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Effects of close surgical margins on prognosis and recurrence of oral squamous cell carcinoma

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Abstract (J Korean Assoc Oral Maxillofac Surg 2025;51:161-167)

Objectives: To assess the relationships of close surgical margins with recurrence and prognosis of oral squamous cell carcinoma (OSCC).

Materials and Methods: This retrospective study consisted of 198 patients who were diagnosed with OSCC based on histopathology. All patients underwent wide local tumor resection and neck dissection, followed by or preceded by chemotherapy and/or radiotherapy. The tumor variables assessed were the pathological stage of disease, involvement site, tumor size, margin status, tumor differentiation, bone involvement if any, presence of lymphovascular or perineural invasion, adjuvant therapies including chemotherapy and radiotherapy, lymph node involvement, and ratio.

Results: The outcome of the disease based on margins was statistically significant, with close mar- gins associated with increased risk of disease fatality. Recurrence was associated with close margins, followed by adequate margins, and the relation-ship was significant within the first 2 years. Tumor stage and size significantly correlated with margin status. Close surgical margins correlated with one positive lymph node.

Conclusion: Close surgical margins are strong predictors for determining prognosis of OSCC.

Key words: Oral squamous cell carcinoma, Surgical margins, Prognostic factor, Recurrence

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I. Introduction

Oral squamous cell carcinoma (OSCC) is one of the most prevalent malignancies and the sixth most frequent cancer in the world. The global incidence of new cases annually is estimated to be approximately 170,000[1]. In India, OSCC ranks among the top three types of cancer.

Access to treatment in rural areas is inadequate, with limited health services, poor treatment outcomes, and unaffordable costs to patients. Although clinical diagnosis is determined by examining the oral cavity and tongue using current diagnostic tools, most patients present at advanced stages of the cancer, limiting chances of their survival. The cancer often occurs primarily after the fifth decade of life; however, current data show a decrease in average age. The incidence of oral cancer in young adults is relatively low and influenced by geographic, environmental, and genetic factors.

The management of OSCC is usually surgery in conjunction with adjuvant radiotherapy with or without chemotherapy. Recently, immunotherapy and targeted therapy have demonstrated promising outcomes and have been approved for patients with recurrence/metastasis[2]. Continued advancements in research as well as increased awareness and early diagnosis and treatment are crucial for improving the outcomes and survival rates.

The goal of surgical resection is to achieve complete excision of the tumor with an uninterrupted margin of the normal tissue. Despite recent advances, the 5-year survival rate is poor. Prognostic indicators are critical in determining the

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likely course and outcome of the disease and include tumor parameters (size, depth of invasion, thickness, stage), histological grade, lymph node involvement, metastasis, margins, perineural invasion, patient factors (age, lifestyle factors, comorbidities), and genetic and molecular markers[3]. Margin status, nodal status, advanced T stage, and lymphovascular and perineural invasion determine the need for postoperative adjuvant therapy.

Recurrence and disease-free survival are critical considerations in the management of OSCC. Early detection, comprehensive treatment, and regular follow-up play pivotal roles in improving outcomes. The prognostic effect of margin status has been examined in several studies; however, the results are inconclusive in terms of recurrence and overall survival.

The aim of the present study was to assess the association of close surgical margins with recurrence and prognosis of OSCC.

II. Materials and Methods

This retrospective study consisted of 198 patients from 2012 to 2018 who reported to the Department of Oral and Maxillofacial Surgery, Faculty of Dental Sciences and Department of Surgical Oncology, Ramaiah University of Applied Sciences, Bengaluru, India.

The study included patients who were diagnosed with OSCC based on histopathology and had no other history of head and neck cancers. All patients underwent wide local tumor resection and neck dissection, followed by or preceded by chemotherapy and/or radiotherapy. The demographic data, case history, and histopathology reports were analyzed to predict the recurrence and disease prognosis up to 5 years postoperatively. Incisional biopsy reports were also analyzed to validate the excisional histopathology reports. Approval was obtained from the University Ethics Committee for Human Trials of Ramaiah University of Applied Sciences (No. EC-24/133-PG-FDS).

The variables assessed in the study included demographic details, pathological stage of disease, tumor size, tumor margins, tumor differentiation, tumor site, disease prognosis, bone involvement if any, presence of lymphovascular or perineural invasion, adjuvant therapies including chemotherapy and radiotherapy, lymph node involvement, and ratio.

The margins were classified as more than adequate (>10 mm), adequate (≥5 to 10 mm), and close (<5 mm).(Fig. 1)

The treatment protocol was based on expert opinions from the surgical team, medical oncology team, and radiation oncology team as discussed during meetings. Radiotherapy or chemotherapy was advised for all patients with close or positive margins, positive lymph node, extranodal spread with advanced pathologic stage of the tumor, perineural invasion,

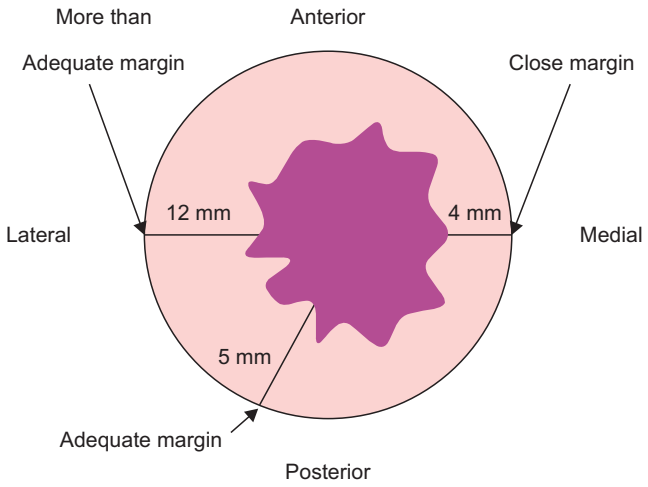

Fig. 1. Types of surgical margins.
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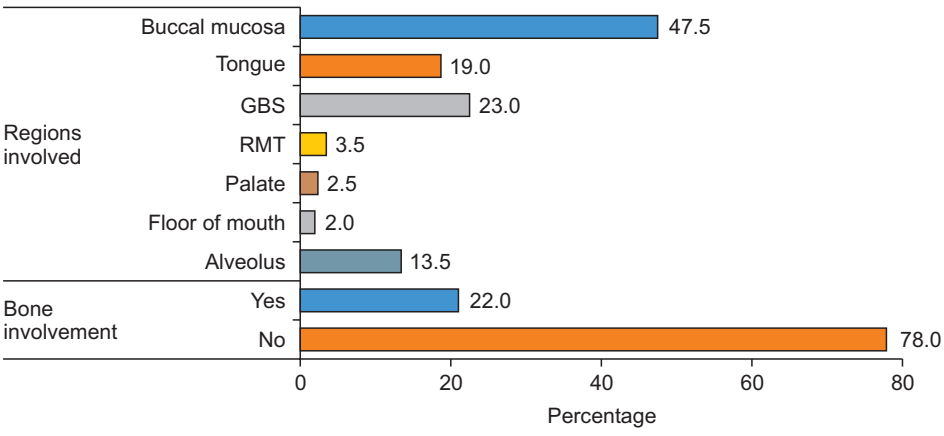

Fig. 2. Distribution of soft and hard tissue involvement among study patients. (GBS: gingivobuccal sulcus, RMT: retromolar trigone)
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or lymphovascular invasion.

The follow-up protocol for the patients included a physical examination of available patients with clinical evaluation for evidence of recurrence, metastasis, and disease-free intervals. Patients for whom a physical follow-up was not possible were contacted by telephone, and prognosis following treatment was elicited verbally through dialogue.

Prognosis was classified as disease-free survival, fatal, and recurrence including secondary recurrence. The timing of recurrence and fatality if present was also recorded. Cases of death due to reasons other than disease were excluded from the study.

IBM SPSS Statistics (ver. 22.0; IBM) was used to perform statistical analyses.

Descriptive analysis of all the explanatory and outcome parameters was performed using frequency and proportions for categorical variables and mean and standard deviation (SD) for continuous variables.

The chi square test was used to correlate the disease-free survival status, American Joint Committee on Cancer (AJCC) staging, histopathological differentiation, perineural invasion, and lymphovascular invasion with margin status.

For comparison of the mean tumor size parameters and the lymph nodes with margin status, the Kruskal–Wallis test was used followed by Dunn's post hoc test. The level of statistical significance was set at $P<0.05$.

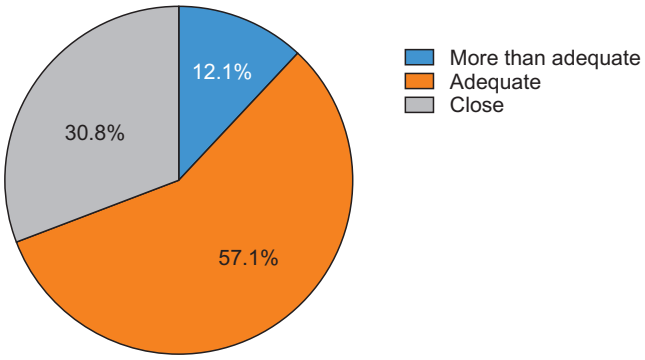

Fig. 3. Margin distribution.
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III. Results

The buccal mucosa (47.5%) was the most commonly affected site of OSCC, followed by the gingivobuccal sulcus and tongue. The majority of cases (78.0%) in the study did not show any bone involvement.(Fig. 2)

Regarding margin status, 57.1% of patients had adequate margins followed by 30.8% with close margins and 12.1% with more than adequate margins.(Fig. 3)

The majority of cases was in Stage 4a; more cases were observed in the close margins group (42.6%) followed by the adequate margins group (37.2%). The AJCC stage based on margin status was statistically significant (P=0.02).(Table 1)

Regarding the histopathological differentiation of the tumor, the majority of cases was moderately differentiated and not statistically significant based on margins.(Table 2)

The mean tumor size showed a significant difference between various margin groups. Multiple comparison between the various margin groups revealed greater tumor size (length, width, depth) in the close margins group, followed by the adequate margins group and more than adequate margins group

Table 1. Correlation of American Joint Committee on Cancer (AJCC) stage with margin status

Variable	Category	More than adequate	Adequate	Close	*P*-value
		n (%)	n (%)	n (%)	
AJCC stage	Stage 1	4 (16.7)	20 (17.7)	5 (8.2)	0.02*
	Stage 2	6 (25.0)	34 (30.0)	8 (13.1)	
	Stage 3	6 (25.0)	15 (13.3)	22 (36.1)	
	Stage 4a	8 (33.3)	42 (37.2)	26 (42.6)	
	Stage 4b	0 (0.0)	2 (1.8)	0 (0.0)	

*Statistically significant.
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Table 2. Correlation of histopathological differentiation with margin status

Variable	Category	More than adequate	Adequate	Close	*P*-value
		n (%)	n (%)	n (%)	
Histopathological differentiation	Well differentiated	8 (33.3)	43 (38.1)	14 (23.0)	0.34
	Moderately differentiated	16 (66.7)	69 (61.0)	46 (75.4)	
	Poorly differentiated	0 (0.0)	1 (0.9)	1 (1.6)	

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Table 3. Comparison of mean tumor size parameters (in cm) based on margin status

Parameter	Margin	n	Mean	Standard deviation	*P*-value	Significant difference	*P*-value
Length	More than adequate	24	2.16	1.21	<0.001*	More than adequate *vs*. adequate	0.040*
	Adequate	113	2.99	1.73		More than adequate vs. close	<0.001*
	Close	61	3.78	1.77		Adequate vs. close	0.001*
Width	More than adequate	24	1.46	0.83	0.001*	More than adequate vs. adequate	0.040*
	Adequate	113	2.08	1.36		More than adequate vs. close	0.001*
	Close	61	2.69	1.53		Adequate vs. close	0.007*
Depth	More than adequate	24	1.01	0.64	0.020*	More than adequate vs. adequate	0.380
	Adequate	109	1.32	1.05		More than adequate vs. close	0.010*
	Close	60	1.78	1.25		Adequate vs. close	0.020*

*Statistically significant.

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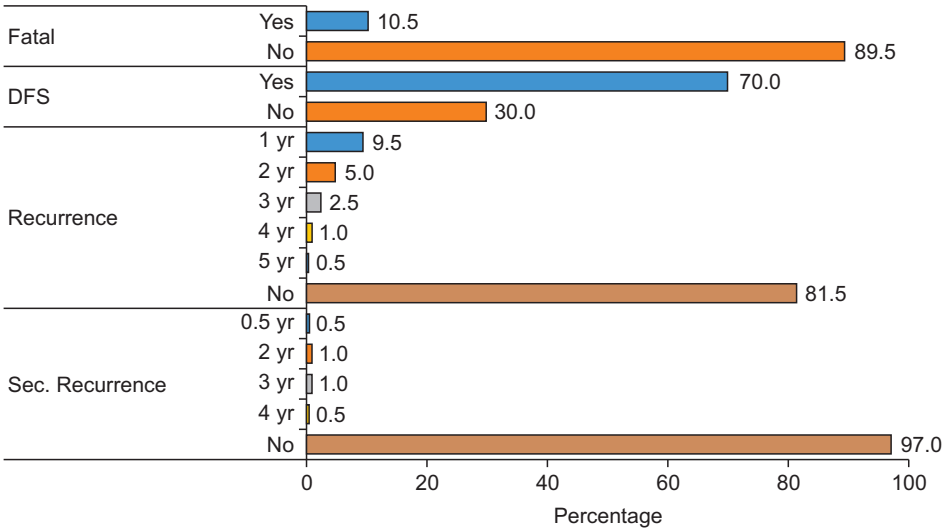

Fig. 4. Distribution of OSCC characteristics among study patients. (OSCC: oral squamous cell carcinoma, DFS: disease free survival, Sec.: secondary)
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with statistical significance.(Table 3)

Among all patients, 10.5% succumbed to the disease and 70.0% were disease-free. Similarly, the majority of cases did not show any recurrence or secondary recurrence (81.5% and 97.0%, respectively).(Fig. 4)

Patients with adequate margins had a better disease-free survival than subjects with close margins and the outcome of the disease based on margins was statistically significant. Patients with close margins had a statistically significant increased risk of disease fatality compared with subjects with adequate margins. Recurrence was more highly associated with close margins than adequate margins, which was significant within the first 2 years.(Table 4)

The mean number of total positive lymph nodes (range 0-10 nodes) with margin status did not show statistical significance between the different margins. The possibility of a positive lymph node existed in close margins. More numerous lymph nodes were excised in the close margins group (range 0-50 nodes) but was statistically non-significant.(Table 5)

The majority of cases did not show any perineural or lymphovascular invasion, and statistical significance was not observed among the types of margins.(Table 6)

IV. Discussion

OSCC is one of the most common head and neck malignancies andis of concern due to its prevalence and effect on patients' quality of life. The goal of surgical management is to achieve complete resection of the tumor along with an uninterrupted margin of normal tissue to maximize the chances of a successful outcome and minimize the likelihood of residual disease. The challenges in managing OSCC are reflected in the poor 5-year survival rate despite advancements in treatment and surgical techniques. A comprehensive and individualized approach to treatment considering margin status, nodal involvement, advanced pathological tumor stage, and lymphovascular and perineural invasion as well as other risk factors is essential for optimizing patient outcomes and determining the need for postoperative adjuvant therapy and prognosis of the disease.

Table 4. Correlation of disease outcome with margin status

Variable	Category	n	Margin status				Total	Chi-square value	*P*-value
			More than adequate	Adequate	Close	Not applicable			
Fatal	No	Count	24	108	44	1	177	27.98	0.001*
		%	100.0	96.4	72.1	100.0	89.4		
	Yes	Count	0	4	17	0	21		
		%	0.0	3.6	27.9	0.0	10.6		
Disease-free survival	No	Count	4	17	37	1	59	43.54	0.001*
		%	16.7	15.2	60.7	100.0	29.8		
	Yes	Count	20	95	24	0	139		
		%	83.3	84.8	39.3	0.0	70.2		
Recurrence	1	Count	4	7	8	0	19	20.69	0.147
		%	16.7	6.3	13.1	0.0	9.6		
	2	Count	0	2	8	0	10		
		%	0.0	1.8	13.1	0.0	5.1		
	3	Count	0	2	3	0	5		
		%	0.0	1.8	4.9	0.0	2.5		
	4	Count	0	1	1	0	2		
		%	0.0	0.9	1.6	0.0	1.0		
	5	Count	0	1	0	0	1		
		%	0.0	0.9	0.0	0.0	0.5		
	No	Count	20	99	41	1	161		
		%	83.3	88.4	67.2	100.0	81.3		
Secondary recurrence	0.5 years	Count	0	0	1	0	1	11.38	0.49
		%	0.0	0.0	1.6	0.0	0.5		
	2 years	Count	0	0	2	0	2		
		%	0.0	0.0	3.3	0.0	1.0		
	3 years	Count	1	0	1	0	2		
		%	4.2	0.0	1.6	0.0	1.0		
	4 years	Count	0	1	0	0	1		
		%	0.0	0.9	0.0	0.0	0.5		
	No	Count	23	111	57	1	192		
		%	95.8	99.1	93.4	100.0	97.0		

*Significant.

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Table 5. Comparison between the mean number of total positive and total excised lymph nodes based on margin status

Parameter	Margin	n	Mean±standard deviation	*P*-value
Total positive lymph nodes	More than adequate	24	0.96±1.71	0.29
	Adequate	113	0.73±1.40	
	Close	61	1.08±1.78	
Total lymph nodes excised	More than adequate	24	10.46±13.31	0.71
	Adequate	113	11.07±12.85	
	Close	61	12.54±13.41	

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Table 6. Comparison between perineural invasion and lymphovascular invasion based on margin status

Variable	Category	More than adequate	Adequate	Close	*P*-value
		n (%)	n (%)	n (%)	
Perineural invasion	Yes	3 (12.5)	9 (8.0)	7 (11.5)	0.66
	No	21 (87.5)	104 (92.0)	54 (88.5)	
Lymphovascular invasion	Yes	3 (12.5)	14 (12.5)	12 (19.7)	0.42
	No	21 (87.5)	98 (87.5)	49 (80.3)	

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The present study included 198 patients (64% females and 36% males) from 2012 to 2018 with ages ranging from 16-80 years (mean=51.9 years). The highest number of cases was moderately differentiated (66%), and histological differentiation based on margin status was not significant.

Buccal mucosa (47.5%) was the most commonly affected site (Fig. 2), followed by gingivobuccal sulcus (23.0%) and tongue (19.0%). In addition, 78.0% of patients had no bone involvement, 38% of patients were in Stage 4a, 24% were in Stage 2, and 22% in Stage 3. Adequate margins were

achieved in 57.1% of patients, close margins in 30.8%, and more than adequate margins in 12.1%.

Patients with adequate and more than adequate margins had a better disease-free survival compared with subjects with close margins (i.e., the disease outcome based on surgical margins showed statistical significance $P<0.001$). Patients with close margins had increased risk of disease fatality compared with subjects with adequate and more than adequate margins. Recurrence was associated with close margins, followed by adequate margins, which was significant within the first 2 years. However, no recurrence (5 years) was observed in subjects with more than adequate margins. Dillon et al.[4] reported similar results in which significantly higher disease-free survival (78%) was observed in the clear surgical margins group ($P=0.01$). They inferred that close margins are an adverse risk feature associated with a decreased disease-free and overall survival. Sutton et al.[5] also reported that close margins indicate poor prognosis in terms of local recurrence and overall survival and is a significant indicator of aggressive disease. According to Suresh et al.[6], negative margins showed a significant effect on patients' disease-free and overall survival rates. Dissanayaka et al.[7] reported that patients with clear tumor margins showed a higher survival than subjects with a close or involved margin.

Mean tumor length showed a significant difference regarding margin status. Multiple comparison between margin types revealed greater tumor size in close margins, followed by adequate margins and smaller tumor size in more than adequate margins. Bajwa et al.[8] and Dik et al.[9] also had similar results showing a significant association between tumor diameter and margin status. Tumor diameter and thickness were larger in the close margins group.

Tumor stage significantly correlated with margin status. Close margins were associated with advanced stages of the tumor; similar results were observed by Dissanayaka et al.[7], who reported tumor stage as a significant prognostic indicator of survival.

The total numbers of mean positive lymph nodes and excised lymph nodes showed no significant difference between margin stages. In patients with close surgical margins, when correlation is done with pTNM (pathological tumour, nodes and metastasis), it is seen that it is associated with one positive lymph node. This in-turn correlates with recurrence and prognosis.

The correlation of perineural invasion and lymphovascular invasion between the margins was not significant, in contrast to the results by Sutton et al.[5].

V. Conclusion

Close surgical margins are strong predictors of prognosis of OSCC. Close surgical margins are more commonly associated with a higher stage and tumor size than are adequate and more than adequate margins and can be an indicator for predicting disease prognosis.

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Authors' Contributions

Conceptualization, review, editing and supervision by K.P. Conceptualization, investigation, writing- original draft preparation by A.N. Conceptualization, Data collection by J.A.T. and S.M.

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Ethics Approval and Consent to Participate

Approval was obtained from the University Ethics Committee for Human Trials of Ramaiah University of Applied Sciences (No. EC-24/133-PG-FDS). The written informed consent was waived by the IRB because of the retrospective nature of the study.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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