus 12 (19.7%). Nodal positivity was highest in the tongue of 14 (40%) patients, followed by the alveolus and buccal mucosa in seven (58%) and six (50%) patients, respectively [Table 1].

Among the T1 lesions, all four patients were node-negative. In T2 lesions out of the 13 patients, five (38%) were node-positive. In T3 lesions, 14 out of 22 (63%) patients were node-positive, and in T4 lesions in 24 patients, 50% were node-positive [Table 2].

Among the 61 patients, 13 were cytologically positive, and 48 were cytologically negative. All positive patient necks were addressed using comprehensive neck dissection (CND). Of the 13 patients 7 patients were treated with composite resection with pectoralis major myocutaneous (PMMC) flap reconstruction.

Of the 48 cytologically negative patients, sentinel lymph node biopsy (SLNB) with frozen, composite resection with PMMC flap reconstruction, and bilateral neck were performed in 28, 19, and 1 patients, respectively. Of the 28 SLNB done and were frozen. Frozen results came positive in 7 patients and converted to CND. Frozen-negative patients were diagnosed with SND. The bilateral neck was addressed in one patient. Right side SLND with SND and left side of the neck CND were performed. Among the 22 SND group, the final HPE was node-negative in 19 and metastatic nodes (but FNAC and SLNB negative) 3 patients. In 19 patients who were treated with composite resection with PMMC flap reconstruction, CND was performed as part of the procedure even though the cytology results were negative. Among the 19 final HPE showed 16 negative nodal status and metastatic nodes in 3 patients.

Six patients were cytology-negative, and the final HPE result was positive in six patients. Neither USG

ISSN (O): 2687-5365; ISSN (P): 2753-6556

nor FNAC was detected in these 6 patients. Cytology and SLNB results were negative in three patients. Of these six patients, three were already treated with CND despite preoperative negative nodal status. The remaining three patients who underwent SLNB did not have metastatic nodes and underwent SND rather than CND. All 6 node-positive patients received adjuvant radiation [Table 3 and Figure 1].

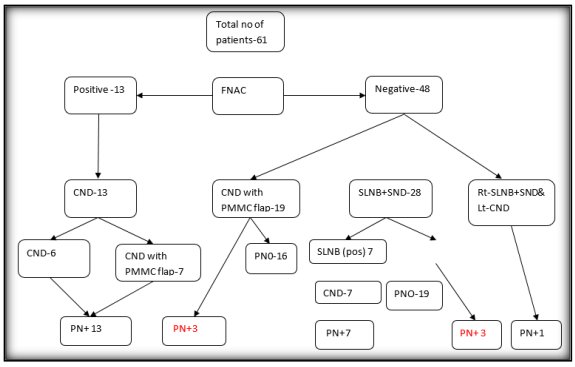

Figure 1: Study methodology and results of the study

All parameters of accuracy (sensitivity, specificity, PPV, and NPV) were > 70% with USG. FNAC had 100% PPV and specificity. The FNAC has an extremely low sensitivity of 40%. Both CT and MRI have low values of accuracy compared with USG and FNAC, and the accuracy parameters of Contrast CT are slightly better than those of MRI. The following table represents the parameters of accuracy (PPV, NPV, Sensitivity and Specificity) of USG, FNAC Nodes, Contrast CT, MRI compared with HPE Nodal Status; when combining USG and FNAC, the sensitivity improved to 72% and NPV remained between USG and FNAC at 68%. PPV and specificity were 100%, similar to those of FNAC. The overall accuracy of the combined modality was 75% [Table 4].

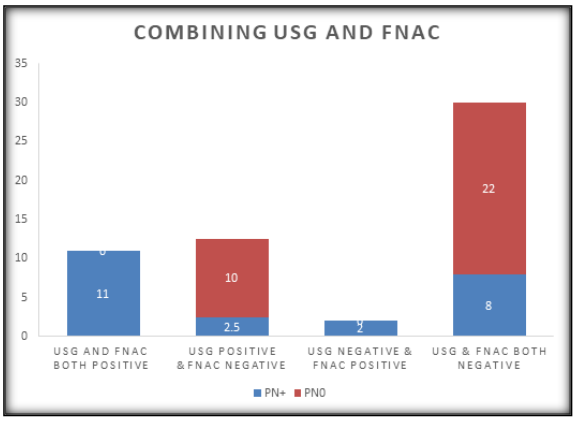

Figure 2: Combining USG and FNAC

Of the 13 FNAC-positive cases, USG revealed metastatic nodes in 11 patients. FNAC was negative in 48 patients and false negative in eight patients, but USG was able to detect metastatic nodes in eight patients. The remaining 32 patients who underwent USG were falsely diagnosed in 10 patients, and 22 patients correctly predicted node-negativity [Figure 2].

Table 1: Primary subsite of malignancy and nodal positivity.

Subsite	Frequency (%)	Nodal positivity
Tongue	35 (57.4%)	14 (40%)
Buccal Mucosa	12 (19.7%)	6 (50%)
Alveolus	12 (19.7%)	7 (58%)

Table 2: T stage-wise nodal positivity distribution

T Stage	Frequency	Node negative	Node positive
T1	4	4 (100%)	0 (0%)
T2	13	8 (62%)	5 (38%)
T3	22	8 (37%)	14 (63%)
T4	24	12 (50%)	12 (50%)

Table 3: Study methodology and outcomes

Parameter	Frequency	Outcome details
Cytology Positive	13	All underwent CND. 7 treated with composite resection and PMMC flap.
Cytology Negative	48	28 underwent SLNB with a frozen section.
SLNB Frozen Results	28	Frozen Positive: 7 converted to CND; Frozen Negative: 21 underwent SND.
Bilateral Neck Addressed	1	Right SLND with SND; Left CND.
SND Group Final HPE	22	Node Negative: 19; Metastatic Nodes: 3 (FNAC & SLNB negative).
Composite Resection with PMMC Flap	19	CND as part of the procedure. Final HPE: 16 negatives, 3 metastatic.
Cytology Negative, Final HPE Positive	6	Not detected by USG or FNAC. Treated as follows:
		3 treated with CND despite negative nodal status preoperatively.
		3 underwent SLNB (negative), treated with SND instead of CND.
Node Positive Patients (Adjuvant RT)	6	All received adjuvant radiation.

Abbreviations: CND - Comprehensive Neck Dissection, SND - Selective Neck Dissection, SLNB - Sentinel Lymph Node Biopsy, PMMC - Pectoralis Major Myocutaneous Flap, HPE - Histopathological Examination, RT - Radiation Therapy.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 4: Accuracy of USG, FNAC nodes, contrast CT, MRI with HPE nodal status

		Final HPE Nodal Status		PPV	NPV	Sensitivity	Specificity
		Positive	Negative				
USG	Positive	21	8	72.40%	71.90%	70.00%	74.20%
	Negative	9	23				
FNAC Nodes	Positive	12	0	100.00%	63.30%	40%	100%
	Negative	18	31				
Contrast CT	Positive	10	5	66.70%	72.70%	76.90%	61.50%
	Negative	8	3				
MRI	Positive	13	8	61.90%	71.40%	76.40%	55.60%
	Negative	4	10				
USG and FNAC	Positive	13	0	100%	68%	72%	100%
	Negative	15	33				

DISCUSSION

In this study, FNAC showed 100% PPV and specificity. FNAC is an invasive procedure compared with other tests. However, FNAC has an extremely low sensitivity (40%). Combined with USG, the sensitivity improved to 72%. FNAC can be used as a confirmatory tool to study lymph node metastasis in head and neck carcinomas. Preoperative USG neck and FNAC aided by preoperative SLNB can improve the accuracy of detecting nodal positivity. By following these methods, we can avoid CND-related complications by performing SND. We safely avoided CND with 5-10% false negativity. Preoperative USG with FNAC of the neck nodes is easy, cost-effective, and reliable in detecting metastatic lymph nodes. Aided by this modality, perioperative SLNB further amplifies its benefit by detecting metastatic lymph nodes, and we can safely avoid CND.

SLNB is not the standard of care for oral cavity cancers.[12] However, many single-institution studies and two multi-institution studies have validated SLNB in oral cancers with high detection rates (approximately 95%) and negative predictive values (88-100%).[13-17] In our study, the detection rate was 89.5% and the negative predictive value was 94%. Three Meta-analyses by Paleri et al,[18] Govers et al,[19] and Thompson et al,[20] based on pooled data samples have also confirmed its use in the staging and treatment of early-stage head and neck cancers.

Horváth et al. observed a similar result when they studied the accuracy of the parameters of preoperative diagnostic workup in patients with head and neck cancers and nodal metastasis who underwent neck dissection. In their study, the sensitivity of both imaging (CT, MRI, US) and FNAC was approximately 80%, but the specificity was 73.9% and 100%, respectively. The positive predictive values of imaging modalities and FNAC were 82.8% and 100%, respectively. They also observed negative predictive values were 73.9% and 66.6%, respectively.[21]

Despite being costly tests and involving infrastructure, both CT and MRI have low values of accuracy compared with USG and FNAC. Out of CT and MRI, the accuracy parameters of Contrast CT were slightly better than MRI. Overall, all the parameters of accuracy were above 70% with USG, with a correct balance between all the parameters of accuracy. Considering its accuracy and other advantages, such as ease of use and low cost, USG can be widely recommended as a screening tool to study lymph node metastasis in head and neck carcinoma. Baatenburg et al. and Prayer et al. in their studies observed an accuracy rate of around 70%, which is similar to our study results.[22,23] But a study by Mehta et al. observed a sensitivity of 93.3% and specificity of 27.7% for USG and they suggested it as a good screening tool.[24]

Bhandari et al. performed a systematic review and meta-analysis of the management of clinically negative lymph nodes (cN0) in primary lip squamous cells. They concluded that their results were insufficient to justify elective treatment of the neck in primary cN0 lip SCC. They also suggested that close observation would be a viable option.[25] Abu-Ghanem et al. showed that END can significantly decrease the risk of regional nodal recurrence with improved disease-specific survival in patients with early-stage cT1-T2N0 oral tongue squamous cell carcinoma.[26] Later Chung et al. recommended SNB instead of END for carefully chosen patients with cN0 OSCC since it offers acceptable oncological results by long-term observation, retaining high accuracy rates.[27]

Dabirmoghaddam et al. assessed the Ultrasound-guided fine needle aspiration cytology in cervical metastasis among patients undergoing elective neck dissection and observed accuracy of Ultrasound-guided fine needle aspiration cytology, Ultrasound and palpation was 96%, 68% and 70%, respectively.[28] So, combining USG and FNAC, Ultrasound-guided fine needle aspiration cytology can be considered. De Bondt et al. did a meta-analysis and suggested that US-guided FNAC showed better diagnostic performance compared with US, CT, and MRI.[29]

In this study, we observed good specificity and PPV of USG. Similarly, Knappe et al, Takes et al, and Dammann et al studied US-guided FNAC and observed good sensitivity and specificity parameters.[30-32] Hence it can be suggested as a good confirmatory and screening tool, and further research can be directed at assessing the accuracy of US-guided FNAC.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Limitation

One limitation of the study is that it was conducted in a tertiary care teaching institution where the standards of care are high, and the parameters of the accuracy obtained in our study can be high compared to the same tests when applied in a secondary care institution.

CONCLUSION

Preoperative USG of the neck and FNAC aided by preoperative SLNB can detect nodal positivity. By following these methods, we can avoid CND-related complications by performing SND. Preoperative USG with FNAC of the neck nodes is easy, cost-effective, and reliable in detecting metastatic lymph nodes. Aided by this modality, preoperative SLNB further amplifies its benefit by detecting metastatic lymph nodes, and we can avoid CND with 5-10%% false negatives.

Overall, all parameters of accuracy were above 70% with USG. FNAC had 100% PPV and specificity. The FNAC has an extremely low sensitivity of 40%. Both CT and MRI have low values of accuracy compared with USG and FNAC, and the accuracy parameters of Contrast CT are slightly better than those of MRI. Hence, we concluded that CT and MRI are less accurate than USG. USG being an easy, simple and low-cost tool, it can be used as a screening tool and FNAC can be a good confirmatory tool.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556