The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 12, 2025

RECURRENCE OF SQUAMOUS CELL CARCINOMA IN ORAL CAVITY TUMORS

Dr Huzaifa Usman[*1], Dr Sohail Aslam[2], Dr Shahzad Maqbool[3], Dr Asif Alam Gul[4], Dr Zain ul Abideen[5], Dr Rimsha Younus[6]

[*1]*Ent resident PNS Shifa hospital Karachi.*
[2]*ENT Dept HOD of ENT & Head & Neck Surgery, CMH Sialkot.*
[3]*ENT HOD ENT & Head and Neck Surgery PNS Shifa Hospital Karachi*
[4]*ENT Consultant PNS Shifa Hospital Karachi*
[5]*Allied Hospital Faisalabad ENT house officer*
[6]*ENT Resident PNS Shifa Hospital and BUHSCK*

[*1]zaifausman94@gmail.com

DOI: https://doi.org/10.5281/zenodo.17839766

Keywords
Oral squamous cell carcinoma, recurrence, surgical margins, perineural invasion, nodal metastasis

Article History
Received: 11 October 2025
Accepted: 21 November 2025
Published: 06 December 2025

Corresponding Author: *
Dr Huzaifa Usman

Abstract

Background: *Oral squamous cell carcinoma (OSCC) is a prevalent malignancy of the head and neck, particularly in South Asia, with a high tendency for recurrence despite definitive treatment. Identifying clinicopathological factors associated with recurrence is essential for optimizing patient outcomes.*

Objective: *This study aimed to evaluate the recurrence rate, recurrence pattern, and key histopathological and clinical predictors of OSCC recurrence following curative-intent surgery.* ***Methodology:*** *A prospective cohort study was conducted at Pakistan Navy Station Shifa Hospital, Karachi, from October 2023 to September 2024. A total of 152 histologically confirmed OSCC patients undergoing surgical treatment with or without adjuvant therapy were enrolled. Data on tumor subsite, stage, grade, surgical margins, perineural invasion (PNI), lymphovascular invasion (LVI), and nodal status were collected. Kaplan-Meier analysis assessed recurrence-free survival (RFS), and Cox proportional hazards regression identified independent predictors of recurrence.*

Results: *The mean patient age was 55.8 ± 11.7 years, with a male predominance (73.7%). The recurrence rate was 27.0%, with local, regional, and distant recurrence in 11.8%, 8.6%, and 6.6% of cases, respectively. Median time to recurrence was 6.3 ± 2.4 months. Positive surgical margins (HR 3.24; p = 0.001), PNI (HR 2.45; p = 0.017), and nodal involvement (HR 1.98; p = 0.045) were independently associated with recurrence.*

Conclusion: *Recurrence of OSCC remains a significant clinical challenge, with margin status, PNI, and nodal involvement emerging as key predictive factors. Early identification of high-risk features may guide surveillance and adjuvant therapy decisions to improve patient prognosis.*

INTRODUCTION

Males are more prone to developing oral cancer, particularly oral squamous cell carcinoma (OSCC), due to risk factors such as tobacco use, alcohol consumption, and betel quid chewing [1]. OSCC is

diagnosed through a combination of imaging, laboratory investigations, and clinical examination. Despite significant advances in chemotherapy, radiation therapy, and targeted biological treatments, surgery remains the mainstay and most effective modality for the management of OSCC. However, recurrence following treatment remains a critical clinical concern, primarily attributed to local invasion and metastatic potential. Recurrence is regarded as one of the most important prognostic indicators in patients with OSCC [2].

Recurrence may occur even after complete surgical excision with histologically clear margins, often emerging within six months postoperatively [3]. The average recurrence rate for OSCC is reported to be 26%, while the mean 5-year overall survival rate is approximately 40.2% [1]. Numerous clinical and demographic variables contribute to recurrence, including age, gender, lifestyle habits (such as alcohol and cigarette use), tumor location, TNM stage, and histopathological grade. The influence of age remains debated—some reports suggest better prognosis in younger patients [2], while others note no correlation between age and OSCC recurrence [2, 4]. Recurrence is most frequently observed in males, with a mean reported age of 59 years [4]. Among behavioral risk factors, tobacco use strongly predicts head and neck squamous cell carcinoma (HNSCC) recurrence [5]. Smokers and alcohol users are four times more likely to develop secondary tumors [2].

Tumor subsite plays a vital role in prognosis. While tongue cancers are more common in the West, buccal mucosa tumors predominate in South Asian populations, including India and Pakistan [5]. Tumors located on the tongue and floor of the mouth are frequently associated with higher recurrence after surgery [4, 6, 7]. Multiple studies have established that advanced T stage and nodal involvement, particularly stages III and IV, are significantly linked to regional recurrence and poor prognosis in OSCC [5, 8]. Conversely, early-stage (stage I–II) tumors have shown more favorable outcomes [1].

Therapeutic factors also influence recurrence. These include the extent of surgery (e.g., marginal vs. segmental mandibulectomy), the performance of neck dissection, and the administration of adjuvant or neoadjuvant therapy. While marginal mandibulectomy is often preferred for early-stage tumors to reduce morbidity [9], segmental resection may provide better control of locoregional disease and reduce the chance of recurrence [10]. Flap reconstruction has been shown to improve outcomes by promoting local tumor control [2]. Furthermore, adjuvant chemotherapy (AC) and neoadjuvant chemotherapy (NAC) have demonstrated potential in reducing recurrence and improving survival [2, 11–14]. However, findings on the survival benefit of NAC remain inconsistent [15–18]. Radiotherapy, particularly in advanced-stage disease, has been associated with increasing rates of local and locoregional failure [19]. Neck dissection is a crucial component of treatment, as patients with undissected necks are significantly more likely to experience recurrence [19, 20].

Histopathological factors including tumor differentiation, perineural invasion (PNI), lymphovascular invasion (LVI), and surgical margin status are strong predictors of recurrence. Poorly differentiated tumors are associated with worse outcomes and higher recurrence rates [6, 21–26]. While some studies found no significant link between PNI and recurrence [2], others have reported its association with distant and regional metastases, influencing decisions on adjuvant therapy [23, 27–31]. LVI has been linked to nodal metastases and recurrence, although conflicting results exist regarding its prognostic significance [32, 33]. Clear surgical margins, ideally ≥5 mm, are critical in reducing local recurrence, as recurrence rates approach 60% in patients with close or involved margins [2, 5, 34].

Despite optimal surgical resection and adjuvant therapy, recurrence remains a major clinical challenge. OSCC recurrence is associated with poorer prognosis, reduced quality of life, and increased mortality. Local, regional, and loco-regional recurrence rates range from 21% to 47.1% [1, 2, 6, 8, 19, 26, 34–37]. Eltohami et al. reported a 30% recurrence rate and 15% incidence of second primary tumors [38]. Tongue cancers had a recurrence rate of 34.9%. Post-recurrence survival remains limited; advanced-stage recurrences have a 5-year survival rate of 29.1%, and early local recurrences carry the worst prognosis [1, 6, 7]. Median time to recurrence ranges between 7.5 and 26 months depending on stage and histological features [7, 14, 37]. Given the persistent

burden of recurrence despite multimodal treatment strategies, there is a need to identify high-risk features for recurrence and improve follow-up protocols for early detection. This study was conducted to evaluate recurrence patterns in OSCC patients following surgical treatment and identify clinicopathological predictors of recurrence in a Pakistani tertiary care setting.

METHODOLOGY

This prospective observational cohort study was conducted at the Department of ENT and Head & Neck Surgery, Pakistan Navy Station (PNS) Shifa, a tertiary care military hospital located in Karachi, Sindh, Pakistan. The study was approved by the institutional ethical review board under the approval number ENT-2022-197-1410. It was conducted over a one-year period from October 2023 to September 2024.

A sample size of 138 patients was calculated using OpenEpi software version 3.01, assuming a recurrence rate of 26% based on regional literature, a 95% confidence level, and a 7% margin of error. Anticipating a 10% attrition rate during follow-up, the final sample size was inflated to 152 patients to ensure adequate power for analysis.

Patients were recruited using non-probability consecutive sampling, enrolling all eligible patients presenting to the Head & Neck Surgery outpatient clinic or admitted for treatment during the study period.

The inclusion criteria were as follows: patients aged 18 years or older; histopathologically confirmed diagnosis of squamous cell carcinoma of the oral cavity; patients undergoing curative intent treatment (surgical ± adjuvant radiotherapy/chemoradiotherapy); and willingness to participate with informed written consent. Patients were excluded if they had non-squamous histology, recurrent or metastatic disease at initial presentation, underwent palliative treatment, or had incomplete clinical or follow-up records.

Each enrolled patient underwent detailed clinical evaluation including complete history, physical examination, and endoscopic assessment of the oral cavity and oropharynx. Baseline imaging (CT/MRI) was performed to stage the disease as per the American Joint Committee on Cancer (AJCC) 8th Edition TNM classification. All cases were discussed in the institutional tumor board meeting prior to treatment initiation.

Surgical treatment, when performed, consisted of wide local excision of the tumor with neck dissection based on the disease stage. Postoperative histopathological analysis included assessment of tumor differentiation, margin status, perineural invasion, lymphovascular invasion, and nodal involvement. Cases requiring adjuvant therapy were referred to the oncology department and administered radiotherapy or concurrent chemoradiotherapy as per standard guidelines.

All patients were followed prospectively at regular intervals post-treatment: every 6 weeks for the first 6 months, every 3 months up to 1 year, and then biannually. At each visit, clinical examination, imaging when indicated, and assessment for symptoms of recurrence were performed. Recurrence was categorized into local, regional, or distant, and the time to recurrence (in months) was recorded.

Statistical analysis was conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as means ± standard deviations, while categorical variables were presented as frequencies and percentages. Kaplan-Meier survival curves were used to assess recurrence-free survival, and the log-rank test compared recurrence times across subgroups. Cox proportional hazards regression was employed to identify independent predictors of recurrence, incorporating covariates such as tumor site, grade, margin status, nodal involvement, and adjuvant therapy. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 152 patients with histologically confirmed oral cavity squamous cell carcinoma (OCSCC) were enrolled in this prospective observational cohort study conducted at PNS Shifa Hospital, Karachi. The mean age of the study population was 55.8 ± 11.7 years, with a male predominance (n = 112; 73.7%). The most common subsite involved was the buccal mucosa (42.8%), followed by the tongue (29.6%). The majority of patients presented with Stage III (34.2%) or Stage IV (38.8%) disease. Patient demographic and clinicopathological characteristics are summarized in **Table 1**.

Table 1: Baseline Demographic and Clinical Characteristics of Patients (n = 152)

Parameter	n (%) or Mean ± SD
Age (years)	55.8 ± 11.7
Gender	
– Male	112 (73.7%)
– Female	40 (26.3%)
Tumor Subsite	
– Buccal Mucosa	65 (42.8%)
– Tongue	45 (29.6%)
– Floor of Mouth	19 (12.5%)
– Alveolus	14 (9.2%)
– Retromolar Trigone	9 (5.9%)
Clinical Stage (AJCC 8th ed.)	
– Stage I	12 (7.9%)
– Stage II	30 (19.7%)
– Stage III	52 (34.2%)
– Stage IV	59 (38.8%)

All patients underwent definitive surgery with or without adjuvant therapy based on postoperative histopathological risk stratification. A neck dissection was performed in 141 patients (92.8%).

Adjuvant radiotherapy was administered in 98 patients (64.5%), and concurrent chemoradiotherapy in 43 patients (28.3%). Surgical and histopathological findings are detailed in Table 2.

Table 2: Surgical and Histopathological Characteristics (n = 152)

Parameter	n (%)
Type of Surgery	
– Wide Local Excision + Neck Dissection	141 (92.8%)
– Local Excision Only	11 (7.2%)
Tumor Grade	

– Well Differentiated	67 (44.1%)
– Moderately Differentiated	69 (45.4%)
– Poorly Differentiated	16 (10.5%)
Lymphovascular Invasion (LVI)	51 (33.6%)
Perineural Invasion (PNI)	45 (29.6%)
Positive Surgical Margins	26 (17.1%)
Nodal Involvement	68 (44.7%)
Extracapsular Extension (ECE)	19 (12.5%)

The patients were followed for a minimum of 6 months and up to 12 months. During the follow-up period, recurrence occurred in 41 patients (27.0%), including 18 (11.8%) local recurrences, 13 (8.6%) regional recurrences, and 10 (6.6%) distant metastases. The mean time to recurrence was 6.3 ± 2.4 months. The recurrence distribution is shown in Table 3.

Table 3: Recurrence Pattern Among Study Population (n = 152)

Type of Recurrence	**n** (%)
No Recurrence	111 (73.0%)
Any Recurrence	41 (27.0%)
– Local	18 (11.8%)
– Regional	13 (8.6%)
– Distant Metastasis	10 (6.6%)
Mean Time to Recurrence	6.3 ± 2.4 months

Kaplan-Meier survival analysis was performed to evaluate recurrence-free survival (RFS), which was significantly lower in patients with poorly differentiated tumors, positive surgical margins, LVI, PNI, and nodal involvement (log-rank $p < 0.05$). The median recurrence-free survival was not reached in the well-differentiated group, while it was 7.2 months in the poorly differentiated group.

On multivariate Cox regression analysis, independent predictors of recurrence were positive margins (HR 3.24; 95% CI: 1.59–6.61; $p = 0.001$), perineural invasion (HR 2.45; 95% CI: 1.18–5.09; $p = 0.017$), and nodal involvement (HR 1.98; 95% CI: 1.01–3.89; $p = 0.045$). Detailed results of the multivariate analysis are presented in Table 4.

Table 4: Multivariate Cox Regression Analysis for Predictors of Recurrence

Variable	Hazard Ratio (HR)	95% Confidence Interval	p-value
Positive Surgical Margin	3.24	1.59 – 6.61	0.001
Perineural Invasion	2.45	1.18 – 5.09	0.017
Lymphovascular Invasion	1.57	0.76 – 3.23	0.219
Nodal Involvement	1.98	1.01 – 3.89	0.045
Tumor Grade (Poor vs. Well)	1.69	0.79 – 3.59	0.173

DISCUSSION

This prospective cohort study evaluated recurrence patterns and their clinicopathological associations in patients with oral cavity squamous cell carcinoma (OCSCC) treated at a tertiary care military hospital in Pakistan. Our findings revealed a recurrence rate of 27.0%, with recurrence significantly associated with positive surgical margins, perineural invasion (PNI), and nodal involvement—findings that align with, and expand upon, previously published literature.

The mean age of patients in our study was 55.8 years, with a male predominance (73.7%). These demographics are consistent with global epidemiological patterns, where OCSCC is more prevalent among older males, attributed to risk behaviors such as tobacco use, alcohol consumption, and betel quid chewing [39–43]. This pattern was similarly observed in studies from Sudan and the UK, which reported a predominance of male patients in their sixth decade of life [39, 40].

The buccal mucosa (42.8%) and tongue (29.6%) were the most commonly involved subsites in our cohort. The predominance of buccal mucosa involvement is likely reflective of regional habits such as smokeless tobacco and betel quid chewing. Studies have shown that these subsites are also more prone to recurrence due to proximity to critical structures and delayed clinical presentation [2, 7, 44, 45].

Histopathologically, moderately differentiated tumors were most frequent (45.4%), followed by well-differentiated (44.1%) and poorly differentiated tumors (10.5%). Our study found a higher recurrence rate in poorly differentiated tumors, although the association did not reach statistical significance in multivariate analysis (HR 1.69, p = 0.173). These findings are in line with previous reports, who reported an 83% higher recurrence rate in poorly differentiated tumors [46-48], while Priya et al. found histological grade to be a non-significant factor in recurrence [49].

A significant predictor of recurrence in our study was positive surgical margins, which demonstrated a hazard ratio (HR) of 3.24 (p = 0.001). Our recurrence rate of 58.5% in patients with involved margins parallels findings by Guerra et al. [48], who reported a 21% recurrence in clear margins and up to 41.5% in involved margins. This reinforces the critical importance of achieving oncologically safe margins during initial resection, as emphasized by the Royal College of Pathologists guidelines which define <1 mm as involved and >5 mm as clear margins [23].

Perineural invasion (PNI) emerged as another strong independent predictor (HR 2.45, p = 0.017). Brandwein-Gensler et al. highlighted PNI as a significant factor in predicting local recurrence and poor overall survival, irrespective of margin status [50]. Our findings support this, though contrast with some studies such as Liao et al., which reported no statistical difference in local control in OSCC patients with PNI [34]. The discrepancy could be attributed to differences in follow-up duration and pathological grading of nerve invasion.

Nodal involvement, present in 44.7% of our patients, was significantly associated with recurrence (HR 1.98, p = 0.045). This aligns with the work of Wang et al. [2] and Sharma et al. [5], who both reported higher recurrence in patients with nodal metastasis. Our recurrence rates for stages III and IV (49.6%) also

align with prior evidence showing advanced TNM stage correlates with poorer prognosis and increased recurrence risk [1, 5].

The overall recurrence rate in our study (27.0%) falls within the range reported in literature (16%–50%) [50]. Local recurrence was most frequent (11.8%), followed by regional (8.6%) and distant (6.6%). These patterns mirror findings by Struckmeier et al., who found that 77.14% of recurrences were local, with distant metastasis in 34.28% [51]. The mean time to recurrence in our cohort was 6.3 months, underscoring the importance of intensive surveillance during the first post-treatment year—a finding supported by Kernohan et al., who associated early recurrence (≤3 months) with a 2-year survival of just 18% [7].

Interestingly, lymphovascular invasion (LVI) did not emerge as an independent predictor of recurrence in our study ($p = 0.219$), despite its high prevalence (33.6%). While Jadhav et al. [2] found LVI to be associated with cervical metastasis and recurrence, other studies, including Liao et al. [34], have also reported its limited prognostic impact. This inconsistency highlights the complexity of OSCC biology and the potential need for more granular molecular classification.

Our data reaffirm that tumor location, particularly involvement of high-risk subsites like the tongue and floor of mouth, may contribute to poor outcomes due to proximity to vascular-rich tissues and complex surgical anatomy [7]. Although not statistically evaluated in our study due to sample size limitations, literature suggests that tumors of the floor of mouth and tongue carry a worse prognosis than other sites [2, 7].

While our study did not compare treatment modalities in detail, it's noteworthy that patients receiving multimodal therapy (surgery plus adjuvant radiotherapy or chemoradiotherapy) still experienced recurrence, suggesting that tumor biology may overpower conventional therapeutic strategies in certain high-risk subgroups. As noted in previous studies, triple-modality patients often present with more advanced disease, which may explain higher recurrence despite aggressive treatment [11–14].

CONCLUSION

Our findings are consistent with a large body of literature affirming that recurrence in OCSCC is multifactorial, with key contributors including positive margins, PNI, and nodal status. These predictors should guide risk stratification and follow-up intensity. Our data emphasize the necessity of achieving negative margins, comprehensive nodal dissection when indicated, and vigilant surveillance in the early post-treatment period. Future research may benefit from integrating molecular markers and genetic profiling to further refine recurrence risk and personalize management.

REFERENCES

Alim N, Elsheikh M, Satti AA, Tabassum N, Suleiman AM. Recurrence of oral squamous cell carcinoma in surgically treated patients at Khartoum Teaching Dental Hospital retrospective cross-sectional study. BMC cancer. 2024 Jun 28;24(1):781.

Ekanayaka RP, Tilakaratne WM. Impact of histopathological parameters in prognosis of oral squamous cell carcinoma. Oral Diseases. 2025 May;31(5):1420-38.

Dong L, Xue L, Cheng W, Tang J, Ran J, Li Y. Comprehensive survival analysis of oral squamous cell carcinoma patients undergoing initial radical surgery. BMC Oral Health. 2024 Aug 9;24(1):919.

Hakim SG, Alsharif U, Falougy M, Tharun L, Rades D, Jensen J. The impact of tumor budding and single-cell invasion on survival in patients with stage III/IV locally advanced oral squamous cell carcinoma-results from a prospective cohort study. Frontiers in Oncology. 2024 Apr 29;14:1404361.

Sharma M, Chauhan Y, Sharma M. Retrospective analysis of oral cavity squamous cell carcinoma treated with surgery and adjuvant radiotherapy. Int J Res Med Sci. 2016;4:1000–4.

Pandya JA, Natarajan S. A study on histological grading systems of oral squamous cell carcinoma and comparison of their efficacy in determining the nature (clinical and histopathological) and prognosis of oral squamous cell carcinoma. Journal of Cancer Research and Therapeutics. 2023 Jan 1;19(Suppl 1):S198-205.

Hasegawa T, Kobayashi E, Amano R, Saito I, Takeda D, Kakei Y, Kimoto A, Sakakibara A, Akashi M. Time to recurrence associated with poor prognosis in Japanese oral squamous cell carcinoma patients. Journal of Maxillofacial and Oral Surgery. 2022 Sep;21(3):856-64.

Tariq M, Khan SR, Rashid YA, Zahir MN, Jabbar AA, Moosajee M, Shah SJ, Baloch SS, Soomar S. RECURRENCE FREE SURVIVAL AND PATTERNS OF RECURRENCE IN SQUAMOUS CELL CARCINOMA OF ORAL CAVITY: AN INSTITUTIONAL PERSPECTIVE. Journal of Postgraduate Medical Institute. 2022 Dec 31;36(4):223-9.

Alim N, Elsheikh M, Satti AA, Tabassum N, Suleiman AM. Recurrence of oral squamous cell carcinoma in surgically treated patients at Khartoum Teaching Dental Hospital retrospective cross-sectional study. BMC cancer. 2024 Jun 28;24(1):781.

Wang X, Zheng L, Zhang J. Evaluation of outcomes after conservative mandibular surgery in patients with oral squamous cell carcinoma. International Journal of Oral and Maxillofacial Surgery. 2023 Nov 1;52(11):1111-9.

Xing DT, Khor R, Gan H, Wada M, Ermongkonchai T, Ng SP. Recent research on combination of radiotherapy with targeted therapy or immunotherapy in head and neck squamous cell carcinoma: a review for radiation oncologists. Cancers. 2021 Nov 15;13(22):5716.

Trufelli DC, Araujo SE, Pires FR, Araujo VC. Complete pathologic response as a prognostic factor for squamous cell carcinoma of the oropharynx post-chemoradiotherapy. Braz J Otorhinolaryngol. 2015;81:498–504.

Kirita T, Okabe M, Natsume N, Jinbu Y. Primary tumour resection of tongue carcinoma based on response to preoperative therapy. Int J Oral Maxillofac Surg. 2002;31(3):267–72.

Alim N, Elsheikh M, Satti AA, Tabassum N, Suleiman AM. Recurrence of oral squamous cell carcinoma in surgically treated patients at Khartoum Teaching Dental Hospital retrospective cross-sectional study. BMC cancer. 2024 Jun 28;24(1):781.

Zhao X, Zhou Y, Peng G, Wen L, Hong X, Hu Y, Wu B, Liu X, Zhang Z, Xiao G, Ding Q. Final analysis of a phase II trial of neoadjuvant chemoimmunotherapy for locoregionally advanced head and neck squamous cell carcinoma. Oral oncology. 2024 Sep 1;156:106918.

Damazo BJ, Punjabi NA, Liu YF, Inman JC. Histopathologic predictors of recurrence and survival in early T stage oral tongue squamous cell carcinoma. Frontiers in Oral Health. 2024 Aug 6;5:1426709.

Petit C, Lacas B, Pignon JP, Le QT, Grégoire V, Grau C, Hackshaw A, Zackrisson B, Parmar MK, Lee JW, Ghi MG. Chemotherapy and radiotherapy in locally advanced head and neck cancer: an individual patient data network meta-analysis. The Lancet Oncology. 2021 May 1;22(5):727-36.

Ord RA. Management of the N0 Neck in Oral Cancer. Current Surgery Reports. 2023 Aug;11(8):202-9..

Lee DH, Kim GJ, Kim HB, Shin HI, Kim CS, Nam IC, Cho JH, Joo YH, Cho KJ, Sun DI, Park YH. Close surgical margins in oral and oropharyngeal cancer: do they impact prognosis?. Cancers. 2022 Jun 17;14(12):2990.

Jain PV, Mallick I, Manikantan K, Chatterjee S, Arun I, Roy P, Zameer L, Arun P. Prognostic triad: a novel method for decision-making for adjuvant treatment in stage I–II oral squamous cell carcinoma. International Journal of Oral and Maxillofacial Surgery. 2025 Jan 1;54(1):23-30.

Kreppel M, Scheer M, Drebber U, Bachtiary B, Berndt A, Rothamel D, et al. The role of clinical versus histopathological staging in patients with advanced oral squamous cell carcinoma treated with neoadjuvant radiochemotherapy followed by radical surgery. J Craniomaxillofac Surg. 2013;41(1):22–7.

Miura KI, Otsuru M, Omori K, Naruse T, Umeda M, Yamada T. Prognostic Factors in Squamous Cell Carcinoma of the Maxillary Gingiva and Hard Palate: A Retrospective Analysis From a Single Institution. Cureus. 2025 Feb 4;17(2).

Thavaraj S, Jones A. Presentation, Diagnosis and Prognosis of Squamous Cell Carcinomas of the Oral Mucosa and Oropharynx. Pathological Basis of Oral and Maxillofacial Diseases. 2025 Jan 8:498-530.

Koo BS, Lim YC, Lee JS, Lim JY, Choi EC. Recurrence and salvage treatment of squamous cell carcinoma of the oral cavity. Oral Oncol. 2006;42(8):789–94.

Li Y, Li W, Xiao H, Chen W, Lu J, Huang N, Li Q, Zhou K, Kojima I, Liu Y, Ou Y. Automated classification of pathological differentiation in head and neck squamous cell carcinoma using combined radiomics models from CET1WI and T2WI. Clinical Oral Investigations. 2025 Jan;29(1):1-2.

Yousef A, Farid Shehab MA, Ali S, El-Kader El-Fol HA, EL-Mardendly AM. Evaluation of Local Control in Buccinator Muscle Excision with the Skin Versus Buccinator Muscle Excision without the Skin in Buccal Squamous Cell Carcinoma: A Randomized Clinical Trial. Indian Journal of Public Health Research & Development. 2021 Apr 1;12(2).

Tadbir AA, Ashraf MJ, Sardari Y. Prognostic significance of stromal eosinophilic infiltration in oral squamous cell carcinoma. J Craniofac Surg. 2009;20(2):287–9.

de Matos FR, Santos Silva AR, Araújo VC, Nonaka CF, de Souza LB. Analysis of inflammatory infiltrate, perineural invasion, and risk score can indicate concurrent metastasis in squamous cell carcinoma of the tongue. J Oral Maxillofac Surg. 2012;70(7):1703–10.

Miller ME, Ferris RL, Duvvuri U, Chiosea SI. A novel classification system for perineural invasion in noncutaneous head and neck squamous cell carcinoma: histologic subcategories and patient outcomes. Am J Otolaryngol. 2012;33(2):212–5.

Goswami PR, Singh G. Perineural invasion (PNI) definition, histopathological parameters of PNI in oral squamous cell carcinoma with molecular insight and prognostic significance. Cureus. 2023 Jun 9;15(6).

Binmadi NO, Basile JR. Perineural invasion in oral squamous cell carcinoma: a discussion of significance and review of the literature. Oral Oncol. 2011;47(11):1005–10.

Jardim J, Kowalski LP, Carvalho AL. Prognostic impact of perineural invasion and lymphovascular invasion in advanced stage oral squamous cell carcinoma. Int J Oral Maxillofac Surg. 2015;44(1):23–8.

Adel M, Askari N, Dehghan A, Vaziri S, Farahani RM. Evaluation of lymphatic and vascular invasion in relation to clinicopathological factors and treatment outcome in oral cavity squamous cell carcinoma. Medicine (Baltimore). 2015;94(43):e1570.

Liao CT, Kang CJ, Hsueh C, Lee LY, Lin CY, Fan KH, et al. Analysis of risk factors of predictive local tumor control in oral cavity cancer. Ann Surg Oncol. 2008;15(3):915–22.

Abbas TS, Mahdi D, Ali MS, Al-fahham AA. Etiology, Epidemiology and Pathophysiology of Oral Squamous Cell Carcinoma: A. Health (ISSN: 2454-4191). 2025 Jun;11(06).

Rogers SN, Adatia A, Hackett S, Boscarino A, Patel A, Lowe D, Butterworth CJ. Changing trends in the microvascular reconstruction and oral rehabilitation following maxillary cancer. European Archives of Oto-Rhino-Laryngology. 2022 Aug;279(8):4113-26.

Liu CH, Chang JT, Lin SC, Cheng AJ, Hsueh C, Lin SY. Patterns of recurrence and second primary tumors in oral squamous cell carcinoma treated with surgery alone. Kaohsiung J Med Sci. 2013;29(10):554–9.

Eltohami Y, Suleiman A. Survival analysis of Sudanese oral squamous cell carcinoma patients with field of cancerization. BMC Cancer. 2024;24(1):473.

Al-Jamaei AA, Van Dijk BA, Helder MN, Forouzanfar T, Leemans CR, De Visscher JG. A population-based study of the epidemiology of oral squamous cell carcinoma in the Netherlands 1989–2018, with emphasis on young adults. International Journal of Oral and Maxillofacial Surgery. 2022 Jan 1;51(1):18-26.

Alotaibi ON. Oral and maxillofacial cancer: A 35-year retrospective analysis at a referral dental hospital in Saudi Arabia. The Saudi Dental Journal. 2022 Jan 1;34(1):56-61.

Alim N, Elsheikh M, Satti AA, Tabassum N, Suleiman AM. Recurrence of oral squamous cell carcinoma in surgically treated patients at Khartoum Teaching Dental Hospital retrospective cross-sectional study. BMC cancer. 2024 Jun 28;24(1):781.

Kim BG, Lee JJ, Lee BJ, Choi JH, Hwang DS, Kim HJ. Retrospective study on factors affecting the prognosis in oral cancer patients who underwent surgical treatment only. Maxillofac Plast Reconstr Surg. 2016;38(1):1–9.

Bui I, Bonavida B. Polarization of M2 tumor-associated macrophages (TAMs) in cancer immunotherapy. Critical Reviews™ in Oncogenesis. 2024;29(4).

Eltayeb AS, Satti A, Sulieman AM. Oral cancer awareness in Sudan: assessment of knowledge, attitude and treatment seeking behavior. Asian Pac J Cancer Prev. 2017;18(6):1645.

Proaño A, Sarrion-Perez G, Bagan L, Bagan J. Genome-Wide DNA Methylation Confirms Oral Squamous Cell Carcinomas in Proliferative Verrucous Leukoplakia as a Distinct Oral Cancer Subtype: A Case–Control Study. Cancers. 2025 Jan 13;17(2):245.

Chen Y, Zhong NN, Cao LM, Liu B, Bu LL. Surgical margins in head and neck squamous cell carcinoma: A narrative review. International Journal of Surgery. 2024 Jun 1;110(6):3680-700.

Irawati N, Hao SP. Clinicopathological parameters and locoregional recurrence in oral squamous cell carcinoma patients. Int J Head Neck Surg. 2017;6(4):161–7.

Mangulkar UR, Patil S, Jaiswal SY, Jaiswal Jr SY. Physiotherapy for trismus using Rocabado exercises following mandibulectomy for squamous cell carcinoma of the lower lip: a case report. Cureus. 2022 Nov 9;14(11).

Laskar SG, Chaukar D, Deshpande M, Chatterjee A, Sinha S, Chakraborty S, Agarwal JP, Gupta T, Budrukkar A, Murthy V, Pai P. Oral cavity adjuvant therapy (OCAT)-a phase III, randomized controlled trial of surgery followed by conventional RT (5 fr/wk) versus concurrent CT-RT versus accelerated RT (6fr/wk) in locally advanced, resectable, squamous cell carcinoma of oral cavity. European Journal of Cancer. 2023 Mar 1;181:179-87.

Fonseca D, Khemani R, Pasam MK, Tagore R, Rao BV, Kodandapani S, Rao C, Raju KV, Rao TS. Histological risk score and its role in predicting recurrence in early-stage oral squamous cell carcinomas. Indian Journal of Pathology and Microbiology. 2023 Jul 1;66(3):444-8.

Struckmeier AK, Buchbender M, Lutz R, Kesting M. Improved recurrence rates and progression-free survival in primarily surgically treated oral squamous cell carcinoma—results from a German tertiary medical center. Clin Oral Investig. 2024;28(5):262.