



ISSN Print: 2394-7489  
ISSN Online: 2394-7497  
IJADS 2024; 10(4): 249-254  
© 2024 IJADS  
[www.oraljournal.com](http://www.oraljournal.com)  
Received: 26-10-2024  
Accepted: 20-11-2024

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## Oral squamous cell carcinoma: The impact of poorly fitting dental prostheses on oncogenesis

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DOI: <https://doi.org/10.22271/oral.2024.v10.i4d.2071>

### Abstract

Oral Squamous Cell Carcinoma (OSCC) is one of the most common malignancies in the oral region, accounting for approximately 90% of oral cancer cases. Its etiology is multifactorial, involving systemic risk factors such as smoking, alcohol consumption, and viral infections, particularly human papillomavirus (HPV). Additionally, chronic irritation from poorly fitting dental prostheses has been identified as a relevant local cofactor capable of creating an inflammatory environment that fosters malignant transformation of squamous epithelium. The literature highlights that constant friction and ulcerations caused by ill-fitting prostheses stimulate the release of reactive oxygen species and pro-inflammatory cytokines, promoting carcinogenesis. At the molecular level, mutations in tumor suppressor genes and epigenetic alterations associated with these processes have been documented. However, the specific mechanisms linking chronic mechanical irritation to OSCC development require further research. Prognosis largely depends on early diagnosis, as five-year survival rates decrease significantly in advanced cases. Emerging technologies, such as artificial intelligence and multimodal optical devices, show potential for improving early detection of premalignant lesions, complementing conventional strategies. Moreover, promoting healthy habits and regular monitoring in patients with dental prostheses are fundamental to preventing oral cancer development. In conclusion, OSCC represents a clinical and public health challenge requiring a comprehensive approach. Proper adaptation of dental prostheses, along with prevention programs, early diagnosis, and multidisciplinary management, can significantly reduce the incidence and burden of this disease in the population.

**Keywords:** Squamous cell carcinoma, Poorly fitting dental prostheses, Chronic irritation, Oral oncogenesis, Risk factors

### 1. Introduction

Oral cancer is one of the leading causes of morbidity and mortality associated with malignancies worldwide, with increasing incidence and prevalence in various regions. This type of cancer includes lesions primarily affecting the mucosa of the oral cavity and oropharynx, highly influenced by risk factors such as tobacco and alcohol consumption, as well as viral infections like Human Papillomavirus (HPV) <sup>[1, 2]</sup>. Early identification of these lesions is critical, as advanced-stage diagnosis is associated with a significant reduction in five-year survival rates <sup>[3]</sup>.

Early diagnosis and the implementation of preventive strategies play a crucial role in managing this disease. Tools such as fluorescence and multimodal optical devices have shown promising results in detecting premalignant lesions, complementing conventional clinical inspection methods <sup>[4, 5]</sup>. Moreover, advancements in artificial intelligence and deep learning have opened new possibilities for the automated identification of malignant transformations, allowing faster and more accurate patient evaluations <sup>[6, 7]</sup>.

In this context, current research emphasizes the importance of combining traditional methods of prevention and diagnosis with innovative technologies to improve clinical outcomes and reduce the burden of this disease <sup>[8, 9]</sup>.

Squamous cell carcinoma (SCC) is a type of cancer originating from squamous epithelial cells that line various body surfaces, including the skin, respiratory tract, esophagus, oral cavity, and other structures.

It is the second most common form of skin cancer after basal cell carcinoma but can also affect internal tissues. Its incidence and clinical behavior vary widely depending on anatomical location, environmental factors, and genetic predisposition.

The most common type of oral cancer is squamous cell carcinoma (SCC), accounting for approximately 90% of all malignancies in the oral region, and is most prevalent in men over 50 years old [10]. Tobacco and alcohol consumption are the primary risk factors for oral SCC, while ultraviolet (UV) radiation exposure plays a significant role in cutaneous SCC [11].

Its etiology is multifactorial, with tobacco and alcohol consumption being the main risk factors. Other contributors include HPV infection, poor oral hygiene, chronic irritation, and prolonged sun exposure in cases of lip cancer [12]. Additionally, a potential link with chronic oral inflammation has been suggested, possibly associated with the microbiome and chronic infections [13, 14].

Oral squamous cell carcinoma (OSCC) is characterized by its high aggressiveness and invasive capacity, with a tendency to metastasize primarily to cervical lymph nodes [15]. Precursor lesions of OSCC often include leukoplakia and erythroplakia, which may evolve into invasive carcinoma. However, cancer can also arise spontaneously in previously healthy mucosa, predominantly affecting the lateral border of the tongue, the floor of the mouth, and the gums [13, 16].

At the molecular level, OSCC carcinogenesis is associated with dysfunction in oncogenes and tumor suppressor genes. Mutations in genes, along with overexpression of the epidermal growth factor receptor, have been identified, accelerating tumor growth and invasion [17]. These genetic and epigenetic changes, combined with environmental factors, facilitate the malignant transformation of the squamous epithelium of the oral cavity [14, 17]. The disease is characterized by variable aggressiveness, depending on factors such as anatomical location, degree of differentiation, and extent of tumor invasion.

In the context of dental prostheses, an ill-fitting complete denture can play a significant role in the development of OSCC. Poorly fitting prostheses can cause chronic irritation, ulcerations, and repeated trauma to oral tissues, creating an environment conducive to cellular malignancy. Constant friction and chronic inflammation induced by a poorly adapted prosthesis can promote the accumulation of reactive oxygen species, as well as the production of pro-inflammatory cytokines, contributing to the emergence of premalignant lesions such as leukoplakias or erythroplakias, known risk factors for OSCC [18, 19].

The prognosis of OSCC largely depends on the stage at which it is diagnosed. Five-year survival rates remain low, hovering around 50% for patients with advanced disease, underscoring the importance of early diagnosis [15]. The standard treatment includes surgery for the resection of the primary tumor, accompanied by radiotherapy and, in some cases, chemotherapy or targeted therapies [17]. In recent years, new treatments, such as immune checkpoint inhibitors and photodynamic therapy, have emerged, offering promise for advanced or recurrent cases [18, 19].

The Mexican Ministry of Health has developed various programs focused on the prevention and control of oncological diseases, with special attention to oral cancer, whose incidence has shown a significant increase in recent years. Through the Specific Action Program for Cancer Prevention and Control, strategies are implemented to ensure

early detection and timely treatment of these pathologies, aiming to mitigate the growing impact of this type of cancer on the population [20].

The Oral Health Program, in turn, promotes preventive and educational activities aimed at preserving oral health. This program emphasizes the importance of early identification of precancerous lesions and fostering healthy habits that reduce risk factors such as tobacco and alcohol consumption, the primary drivers of the increase in oral cancer cases [21].

Efforts have also been reinforced through the integration of specialized services in pathology and oral medicine. These initiatives aim not only to ensure the timely diagnosis of severe oral diseases but also to provide specialized care to a population facing a 150% increase in oral cancer cases nationwide [22].

This review highlights the clinical relevance of identifying well-differentiated squamous cell carcinoma in patients with ill-fitting complete dentures. It establishes the impact of chronic irritation as a potential cofactor in oncogenesis and underscores the need for a multidisciplinary approach in evaluating and treating patients with dental prostheses. It is crucial that patients with poorly fitting dentures receive adequate clinical follow-up to prevent severe complications and enable early detection of suspicious lesions in the oral cavity.

Given the complexity of its etiology and the clinical implications of this type of cancer, a comprehensive analysis of the scientific literature is necessary. This review aims to explore the risk factors, molecular mechanisms, and preventive strategies associated with OSCC, with a particular emphasis on the role of ill-fitting dental prostheses as a cofactor in its development.

## 2. Methodology

A literature review was conducted to examine the association between oral squamous cell carcinoma (OSCC) and the use of ill-fitting dental prostheses. This approach aimed to synthesize and analyze the available evidence to identify patterns, risk factors, biological mechanisms, and clinical management strategies related to this association.

The objective was to identify and analyze relevant literature exploring the relationship between poorly fitted dental prostheses and chronic irritation as a cofactor in the development of OSCC.

### Inclusion criteria

- Publications in indexed and peer-reviewed journals
- Original studies, systematic reviews, narrative reviews, and case reports

### Articles published in recent years

- Focus on OSCC and its relationship with prosthetic factors.
- Articles in English and Spanish.

### Exclusion criteria

- Studies unrelated to the oral cavity or involving cancers other than OSCC.
- Duplicate publications or those with insufficient data for analysis.
- Studies conducted on animals or experimental models without clinical analyses.

### Search strategy

Recognized electronic databases such as PubMed/MEDLINE,

Scopus, Web of Science, Embase, and SciELO were consulted. Additionally, bibliographies of selected articles were reviewed to identify additional relevant studies. Keywords combined with Boolean operators were used for the search, including: "Oral squamous cell carcinoma" and "poorly fitted dentures", "Chronic irritation" and "dental prosthesis" and "oral cancer", "Prosthetic trauma" and "oral malignancy".

All relevant articles found in the databases were identified. Duplicates were removed, and inclusion/exclusion criteria were applied to titles and abstracts. Full-text articles were reviewed to assess relevance.

For the analysis and synthesis of data, the extracted information was organized into key categories such as: risk factors related to poorly adapted prostheses, biological mechanisms of chronic irritation and carcinogenesis, clinical characteristics of prosthesis-associated carcinoma, and methods for prevention, diagnosis, and clinical management. A descriptive and qualitative analysis of the information was performed, highlighting trends and gaps in current knowledge.

### Ethical considerations

No ethical approval was required as no patient data or experiments were included. All sources of information were cited in accordance with intellectual property standards.

### 3. Results

Squamous cell carcinoma (SCC) is the most common malignant neoplasm in the oral cavity, accounting for approximately 90% of cases. Its etiology is multifactorial, with risk factors including tobacco and alcohol consumption, human papillomavirus (HPV) infections, and chronic trauma, such as that caused by poorly fitted dental prostheses. This article reviews recent advances in the diagnosis, risk factors, and treatment of SCC, integrating key findings from contemporary studies. It emphasizes the importance of early detection and preventive strategies to improve patient survival and quality of life.

Oral squamous cell carcinoma (OSCC) represents a significant public health concern due to its high morbidity and mortality. According to the Global Cancer Observatory (2020), approximately 377,000 new cases of oral cancer and 177,000 related deaths were estimated worldwide [23]. The incidence varies geographically, being highest in regions such as South Asia, parts of Eastern Europe, and some areas of Latin America, where risk factors such as tobacco use and poorly adapted dental prostheses are prevalent. These differences reflect variations in risk factor prevalence and cultural practices [23].

#### 3.1 Epidemiology and Risk Factors

OSCC accounts for approximately 90% of malignant neoplasms in the oral cavity, being more prevalent in men over 50 years old. However, in recent years, an increase in cases among women and young adults has been observed, attributed to growing tobacco and alcohol consumption in these populations [10, 12]. In Mexico, a 150% increase in oral cancer incidence has been reported over the past decades, highlighting it as an emerging public health issue [22].

A study revealed significant differences in the global incidence of SCC, with the highest rates in India, Sri Lanka, and Pakistan, primarily due to the use of chewable tobacco and areca nut. In contrast, cases in Western countries are more commonly associated with alcohol consumption and HPV.

These epidemiological differences underscore the importance of region-specific prevention strategies [24].

#### Key Risk Factors

**Tobacco and alcohol consumption:** These are the main risk factors for the development of SCC in the oral cavity. Studies have shown that the combined use of tobacco and alcohol has a synergistic effect, increasing the risk of oral carcinogenesis by up to 30 times [12, 13, 25]. Tobacco contains multiple carcinogens that induce DNA mutations in oral epithelium, while alcohol acts as a solvent, facilitating the penetration of these carcinogens into epithelial cells.

- **Human papillomavirus (HPV) infection:** Primarily associated with lesions in the oropharynx, its incidence has increased due to changes in sexual behaviors [14].
- **Poor oral hygiene:** Linked to chronic inflammation and alterations in the oral microbiome, which favor the development of precursor lesions [13].
- **Chronic irritation from poorly fitted prostheses:** Constant friction and repeated ulcerations in oral tissues can trigger malignant transformations [18, 19].

#### 3.2 Molecular Mechanisms and Pathogenesis

**The development of OSCC is associated with a series of genetic and epigenetic alterations:**

- **Genetic mutations:** Recurrent mutations have been identified in genes such as TP53, PIK3CA, and CDKN2A, which are involved in cell cycle regulation and apoptosis [17].
- **Epigenetic dysregulation:** Changes such as hypermethylation of tumor suppressor genes and overexpression of the epidermal growth factor receptor (EGFR) contribute to tumor growth [14].
- **Inflammatory microenvironment:** Chronic inflammation, associated with mechanical irritation or infections, creates a favorable environment for uncontrolled proliferation and the accumulation of reactive oxygen species (ROS), promoting malignant transformation [19].

Human papillomavirus (HPV) infection, particularly genotypes 16 and 18, has emerged as a significant etiological factor in a subgroup of oral SCCs [26]. HPV can integrate its DNA into the host genome, leading to the expression of oncoproteins that inactivate key tumor suppressors such as p53 and Rb, facilitating malignant transformation. This mechanism is more prevalent in developed regions where tobacco consumption is less dominant.

#### 3.3 Chronic oral trauma and Poorly fitted dental prostheses

Chronic irritation of the oral mucosa, such as that caused by poorly fitted dental prostheses, has been implicated in oral carcinogenesis [27]. Constant mechanical trauma can induce chronic inflammation and compensatory, often abnormal, cell proliferation, increasing the risk of mutations and malignant transformation [18, 19]. Furthermore, this persistent trauma may contribute to the development of precursor lesions, such as leukoplakia, heightening the risk of progression to invasive carcinoma. However, further research is needed to confirm this association.

#### 3.4 Field Cancerization

The "field cancerization" phenomenon describes the presence of multiple areas of premalignant epithelium in the oral cavity

due to continuous and prolonged exposure to carcinogenic agents [28]. This increases the risk of recurrence and the development of multiple malignant lesions, complicating treatment strategies.

### 3.5 Clinical Presentation and Diagnosis

#### 3.5.1 Clinical Presentation

Oral SCC can manifest as chronic, non-healing ulcers, leukoplakias, erythroplakias, or exophytic masses [29]. The most common sites include the tongue, floor of the mouth, and buccal mucosa. Symptoms may be nonspecific in early stages, contributing to delayed diagnoses.

A recent case reported an unusual presentation of SCC in the floor of the mouth resembling an abscess [30]. This highlights the importance of differential diagnosis and early biopsy to identify suspicious lesions.

#### 3.5.2 Diagnosis

Early diagnosis is crucial to improving survival, as over 50% of cases are identified at advanced stages, with five-year survival rates rarely exceeding 50%. However, the implementation of new technologies has significantly enhanced early detection capabilities:

Clinical evaluation should be complemented by diagnostic techniques such as incisional biopsies and histopathological analysis [30]. Advanced imaging methods like CT and MRI are useful for determining tumor extent and characteristics.

Optical devices and fluorescence techniques allow identification of suspicious areas through changes in tissue autofluorescence, aiding in the detection of premalignant lesions like leukoplakia and erythroplakia [4, 5].

#### **Circulating tumor DNA detection is emerging as a promising tool for early diagnosis.**

Artificial intelligence and predictive models can improve diagnostic accuracy by analyzing images of oral lesions.<sup>30</sup> Recent studies have shown that deep learning algorithms can analyze oral images and predict malignant transformations with over 90% accuracy [6, 7]. This accelerates the diagnostic process and reduces human error in interpreting clinical images.

### 3.6 Treatment

#### 3.6.1 Surgical Treatment

Surgery remains the treatment of choice for localized SCC in early stages. Studies have demonstrated that salvage surgery can provide significant benefits in terms of overall survival and quality of life, despite the associated morbidity [31]. Tumor resection is the primary treatment, often complemented by radiotherapy and chemotherapy in advanced cases [17].

#### 3.6.2 Radiotherapy and Chemotherapy

These treatments are essential for inoperable or metastatic cases. Combining radiotherapy with EGFR inhibitors, such as cetuximab, has shown efficacy in improving survival in selected patients [25, 29].

#### 3.6.3 Targeted Therapies and Personalized Medicine

Advances in understanding the molecular biology of SCC have led to the development of targeted therapies, such as EGFR inhibitors. Identifying genetic and epigenetic biomarkers is crucial for the development of individualized treatments, which promises to revolutionize SCC management in the coming years [26].

### 3.6.4 Emerging Therapies

- **Immunotherapy:** Immune checkpoint inhibitors (e.g., anti-PD-1 agents) have shown promising results in advanced or metastatic cases [18].
- **Photodynamic therapy:** This technique uses light and a photosensitizing agent to selectively destroy tumor cells, with encouraging results in superficial lesions [18].
- **Targeted therapy:** EGFR inhibitors, such as cetuximab, have demonstrated efficacy in reducing tumor growth in selected patients [14].

### 3.7 Prognosis

The prognosis of OSCC primarily depends on the stage at the time of diagnosis. In early stages, five-year survival rates exceed 80%, while in advanced stages, they drop to 50% or lower [15]. Early detection and timely treatment are critical to improving clinical outcomes.

### 3.8 Prevention and Control

Primary prevention is essential to reduce the incidence of OSCC. Various researchers have emphasized the importance of reducing tobacco and alcohol consumption through strict regulation, awareness campaigns, and oral hygiene promotion, along with regular oral exams to detect premalignant lesions early [12, 13]. HPV vaccination also plays a key role in prevention, particularly in regions with high incidence rates [23].

In Mexico, the Oral Health Program and the Specific Action Program for Cancer Prevention and Control have implemented education and screening campaigns, focusing on high-risk populations [20, 21].

Oral squamous cell carcinoma remains a significant clinical challenge. Advances in diagnosis and treatment have improved outcomes, but prevention and early detection are key to reducing the global burden of this disease. A multidisciplinary approach and further research are necessary to optimize care and improve patient prognosis.

### 4. Conclusions

Oral squamous cell carcinoma (OSCC) is a highly prevalent and aggressive neoplasm, with an etiology influenced by well-established risk factors such as smoking, alcohol, and viral infections, along with local conditions like chronic irritation. This review highlights that poorly fitted dental prostheses can play a significant cofactor role in oral carcinogenesis by creating an inflammatory microenvironment that promotes the malignant transformation of squamous epithelium.

Advances in understanding the molecular mechanisms associated with OSCC, including mutations in tumor suppressor genes and epigenetic alterations, have enhanced knowledge of its pathogenesis. However, significant gaps remain in the evidence specifically linking chronic mechanical trauma to the development of oral cancer, underscoring the need for further research.

From a clinical perspective, early diagnosis remains the main challenge to improving survival rates, which remain low in advanced stages. The integration of emerging technologies, such as artificial intelligence and multimodal optical devices, holds promise for optimizing the identification of premalignant and malignant lesions, complementing traditional clinical evaluation methods. Additionally, oral health education and the promotion of healthy habits are essential strategies to reduce the incidence of this cancer.

In terms of prevention, public health programs should

prioritize the identification of local risk factors, such as chronic irritation from poorly fitted dental prostheses, and encourage the implementation of early corrective measures. This requires multidisciplinary collaboration, integrating dentists, oncologists, and other healthcare professionals to provide comprehensive and effective patient care.

In conclusion, OSCC is a complex disease that demands a comprehensive preventive, diagnostic, and therapeutic approach. Proper adaptation and follow-up of dental prostheses, along with prevention and early detection strategies, are key to mitigating the impact of this pathology on the population. Future research should focus on strengthening the evidence on local factors and exploring innovative interventions to improve clinical outcomes and reduce the burden of this disease.

#### Conflict of Interest

Not available

#### Financial Support

Not available

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#### **How to Cite This Article**

Tijerina MCT, Rangel SS, Fierro NC. Oral squamous cell carcinoma: The impact of poorly fitting dental prostheses on oncogenesis. *International Journal of Applied Dental Sciences.* 2024;10(4):249-254.

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