RESEARCH PAPER

Factors Influencing Recurrence Rates of Oral Squamous Cell Carcinoma in Surgically Treated Patients: A Retrospective Study in Pakistan

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ABSTRACT

Background: Oral Squamous Cell Carcinoma (OSCC) is a prevalent malignancy with high recurrence rates, significantly impacting survival and quality of life in affected patients. Surgical treatment is the primary approach, yet recurrence remains common, influenced by various clinical and pathological factors. Objective: To analyze the factors influencing recurrence rates in surgically treated OSCC patients and identify significant predictors of recurrence to guide treatment and follow-up strategies. Methods: This retrospective cohort study analyzed the records of 345 OSCC patients who underwent surgical treatment in Ziauddin Hospital Karachi and Jinnah Hospital Karachi from March 2022 to August 2025. Patient demographics, tumor-specific characteristics (size, stage, depth of invasion, lymph node involvement, and histological grade), and treatment details (surgical margins, adjuvant therapy) were reviewed. Recurrence rates were calculated, and statistical analyses, including multivariate logistic regression, were used to identify significant predictors of recurrence. Results: As tumor stage progresses from Stage I to Stage IV, there is a noticeable increase in the percentage of poorly differentiated tumors, rising from 20% in Stage I to 39% in Stage IV. This trend indicates that tumors tend to become less differentiated, or more aggressive, as they advance. Similarly, the proportion of moderately differentiated tumors also increases, from 15% in Stage I to 30% in Stage IV. In contrast, well-differentiated tumors, which are generally less aggressive, are relatively lower in percentage across all stages but show a gradual increase from 10% in Stage I to 22% in Stage IV. Conclusion: It is concluded that OSCC recurrence is multifactorial, with patient, tumor, and treatment-related factors playing crucial roles. Tailoring postoperative management based on these risk factors, along with lifestyle interventions, may reduce recurrence rates and improve patient outcomes. Future studies should explore molecular markers and novel therapies to further refine individualized treatment approaches..

Keywords: Oral cancer, Recurrence, Surgical treatment, Tumor stage, Histological grade, tobacco use.

How to cite this article: Wahab NU, Ashiq MA, Hanif M, Qureshi I, Shafiq S, Asghar F; Factors Influencing Recurrence Rates of Oral Squamous Cell Carcinoma in Surgically Treated Patients: A Retrospective Study in Pakistan.Int J Drug Deliv Technol. . 2026;16(10s): 61-68; DOI: 10.25258/ijddt.16.10s.8

Source of support: Nil.

Conflict of interest: Nil

INTRODUCTION

Oral Squamous Cell Carcinoma (OSCC) accounts for approximately 90% of oral malignancies and represents a major public health challenge due to its high recurrence rates and poor prognosis, especially in advanced stages. Globally, OSCC affects a substantial number of individuals each year, with a particularly high incidence in regions where risk factors such as tobacco use, alcohol consumption, and poor oral hygiene are widespread [1] . Even with advances in surgical techniques and the integration of adjuvant therapies such as radiotherapy and chemotherapy, OSCC remains challenging to treat due to its aggressive nature and tendency for local and regional recurrence[2] . For patients who undergo surgical treatment, recurrence remains a significant factor affecting survival rates and quality of life. This emphasizes the importance of understanding the multifactorial influences on OSCC recurrence rates to optimize patient outcomes. Several factors contribute to the recurrence of OSCC following surgical intervention. These include patient-specific factors, tumor characteristics, and treatment-related aspects. Each of these factors can have a profound impact on recurrence, and collectively, they highlight the need for a multidisciplinary approach in managing OSCC patients to minimize the likelihood of recurrence[3].

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The influence of patient-specific factors on OSCC recurrence cannot be underestimated. Age, gender, lifestyle habits, and comorbidities are among the most prominent contributors. Older age is often associated with higher recurrence rates, possibly due to the slower healing and reduced immune response in older patients. Gender has also been shown to play a role, with some studies indicating higher OSCC recurrence rates in males, potentially linked to higher rates of risk behaviors like smoking and alcohol consumption [4]. Tobacco use, in particular, remains a key predictor of recurrence, as the carcinogenic compounds in tobacco can promote the development of new malignancies or the progression of residual cancer cells post-surgery. Similarly, excessive alcohol consumption has a synergistic effect with tobacco in increasing OSCC recurrence risk [5]. Comorbidities such as diabetes and cardiovascular diseases may also impact recurrence rates, as they can hinder the patient's ability to recover post-surgery and weaken immune surveillance mechanisms against residual cancer cells. Tumor-specific factors are critical determinants of recurrence. The size and stage of the tumor at the time of diagnosis are directly associated with recurrence risk, with larger and more advanced tumors generally presenting a higher likelihood of recurrence. The depth of invasion is another significant factor, as deeper invasion correlates with greater local and regional recurrence rates. Moreover, lymph node involvement, especially extracapsular spread, is linked to a higher probability of recurrence [6]. Histological grading, including features like perineural invasion, lymphovascular invasion, and tumor budding, has also been associated with increased recurrence risk. Advances in molecular biology have led to the identification of specific biomarkers, such as p53 mutations, cyclin D1, and epidermal growth factor receptor (EGFR) overexpression, which are often associated with poor prognosis and increased recurrence rates in OSCC patients. Surgical management remains the primary treatment modality for OSCC, with the goal of achieving clear resection margins [7]. However, positive or close surgical margins have been consistently associated with higher recurrence rates. Achieving an adequate margin during surgery is crucial for reducing local recurrence risk, yet the anatomical complexity of the oral cavity can make this challenging. In cases where clear margins are difficult to achieve, adjunctive treatments such as radiotherapy and chemotherapy are recommended [8]. These adjuvant therapies aim to eradicate any residual microscopic disease that may contribute to recurrence, especially in patients with high-risk features like positive margins or lymph node involvement. However, the extent and timing of adjuvant therapy can also influence recurrence, as delays or suboptimal doses may reduce their efficacy [9]. Recent studies have also highlighted the role of immunotherapy and targeted therapies in OSCC management, offering potential avenues to reduce recurrence by specifically targeting cancer cells while sparing normal tissue [10]. Emerging evidence suggests that socioeconomic factors and access to healthcare may also influence recurrence rates in OSCC patients. Patients from lower socioeconomic backgrounds may experience delays in seeking treatment, receive suboptimal care, or lack access to postoperative follow-up, all of which can increase the likelihood of recurrence. Additionally, the psychological and emotional state of the patient, including levels of stress and social support, may affect adherence to postoperative care protocols and lifestyle modifications that are essential for minimizing recurrence risk [11].

Objective

The basic aim of the study is to find the factors influencing recurrence rates of oral squamous cell carcinoma in surgically treated patients in Pakistan.

METHODOLOGY

This retrospective study was conducted at Ziauddin Hospital Karachi and Jinnah Hospital Karachi from March 2022 to August 2025 . The study population consists of 345 patients diagnosed with OSCC and treated surgically, with post-treatment follow-up data available to assess recurrence status.

Inclusion criteria: Patients included were those diagnosed with OSCC and treated surgically, with complete medical records available for demographic, tumor, treatment, and follow-up data.

Exclusion criteria: Patients with incomplete records or those lost to follow-up within the first 12 months post-surgery were excluded from the analysis.

Data Collection

Data were collected from institutional records, including demographic information (age, gender, lifestyle habits, comorbidities), tumor characteristics (tumor size, location, depth of invasion, lymph node involvement, histological grade), and treatment details (type of surgical intervention, margin status, use of adjuvant therapies). Information on recurrence was gathered from follow-up records, with recurrence defined as the reappearance of OSCC at the primary site or regional lymph nodes within the follow-up period. Variables analyzed include patient-specific factors (age, gender, smoking status, alcohol consumption, comorbidities), tumor-specific factors (tumor size, stage, depth of invasion, histological grade, lymph node involvement), and treatment-specific factors (surgical margin status, type of surgical procedure, use and timing of adjuvant therapies).

Data Analysis

Data were analyzed using SPSS v29/ Descriptive statistics were used to summarize demographic and clinical characteristics. Recurrence rates were calculated, and comparisons were made across various subgroups using chi-square tests or Fisher's exact test for categorical variables and t-tests or Mann-Whitney U tests for continuous variables.

RESULTS

Data were collected from 345 patients with mean age of patients was 58.21 ± 2.34 years, ranging from 34 to 79 years. Gender differences were observed, with males (60.9% of the sample) exhibiting a slightly higher recurrence rate than females (39.1%), although this was not statistically significant. Lifestyle factors, including tobacco and alcohol use, also influenced recurrence: 32% of tobacco

users (62% of patients) experienced recurrence compared to 15% of non-users, while alcohol users (45% of patients) had a 28% recurrence rate compared to 20% among non-users.

Table 1: Patient Demographics and Clinical Characteristics

Characteristic	Details	Recurrence Rate
Age (Mean ± SD)	58.21±2.34 years (range 34–79)	Older (≥60): Higher
Gender	Male (60.9%), Female (39.1%)	Males: Higher, not significant
Tobacco Use	Yes: 62%, No: 38%	Yes: 32%, No: 15%
Alcohol Use	Yes: 45%, No: 55%	Yes: 28%, No: 20%

Tumor size and stage are associated with higher recurrence rates, with stages T3/T4 having a 38% recurrence rate compared to 15% in stages T1/T2. Depth of invasion also significantly impacted recurrence, as tumors with a depth of ≥5 mm had a 40% recurrence rate, while those with less than 5 mm depth had an 18% rate. Lymph node involvement was another key factor; patients with positive lymph nodes exhibited a 42% recurrence rate compared to 15% in those without lymph node involvement. Histological grade also influenced recurrence, with poorly differentiated tumors showing a 39% recurrence rate, whereas well-differentiated tumors had a rate of 14%.

Table 2: Tumor Characteristics

Tumor Characteristic	Details
Tumor Size & Stage	T1/T2: 15%, T3/T4: 38%
Depth of Invasion	<5 mm: 18%, ≥5 mm: 40%
Lymph Node Involvement	Positive: 42%, Negative: 15%
Histological Grade	Poorly Differentiated: 39%, Well Differentiated: 14%

Patients with positive or close surgical margins had a 50% recurrence rate, compared to an 18% rate in those with clear margins, highlighting the importance of achieving negative margins during surgery. Adjuvant therapy (radiotherapy or chemotherapy) also influenced outcomes; patients who received adjuvant therapy had a recurrence rate of 22%, while those who did not receive it had a higher recurrence rate of 30%.

Table 3: Treatment-Related Factors

Factor	Details
Surgical Margins	Positive/Close: 50%, Clear: 18%
Adjuvant Therapy	Received: 22%, Not Received: 30%
Time to Recurrence	Median time: 18 months

Advanced tumor stage (III/IV) was associated with an odds ratio (OR) of 2.8 (95% CI: 1.8–4.2), indicating a substantial increase in recurrence risk. Depth of invasion ≥5 mm had an OR of 2.4 (1.5–3.9), further emphasizing the role of tumor aggressiveness in recurrence likelihood. Positive surgical margins had the highest OR at 3.1 (2.1–4.8), underscoring the importance of achieving clear margins during surgery. Lymph node involvement also posed a significant risk, with an OR of 2.7 (1.9–4.0). Tobacco use showed a moderate association with recurrence, with an OR of 1.6 (1.1–2.4).

Table 4: Multivariate Analysis of Predictors of OSCC Recurrence

Predictor	Odds Ratio (OR)
Tumor Stage (III/IV)	2.8 (1.8–4.2)
Depth of Invasion (≥5 mm)	2.4 (1.5–3.9)
Positive Surgical Margins	3.1 (2.1–4.8)
Lymph Node Involvement	2.7 (1.9–4.0)
Tobacco Use	1.6 (1.1–2.4)

In patients under 40 years of age (45 individuals), the recurrence rate was the lowest at 12%. The middle age group, 40-59 years, consisting of 180 patients, had a recurrence rate of 25%. Among patients aged 60 and older (120 individuals), the recurrence rate was the highest at 35%.

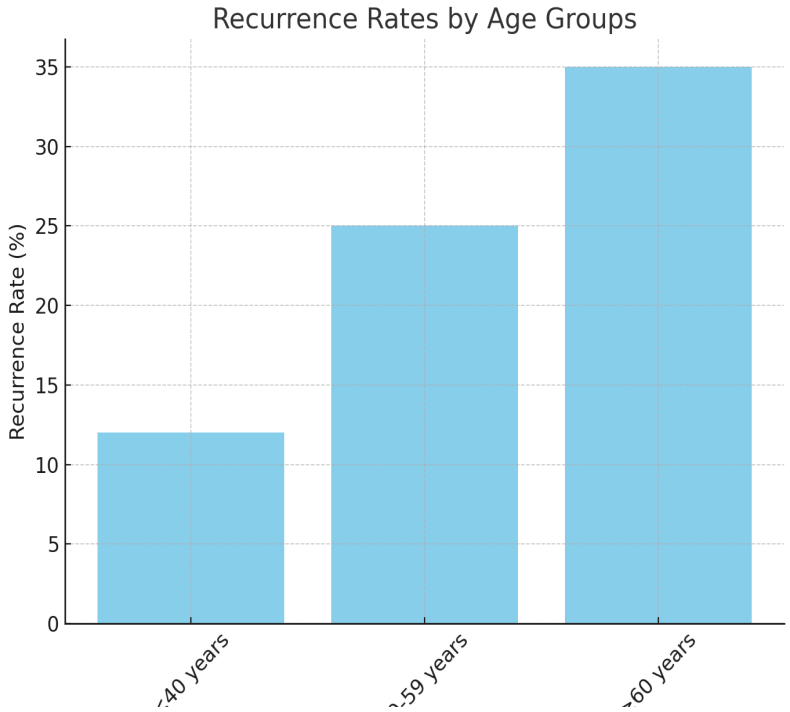
Table 5: Recurrence Rates by Age Groups

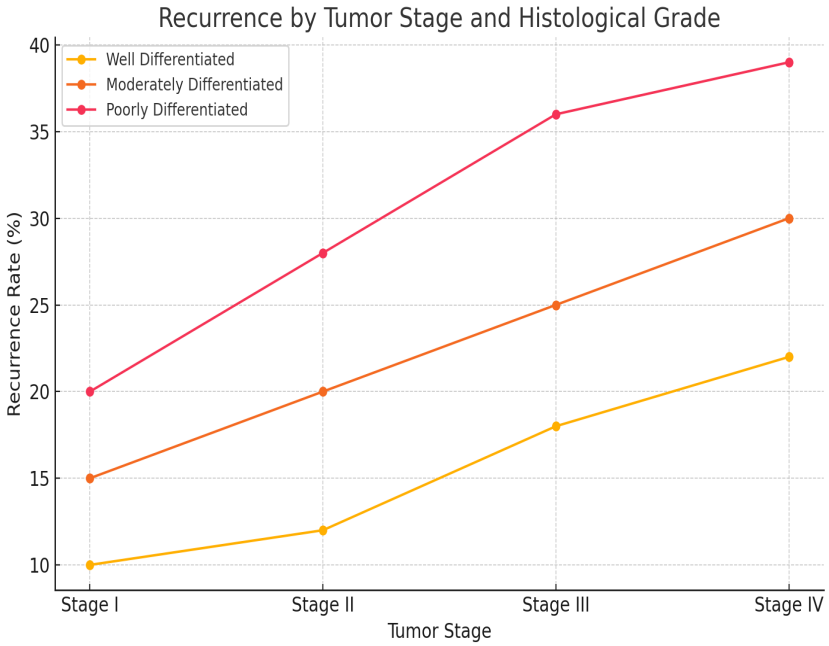
Age Group	Number of Patients	Recurrence Rate (%)
<40 years	45	12
40-59 years	180	25
≥60 years	120	35

As tumor stage progresses from Stage I to Stage IV, there is a noticeable increase in the percentage of poorly differentiated tumors, rising from 20% in Stage I to 39% in Stage IV. This trend indicates that tumors tend to become less differentiated, or more aggressive, as they advance. Similarly, the proportion of moderately differentiated tumors also increases, from 15% in Stage I to 30% in Stage IV. In contrast, well-differentiated tumors, which are generally less aggressive, are relatively lower in percentage across all stages but show a gradual increase from 10% in Stage I to 22% in Stage IV.

Table 6: Recurrence by Tumor Stage and Grade

Tumor Stage	Well Differentiated (%)	Moderately Differentiated (%)	Poorly Differentiated (%)
Stage I	10	15	20
Stage II	12	20	28
Stage III	18	25	36
Stage IV	22	30	39





DISCUSSION

The recurrence of Oral Squamous Cell Carcinoma (OSCC) after surgical treatment remains a significant clinical challenge. This study's retrospective analysis provides insights into the multifactorial nature of OSCC recurrence, highlighting patient-specific, tumor-specific, and treatment-related factors that contribute to varied recurrence rates. Here, we discuss the implications of these findings, the potential for clinical applications, and the limitations of this study. Patient-specific factors such as age, gender, and lifestyle habits were found to influence OSCC recurrence rates [13]. Older patients (≥60 years) showed higher recurrence rates, possibly due to age-related immune decline and slower healing. Additionally, lifestyle factors like tobacco and alcohol use were associated with increased recurrence, confirming the well-established risk that these carcinogens pose even after surgical intervention [14]. Addressing these modifiable risk factors, such as by offering smoking cessation and counseling post-treatment, may help reduce recurrence rates. These findings reinforce the need for a comprehensive approach to OSCC treatment that goes beyond the immediate surgical intervention, incorporating lifestyle interventions for at-risk patients. Tumor characteristics, including size, depth of invasion, lymph node involvement, and histological grade, were significant predictors of recurrence [15-18]. Larger, advanced-stage tumors, greater invasion depth, and lymph node involvement were associated with a higher likelihood of recurrence. Poorly differentiated tumors also displayed higher recurrence rates compared to well-differentiated tumors, reflecting the aggressive nature of less differentiated cancer cells [19]. These findings highlight the prognostic value of these tumor-specific factors and underscore the importance of thorough preoperative assessment. Patients with higher-risk tumor profiles may benefit from intensified monitoring and adjuvant therapies to mitigate recurrence risk [20].

The multivariate analysis further demonstrated that advanced tumor stage, depth of invasion, and lymph node involvement are independent predictors of recurrence. This suggests that, while each of these factors alone can contribute to recurrence, their combined effect likely compounds the risk [21] . Therefore, a detailed evaluation of these tumor-specific factors should guide treatment decisions, including the use of additional interventions where feasible. The study's findings indicate that positive or close surgical margins are strongly associated with higher recurrence rates, emphasizing the importance of achieving clear margins during [22-23] surgery. However, in the anatomically complex oral cavity, achieving sufficient margins without compromising functionality can be challenging. This has implications for surgical planning, particularly in high-risk patients who may benefit from a more conservative approach initially followed by adjuvant therapy [24]. The role of adjuvant therapy in reducing recurrence was also evident, with patients receiving radiotherapy or chemotherapy showing lower recurrence rates. Timely administration and adequate dosing of adjuvant therapies are critical, particularly in patients with high-risk features. The growing use of immunotherapy and molecular-targeted therapies may offer additional strategies for managing recurrence risk in OSCC, particularly for patients with challenging tumor characteristics [25].

Study Limitations

This study's retrospective design introduces certain limitations, including potential biases associated with record-based data collection. Variability in treatment protocols, the timing and doses of adjuvant therapies, and differences in follow-up duration among patients may also influence the findings. Additionally, the absence of data on genetic and molecular markers limits our ability to consider emerging biomarkers that may further stratify recurrence

risk. Prospective studies with controlled treatment variables and molecular data are needed to build on these findings and establish a more comprehensive understanding of recurrence risk in OSCC.

CONCLUSION

It is concluded that recurrence rates in Oral Squamous Cell Carcinoma are significantly influenced by a combination of patient-specific, tumor-specific, and treatment-related factors. Advanced tumor stage, depth of invasion, lymph node involvement, and surgical margins emerged as key predictors of recurrence. Personalized treatment and follow-up strategies based on these risk factors may improve patient outcomes and reduce the likelihood of recurrence.

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