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Factors associated with follow-up attendance of patients with oral squamous cell carcinoma: A retrospective cohort study

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Abstract

Background: This study examined the postoperative follow-up attendance of oral squamous cell carcinoma (OSCC) patients, evaluated some of the factors associated with it, and assessed its relationship with early detection of postoperative disease progression.

Methods: An exploratory retrospective cohort study of 430 OSCC patients was conducted. We examined associations of follow-up attendance within the first year after surgery with selected demographic and clinical factors, and with early detection of disease progression.

Results: The mean number of follow-up visits within the first year after surgery was 3.9 out of the 12 recommended at our center; few patients were fully adherent. Age ≥70 years, unmarried status, high education level, and negative history of surgery for premalignant or malignant lesions from oral cavity or other sites were significantly associated with lower follow-up attendance. Greater follow-up attendance was significantly associated with early detection of disease progression during the first year after surgery ($p = 0.025$).

Conclusions: Adherence to follow-up visits was poor. Several sociodemographic and clinical factors were related to follow-up attendance, greater follow-up attendance was significantly associated with early detection of disease progression, and these should be further explored in future research.

KEYWORDS

disease progression, operative, risk factors, squamous cell carcinoma of head and neck, surgical procedures

1 | INTRODUCTION

Oral squamous cell carcinoma (OSCC) represents a common cancer worldwide, and accounts for more than 90% of all oral malignancies.[1,2] With approximately 370 000 patients newly diagnosed with OSCC and 200 000 mortalities from OSCC each year, the global burden of this disease is high, and it constitutes a real public health issue.[3,4]

Although tremendous improvements have been made in therapeutic strategies, radical surgery remains the standard treatment of choice for resectable OSCC.[2,5–7] However, the postoperative local recurrence and regional metastasis rates of OSCCs remain high despite radical tumor resection and cervical lymph node dissection, especially among patients with advanced diseases.[5,8–11] Moreover, the development of multiple primary carcinomas is a known phenomenon in OSCC,[5,8,12–14] which can significantly impact the prognosis of the patient.

Early detection of disease progression, alongside prompt and effective treatment, are crucial in improving the prognosis of OSCC patients.[15–18] Despite the accessibility of the oral cavity and neck for inspection, local recurrence and regional metastasis can be occult in early stages. As these may remain undetectable by patients themselves, regular clinical follow-ups are crucial. At our institute, monthly follow-up visits within the first year after surgery are recommended for OSCC patients.[19] The NCCN guidelines recommend an exam every 1–3 months within the first year after surgery.[20] However, nonadherence to such follow-up regimes tends to occur in clinical practice.

To the best of our knowledge, no previous study examined the postoperative follow-up attendance of OSCC patients. Moreover, the relationship between clinical follow-up visits and early detection of local recurrence and regional metastasis remains unknown. The primary aims of this exploratory retrospective study were therefore to assess the follow-up attendance of OSCC patients following surgery, identify some of its sociodemographic and clinical correlates, and further determine its relationship with early detection of postoperative disease progression. We hypothesized that follow-up attendance would be significantly associated with early detection of disease progression during the first year after surgery.

2 | MATERIALS AND METHODS

2.1 | Study sample

A retrospective cohort study involving OSCC patients who underwent surgery at the Department of Oral and Maxillofacial Surgery of Peking University Shenzhen Hospital between August 2017 and March 2021 was conducted. All surgeries were performed by a single surgical team. At our institute, monthly follow-up visits are recommended for OSCC patients within the first year after surgery, which is more frequent than the NCCN guidelines and some other institutes from China recommend. There is a standardized protocol for follow-up instruction at our institute, and instructions for monthly follow-up visits within the first year after surgery were provided to the OSCC patients both verbally and in writing when they left the hospital. The inclusion criteria were as follows: (1) OSCC patients who underwent surgery at our institute; (2) age ≥18 years; and (3) literate in Chinese. The exclusion criteria were as follows: (1) postoperative survival time <1 year; and (2) the presence of concurrent malignancies at other body sites; and (3) patients with recurrent, metastatic, and palliative OSCCs.

2.2 | Measures and outcome definitions

Our primary outcomes involved the number of follow-up visits within the first year after surgery, and the early detection of postoperative disease progression of OSCC patients. In this study, early detection of disease progression was defined as no more than 1 month from first notice of signs and symptoms of local recurrence and/or regional metastasis to definitive diagnosis, or recurrence and/or metastasis being detected in patients with no complaints of symptoms or signs at the time of the follow-up visits. Early detection was coded dichotomously (yes/no) for the analysis. Patients received physical examinations and necessary auxiliary examinations from our senior professional doctors with rich clinical experience during follow-up visits.

The follow-up attendance of patients was derived from outpatient records. Sociodemographic, baseline clinical, and disease-related variables were collected from the medical records as factors potentially associated with follow-up attendance. Sociodemographic factors included age, sex, marital status, employment status, education level, and residential location. Employment status was divided into two groups based on whether the patients had stable jobs or not. Education levels were divided into three categories based on duration of education: low (0–6 years), middle (7–12 years), and high (≥13 years). Residential location was classified as within or outside of Shenzhen. Baseline clinical factors included body mass index (BMI, kg/m^2, coded as <18.5, >18.5 and <25, and ≥25) and comorbidity. Comorbidities were evaluated using Adult Comorbidity Evaluation-27 (ACE-27), and

divided into none-to-mild and moderate-to-severe.[21] Disease-related factors involved tumor stage and surgical history (coded yes/no). Tumor stages were divided into I–II and III–IV based on the 8th AJCC guidelines of oral cancer.[22] Surgical history included previous surgery prior to the baseline surgery for premalignant or malignant tumors from oral cavity or other sites, other types of non-oncological surgery, such as cardiac surgery or spinal repair, were not included in this variable. The investigators hypothesized that pervious surgery for premalignant or malignant lesions might be associated with concerns of patients, which may affect the treatment adherence.

2.3 | Statistical analysis

Data analyses were performed using Statistic Package for Social Science (SPSS) version 26.0 (IBM Corp., Armonk, NY). Descriptive frequencies were expressed as percentage, number, median, and mean (SDs), as appropriate. The distribution of counts of follow-up attendance approximated a Poisson distribution, and mean and variance of the model were identical. To identify the independent associated factors of follow-up attendance, univariate statistical analysis was performed using Poisson regression analysis and variables with p-value <0.1 were further analyzed using multivariable stepwise Poisson regression. Multivariate logistics regression analysis was used to identify the relationship between follow-up attendance and early detection of postoperative disease progression during the first year after surgery. Statistical significance was considered as p-value <0.05.

This study was approved by the Ethics Committee of Peking University School Shenzhen Hospital (Shenzhen, China), which waived the requirement for written informed consent, and all procedures conformed to the tenets of the Helsinki Declaration.

3 | RESULTS

3.1 | Study sample

A total of 430 OSCC patients were included in this retrospective cohort study. Among these patients, 298 were male, and the mean age was 54.9 ± 13.4 years (range, 23–89 years). The median of follow-up duration from time of surgeries was 26 months (range, 13–55 months). During the follow-up period, 363 (84.4%) patients were free of local recurrences and regional metastases, 22 (5.1%) developed local recurrence only, 39 (9.1%) developed regional metastasis only, while 6 (1.4%) developed concurrent local recurrence and regional metastasis. Postoperative disease progression was detected within 1–36 months after surgery (median, 7 months). Overall, 40.3% (n = 27) of postoperative disease progression occurred within 6 months, 83.6% (n = 56) occurred within 1 year, and 98.5% (n = 66) occurred within 2 years after surgery. The sociodemographic and clinical characteristics of all patients are summarized in Table 1.

3.2 | Follow-up attendance

The mean number of follow-up visits within the first year after surgery was 3.9 ± 2.9 out of 12 visits recommended by our treatment center (range, 0–12). During this period, 54 (12.6%) patients did not attend any follow-up visits, 255 (59.3%) attended ≤5 follow-up visits, and only 7 (1.6%) adhered to the monthly follow-up regime. The number of follow-up visits within this period is summarized in Figure 1.

3.3 | Factors associated with follow-up attendance

Based on findings from univariate analyses using Poisson regression analysis, age, BMI, marital status, employment status, surgical history, and education level ($p < 0.1$) were further analyzed using multivariable stepwise Poisson regression to identify factors independently associated with follow-up attendance of OSCC patients. In univariate analyses, sex, residential location, comorbidity, and tumor stage were not significantly associated with follow-up attendance. The results of multivariable analysis showed that patients with age ≥70, unmarried status, and negative surgical history attended significantly fewer follow-up visits within the first year after surgery. Compared with patients with high education level, patients with middle education level were more likely to attend follow-up visits, while the difference was not significant for those with low education level. No significant association was shown for BMI or employment status in the multivariable model. These results are shown in Table 2.

3.4 | Association of follow-up visits with early detection of postoperative disease progression

Overall, local recurrences and/or regional metastases were reported in 67 (15.6%) patients during the follow-up

TABLE 1 Patient characteristics.

Characteristics	*N* or median/mean value ± SD	Percentage
Total	430	100%
Sex		
Male	298	69.3%
Female	132	30.7%
Age (years)	54.9 ± 13.4 (range, 23–89)	
Follow-up duration (months)	26 (range, 13–55)	
Disease progression		
None	363	84.4%
Local recurrence	22	5.1%
Regional metastasis	39	9.1%
Both	6	1.4%
Time of disease progression		
1st year after surgery	56	83.6%
2nd year after surgery	10	14.9%
3rd year after surgery	1	1.5%
BMI		
<18.5	63	14.7%
18.5–24.9	255	59.3%
≥25	112	26.0%
Employment status		
Unemployed	210	48.8%
Employed	220	51.2%
Education level		
Low	89	20.7%
Middle	264	41.4%
High	77	17.9%
Marital status		
Married	381	88.6%
Unmarried	49	11.4%
Surgical history		
Positive	104	24.2%
Negative	326	75.8%
Tumor stage		
I–II	210	48.8%
III–IV	220	51.2%
Residential location		
Within Shenzhen	94	21.9%
Outside of Shenzhen	336	78.1%

Note: "Surgical history" refers to prior surgery for premalignant or malignant lesions in any location.
Abbreviations: BMI, body mass index; SD, standard deviation.

period, and postoperative disease progression developed within the first year after surgery in 56 (13.0%). Multivariate logistics regression analysis showed that more frequent attendance at follow-up visits during the first year was significantly associated with early detection of postoperative disease progression during the first year after surgery (odds ratio, 1.28; confidence interval, 1.03–1.59; $p = 0.025$) (Table 3).

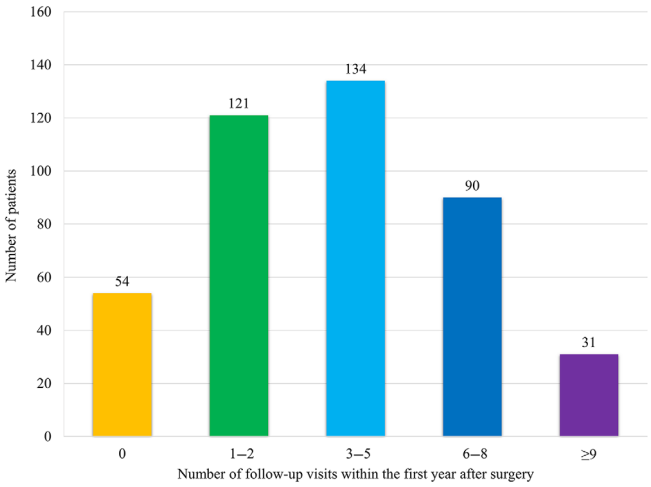

FIGURE 1 The number of follow-up visits of OSCC patients within the first year after surgery. [Color figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

This exploratory retrospective study revealed several important findings regarding the follow-up attendance of OSCC patients at our institute, only 1.6% of patients attended follow-up visits every month, this highlighted that the majority of OSCC patients did not adhere to the monthly follow-up regime within the first year after surgery.

The results suggested that greater attendance at follow-up visits during the first year was significantly associated with early detection of postoperative disease progression during the first year after surgery, including local recurrences and regional metastases. Ingeborg et al. reported that most recurrences of first primary tumors occurred within the first 2 years post-treatment.[12] In our study, most of the postoperative disease progression occurred within the first year after surgeries (56 of 67 patients). The developments of postoperative second primary carcinomas and precancerous lesions are prevalent among OSCC patients.[10,12–14,23] Despite the accessibility of the oral cavity and neck for inspection, local recurrences and regional metastases can be occult in early stages, and not easy for patients themselves to detect. Clinical follow-up appointments involving physical and auxiliary examinations are therefore crucial. Considering the high local recurrence and regional metastasis rates of OSCC, and their propensities to develop within the first year after surgery, we recommend that OSCC patients attend monthly follow-up visits during this period to allow for early detection and timely treatment for both disease progression and new primary tumors. However, it must be noted that the current NCCN practice guidelines recommend a follow-up visit every 1–3 months within the first year after surgery, which is less frequent than our regimen of follow-up visit. Further study is needed to justify the need for monthly follow-up visits within the first year after surgery.

In this study, age was significantly associated with follow-up attendance, with patients aged ≥70 years being less likely to attend follow-up visits. It is possible that this may be attributed to diminished functional capacity and limited mobility of some patients in this age group, but further study is needed to confirm the hypothesis and examine the other associated factors of barriers to adherence among older OSCC patients. Measures should be taken to promote the adherence to follow-up visits of older OSCC patients.

In terms of marital status, married patients were more likely to attend follow-up visits. In line with this, Manski et al. reported that unmarried patients were less likely to have dental care coverage in the United States,[24] while Osterberg et al. reported that unmarried patients were less likely to utilize dental services in Sweden.[25] Furthermore, Ballard et al. reported that married OSCC patients appeared to experience higher levels of hope.[26] We therefore postulate the important role of encouragement and prompting from spouses in ensuring regular follow-up attendance among OSCC patients.

The association between higher education level and better prognosis among cancer patients has been reported by several studies,[27,28] although the exact underlying mechanisms remain unknown. A previous study reported that patients with low education levels had lower oral health awareness.[29] However, in the present study, patients with high education levels were less likely to attend regular follow-up visits compared with those with middle education levels. Further study is needed to examine the relationship between education level and adherence to follow-up visits of OSCC patients.

Our findings also suggest that a prior history of surgery for premalignant or malignant lesions from oral cavity or other sites was significantly associated with follow-up attendance (note that patients with recurrent oral cancer were excluded from this study). Higher attendance at follow-up visits was observed among patients with positive surgical histories may suggest that such patients tend to be more conscious about their disease status and have higher treatment adherence. It would be valuable to examine the beliefs and expectations of these patients in future research.

While unemployment was significantly associated with lower follow-up attendance in the univariate analysis model, its significance did not persist in further multivariable stepwise Poisson regression analysis. Further

TABLE 2 Poisson regression analysis predicting follow-up attendance from selected demographic and clinical variables.

Characteristics	*N*	Median (25%, 75%)	Model 1[a]		Model 2[a]	
			OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age						
<70	373	4 (2, 6)	Reference		Reference	
≥70	57	2 (1, 4)	0.65 (0.50–0.83)	<0.001[b]	0.73 (0.56–0.94)	0.018[c]
Sex						
Female	132	3 (1, 6)	Reference			
Male	298	4 (2, 6)	1.04 (0.89–1.22)	0.587		
Comorbidity						
Moderate-to-severe	125	4 (1, 6)	Reference			
None-to-mild	305	3 (2, 6)	1.00 (0.85–1.17)	0.991		
BMI (kg/m^2)						
<18.5	63	3 (1, 5)	Reference		Reference	
18.5–24.9	255	4 (1, 6)	1.25 (0.98–1.60)	0.079[b]	1.17 (0.91–1.49)	0.224
≥25	112	4 (2, 6)	1.22 (0.97–1.53)	0.084[b]	1.19 (0.95–1.48)	0.135
Education level						
High	77	3 (1, 5)	Reference		Reference	
Middle	264	4 (2, 7)	1.42 (1.12–1.79)	0.004[b]	1.30 (1.03–1.65)	0.030[c]
Low	89	4 (2, 6)	1.26 (1.04–1.53)	0.021[b]	1.19 (0.98–1.45)	0.083
Marital status						
Married	381	4 (2, 6)	Reference		Reference	
Unmarried	49	2 (1, 5)	0.69 (0.53–0.90)	0.006[b]	0.72 (0.55–0.93)	0.012[c]
Employment status						
Employed	220	3 (1, 5)	Reference		Reference	
Unemployed	210	4 (2, 6)	1.23 (1.06–1.42)	0.005[b]	1.09 (0.93–1.27)	0.297
Surgical history						
Negative	326	3 (1, 6)	Reference		Reference	
Positive	104	4 (2, 6.25)	1.19 (1.01–1.39)	0.038[b]	1.19 (1.02–1.39)	0.030[c]
Tumor stage						
I–II	210	3 (2, 6)	Reference			
III–IV	220	4 (1, 5)	0.95 (0.82–1.10)	0.476		
Residential location						
Outside of Shenzhen	336	3.5 (1.25, 7)	Reference			
Within Shenzhen	94	4 (1, 6)	0.95 (0.80–1.13)	0.586		

Note: "Surgical history" refers to prior surgery for premalignant or malignant lesions in any location.
Abbreviations: CI, confidence interval; OR, odds ratio.
[a]Model 1 is a univariate analysis. Model 2 uses stepwise regression to screen variables based on model 1.
[b]*p*-value <0.1.
[c]*p* value <0.05.

studies are thereby warranted to examine this relationship. We further found no association between follow-up attendance and sex, comorbidities, BMI, tumor stage, and residential location.

This study had several limitations. First, other potential associated factors such as anxiety, self-efficacy, beliefs about the necessity of follow-up visits, adjuvant treatment, and socioeconomic level were not included in the present study. Second, the first postoperative year may not be sufficient to produce reliable findings regarding the follow-up attendance of OSCC patients or its influence on disease progression

TABLE 3 Multivariate logistics regression analysis examining relationship between follow-up attendance and early detection of disease progression.

		Model 1[a]		Model 2[a]	
Characteristics	***N*/Mean ± SD**	**OR (95% CI)**	***p* value**	**OR (95% CI)**	***p* value**
Follow-up attendance	4.8 ± 3.1	1.28 (0.98–1.67)	0.066	1.28 (1.03–1.59)	0.025[b]
Age					
<70	48	1 (Reference)			
≥70	8	1.04 (0.14–7.64)	0.971		
Sex					
Male	37	1 (Reference)			
Female	19	1.53 (0.29–8.09)	0.619		
Comorbidity					
None-to-mild	41	1 (Reference)			
Moderate-to-severe	15	0.85 (0.20–3.65)	0.829		
Education level					
Low	11	1 (Reference)			
Middle	38	1.75 (0.34–8.85)	0.501		
High	7	2.10 (0.18–23.91)	0.550		
Marital status					
Married	47	1 (Reference)			
Unmarried	9	0.73 (0.10–5.40)	0.760		
Employment status					
Unemployed	27	1 (Reference)			
Employed	29	0.79 (0.17–3.54)	0.754		
Surgical history					
Positive	18	1 (Reference)			
Negative	38	1.62 (0.42–6.23)	0.484		
Tumor stage					
I–II	16	1 (Reference)			
III–IV	40	0.92 (0.21–4.07)	0.917		

Note: "Surgical history" refers to prior surgery for premalignant or malignant lesions in any location.
[a]Model 1 is a multivariate analysis that incorporates all variables. Model 2 uses stepwise regression to screen variables based on Model 1.
[b]*p* value <0.05.

detection. Third, it is possible that some patients may be followed by different teams from different treatment centers, which may affect the results. Moreover, this is a single-center exploratory retrospective study. Recommendations regarding the primary outcome variable, namely follow-up attendance within the first year after surgery, was more frequent at our institute than recommended by the NCCN guidelines. Further multicenter prospective study is necessary to replicate the findings as well as to identify the relationship between the factors mentioned above and follow-up attendance.

5 | CONCLUSION

In the current exploratory retrospective study, the majority of OSCC patients did not adhere to the monthly follow-up regime during the first postoperative year, and this non-adherence was significantly associated with age ≥70 years, unmarried status, high education level, and negative surgical history for premalignant or malignant lesions. Clinical follow-up visits were preliminarily found to be associated with early detection of local recurrence and regional metastasis. Attention should be paid to the adherence to follow-up visits of OSCC patients,

especially those of elderly age, unmarried status, and negative surgical history for premalignant or malignant tumors from oral cavity or other sites. Further study is necessary to examine these and other potential barriers to adherence and seek effective measures that help improve adherences to follow-up visits of OSCC patients.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

ETHICS STATEMENT

This study was approved by the Ethics Committee of Peking University School Shenzhen Hospital (Shenzhen, China).

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