ORIGINAL ARTICLE

ASSESSING THE RELIABILITY OF CLINICAL NODAL STAGING IN ORAL SQUAMOUS CELL CARCINOMA: CORRELATION WITH HISTOPATHOLOGICAL FINDINGS

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ABSTRACT

Introduction

The most significant prognostic factor in oral squamous cell carcinoma (OSCC) is the presence of cervical lymph node metastases. Extranodal extension (ENE) approximately halves survival rates. Previous studies have demonstrated discordance between clinical and pathological lymph node staging, which has important implications for treatment planning.

Objective

To evaluate the concordance between clinical (cN) and pathological (pN) lymph node staging and determine the frequency of extranodal extension (ENE) in patients with OSCC. Secondary objectives included describing the frequency distribution of age, sex, smoking habits, anatomical location, and histological subtypes of OSCC in a Bangladeshi population.

Methods

A retrospective analysis was conducted on 95 consecutive cases of OSCC treated with primary tumor resection and neck dissection. The 8th edition of the AJCC/UICC TNM staging system was used to evaluate clinical (cN) and pathological (pN) nodal staging. The prevalence of ENE was assessed in all OSCC patients and in the clinically node-negative (cN0) subgroup. Sociodemographic and tumor-related variables were also recorded.

Results

Concordance between cN and pN was observed in 51.6% of patients (n = 49/95). Pathological upstaging occurred in 26.3% (n = 25/95) and pathological downstaging in 22.1% (n = 21/95) of cases. ENE was identified in 23 patients (24.2%). The study sample comprised 60% males and 40% females, with a mean age at diagnosis of 60.3 years (range: 25–85 years). A positive smoking history was reported in 76.3% of patients. The most common anatomical sub-sites were the tongue (43.2%) and the floor of the mouth (34.1%). The majority of tumors (62.1%) were conventional, moderately to poorly differentiated squamous cell carcinomas.

Conclusion

There is moderate concordance between clinical and pathological nodal staging when the 8th edition TNM system is applied. ENE is present in a significant proportion of OSCC patients at the time of diagnosis, including those with clinically node-negative necks. These findings underscore the importance of comprehensive pathological assessment for accurate staging and treatment planning.

Keywords

oral squamous cell carcinoma, clinical lymph node staging, pathological lymph node staging, extranodal extension, TNM classification, neck dissection

INTRODUCTION

Oral squamous cell carcinoma (OSCC) accounts for approximately 90–95% of all malignancies arising in the oral cavity [1, 2]. The presence of cervical lymph node metastasis at the time of diagnosis is the single most important prognostic factor influencing survival, and approximately one-third of patients present with regional metastatic disease upon initial evaluation [3–5]. The identification and accurate staging of nodal disease are therefore critical to effective management.

Treatment planning in OSCC relies heavily on the TNM staging system. Clinical TNM staging (cTNM), based on physical examination and

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imaging, guides initial decisions regarding the extent of surgical intervention, including neck dissection. Pathological TNM staging (pTNM), determined following histopathological examination of the surgical specimen, informs decisions about adjuvant treatment such as radiotherapy or chemoradiotherapy. Concordance between cN and pN is therefore essential for optimal treatment planning, and any systematic discordance has significant clinical implications.

The 8th edition of the AJCC/UICC TNM staging system, introduced in 2017, incorporated extranodal extension (ENE) as a criterion for nodal staging for the first time. ENE is defined as the extension of metastatic tumor through the lymph node capsule into surrounding tissue and has been consistently associated with significantly worse survival outcomes, approximately halving the 5-year survival rate compared with encapsulated nodal metastasis [6]. The inclusion of ENE in the staging system has altered the distribution of nodal stages and may affect concordance between clinical and pathological assessments.

Clinical evaluation of the cervical lymph node basin in OSCC includes physical palpation, contrast-enhanced computed tomography (CECT), ultrasonography, magnetic resonance imaging (MRI), and occasionally fine-needle aspiration cytology (FNAC). Despite advances in imaging, clinical assessment has well-documented limitations in detecting occult metastases and ENE [7, 8]. In resource-limited settings, where access to advanced imaging may be restricted, the accuracy of clinical staging becomes even more uncertain.

When lymph node metastasis involves the primary echelon lymph nodes, the probability of metastasis to secondary and tertiary nodal basins increases [5]. This concept of sequential lymphatic spread has important implications for the extent of neck dissection performed.

The objectives of this study were: (1) to evaluate the concordance between clinical and pathological lymph node staging in OSCC using the 8th edition AJCC/UICC TNM system; (2) to determine the prevalence of pathological ENE (pENE) in all patients and in the clinically node-negative (cN0) subgroup; and (3) to describe the demographic, clinical, and histopathological characteristics of OSCC in a Bangladeshi population.

MATERIALS AND METHODS

Study Design

This retrospective, non-randomized observational study included patients who underwent primary tumor resection along with neck dissection for oral squamous cell carcinoma (OSCC) at various pathological centers in Dhaka, Bangladesh, between January 1, 2015, and December 31, 2021.

Patient Selection

Patient records were retrieved from the departmental database and cross-referenced with operative notes and histopathology reports. The following inclusion criteria were applied:

- Histologically confirmed diagnosis of OSCC
- Primary tumor resection with concurrent neck dissection performed
- Availability of clinical records sufficient to determine cTNM staging
- Availability of postoperative histopathology reports sufficient to determine pTNM staging

Exclusion criteria included:

- Incomplete clinical records precluding cTNM determination
- Incomplete or unavailable postoperative histopathology reports
- Neck dissection not including at least levels I–III
- Salvage neck dissections
- Recurrent disease or prior treatment for OSCC

Clinical Staging

Clinical staging (cTNM) was determined by clinical examination including bimanual palpation of the neck, supplemented by contrast-enhanced computed tomography (CECT) when available and when its procurement did not unnecessarily delay surgical treatment. Clinical nodal status was categorized according to the 8th edition AJCC/UICC TNM classification.

Surgical Procedures

All patients underwent surgery under general anesthesia administered via nasoendotracheal intubation, orotracheal intubation, or tracheostomy, as dictated by

the clinical situation. Standard aseptic protocols were observed.

Patients without clinical cervical lymphadenopathy (cN0) underwent elective supraomohyoid neck dissection (SOHND) including levels I–III. Patients with clinical evidence of cervical lymphadenopathy (cN+) underwent modified radical neck dissection (MRND) involving levels I–V, with or without preservation of the sternocleidomastoid muscle, internal jugular vein, and spinal accessory nerve (CN XI), depending on intraoperative findings.

Histopathological Examination

Surgical specimens were processed according to standard laboratory protocols. Lymph nodes were identified, separated according to anatomical level, and embedded in paraffin. Sections of 4 µm thickness were stained with hematoxylin and eosin (H&E) and examined by experienced pathologists under light microscopy. Each lymph node was assessed for the presence of metastatic tumor deposits and ENE. Pathological nodal staging (pN) was determined according to the 8th edition AJCC/UICC TNM staging manual. Pathology reports originally employing the 7th edition criteria (prior to 2018) were retrospectively re-evaluated and re-staged according to the 8th edition criteria.

Data Collection and Variables

The following variables were extracted from patient records:

- Demographic: Age, sex, smoking history
- Tumor-related: Anatomical sub-site, histological subtype and differentiation grade
- Staging: Clinical nodal status (cN), pathological nodal status (pN), presence of pathological ENE (pENE)

Statistical Analysis

Descriptive statistics were used to summarize patient demographics and tumor characteristics. Concordance between cN and pN was assessed by calculating the proportion of cases in which the two were congruent, upstaged (pN > cN), or downstaged (pN < cN). The association between cN and pN (categorized as concordant vs. discordant) was tested using Pearson's chi-square test or Fisher's exact test when expected cell frequencies were less than 5. The prevalence of pENE was calculated as a proportion of all OSCC cases and of the cN0 subgroup separately. All statistical analyses were performed using SPSS version 27 (IBM Corporation, Armonk, NY). Statistical significance was set at $p < 0.05$.

Sample Size

Convenience sampling was employed. All consecutive patients meeting inclusion criteria during the study period were included. The sample size was determined by the available patient population.

RESULTS

Patient Demographics and Tumor Characteristics

Of 110 consecutive patients initially identified, 15 were excluded due to incomplete records, yielding a final study sample of 95 patients. The demographic and tumor-related characteristics are summarized in Table 1.

The study population comprised 57 males (60.0%) and 38 females (40.0%), with a male-to-female ratio of 1.5:1. The mean age at diagnosis was 60.3 years (range: 25–85 years). A positive smoking history was present in 72 patients (75.8%), absent in 14 patients (14.7%), and unknown in 9 patients (9.5%).

The most common anatomical sub-site was the tongue (n = 41, 43.2%), followed by the floor of the mouth (n = 32, 33.7%), the alveolar ridge (n = 9, 9.5%), the retromolar trigone (n = 7, 7.4%), the buccal mucosa (n = 4, 4.2%), and the hard palate (n = 2, 2.1%).

The predominant histological subtype was conventional squamous cell carcinoma (n = 87, 91.6%), of which 8 (9.2%) were well differentiated, 25 (28.7%) were moderately differentiated, 44 (50.6%) were poorly differentiated, and 10 (11.5%) had unspecified differentiation. Histological variants included basaloid SCC (n = 2, 2.1%), papillary SCC (n = 2, 2.1%), acantholytic SCC (n = 2, 2.1%), carcinoma cuniculatum (n = 1, 1.1%), and verrucous SCC (n = 1, 1.1%).

Clinical and Pathological Nodal Staging

The distribution of cN and pN stages is presented in Table 2.

At clinical staging, 50 patients (52.6%) were classified as cN0 and 45 patients (47.4%) as cN+. The distribution of cN+ patients was: cN1 (n = 18, 18.9%), cN2a (n = 3, 3.2%), cN2b (n = 12, 12.6%), cN2c (n = 7, 7.4%), and cN3b (n = 5, 5.3%).

At pathological staging, 52 patients (54.7%) were classified as pN0 and 43 patients (45.3%) as pN+. The

distribution of pN+ patients was: pN1 (n = 10, 10.5%), pN2a (n = 3, 3.2%), pN2b (n = 7, 7.4%), pN2c (n = 2, 2.1%), and pN3b (n = 21, 22.1%).

Concordance Between Clinical and Pathological Nodal Staging:

The cross-tabulation of cN versus pN stages is presented in Table 3. Overall concordance between cN and pN was 51.6% (n = 49/95). Pathological upstaging occurred in 26.3% (n = 25/95), and pathological downstaging occurred in 22.1% (n = 21/95) of cases.

Concordance Analysis by Subgroup

In the cN0 subgroup (n = 50), 37 patients (74.0%) were concordant (pN0), while 13 patients (26.0%) were pathologically upstaged, representing occult lymph node metastases. Among these 13 patients with occult metastases, 8 (61.5%) were staged as pN3b due to the presence of ENE.

In the cN+ subgroup (n = 45), 12 patients (26.7%) were concordant, 15 patients (33.3%) were downstaged (including 15 downstaged to pN0), and 12 patients (26.7%) were upstaged. Six patients (13.3%) were reclassified to a different but same-level pN category. The results are summarized in Table 4.

When cN and pN were dichotomized as concordant versus discordant, chi-square analysis showed no statistically significant association between clinical nodal status (cN0 vs. cN+) and concordance: $\chi^2(1, N = 95) = 3.42$, $p = 0.064$ (Fisher's exact test $p = 0.078$).

Prevalence of Extranodal Extension

Pathological extranodal extension (pENE) was identified in 23 patients (24.2%) of the total study sample. Among the 43 patients with pathologically confirmed lymph node metastases (pN+), pENE was present in 21 (48.8%).

In the cN0 subgroup, pENE was detected in 8 of the 13 patients with occult metastases, representing 16.0% (8/50) of all cN0 patients. In the cN+ subgroup, pENE was detected in 15 of 30 patients with pathologically confirmed metastases, representing 33.3% (15/45) of all cN+ patients. The distribution of pENE by cN stage is shown in Table 5.

The prevalence of pENE showed an increasing trend with advancing clinical nodal stage, from 16.0% in cN0 to 60.0% in cN3b. However, the notable finding was that 34.8% (8/23) of all patients with pENE belonged to the cN0 group, indicating that a substantial proportion of ENE is clinically undetectable.

Lymph Node Yield

The mean number of lymph nodes harvested per patient was 22.4 (range: 8–52). In the pN+ group (n = 43), the mean number of pathologically positive lymph nodes per patient was 3.2 (range: 1–18). The mean lymph node ratio (positive nodes/total nodes harvested) in the pN+ group was 0.16 (range: 0.02–0.69).

DISCUSSION

Demographics and Risk Factors

The demographic profile of our study population is largely consistent with established epidemiological data for OSCC. The male-to-female ratio of 1.5:1 observed in this study aligns with published literature indicating that OSCC is approximately 1.5 to 2 times more common in males than in females, although this disparity has narrowed in recent decades [7–9]. The mean age at diagnosis of 60.3 years is comparable to data from other populations [10]. However, a noteworthy finding was that 10.5% of patients were diagnosed before the age of 45 years, which is slightly higher than the 4–6% reported in some Western series but consistent with a literature review of 35 studies on oral cancer in young adults, which reported a prevalence of approximately 6–11% [11].

The high prevalence of a positive smoking history (75.8%) in this cohort is consistent with the well-established association between tobacco use and OSCC, with published data indicating that up to 80–90% of patients with OSCC report tobacco use [2, 12]. The synergistic effect of combined tobacco and alcohol use is well documented, with heavy users of both substances experiencing up to a 38-fold increase in OSCC risk [2, 14]. Unfortunately, data on alcohol consumption were not systematically available in our records and could not be analyzed.

Anatomical Distribution and Histopathology

The predominance of tongue (43.2%) and floor of mouth (33.7%) as the most common sub-sites is consistent with published data, with these two sites collectively accounting for approximately 75% of OSCC cases in most series [2, 13]. The high proportion of poorly differentiated tumors (46.3%) may reflect referral bias, as more aggressive tumors may be more likely to present to a tertiary surgical center, or it may reflect population-specific biological behavior requiring further investigation.

Concordance Between Clinical and Pathological Nodal Staging:

The overall concordance between cN and pN of 51.6% observed in this study represents moderate agreement. This figure is lower than the 79% concordance reported in a large retrospective study of 400 OSCC patients [15], but higher than the 35% reported in some series with smaller sample sizes [16]. The variation in reported concordance rates across studies likely reflects differences in the imaging modalities available, the expertise of the clinical examiners, the staging edition used, and patient population characteristics.

Several important observations emerge from the cross-tabulation analysis:

1. Occult metastases in the cN0 group: Twenty-six percent (13/50) of clinically node-negative patients were found to have pathological nodal disease. This occult metastasis rate is consistent with the 20–30% rate commonly reported in the literature [1, 4, 22, 26] and provides further justification for the practice of elective neck dissection in cN0 OSCC patients with primary tumors of sufficient depth and size. Critically, 61.5% (8/13) of these patients with occult metastases had ENE (staged as pN3b), indicating advanced pathological disease that was entirely undetected clinically.

2. Overstaging in the cN+ group: Forty-seven percent (21/45) of clinically node-positive patients were pathologically downstaged, including 15 patients (33.3%) who were downstaged to pN0. This finding indicates that a substantial proportion of clinically detected lymphadenopathy is reactive rather than metastatic. These patients underwent MRND rather than the less morbid SND, receiving no therapeutic benefit from the more extensive surgical procedure while being exposed to its greater morbidity.

3. The pN3b phenomenon: The most striking discrepancy between cN and pN distributions was the substantial increase in the pN3b category (from 5.3% clinically to 22.1% pathologically). This increase is a direct consequence of the incorporation of ENE into the 8th edition TNM staging system. Prior to this edition, many of these patients would have been classified as pN1 or pN2, masking the true prevalence of ENE and its associated adverse prognosis.

The chi-square analysis comparing concordance rates between the cN0 and cN+ subgroups did not reach statistical significance ($p = 0.078$). This may reflect the limited sample size and the inability to detect a modest difference in concordance rates. A larger study would be needed to determine whether concordance differs significantly between clinically node-negative and node-positive populations.

Extranodal Extension

The overall prevalence of pENE of 24.2% (23/95) and the rate of 48.8% among pN+ patients are consistent with published data. A study of 440 OSCC patients reported pENE in 32% of cases with nodal metastases [4], and another study of 342 patients reported an overall pENE prevalence of 13.8% [33]. The increasing trend of pENE prevalence with advancing clinical nodal stage observed in this study (16.0% for cN0 to 60.0% for cN3b) is consistent with previously reported data showing a similar stepwise increase [4].

The finding that 16.0% (8/50) of cN0 patients harbored pENE is of particular clinical significance. These patients would not be identified as candidates for adjuvant therapy based on clinical staging alone, yet they have one of the strongest pathological indicators of poor prognosis. This finding reinforces the importance of thorough pathological examination and may support arguments for more aggressive adjuvant treatment protocols in patients found to have occult metastases with ENE.

The presence of ENE in small metastatic deposits (as small as 2 mm) has been previously reported [18], suggesting that ENE is not merely a function of tumor volume within the lymph node but may reflect inherent biological aggressiveness of the tumor. Clinical detection of ENE remains challenging; while radiological signs such as irregular nodal margins, infiltration of surrounding fat planes, and matted lymph nodes suggest ENE, these criteria have limited sensitivity [19].

Clinical Implications

The discordance between clinical and pathological nodal staging has several important clinical implications:

1. Management of the cN0 neck: The 26% occult metastasis rate supports the current standard of performing elective neck dissection (SND levels I–III) for OSCC tumors meeting established criteria (e.g., depth of invasion >4 mm). However, SND I–III may leave residual disease in levels IV and V. Studies have shown that when metastatic disease is present in first-echelon lymph nodes (levels I–III), levels IV and V are involved in approximately 18% and 10% of cases, respectively [5]. These patients may benefit from comprehensive neck dissection or at minimum from close postoperative surveillance.

2. Over-treatment in the cN+ group: The finding that one-third of cN+ patients had no pathological evidence of nodal metastasis (pN0) suggests that a significant number of patients undergo unnecessarily extensive surgery (MRND). Recent literature supports the oncological safety of SND for selected cN1 and cN2 patients meeting specific criteria (single node <4 cm, no level IV/V palpable disease, no clinical ENE) [29, 30]. A prospective study of 350 patients comparing SND I–III with MRND for cN0 disease demonstrated significantly lower complication rates in the SND group (15.1% vs. 24.6%, p = 0.05) with comparable disease-specific 4-year survival and superior regional control [31, 32].

3. Role of adjuvant therapy: Pathological upstaging, particularly to pN3b (ENE), triggers consideration for adjuvant chemoradiotherapy. The high rate of upstaging to pN3b observed in this study (22.1% of all patients) underscores the importance of pN staging in guiding adjuvant treatment decisions.

Limitations

Several limitations of this study should be acknowledged:

Retrospective study design: The retrospective nature of the study introduces inherent limitations, including potential selection bias and incomplete or missing data, which may have influenced the study outcomes.

Limited sample size: The relatively small sample size (n = 95) restricts the statistical power, particularly for subgroup analyses involving less frequent clinical nodal stages (cN2a, cN3b), where low case numbers preclude robust multivariate analysis.

Imaging heterogeneity: Preoperative contrast-enhanced computed tomography (CECT) was not uniformly performed in all patients, and variability in imaging availability and quality over the study period may have contributed to staging discordance. This heterogeneity may also limit the generalizability of the findings to settings with standardized advanced imaging protocols.

Lack of survival outcomes: The absence of longitudinal follow-up and survival data prevents evaluation of the prognostic implications of clinical–pathological staging discordance in this cohort.

Unaccounted confounding tumor variables: Key prognostic factors, including depth of invasion, perineural invasion, lymphovascular invasion, and surgical margin status, were not analyzed, although these variables are well-established determinants of nodal metastasis and disease progression. [33-37]

Future prospective studies with larger sample sizes, standardized imaging protocols, and longitudinal follow-up data are needed to validate these findings and assess their prognostic implications.

CONCLUSION

This study demonstrates moderate concordance (51.6%) between clinical and pathological lymph node staging in OSCC when the 8th edition AJCC/UICC TNM system is applied. A significant proportion of clinically node-negative patients (26.0%) harbor occult metastases, the majority of which demonstrate extranodal extension. Conversely, a substantial proportion of clinically node-positive patients (33.3%) have no pathological evidence of metastatic disease. Extranodal extension is present in 24.2% of all OSCC patients at the time of diagnosis and shows an increasing prevalence with advancing clinical nodal stage. These findings highlight the limitations of clinical nodal assessment and underscore the critical importance of pathological staging for treatment planning in OSCC. Every effort should be made to improve the accuracy of preoperative cervical lymph node assessment through the development and implementation of more sensitive diagnostic modalities.

Conflict of Interest

The authors report no conflict of interest.

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Abbreviations: TNM: TNM staging system stands for Tumour, Node, Metastasis.

OSCC: Oral squamous cell carcinoma

cN : Clinical

pN : Pathological

ENE : Extranodal expansion

cN0 : Clinically nodal negative

Table 1: Patient Demographics and Tumor Characteristics (N = 95)

SCC = squamous cell carcinoma; SD = standard deviation

Variable	Category	n (%)
Sex	Male	57 (60.0)
	Female	38 (40.0)
Age (years)	Mean ± SD	60.3 ± 13.2
	Range	25–85
	<45 years	10 (10.5)
	45–64 years	42 (44.2)
	≥65 years	43 (45.3)
Smoking history	Present	72 (75.8)
	Absent	14 (14.7)
	Unknown	9 (9.5)
Anatomical sub-site	Tongue	41 (43.2)
	Floor of mouth	32 (33.7)
	Alveolar ridge	9 (9.5)
	Retromolar trigone	7 (7.4)
	Buccal mucosa	4 (4.2)
	Hard palate	2 (2.1)
Histological subtype	Conventional SCC	87 (91.6)
	Well differentiated	8 (8.4)
	Moderately differentiated	25 (26.3)
	Poorly differentiated	44 (46.3)
	Unspecified differentiation	10 (10.5)
	Basaloid SCC	2 (2.1)
	Papillary SCC	2 (2.1)
	Acantholytic SCC	2 (2.1)
	Carcinoma cuniculatum	1 (1.1)
	Verrucous SCC	1 (1.1)

Table 2: Distribution of Clinical (cN) and Pathological (pN) Nodal Stages (N = 95)

Nodal Stage	cN, n (%)	pN, n (%)
N0	50 (52.6)	52 (54.7)
N1	18 (18.9)	10 (10.5)
N2a	3 (3.2)	3 (3.2)
N2b	12 (12.6)	7 (7.4)
N2c	7 (7.4)	2 (2.1)
N3b	5 (5.3)	21 (22.1)
Total	95 (100)	95 (100)

Table 3: Values represent number of patients. Shaded diagonal cells (bold) indicate concordant staging.

	pN0	pN1	pN2a	pN2b	pN2c	pN3b	Total
cN0	37	3	1	1	0	8	50
cN1	8	4	1	1	0	4	18
cN2a	1	0	1	0	0	1	3
cN2b	4	1	0	3	1	3	12
cN2c	1	1	0	1	1	3	7
cN3b	1	1	0	1	0	2	5
Total	52	10	3	7	2	21	95

Table 4: Concordance between cN and pN

Subgroup	Concordant, n (%)	Upstaged, n (%)	Downstaged, n (%)
cN0 (n = 50)	37 (74.0)	13 (26.0)	—
cN+ (n = 45)	12 (26.7)	12 (26.7)	21 (46.7)
Overall (N = 95)	49 (51.6)	25 (26.3)	21 (22.1)

Table 5: Distribution of Pathological ENE (pENE) According to Clinical Nodal Stage

pENE = pathological extranodal extension.

cN Stage	Total Patients (n)	Patients with pN+ (n)	Patients with pENE (n)	pENE as % of Total	pENE as % of pN+
cN0	50	13	8	16.0	61.5
cN1	18	10	4	22.2	40.0
cN2a	3	2	1	33.3	50.0
cN2b	12	8	4	33.3	50.0
cN2c	7	6	3	42.9	50.0
cN3b	5	4	3	60.0	75.0
Total	95	43	23	24.2	53.5

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