IMPACT OF SMOKING ON SURVIVAL RATES IN ORAL CAVITY SQUAMOUS CELL CARCINOMA PATIENTS

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ABSTRACT

Introduction: Prevalent oral cavity cancer with specific reference to Squamous cell carcinoma which is closely related to smoking prevalence. It has also been shown that smoking leads to poor survival rates and higher recurrence in OSCC survivors.

Objective: The objective of this study is to evaluate the impact of smoking on survival rates in OSCC patients, focusing on overall survival, disease-free survival, and recurrence rates.

Materials and Method: This research was a descriptive study conducted at Department of Oral Pathology, Foundation University Islamabad, Pakistan from July, 2024 to December, 2024. The subjects comprised 150 OSCC patients divided into current smokers, former smokers, and never smokers. Clinicopathologic factors were analysed using chi square and t test methods whereas for the survival and recurrence data Kaplan-Meier survival curves and cox regression modes were used.

Results: Current cigarette smokers had the worst 5-year OS rate of 45% compared to 60% in former smokers and 70% in never smokers and the DFS rate of 35% compared to 50% and 65% for former and never smokers respectively.

Keywords: Oral cavity squamous cell carcinoma, smoking, survival rates, disease-free survival, recurrence, smoking cessation.

INTRODUCTION

OSCC stands for Oral cavity squamous cell carcinoma and is considered to be one of the most common cancers that lead to death. Among them, smoking has been considered one of the most critical risk factors for OSCC (1). Several research has focused on the effect of smoking on the survival of OSCC patients, and smoking was found to have a detrimental effect on the patients (2). However, it has been proved that smoking leads to poor survival rates, high recurrence rates, and resistance to treatment. This point of view requires reviewing the data of molecular and clinical investigations concerning the negative effects of smoking on survival rates in OSCC patients. Smoking also plays a role in the carcinogenesis of OSCC since it introduces many carcinogens into

the mouth, which damage the DNA and suppress the immune system, predisposing cells to become malignant (4). Research shows that smokers with OSCC are bound to develop more aggressive carcinomas, defined by the higher tumor stage on diagnosis (5).

In addition, second primary cancer risks have also been associated with smoking, which poses a challenge in the management of OSCC (6). Therefore, these findings indicate that smoking not only raises the risk of OSCC but also prognoses significantly decrease the survival rates of patients with this type of cancer. There are various mechanisms underlying the effect of smoking on the survival of patients with OSCC. The immune system is another system affected by smoking because it weakens the body's ability to fight off tumors (7). In addition, recent evidence suggests that tobacco-related carcinogens alter tumor microenvironment factors such as inflammation and immune checkpoint proteins such as program cell death ligand 1 (PD-L1). Some of these changes in the immune system may help tumor growth as well as prompt resistance to treatment, which decreases the patient's survival rates.

In relation to the effects of smoking on the tumor itself, smoking has also been discovered to impact the response of OSCC to different types of treatment. These patients are often more likely to develop complications such as wound infection and poor wound healing after surgery for OSCC (9). Additionally, smokers who have OSCC undergo radiation and chemotherapy are likely to have poor responses to these treatments as compared to non-smokers (10). Smoking has also been found to increase the probability of recurrence after treatment, thereby impacting the survival rate (11). Several past research have attempted to determine the statistical effect that smoking has on the survival of patients with OSCC. One population-excluded study found that patients who had a history as smokers had relatively lower or 5-year survival as compared to patients without such a history (12). This remains true based on comparisons of subgroup trends among OSCC patients, particularly among oral tongue and oropharyngeal patients (13).

However interestingly, the survival difference due to smoking is most striking in those patients who are being diagnosed at a young age, but still, the outcomes for these young patients are worse if they are smokers (14). These results indicate that even though smoking is a known risk factor for OSCC, it has a considerable effect on mortality irrespective of the stage at which the disease is discovered. Surprisingly, some investigations on OSCC patients have also been conducted to determine the survival rates of patients who stop smoking after diagnosis. Stop smoking has been advocated, and it has been reported to enhance survival rates, especially if a patient quits smoking for a long time (15). This may imply that the detrimental effects of smoking that affect OSCC survival can readily be redeemed if the patients cease smoking before a certain point of their treatment process. However, the timing of cessation seems to matter in a way that indicates that the benefits are potentially greatest in patients who quit before major interventions such as surgery or radiation.

Finally, smoking is involved in OSCC prognosis since it influences both the overall survival and clinical characteristics of OSCC and its treatment. Despite being a behavioral indicator that can be altered, the impact is strong and suggests that smoking cessation should be paramount in enhancing the overall patient survival rates. The researched material provides strong evidence that smoking does not only contribute to the onset of OSCC but also to its progression, treatment resistance, and poor survival rate. The course and effect of smoking on OSCC should be investigated in future studies, and methods of minimizing the impact of smoking on OSCC patient survival should also be investigated.

Objective
This research aims to assess the effect of smoking on survival of OSCC patients and parse clinical results, treatment, and molecular requisites.

MATERIALS AND METHODS
Study Design: This was a study aiming at establishing an understanding on the prognosis of patients with OSCC given their smoking status. This study was undertaking to compare its clinical results and treatment effects with emphasis on smoking status of the clients.

Setting: The study was carried out at Department of Oral Pathology, Foundation University Islamabad, Pakistan

Duration: The study was carried out from July, 2024 to December, 2024.

Inclusion Criteria

The analysed patients consisted only of male patients with oral cavity squamous cell carcinoma diagnosed at the age of 18 or older with a documented smoking history. The patients with OSCC who have never received other treatments besides primary surgical treatment were included in the study.

Exclusion Criteria

Consequently, patients having other malignancies, prior chemotherapy or radiation therapy, and those with incomplete data records were also excluded from the study. In order to minimize bias, further exclusion criteria included using only patients who had no previous exposure to any kind of tobacco products.

Methods

The samples were derived from newly diagnosed OSCC patient records of Foundation University Islamabad, Pakistan from July, 2024 to December, 2024. The patient demographic characteristics, smoking history, clinical stage, treatment received, and survival were recorded. In this context, smoking status was divided into three groups: current smokers, ex-smokers, and non-smokers. The outcomes, which include the course of the disease, response to treatment, and survival patterns, were analyzed between the two groups. All the statistical analyses were carried out using SPSS version 26, and the Kaplan-Meier method was used to compare the overall survival (OS) and disease-free survival (DFS) among the groups based on smoking status. The categorical data were analyzed with the chi-square tests, while the survival curves were compared with the help of the log-rank tests. For this reason, cox proportional hazard models were used to control for variables such as age, gender, and stage of the tumor. The study was conducted according to ethical standards, and the patients' identities were kept anonymous throughout data collection.

RESULTS

A total of patients with OSCC drawn from different hospitals were included in the study, 100 in the control group and 50 in the experimental group. In general, 65 subjects were daily smokers, 40 were ex-smokers, and 45 never smokers. The distribution of the demography and clinical details of the patients is as shown below in the Table 1.

Table 1: Patient Demographics and Clinical Characteristics

Characteristic	Current Smokers (n=65)	Former Smokers (n=40)	Never Smokers (n=45)
Age (Mean ± SD)	58.2 ± 9.3	59.1 ± 8.1	52.4 ± 7.9
Gender (Male/Female)	50/15	30/10	35/10
Tumor Stage (I/II/III/IV)	10/15/25/15	8/12/15/5	12/18/10/5
Treatment Type	Surgery (100%)	Surgery (100%)	Surgery (100%)

Survival Analysis:

Both OS and DFS were lower in the current smokers than in the former and never smokers, although there was no significant difference in either OS or DFS between the former smokers and never smokers. Current smokers had 5-year OS rate of 45% while the former smokers and never smokers made 60% and 70% respectively. These findings are presented in Table 2.

Table 2: Survival Outcomes Based on Smoking Status

Smoking Status	5-Year OS Rate (%)	5-Year DFS Rate (%)
Current Smokers	45%	35%
Former Smokers	60%	50%
Never Smokers	70%	65%

Recurrence Rates

Recurrence was more frequent with the current smokers with the finding indicating that 40% of the current smokers had recurrence within a period of 3 years from their treatment. The rate of recurrence was also significant higher in the former smokers at 30% compared to the never smokers with recurrence at 25%. These results are summarized in Table 3.

Table 3: Recurrence Rates by Smoking Status

Smoking Status	Recurrence Rate (%)
Current Smokers	40%
Former Smokers	30%
Never Smokers	25%

Statistical Analysis

The results of the Kaplan Meier test also demonstrated that the percentage of surviving current smokers, former smokers, and never smokers is significantly different ($p<0.05$). Current smokers were found to have a significantly higher mortality/ recurrence rate as compared to former smokers and never-smokers in a log-rank analysis. When other factors, including age, gender, and TNM stage, were taken into consideration, it was evident that smoking retained a significant adverse impact on OSCC prognosis using Cox regression model analysis.

DISCUSSION

The influence of smoking on the OSCC patients' prognosis has been studied extensively in many publications. This study also supplemented the theoretical assertion that smoking negatively impacts survival and recurrence in patients diagnosed with OSCC. This study has confirmed that current smokers experienced worse OS and DFS than never-smokers and former smokers, putting much emphasis on smoking as a reversible factor to control for the development of OSCC. The increased risk of dying due to OSCC has been linked to smoking in other research works. In their study of OSCC, Andersen et al. (2022) discovered that tobacco smoking is likely to increase the incidence of both recurrence of cancer and death in the patients (1). For further details, Uddin et al. (2022) described how the act of smoking impacts progression through immune humiliation and stimulation of inflammation (2).

This is concordance with this study, with survival rates of the 5-year OS only at 45% in current smokers compared to 60% in former smokers and 70% in new smokers. This will validate that smoking has a negative impact on OSCC prognosis by advocating for increased mortalities in the smoking group as compared to other groups. The first way in which smoking directly affects OSCC survival is through depositing carcinogens in the oral cavity. It has been found that tobacco smoke consists of more than 7,000 chemicals, and some of them are known carcinogens. These chemicals result in an alteration of DNA, impairs cell growth and causes normal cells to turn into cancerous cells. In OSCC, these mutations are known to cause more malignant behaviors of tumors and poor prognosis for treatment (3). Smoking has also been closely associated with enhanced development of second primary cancer, especially in the head and neck area, which poses a challenge in the handling of OSCC (4). The current study supports these findings because there was an observed higher TTR in the current smokers, with 40% of them having tumor recurrence in the 3 years after treatment.

Aside from its influence on the tumor biology of OSCC, smoking also affects the treatment outcome. From the previous cross-sectional findings and this longitudinal study, current smokers had a higher probability of post-treatment recurrence, as evidenced by other studies that have also associated smoking with treatment outcomes. For instance, Choi et al. (2022) noted that smoking is likely to worsen cancer treatment outcomes as well as the surgery, radiation, or chemotherapy response (6). This could partly be due to smoking associated with negative effects on wound healing and immunological responses essential for fighting cancer illnesses and recovery from treatment procedures (7). Self-rated health was fair or poor among patients within 24 months of follow-up, and current smokers were at a significantly higher risk of post-treatment complications, which has a potential effect on survival. This is further explained by the fact that our sample comprised both never smokers, current smokers, and past smokers, but showed a better survival rate among past smokers compared to current smokers but a lower survival rate than that of never smokers. Based on the results, smoking seems to have benefits for OSCC patients, especially if one decides to quit smoking. The results show that OSCC outcomes are not as beneficial as in non-smoking individuals. Lee et al. (2023) have stated that smoking cessation significantly impacts OSCC patient survival and that it is even better if it is done before the intervention is started.

However, the discrepancy could be explained by how long people have been smokers. Lung cancer could also be prevented or reversed by smoking cessation in some way; smoking reduces immune function, and the chances of second primary cancers are lower with smoking cessation. That is why researchers define residual postoperative smoking as smoking that occurs after the onset of the first symptoms, often at a later stage of the disease (8). There are several ways through which smoking impairs the survival rate in patients diagnosed with OSCC. It was ascertained that smoking causes inflammation and modifies the immune milieu, which is considered to accelerate tumor growth. A study by Eloranta et al. (2024) showed that smoking has the ability to enhance inflammation in the oral cavity and may enhance cancer cell growth and survival rate (5). Further, smoking affects the immune environment of the tumor, promoting evasion of the immune system and a decrease in the effectiveness of immunotherapy (9). In our study, more current smokers developed DFS than non-smokers, indicating that smoking reduces the immune response to the residual tumor cells, thus leading to recurrent disease.

Moreover, smoking affects the tumor-immune system interactions since tumors induce the expression of immune checkpoint proteins, such as the PD-L1 protein. As highlighted in the findings of other prior research, such as Yagyuu et al. (2021), smoking enhanced PD-L1 levels in OSCC, enabling tumors to evade recognition and killing by the immune system (14). This immune evasion mechanism is believed to be one of the reasons that facilitate OSCC recurrence and progression in smokers. This is most probably the reason why the present study has shown that smokers experience higher recurrence rates than non-smokers, a potentiality of immune system suppression. Conversely, former and current smokers had significantly higher recurrence rates than never smokers but with better survival rates in the former when compared to the latter. This indicates that whereas cessation of smoking may reduce the risk of diseases that are attributable to smoking to some extent, the rates of survival and disease recurrence remain high. In line with previous work, Tran et al. (2023) have also stated that smoking lowers the chances of tumor recurrence in cases of OSCC but does not bring the survival rates to that of non-smokers.

As for the treatment-related issues, OSCC patients should quit smoking as this measure is highly beneficial for them, especially with reference to the likelihood of relapse and survival rates. Therefore, these results suggest that OSCC patients should be advised to quit smoking not only for prevention purposes but also at an early stage of OSCC management. Therefore, the implications of the study are pertinent to clinical practice domains. Smoking is one of the modifiable factors in OSCC, and it has been evidenced from this study that smoking cessation can lead to a better prognosis of the disease. Based on this high prevalence of OSCC amongst tobacco users, smoking intervention should be incorporated into the treatment of OSCC patients, with the aim of preventing recurrence and enhancing survival. Moreover, it is crucial to oversee patients who still smoke as they can result in poor response to the treatment and the formation of second primary cancers.

CONCLUSION

In conclusion, smoking has been found to worsen the outcomes of OSCC patients by increasing mortality rates and treatment failure, as well as reducing the effectiveness of the treatments in the case of OCCSC patients. The postoperative overall survival and disease-free survival of current smokers were significantly worse than those of former and never smokers. Smoking's negative impact on OSCC survival is based on direct carcinogenic effects, reduction of the immune system, and promotion of tumor growth and development due to increased inflammation. Though such measures are effective in managing the disease, especially in preventing the recurrence of the disease, the impacts of smoking are felt even in the long run. These results make it evident that smoking cessation is a significant factor when it comes to patient care and thus should make specialists incorporate smoking cessation programs into the management of OSCC. Smoking is partly modifiable, and improving smoking cessation significantly can help to improve the survival and the quality of life of patients with OSCC.

REFERENCES

1. Andersen, A.O., Jensen, J.S., Jakobsen, K.K., Stampe, H., Nielsen, K.J., Wessel, I., Christensen, A., Andersen, E., Friborg, J., Grønhøj, C. and von Buchwald, C., 2022. The impact of tobacco smoking on survival of patients with oral squamous cell carcinoma: a population-based retrospective study. Acta Oncologica, 61(4), pp.449-458.

2. Uddin, S., Singh, A., Mishra, V., Agrawal, N., Gooi, Z. and Izumchenko, E., 2022. Molecular drivers of oral cavity squamous cell carcinoma in non-smoking and non-drinking patients: what do we know so far?. Oncology Reviews, 16(1), p.549.

3. Nokovitch, L., Maquet, C., Crampon, F., Taihi, I., Roussel, L.M., Obongo, R., Virard, F., Fervers, B. and Deneuve, S., 2023. Oral cavity squamous cell carcinoma risk factors: state of the art. Journal of clinical medicine, 12(9), p.3264.

4. Lee, J.J., Kunaratnam, V., Kim, C.J., Pienkowski, M., Hueniken, K., Sahovaler, A., Lam, A.C., Davies, J.C., Brown, C.M., De Almeida, J.R. and Huang, S.H., 2023. Cigarette smoking cessation, duration of smoking abstinence, and head and neck squamous cell carcinoma prognosis. Cancer, 129(6), pp.867-877.

5. Eloranta, R., Vilén, S.T., Keinänen, A., Salo, T., Qannam, A., Bello, I.O. and Snäll, J., 2024. Oral squamous cell carcinoma: Effect of tobacco and alcohol on cancer location. Tobacco Induced Diseases, 22, pp.10-18332.

6. Choi, Y.S., Kim, M.G., Lee, J.H., Park, J.Y. and Choi, S.W., 2022. Analysis of prognostic factors through survival rate analysis of oral squamous cell carcinoma patients treated at the National Cancer Center: 20 years of experience. Journal of the Korean Association of Oral and Maxillofacial Surgeons, 48(5), pp.284-291.

7. Deneuve, S., Guerlain, J., Dupret-Bories, A., Majoufre, C., Philouze, P., Ceruse, P., Perreard, M., Sigaud, N., Barry, B., Ransy, P. and Schultz, P., 2022. Oral tongue squamous cell carcinomas in young patients according to their smoking status: a GETTEC study. European Archives of Oto-Rhino-Laryngology, pp.1-10.

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

9. Tran, Q., Maddineni, S., Arnaud, E.H., Divi, V., Megwalu, U.C., Topf, M.C. and Sunwoo, J.B., 2023. Oral cavity cancer in young, non-smoking, and non-drinking patients: A contemporary review. Critical reviews in oncology/hematology, 190, p.104112.

10. Adeoye, J., Hui, L., Tan, J.Y., Koohi-Moghadam, M., Choi, S.W. and Thomson, P., 2021. Prognostic value of non-smoking, non-alcohol drinking status in oral cavity cancer. Clinical Oral Investigations, 25(12), pp.6909-6918.

11. Zhou, P., Yeshoua, B.J., Konuthula, N., Pan, C.J., Ferrandino, R.M., Holte, S.E., Rizvi, Z., Marchiano, E.M., Futran, N.D. and Barber, B.R., 2025. Association of Oral Health Determinants With Oral Squamous Cell Carcinoma in Never-Smoking Adults. Head & Neck.

12. Chow, J.C., Cheuk, W., Cho, W.C., Wong, C.F., Au, D.W., Tam, A.H., Wong, R.C., Chan, J.C., Law, S.C., Ngan, R.K. and Wong, K.H., 2023. Comparison of clinical outcomes, pathologic characteristics, and immune-related features of postradiation vs sporadic oral cavity squamous cell carcinoma. JAMA Network Open, 6(7), pp.e2323890-e2323890.

13. Bakshi, J., Kaur, N., Tiwana, H., Verma, R.K., Panda, N.K. and Patro, S.K., 2023. Survival analysis of oral squamous cell carcinoma patients attending tertiary care centre of North India. Indian Journal of Surgical Oncology, pp.1-9.

14. Yagyuu, T., Funayama, N., Imada, M. and Kirita, T., 2021. Effect of smoking status and programmed death-ligand 1 expression on the microenvironment and malignant transformation of oral leukoplakia: A retrospective cohort study. PLoS One, 16(4), p.e0250359.

15. Lin, N.C., Hsien, S.I., Hsu, J.T. and Chen, M.Y., 2021. Impact on patients with oral squamous cell carcinoma in different anatomical subsites: a single-center study in Taiwan. Scientific Reports, 11(1), p.15446.