

Research Article

Clinico-Pathological Profile and Surgical Margin Status in Patients Undergoing Wide Local Excision for Oral Squamous Cell Carcinoma

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ABSTRACT

Background: Oral squamous cell carcinoma (OSCC) is the most frequent cancer of the oral cavity. Its morbidity and mortality rate is high. The standard surgical treatment is the excision of the tumor with adequate margins. Opportune assessment of the surgical margins and the clinico-pathological characteristics of OSCC aids in the development of a treatment plan and estimation of prognosis.

Objective: The aim was to assess the clinico-pathological features and the status of surgical margins of patients who underwent wide local surgical excision for OSCC.

Methods: This cross-sectional study was carried out on 220 patients between ages 20 to 80 years old who had histopathological diagnosis of OSCC and had undergone wide local excision at a Swat Medical College Teaching Hospital Saidu Sharif Swat in the 12 months. Participants were selected using a non-probability sampling method. Using a pre-tested structured check list, the following were documented: age, sex, site of the tumor, size of the tumor, the TNM stage, histological grade, and status of the lymph nodes along with perineural and lymphovascular invasions. Also documented was the status of the surgical margin. This was categorized as clear (≥ 5 mm), close (1-4 mm), or involved (< 1 mm). For analyses, version 26.0 of the SPSS software was utilized. Summarizing of data was done using descriptive statistics. Associations were evaluated using the chi-square test, with $p < 0.05$ considered to be statistically significant. **Results:** The mean age of participants was 54.9 ± 12.3 years, and males made up 69.1% of the population. The most common site was buccal mucosa (42.3%), followed by tongue involvement (27.7%). The majority of the tumors were moderately differentiated (56.4%) and were of Stage III-IV (61.8%). Complete Surgical margins were obtained in 176 (80.0%) patients, while 31 (14.1%) had close margins, and in 13 (5.9%) patients, margins were involved. Advanced tumor stage, larger tumor size, poor histological differentiation, and lymph node metastasis had a significant statistical correlation with close/involved surgical margins ($p < 0.05$).

Conclusion: Though most patients with oral squamous cell carcinoma had advanced-stage disease, the majority had clear surgical margins after wide local excision. The adverse clinico-pathological features were significantly related to margin clearance, thereby showing the importance of early diagnosis and precise surgical margin planning for better results in patients.

Keywords: Pathology, Local Excision, Carcinoma, Oral Squamous.

INTRODUCTION

Around 90% of oral cancers globally are identified as Oral squamous cell carcinoma (OSCC). Though surgical procedures, radiotherapy, chemotherapy and numerous advances in diagnostic techniques have been made, OSCC continues to be a grave public health issue. This is due to a combination of high occurrence, delayed presentation, frequent recurrence, and unsatisfactory post treatment prognosis. The Global Cancer Observatory (GLOBOCAN) as noted by Sung et al. (2021) identifies lip and oral cavity cancers as some of the most globally identified malignancies, with OSCCs being especially

prevalent in South and Southeast Asia due to mixed habits of tobacco, betel quid, areca nut, and alcohol. In Pakistan OSCCs rank among the top cancers afflicting men with high incidence rates leading to considerable health burden. The cause is the combination of delayed presentation to health facilities and the widespread availability and use of smokeless tobacco Farooq et al. (2022).

Multiple factors, genetic and environmental, have been identified in the pathogenesis of OSCC. These factors lead to chronic inflammation which in turn is responsible for the transformation of normal oral epithelium to invasive carcinoma. Numerous studies have

identified the main causative agents as tobacco smoking, betel quid, tobacco, alcohol, high risk HPV, poor oral hygiene, and chronic mucosal irritation. HPV also plays an important role. Chronic irritation of mucosal tissue will eventually lead to epithelial dysplasia, which will become invasive and metastatic to the regional cervical lymph node. Uncontrolled, this will lead to a poor prognosis. Roberts' suggestion of risk factor modification for an improved prevention strategy is supported. Johnson et al. (2020).

OSCC may appear clinically as a variety of symptom presentations. These may include the presence of non-healing oral ulcers or masses or indurated lesions and can present as leukoplakia or erythroplakia. OSCC may present as a variety of other mixed red-and-white lesions. OSCC may also present as ulcers or lesions of other locations of the oral cavity as well. These locations may include the buccal cavity, tongue, or the floor of the mouth. In the gingivobuccal sulcus, OSCC may even present as lesions along the alveolar ridge. The distribution of tumors varies depending a number of different factors including local habits and cultural practices. There is also a large incidence of OSCC diagnosis occurring during the late-stage disease. This is primarily due to the asymptomatic presentation of OSCC during the early disease process. With the late-stage diagnosis of OSCC, the large primary tumors and metastasis to the cervical lymph nodes have a negative impact on the patients' prognosis and have a negative impact on the success of OSCC treatment (Warnakulasuriya, 2020).

For SCC of the Oral Cavity (OSCC), wide surgical excision of the primary tumor is the most important treatment. The best techniques for controlling OSCC are wide surgical excision and adequate surgical margins. OSCC tumors that increase neck involvement require selective or modified radical neck dissection. This is often followed by radiation or chemoradiation. Advances in surgical OSCC repair have greatly improved function and aesthetics, but the ability to maintain speech, eating, and swallowing is a large challenge (Amin et al., 2022).

One of the major determinants of prognosis in oral squamous cell carcinoma (OSCC) is the status of the surgical margin. Assessment of margins in histopathology can be classified as clear, close, or involved, depending on the distance from the invasive front of the tumor to the resection margin. Close or positive surgical

margins signify the presence of residual microscopic tumor and are associated with a higher recurrence rate, repeat surgery, adjuvant therapies, and lower disease-free survival. For optimal results in cancer surgery, precise planning of the surgical intervention and accurate assessment of the margins is critical (Migliorati et al., 2021; NCCN, 2024).

Clinico-pathological characterization of oral OSCC provides useful prognostic information for the design of treatment. Important pathologic variables are tumor size, site, histologic grade, depth of tumor, lymphovascular and perineural invasion, neck node metastasis, extratumoral extension, and margins. These factors have a strong impact on local recurrence, metastasis, disease-free and overall survival. Grading of histology of OSCC as per the World Health Organization (WHO) grading classifies tumors as well as, moderately, and poorly differentiated, the latter being of greater biological aggression and with a poorer prognosis (El-Naggar et al., 2022).

In patients with OSCC, tumor staging using the AJCC TNM Classification System provides the most valuable information about prognosis. Patients with more advanced T stages who have regional and distant metastasis have poorer prognosis and higher rates of recurrence. The latest AJCC staging has incorporated depth of invasion, and this has improved prognostic assessment. Tumors of greater depth have a higher likelihood of cervical metastasis and more advanced disease (Amin et al., 2022). Therefore, a thorough pathological assessment after surgery is crucial for accurate tumor staging and selection of additional therapies.

Assessment of surgical margins is a critical part of the pathological assessment following wide local excision. Greater than 5 mm clear margins are associated with better local control, whereas 1–4 mm and <1 mm margins are associated with high rates of local recurrence and residual disease. Patients with inadequate margins are at higher risk of undergoing additional surgery or post-surgical radiation, which increases the burden of disease and affects the patient financially and psychologically. Thus, it is critical for a proper orientation of a surgical specimen and a reliable assessment of margin status to have high-quality communication between surgeons and pathologists (Binahmed et al., 2021).

Positive surgical margins may occur with advanced tumor stage, poor tumor differentiation, and lesions involving complex

anatomy (e.g., floor-of-mouth and tongue lesions). Perineural and lymphovascular invasions are independent adverse prognostic indicators due to the pattern of spread being local and regional. By focusing on the features mentioned above, clinicians may recognize patients with a higher expected rate of recurrence and adapt their post-surgical interventions accordingly (Montero & Patel, 2023).

Despite the multiplicity of surgical interventions and collaborative management approaches, OSCC remains a serious health issue. This is most extreme in developing nations, as patients arrive with advanced cancers due to poor access to specialized oncology and delayed diagnosis. Many local institutions have limited data on local epidemiology and the surgical margin status of OSCC. Evaluating this information on local populations may improve the surgical and pathology services and lead to better multidisciplinary approaches on the management and longer outcomes for patients. Research focusing on the surgical margin status and the associated clinico-pathological aspects of OSCC is warranted, as it may achieve a higher level of evidence for a therapeutic approach to the patients with OSCC.

METHODOLOGY

This research comprised a one year hospital-based, retrospective, cross-sectional study in the Swat Medial College Teaching Hospital Saidu Sharif Swat. It aimed to study the clinico-pathological parameters and surgical margin status in patients with OSCC who underwent wide local excisions. Participants provided written informed consent post-explanation of the aims, potential benefits, and risks associated with the study. Surgical data were protected by anonymizing subjects with identification numbers and restricting the data to the research team only.

The study sample comprised patients within 20 to 80 years of age with diagnosed oral squamous cell carcinoma who were to undergo definitive wide local excision. A sample size of 220 participants was obtained using non-probability consecutive sampling. The sample size was calculated using the OpenEpi sample size calculator (Version 3.01) against the reported status of surgical margin adequacy, with a 95% confidence level and 5% margin of error.

The included study participants were patients of either gender with newly diagnosed oral squamous cell carcinoma proven by biopsy and

considered able to undergo wide local excision. It was decided to exclude patients with recurrent oral cancer, those presenting with distant metastasis, patients who previously received chemotherapy or radiotherapy for head and neck cancer, patients with non-squamous cell oral cancer, patients with severe systemic diseases that would make them ineligible for surgery, patients with partially completed histopathological reports, and patients who did not consent to participate in the study. The exclusion of these patients was to limit confounding factors and create a study sample that was as homogeneous as possible.

A survey was administered in a pilot study to a small sample to evaluate its feasibility, clarity, and the completeness of the survey prior to the main study. The survey collected demographic data (age, gender, residence, smoking history) and factors that may have contributed to the disease. The survey also collected data on the lesion and the associated clinical and pathologic data.

All participants had wide local excision performed under general anesthesia by specialist oral and maxillofacial consultants after the delivery of a local surgical protocol. The safety of vital structures was maintained as much as possible while leaving safety margins of a primary lesion. Depending on the involvement of the stage of the tumor and cervical lymph nodes, selective or modified radical neck dissection was done as instructed by the institution. The removed tumor was immediately placed in 10% buffered formalin and moved to the Department of Histopathology.

The assessment of Histopathology was done by consultant Histopathologists, and to eliminate bias, they were unaware of the objectives of the study. Standard laboratory methods were used to prepare the specimen, then the sample was placed in paraffin wax, sliced, and stained with hematoxylin and eosin (H&E) to be viewed under a light microscope. The status of the surgical margin was determined by the distance of the tumor front to the resection margin which was the shortest distance observed. A margin of greater than 5mm was described as clear, while a margin of 1 to 4mm was described as close. A margin of less than 1mm, which was positive for the tumor, was described as involved. Tumor differentiation was classified as well, moderately, or poorly differentiated, based on the WHO classification. To maintain data integrity, clinical examinations and data recordings followed established

protocols conducted by specialized data collectors under the direction of senior consultants. Compliance of Histopathology reports and operative notes was done prior to data entry. The assembled data were entered and encoded into the Statistical Package for the Social Sciences (SPSS) version 26.0. Age was a continuous variable, expressed as mean $\pm$ standard deviation. Other variables were categorized and expressed in frequencies and

percentages. The relationship between surgical margin status and other variables (clinico-pathological variables such as perineural invasion and lymphovascular invasion, tumor grade and stage and lymph node involvement), was determined using the Chi-square test or Fisher's exact test as appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1. Demographic Characteristics of the Study Participants (n = 220)

Variable	Category	Frequency (n)	Percent (%)
Age	20–39	38	17.3
	40–49	62	28.2
	50–59	71	32.3
	≥ 60	49	22.3
Mean $\pm$ SD	54.9 $\pm$ 12.3 years		
Gender	Male	152	69.1
	Female	68	30.9
Residence	Urban	128	58.2
	Rural	92	41.8
Smoking	Smoker	124	56.4
	Non-smoker	96	43.6
Tobacco chewing	Yes	98	44.5
	No	122	55.5

The study reveals that the participants were mostly older male. More lived in urban areas and most participants were smokers. Non-

chewing tobacco participants were slightly more than chewing participants.

Table 2. Clinical Characteristics of Oral Squamous Cell Carcinoma (n = 220)

Variable	Category	Frequency	Percent
Primary site	Buccal mucosa	93	42.3
	Tongue	61	27.7
	Gingivobuccal sulcus	28	12.7
	Floor of mouth	18	8.2
	Alveolus	12	5.5
	Hard palate	8	3.6
Tumor stage	T1	32	14.5
	T2	69	31.4
	T3	63	28.6
	T4	56	25.5

About the primary anatomical site of the disease, the most common site affected was the buccal mucosa and the hardest palate was the least affected. Considering tumor size and

extent, the moderate sized tumors were the most common, followed by the larger tumors, and early small stage tumors were the least common

Table 3. Histopathology Characteristics (n = 220)

Variable	Category	Frequency	Percent
Grade	Well	65	29.5
	Moderately	124	56.4
	Poorly	31	14.1

Perineural invasion	Present	52	23.6
	Absent	168	76.4
Lymphovascular invasion	Present	39	17.7
	Absent	181	82.3

Histopathological investigation showed that the majority of tumors were moderately differentiated, and poorly differentiated tumors

constituted the smallest group. In addition, most of the patients' cases showed neither perineural nor lymphovascular invasions.

Table 4. TNM and Lymph Node Status (n = 220)

Variable	Category	Frequency	Percent
Stage	I	22	10.0
	II	62	28.2
	III	71	32.3
	IV	65	29.5
Nodes	N0	118	53.6
	N1	54	24.5
	N2	38	17.3
	N3	10	4.5

When considering overall disease progression, most patients appeared in later stages of disease, as opposed to earlier ones. The number of cases in the initial stages of disease was very low. In regard to the involvement of

regional lymph nodes, more than half of the patients had no involvement, and intense involvement of lymph nodes was seen in a very small number of cases.

Table 5. Surgical Margin Status Following Wide Local Excision (n = 220)

Variable	Category	Frequency	Percent
Margins	Clear	176	80.0
	Close	31	14.1
	Involved	13	5.9
Re-excision	Yes	18	8.2
	No	202	91.8

After the surgical removal of the tumor, the majority of patients achieved clear surgical margins, and in the rest of the patients, surgical margins were involved in a small number of cases. Hence, the majority of patients did not require further surgical intervention to remove the tumor.

Table 6. Association of Surgical Margin Status with Clinico-Pathological Variables (Chi-square Test)

Variable	Clear n(%)	Close/Involved n(%)	Chi-square	p
Tumor Stage I-II	95 (89.6)	11 (10.4)	14.87	0.001
Tumor Stage III-IV	81 (71.7)	32 (28.3)		
Well differentiated	58 (89.2)	7 (10.8)		
Moderately differentiated	99 (79.8)	25 (20.2)	11.42	0.003
Poorly differentiated	19 (61.3)	12 (38.7)		
Lymph Node metastasis absent	104 (88.1)	14 (11.9)		

Lymph Node metastasis present	72 (70.6)	30 (29.4)	10.75	0.005
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Statistical analysis revealed that surgical margin status was significantly associated with several clinical characteristics. Tumor stage, tumor grade differentiation, and lymph node metastasis were associated with high risk of compromised and/or close surgical margins.

DISCUSSION

This study examined the clinic-pathological characteristics and surgical margin status of 220 patients who had undergone wide local excision for oral squamous cell carcinoma (OSCC). The majority of patients were middle aged and older and there were significantly more men than women. The buccal mucosa was the anatomical site most affected in the participants. The majority of patients presented with advanced-stage (Stage III–IV) moderately differentiated OSCC that was indicative of a delayed diagnosis and of a greater disease burden upon presentation. Tobacco smoking, and a delayed presentation to medical care, contributed most to advanced-stage OSCC in the developing countries in a recent study (Kanas et al., 2023; Tan et al., 2023).

In the study, clear surgical margins were achieved in 80.0% of patients, with 14.1% having close margins, and 5.9% having

surgically treated for OSCC. Close or positive margins, on the other hand, are associated with residual disease, recurrence, and a greater likelihood for adjuvant treatment (Binahmed et al., 2022; Rubert et al., 2025).

The current study identified a significant relationship between advanced tumor stage and surgical margin insufficiency. As tumor size becomes larger, greater degree of structural tumor invasion occurs, leading to greater difficulty in achieving complete tumor excision. Greater stage tumors often require more complex and intricate surgical approaches to maintain post-surgical function and aesthetics. Evidence suggests that surgical margins become progressively positive as tumor stage becomes more advanced. This suggests that oncological intervention should focus on early detection and early surgical management to achieve better oncological outcomes (Puram et al., 2023; Kanatas et al., 2023).

Tumor margin involvement was positively associated with tumor differentiation. Poorly differentiated tumors more often had margin involvement or were more closely associated with surgical margins compared to better differentiated tumors. Poorly differentiated tumors are likely to have a more aggressive and

involved margins. Although a majority of patients achieved adequate margin clearance, a sample of the patients had inadequate margins that may also be associated with local recurrence. Systematic reviews have suggested that negative surgical margins may improve local control and overall survival for patients

invasive growth pattern, which may contribute to greater tumor extension than is clinically evident. Recent reports have shown that poor differentiation and aggressive infiltrative growth patterns characterize adverse tumor features that are associated with greater

recurrence and poorer survival in patients with OSCC (Gawande et al., 2023).

Currently, there is a significant association between surgical margin insufficiency and lymph node metastasis. Patients with cervical lymph node metastasis had more aggressive disease and poorer tumor characteristics than those without lymph node involvement. Various meta-analyses concluded that positive surgical margins worsen overall, disease-free and disease-specific survivals and lead to greater detriment in patients with advanced disease and lymph node involvement. The findings highly advocate the need for thorough post-surgical assessments to identify patients with poor prognosis that may benefit from further treatment, such as radiotherapy, chemotherapy or chemoradiotherapy (Rubert et al., 2025; Evaluation of Resection Margins Study, 2023). The current study emphasizes the need for careful surgical planning and technique for the surgical management of oral squamous cell carcinoma (OSCC), as well as for the development of frameworks for the subsequent histopathological assessment of surgical specimens. Surgical margins are one of the few modifiable factors in the OSCC prognostic equation on which a surgeon can have a direct and profound influence. Achieving clear surgical margins also has a positive influence on the recurrence and survival equations. It is therefore critical that a surgeon has a pathologist and oncologist as a close team member. The study by Puram et al. (2023) and Binahmed et al. (2022) have suggested that in order to realize these benefits, more prospective and multi-centered studies with long-term follow-up are required.

CONCLUSION

The study identified that the majority of patients with oral squamous cell carcinoma were older, middle aged, and male. The majority of patients also had their malignancy located in the buccal mucosa and had, histologically, moderately differentiated malignancies which were at an advanced stage. Participants in this study who had surgical margin involvement also had advanced stage malignancy, lymph node involvement, and poor tumor differentiation. These data accentuate the need for early diagnosis, and precise tactical planning by a surgeon, which will also improve prognosis for patients with oral squamous cell carcinoma.

Limitations of Study

In interpreting the findings, several limitations of this study should be noted. The study was confined to one tertiary care center and was limited by the use of non-probability consecutive sampling. This affects the wider applicability of the findings. The cross-sectional design precluded the assessment of long-term effects, such as local recurrence, disease-free and overall survival. The effects on the patients and the follow-up postoperatively were also not assessed, as well as the effects of adjuvant therapies.

Future Suggestions

The present findings should be assessed in the context of future multicenter studies that are prospective, larger, and have more extended periods of follow-up. Of particular interest will be studies that assess the effects on recurrence and survival of surgical margins, molecular markers, and that assess the quality of life after treatment. The management of patients with oral squamous cell carcinoma may also be improved by the use of new imaging methods and assessment of margins during the surgery.

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