e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(7); 928-932

Original Research Article

Correlation between PET-CT and Histopathological T and N Staging in Buccal Mucosa Squamous Cell Carcinoma: A Single-Institution Study

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Received: 01-04-2026 / Revised: 15-05-2026 / Accepted: 21-06-2026

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Conflict of interest: Nil

Abstract

Objective: To determine the concordance between preoperative PET-CT-based clinical staging (cTNM) and final histopathological staging (pTNM) for the primary tumour (T) and regional lymph nodes (N) in patients with buccal mucosa squamous cell carcinoma, using AJCC 8th edition criteria.

Methods: In a prospective observational study, 87 patients with histopathologically proven, operable buccal mucosa squamous cell carcinoma underwent PET-CT-based clinical staging followed by radical surgery with neck dissection. Clinical T and N stage were compared with final pathological T and N stage. Agreement was expressed as the proportion of correctly staged, under-staged (cT<pT / cN<pN), and over-staged (cT>pT / cN>pN) cases, with Cohen's kappa as the measure of agreement.

Results: Overall T-stage concordance was 60.9% (53/87; kappa = 0.403, moderate agreement), with the poorest agreement in pT3 (31.3% correct, 50.0% under-staged) and the best in pT4 (68.8% correct, no over-staging). Overall N-stage concordance was 52.9% (46/87; kappa = 0.306, fair agreement); pN0 was frequently over-staged (30.2%), while pN1 and pN3 were markedly under-staged (42.9% and 94.7% under-staged, respectively).

Conclusion: PET-CT-based clinical staging of buccal mucosa carcinoma shows only moderate agreement with pathological T stage and fair agreement with pathological N stage, with a systematic tendency toward under-staging of higher nodal categories. These findings support cautious preoperative counselling and a low threshold for elective/therapeutic neck dissection even when the clinical neck appears node-negative or minimally involved.

Keywords: Buccal Mucosa Carcinoma; Oral Cavity Cancer; PET-CT; Clinicopathological Correlation; AJCC 8th Edition; TNM Staging; Kappa Agreement.

DOI: 10.25258/ijcpr.18.7.142

Introduction

Oral cavity squamous cell carcinoma is one of the most significant head and neck malignancies worldwide, with a disproportionate burden in South-Central Asia, where tobacco chewing, smoking, and alcohol use remain the principal risk factors. Buccal mucosa is consistently reported as the most frequent oral cavity subsite in Indian institutional series, reflecting the regional prevalence of smokeless tobacco and areca nut chewing habits.

Management planning for buccal mucosa carcinoma - the extent of resection, the need for and laterality of neck dissection, and the likelihood of requiring adjuvant therapy - is largely determined at initial clinical assessment, using clinical examination together with PET-CT of the face and neck (cTNM). The definitive stage, however, is established only after histopathological examination of the resected specimen (pTNM), incorporating parameters such as depth of invasion

and extranodal extension that cannot be reliably assessed preoperatively.

Discordance between the two staging systems, in either direction, has direct clinical consequences: under-staging may lead to inadequate resection margins or omission of indicated neck dissection, while over-staging may expose patients to more extensive surgery or adjuvant treatment than the disease ultimately warrants. While concordance between PET-CT and pathological staging has been described for oral cavity cancer as a whole, site-specific data for buccal mucosa - the most common subsite in this population - remain comparatively limited. This paper reports a prospective cohort study on PET-CT-pathological staging concordance in buccal mucosa carcinoma, with the specific aim of characterizing the direction and magnitude of T- and N-stage discordance in this subsite using AJCC 8th edition criteria.

PET-CT combines the metabolic activity of the tumour, expressed as the maximum standardized uptake value (SUVmax), with cross-sectional anatomical detail, and is widely used for both primary tumour and nodal staging in oral cavity cancer. SUVmax has been reported to correlate with histopathological tumour grade and depth of invasion, and PET-CT nodal positivity broadly parallels pathological nodal status, giving it reasonable overall accuracy for excluding grossly metastatic disease.

Its correlation with final histopathology is, however, imperfect at the level of the individual node or tumour: PET-CT frequently fails to identify micrometastatic or sub-centimetre nodal deposits that fall below its spatial resolution, while inflammatory or reactive nodes can generate false-positive uptake, and neither pattern is reliably distinguished from true metastatic involvement on imaging alone. Extranodal extension, similarly, is identified with far greater certainty on histopathological examination than on PET-CT. This imperfect radiological-pathological correlation is one of the principal drivers of the clinicopathological staging discordance that the present study set out to characterise in the buccal mucosa subsite.

Materials and Methods

Study design and setting: This was a prospective observational study conducted in the Department of Pathology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan.

Participants: A total of 87 patients over 18 years of age, of either sex, with histopathologically proven, operable buccal mucosa squamous cell carcinoma admitted for radical surgery were enrolled after written informed consent. Patients under 18 years of age, those with distant metastatic disease, prior oral cavity/neck surgery, prior head and neck radiotherapy, recurrent disease, prior chemotherapy for any malignancy, or unwillingness for surgery were exclusion criteria.

Staging procedure: All patients underwent detailed history-taking, clinical examination, and radiological staging with whole-body PET-CT as indicated, from which the clinical stage (cTNM) was assigned. After metastatic work-up, patients underwent radical surgery with ipsilateral (or bilateral, where indicated) neck dissection encompassing levels I-V. Resected specimens were fixed in 10% neutral buffered formalin, sectioned, paraffin-embedded, and stained with haematoxylin and eosin, from which the final pathological stage (pTNM) was assigned according to AJCC 8th edition criteria.

Statistical analysis: For both T and N categories, each pathological stage was cross-tabulated against the corresponding clinical stage. Cases were classified as correctly staged (cT=pT, cN=pN), under-staged (cT<pT, cN<pN), or over-staged (cT>pT, cN>pN). Agreement between clinical and pathological staging was quantified using Cohen's kappa statistic, interpreted as: 0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial, and 0.81-1.00 almost perfect agreement.

Results

Of the 87 patients with buccal mucosa squamous cell carcinoma, baseline demographic character istics are summarised in Tables 1 and 2.

Table 1: Age distribution of the study cohort (N = 87)

N	Mean (years)	SD	Median (years)	Minimum	Maximum
87	50.6	11.25	49.00	27	77

Age group (years)	N	%
≤ 40	15	17.2
41-50	30	34.4
51-60	27	31.0
> 60	15	17.2
Total	**87**	**100.0**

The mean age of the cohort was 50.6 ± 11.25 years (median 49 years; range 27-77 years), with the largest proportion of patients in the 41-50 year age group (34.4%).

Table 2: Gender distribution of the study cohort (N = 87)

Gender	N	%
Male	77	88.5
Female	10	11.5
Total	**87**	**100.0**

Males predominated markedly over females, with a male-to-female ratio of approximately 7.7:1 (77 vs. 10).

Clinical versus pathological T staging (n = 87)

Table 3: Cross-tabulation of clinical T stage (cT) against pathological T stage (pT) in buccal mucosa carcinoma (n = 87)

Pathological T stage	cT1		cT2		cT3		cT4		Total	
	N	%	N	%	N	%	N	%	N	%
pT1	2	40.0	2	6.1	0	0.0	0	0.0	4	4.6
pT2	3	60.0	13	39.4	2	16.7	1	2.7	19	21.8
pT3	0	0.0	8	24.2	5	41.7	3	8.1	16	18.4
pT4	0	0.0	10	30.3	5	41.7	33	89.2	48	55.2
Total	**5**	**100.0**	**33**	**100.0**	**12**	**100.0**	**37**	**100.0**	**87**	**100.0**

Column percentages are calculated within each clinical T-stage column.

Table 4: Concordance between clinical and pathological T staging in buccal mucosa carcinoma (n = 87)

Pathological T stage	Total		Correctly staged		Under-staged		Over-staged	
	N	%	N	%	N	%	N	%
pT1	4	100.0	2	50.0	0	0.0	2	50.0
pT2	19	100.0	13	68.4	3	15.8	3	15.8
pT3	16	100.0	5	31.3	8	50.0	3	18.7
pT4	48	100.0	33	68.8	15	31.2	0	0.0
Total	**87**	**100.0**	**53**	**60.9**	**26**	**29.9**	**8**	**9.2**

Cohen's kappa = 0.403 (moderate agreement).

Overall clinical-pathological T-stage concordance in buccal mucosa carcinoma was 60.9% (53/87), with moderate agreement overall (kappa = 0.403).

Concordance was lowest for pT3 (31.3% correctly staged, 50.0% under-staged) and highest for pT4 (68.8% correctly staged, 31.2% under-staged, no over-staging). Early pT1 tumours were correctly staged in only half of cases, with the remainder over-staged clinically; no pT1 case was under-staged.

Clinical versus pathological N staging (n = 87)

Table 5: Cross-tabulation of clinical N stage (cN) against pathological N stage (pN) in buccal mucosa carcinoma (n = 87)

Pathological N stage	cN0		cN1		cN2		cN3		Total	
	N	%	N	%	N	%	N	%	N	%
pN0	30	78.9	2	25.0	11	27.5	0	0.0	43	49.4
pN1	3	7.9	1	12.5	3	7.5	0	0.0	7	8.0
pN2	2	5.3	2	25.0	14	35.0	0	0.0	18	20.7
pN3	3	7.9	3	37.5	12	30.0	1	100.0	19	21.8
Total	**38**	**100.0**	**8**	**100.0**	**40**	**100.0**	**1**	**100.0**	**87**	**100.0**

Column percentages are calculated within each clinical N-stage column.

Table 6: Concordance between clinical and pathological N staging in buccal mucosa carcinoma (n = 87)

Pathological N stage	Total		Correctly staged		Under-staged		Over-staged	
	N	%	N	%	N	%	N	%
pN0	43	100.0	30	69.8	0	0.0	13	30.2
pN1	7	100.0	1	14.2	3	42.9	3	42.9
pN2	18	100.0	14	77.8	4	22.2	0	0.0
pN3	19	100.0	1	5.3	18	94.7	0	0.0
Total	**87**	**100.0**	**46**	**52.9**	**25**	**28.7**	**16**	**18.4**

Cohen's kappa = 0.306 (fair agreement).

Overall clinical-pathological N-stage concordance in buccal mucosa carcinoma was 52.9% (46/87; kappa = 0.306, fair agreement). Staging was most accurate for pN2 (77.8% correct) and least accurate for pN3, where 94.7% of cases were under-staged clinically and only 5.3% were correctly identified. pN0 was correctly staged in 69.8% of cases, with the remainder (30.2%) over-staged; no pN0 case was under-staged, by definition. pN1 showed the least reliable clinical prediction of all categories, with correct staging in only 14.2% and near-equal over- and under-staging (42.9% each).

Discussion

Buccal mucosa was the predominant oral cavity subsite in the parent cohort, consistent with the well-documented regional predominance of smokeless tobacco and areca nut chewing habits in South Asian populations. The moderate T-stage agreement (kappa = 0.403) and fair N-stage agreement (kappa = 0.306) observed here indicate that, even in a subsite that is directly accessible to clinical inspection and palpation, PET-CT-based preoperative staging imperfectly predicts the final pathological stage.

For T staging, our finding of 60.9% concordance in buccal mucosa carcinoma is lower than the 92.4% stage-retention reported by Padma R and Sundaresan [1] in a single-institution series of 198 buccal mucosa carcinoma patients, where only 3% were upstaged and 4.6% downstaged. It is, however, broadly in keeping with Gupta K et al. [2], who reported higher discrepancy rates in oral cavity squamous cell carcinoma generally (21.9% upstaged, 7.9% downstaged), and with Greenberg et al. [3], who documented pathological upstaging in 34-44% of head and neck squamous cell carcinoma cases and argued that pathological staging, rather than clinical staging, should guide treatment decisions. The pattern seen here - disproportionate under-staging of pT3 tumours - is consistent with the recognized difficulty of clinically and radiologically estimating depth of invasion once it approaches intermediate thresholds, a parameter that the AJCC 8th edition incorporates directly into T-category assignment.

For N staging, the fair agreement observed (kappa = 0.306) and the pronounced under-staging of pN1 and pN3 disease parallel the difficulty of detecting limited-volume or microscopic nodal metastases on cross-sectional and metabolic imaging. Chloupek et al. [4] reported a higher, substantial level of agreement for N staging in head and neck cancer overall (kappa = 0.62), while Patil et al.5, studying 22 buccal mucosa carcinoma patients specifically, found that a large proportion of clinically N0 or N1 necks harboured more extensive pathological nodal disease. Taken together with the present findings, this reinforces that a clinically and radiologically reassuring neck in buccal mucosa carcinoma does not reliably exclude occult or under-estimated nodal disease, particularly in the pN1 and pN3 categories.

Comparable overall cT-pT concordance for oral cavity cancer in general has been reported by Dharini et al. [6] and Kreppel et al. [7], both of whom similarly found lower agreement in intermediate T categories than in early or advanced disease, mirroring the pT3 dip seen in this buccal mucosa cohort. Using AJCC 8th edition criteria specifically, Yokota et al. [8] showed that incorporating depth of invasion and extranodal extension into staging improves prognostic discrimination compared with the 7th edition, though at the cost of a measurable degree of stage migration - a phenomenon that plausibly contributes to the T- and N-stage discordance documented here.

For buccal mucosa specifically, Shah and Parikh [9] demonstrated that greater depth of invasion correlated significantly with nodal metastasis in oral tongue and buccal mucosa carcinoma, supporting a mechanistic link between imprecise preoperative depth-of-invasion estimation and the downstream N-stage under-staging observed in our pN1 and pN3 cases. Sultania et al. [10] further validated clinical T staging against depth of invasion and found close correlation with imaging-based depth assessment, suggesting that dedicated radiological protocols for depth-of-invasion measurement could help narrow the cT-pT gap identified in this study.

These findings should be interpreted in the context of a single-institution cohort with a comparatively small buccal mucosa subgroup (n = 87), which limits the precision of stage-specific concordance estimates, particularly for less frequent categories such as pT1 and cN3. This does not affect the validity of the site-specific staging concordance analysis, which was performed directly on the 87 buccal mucosa cases.

Conclusion

In buccal mucosa squamous cell carcinoma, PET-CT-based clinical staging shows only moderate agreement with pathological T stage and fair agreement with pathological N stage, with a consistent tendency toward under-staging of intermediate-to-advanced T3 tumours and of pN1/pN3 nodal disease. These findings support realistic preoperative counselling regarding the possibility of pathological upstaging and argue for a low threshold for elective or therapeutic neck dissection in buccal mucosa carcinoma, even when the PET-CT-assessed neck appears node-negative or only minimally involved.

Acknowledgements: The authors thank the Department of Pathology and Department of Surgical Oncology, Mahatma Gandhi Medical College and Hospital, Jaipur, for institutional support.

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