The American Journal of Medical Sciences and Pharmaceutical Research
ISSN 2689-1026 | Open Access

TYPE Original Research
PAGE NO. 24-28
DOI 10.37547/tajmspr/Volume07Issue10-04

Comprehensive Perspectives on Oral Squamous Cell Carcinoma: HPV, Epidemiological Patterns, Diagnosis, Post-Treatment Challenges

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OPEN ACCESS

SUBMITED 18 September 2025
ACCEPTED 27 September 2025
PUBLISHED 15 October 2025
VOLUME Vol.07 Issue 10 2025

CITATION
Thy Uyen Pham. (2025). Comprehensive Perspectives on Oral Squamous Cell Carcinoma: HPV, Epidemiological Patterns, Diagnosis, Post-Treatment Challenges. The American Journal of Medical Sciences and Pharmaceutical Research, 7(10), 24–28.
https://doi.org/10.37547/tajmspr/Volume07Issue10-04

Abstract

Oral Squamous Cell Carcinoma (OSCC) is the most common type of head and neck cancer, with the highest mortality rate. Traditional causes include smoking, alcohol consumption, tobacco use and betel chewing, while human papillomavirus (HPV) has recently emerged as an additional significant cause. Current challenges include a rising incidence in younger patients, variations in tumor location and biology, and early lesions that often resemble benign conditions, making timely diagnosis difficult.

HPV-positive OSCC shows a better prognosis and treatment response due to the radiosensitivity of HPV-associated tumors. Researchers have developed an HPV-positive OSCC model to study the biological mechanisms of HPV-induced disease and to identify optimal treatment intensity with low toxicity and high efficiency. Furthermore, advances in medicine, such as the use of salivary biomarkers and artificial intelligence, promise to enhance diagnosis in the future.

In addition to treatment, the issues of post-treatment life of patients need to be considered because patients often face mental and physical side effects for a long time after treatment. This review summarizes the current understanding of the role of HPV in OSCC and examines factors such as age, gender, delayed diagnosis, emerging diagnostic methods, and the influence of post-

treatment quality of life on OSCC overall.

Keywords: Postoperative nausea and vomiting, bariatric surgery, morbid obesity, multimodal prophylaxis, triple therapy, anesthesia.

Introduction

Oral Squamous Cell Carcinoma (OSCC) is the most common head and neck cancer, causing a significant health burden and mortality worldwide (AlZoubi et al., 2025). The main causes are smoking, alcohol, and tobacco consumption, and the disease is commonly found in the elderly. However, in recent years, the incidence of OSCC in young people has been reported due to HPV and lifestyle changes. Despite advances in medical technology, the survival rate of OSCC patients is often low due to late diagnosis and high recurrence rates.

HPV-positive OSCC has been shown to have different biological characteristics compared to HPV-negative OSCC. Patients with HPV-positive OSCC often have higher radiosensitivity (meaning their tumors respond better to radiation therapy), better treatment response, and better prognosis than the negative group (Modic et al., 2023). The fact that HPV is both a cause of cancer and associated with a better prognosis has prompted further research into its mechanisms, clinical applications, and the potential to reduce the intensity of treatment for patients.

In addition, many other factors, such as changing epidemiology, difficulties in diagnosis, as well as new advances in the science of diagnosis and information on the quality of life after treatment of patients, also contribute to shaping the comprehensive picture of OSCC. This review aims to systematize the current understanding of OSCC, including the role of HPV, differences in age groups and gender, diagnosis, advances in OSCC diagnostic technology, and discuss the impact of treatment of cancer on the normal life of patients.

Role of HPV in OSCC

HPV contributes greatly to the development and treatment of OSCC. Studies have shown that patients with HPV-positive OSCC often respond better to treatment than patients with HPV-negative OSCC (Modic et al., 2023). To further investigate this issue, scientists have created an HPV-positive OSCC model in immunocompetent (having a normal immune system) mice (Chen, 2023). Because HPV only infects human cells, they have transformed a mouse OSCC cell line to express HPV-16 E6/E7, then testinged in vitro and transplantinged into immunocompetent mice. A new cell line, called MOC1-HPV K1, has reproduced the radiosensitivity of HPV-positive tumors. This allowenables researchers to further studyinvestigate radiotherapy and immunotherapy in conditions that more closely resemble those of real patients. However, this model is limited because it does not originate from the oropharynx - where HPV commonly causes cancer in humans - and the genetic similarity to human tumors is not high, and it lacks the complexity of the real tumor environment.

From a scientific perspective, the radiosensitivity of HPV - positive Oropharyngeal Squamous Cell Carcinoma (OPSCC) has prompted interest in de-escalating treatment. Phase II clinical trials have shown that de-escalation of radiotherapy or chemotherapy can still maintain the treatment effect and reduce toxicity. Thereby, the lives of patients can be improved (Chen, 2023). However, these strategies should only be limited to clinical trials only because the criteria for patient selection and safe implementation are stillremain unclear. Therefore, further studies are needed to safely reduce the intensity of the treatment. Mechanistically, the better response to treatment in HPV-positive OSCC patients may be explained by tumor radiosensitivity and better immune-mediated tumor control. (Hussain et al., 2025)

Currently, approximately 30 HPV types can infect the oral cavity, leading to consequences ranging from latent infection to transformation into OSCC (Baher et al., 2025). Among them, HPV 16 and HPV 18 are high-risk strains and are most likely to transform into OSCC. Taken together, the above studies suggest a dual role for HPC in OSCC: on the one hand, it promotes cancer progression and causes cancer; on the other hand, HPV positivity in OSCC leads to better treatment outcomes

Epidemiological Patterns (Age & Gender)

Traditionally, OSCC is more common in older men, with alcohol, smoking, and tobacco being the causes. However, recent studies have shown that there has been an increase in OSCC cases in younger people worldwide. This change may be due to lifestyle changes and HPV positivity (Yang et al., 2023). In addition to the usual factors such as smoking and alcohol, genetic factors also play a role in the increasing incidence of OSCC in young adults (YA-OSCC) in some regions (Lenoci

et al., 2024). Younger people often receive more aggressive treatment from specialists than older people and therefore have higher survival rates (Yang et al., 2023). Despite their higher survival rates, their 5-year disease-free rates may be worse due to recurrence. (Lenoci et al., 2024).

Studies have shown that oral squamous cell carcinoma differ exhibits bysex-related sexdifferences. In women, tongue cancer is more common, and there are more cases without smoking or drinking. In contrast, men often have a major cause of smoking, drinking alcohol, or chewing betel nut, and often have cancer in the floor of the mouth. Women who smoke are also likely to have tumors transferred to the floor of the mouth, similar to men (Wolfer et al., 2022). In addition, women are often diagnosed five years later, possibly because they belong to the non-smoking group. These differences in tumor location may be explainattributed byto biological and genetic differencevariations. Mechanistically, OSCC tumors in men are more likely to be related to oxidative stress and immune pathways, while in women, they are more likely to be related to metabolism and VEGF signaling. Because of the gender differences in OSCC, further studies on the influence of gender in OSCC patients are needed to provide optimal treatment for patients.

Early Signs and Diagnostic Delays

The main reason for the late diagnosis of OSCC may be associated withthat patients delaying their medical examination. Failure to recognize early signs of the disease, financial difficulties, fear of cancer detection, or difficulty accessing specialized facilities are reasons why many people hesitate to seek medical attention immediately (Swaminathan et al., 2024). Symptoms such as slow-healing mouth ulcers, white/red patches, or persistent lesions are often ignored or thought to be minor, benign problems that can heal on their own over time (Gonzalez-Moles et al., 2022). Some patients self-treat with herbal medicines or folk remedies to reduce discomfort instead of going to the doctor, which further prolongs the diagnosis (Rutkowska et al., 2020). Moreover, the early stages of OSCC are often painless or have only vague symptoms, making many people subjective. Delays typically range from 45 days to nearly 6 months, causing the golden window for treatment to be missed, and many people are only diagnosed when the disease is in its late stages (Mauceri et al., 2022)

Professional delays also play a significant role, with early signs being misdiagnosed as minor lesions, benign infections, and denture irritation (Swaminathan et al., 2024). Clinicians sometimes only provide symptomatic treatment without scheduling appropriate follow-up visits, allowing cancer to develop undetected (González-Moles et al., 2022). Failure to refer patients to specialists in a timely manner is also a cause of treatment delays. Delays in treatment and diagnosis not only increase treatment costs, thereby increasing the financial burden on patients, but also reduce the patient's survival rate of patients.

To avoid delays in treatment and diagnosis, careful monitoring and not being subjective are what patients need to do to prevent cancer from developing further. Not arbitrarily intervening with unproven medical therapies is also a way to help the disease be diagnosed earlier. On the part of experts, it is necessary to closely monitor patients and disease symptoms for timely treatment, avoiding misdiagnosis that causes the disease to develop more strongly.

Advances in Detection & Prevention

In recent years, saliva has emerged as a potential, non-invasive tool for diagnosing OSCC. According to one study, several molecules, including chemerin and MMP-9 (an enzyme that degrades the extracellular matrix, enabling tumor invasion), demonstrated superior diagnostic performance in detecting OSCC using saliva, with a palatability of up to 94% and a balanced accuracy of approximately 93%. In more general head and neck cancers, actin, IL-1β, and IL-8 were also useful in detecting the disease (Khijmatgar et al., 2023). In additionAdditionally, combining multiple markers also helps to increaseenhances the ability to identify cancer. A saliva test combining TPSA, MMP-9, and IL-6 biomarkers can detect early-stage OSCC with high accuracy - identifying 90% of cases and excluding 88% of non-infected individuals (AlZoubi et al., 2025)

Artificial intelligence can also be applied to the diagnosis of OSCC. Deep learning models (Xception + Grad-CAM) achieved high accuracy in OSCC histological classification, with AUC values of around 0.93-0.94. Grad-CAM also increases transparency by visualizing image regions used in predictive diagnosis, reducing subjectivity and assisting pathologists in early detection (Stifanic et al., 2025). A systematic review of AI showed that the accuracy can reach 85%-100%. However, the studies are all based on old data, so more real-world testing is needed before AI is widely used in hospitals

(Warin & Suebnukarn, 2024).

Post-Treatment Challenges & Quality of Life

Following cancer treatment, patients often continue to face a range of psychological and physical health problems that hinder their daily lives. Common chronic effects after OSCC include oral mucositis, salivary gland dysfunction, taste disorders, dental caries, radiotherapy-induced osteonecrosis, and trismus. Each side effect significantly impairs oral function, making it difficult to eat and drink in daily life and ultimately diminishing their overall quality of life (Sanka & Xu, 2023). In addition to the impact on physical challenges, patients also experience high levels of anxiety (16%), worry, and depression (10%). This is thought to be due to limited jaw movement and persistent oral problems. Survivors have reported a lack of information about health care, side effect management, and lifestyle adjustments after treatment (Badr et al., 2017). The first year after treatment is the period of greatest decline in health and quality of life; however, most recover by the third year, with sleep quality and saliva flow reported to be improvedimprove during this period (Shen et al., 2024). However, for chemotherapy patients, dry mouth, sticky saliva, and limited daily activities persist (Nunez-Vera et al., 2024)

Given the challenges patients face in readjusting to normal life, it is essential for specialists to provide guidance on mitigating side effects and promoting effective self-care after treatment.

Conclusion

Oral squamous cell carcinoma (OSCC) remains a major burden due to delayed diagnosis, treatment toxicity, and lasting impact on quality of life. HPV's association with better outcomes enables research into treatment de-escalation, though safety and patient selection require further study. Advances in salivary biomarkers and artificial intelligence may enable earlier and more accurate diagnoses, but large-scale validation is still needed.allow earlier, more accurate diagnosis, but large-scale validation is needed. Focusing on prevention, early diagnosis, and targeted research is essential to improving outcomes and quality of life for OSCC patients

Acknowledgements

I would like to express my deepest gratitude forto Dr. Sanchita Bhatnagar, whose guidance helped withme understanding the cancer mechanisms. I am profoundly thankful to my T.A Sultan Mussakhan for invaluable feedback and thoughtful suggestions that greatly enriched this work and helped shape its direction with clarity and precision. Beyond academic guidance, he also provided valuable insight into what it truly means to work as a scientist – sharing perspective on the challenges and dedication required in a research with advice on how to start my journey on academic research. I also extend my appreciation towards Ingenious Prep for providing this program and resources that enabled the successful completion of this review.

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