Current trends in oral cancer: A review

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Oral cancer remains one of the most common and challenging malignancies of the head and neck region. This review summarizes the incidence, prevalence and mortality rates associated with oral cancer. We also investigated the strategies for early diagnosis, the molecular pathway of carcinogenesis, and the current treatment modalities available for oral cancer.

Keywords: Oral cancer; oral squamous cell carcinoma; tobacco smoking; oral cancer epidemiology


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Introduction

Oral cancers (OC) represent the majority of head and neck cancers with more than half million patients being affected each year worldwide [¹]. More than 90% are squamous cell carcinomas, which are mostly attributed to exogenous factors such as tobacco smoking and heavy alcohol consumption [²]. Advances in cancer research have provided new information on the cellular and molecular processes in carcinogenesis. This has also lead to the identification of biological markers and effective treatment options. The long-term survival rates for late stages, however, remain low. The aim of the present review is to:

1) Investigate the current state of knowledge of OC by focusing on the epidemiology and the associated risk factors.

2) Describe the available strategies for diagnosis and the treatment.

The literature was reviewed for published articles related to oral cancer. Keywords used for the search were: oral cancer; oral squamous cell carcinoma; tobacco smoking; oral cancer epidemiology. The search yielded to thousands of papers. We selected the most relevant articles with a focus on oral cancer epidemiology and risk factors, the most important and innovative tools to perform a correct diagnosis, a brief description of the molecular changes that lead to OC, staging and treatment protocols.
Oral cancer epidemiology

OC is the eighth most common cancer in the world, with the highest prevalence among men (5-year prevalence in men: 401,075) [2]. According to Ferlay et al, the worldwide cases of oral cancer in 2012 in both sexes were about 300,000 (2.1% of the total cancers) and approximately 145,000 cases were fatal[3]. According to the American Cancer society the incidence of OC is higher in developed countries when compared to developing countries, but the mortality rates remain higher in developing countries. In developing countries the incidence of OC is 107,700 in males and the estimated deaths are 61,200 [4].

In south-central Asia, OC is one of the most frequent types of cancer. In India the incidence rate is 12.6 per 100 000 population, and in other countries of Asia OC remains one of the most common cancers [3,6]. Of interest, the incidence rate remains high in several developed countries such as Denmark, Poland, Germany, Scotland, and also in Australia, Japan, New Zealand and the USA [7, 8].

Survival Rates

According to the Surveillance, Epidemiology and End Results Program the overall 5-year relative survival rate is 62.2%. The 5-year survival rate of late-stage OC is only 20% and it is approximately 82% for early stage OC (localized tumor, confined to primary site) [9]. In USA from 1983 to 2006, the five-year survival rate has increased from 52.5% to 60.8% within the time period [10].

Data from the World Health Organization showed a negative trend in the survival rates between 2005-2010 in some countries (e.g., Brazil, Egypt, Germany, Japan, Netherlands, Poland, United Kingdom) [11] where the number of deaths has increased.

Demographic and anatomic sites

Oral cancer arises from mucosa lining of the oral cavity or from the lips. The most common type is squamous cell carcinoma, and the histological grade can vary from well-differentiated keratinizing to un-differentiated non-keratinizing with a high tendency to metastasize.

In the United States the median age at diagnosis for cancer of the oral cavity is 64.5 years of age [12]. The tongue remains the main site affected [13-17], particularly the lateral/ventral posterior area, in older males individuals [18] (Figure 1). Interestingly, a new trend emerged during the last 20 years; the rate of OC (especially tongue cancer) increased in younger patients without any apparent and common risk factors such as tobacco or alcohol consumption [19, 20]. The increased trend of OC in younger patients merits further investigation. Data from 2006-2010 show that the total percentage of cancer of the tongue who occurred in people younger than 45 years old is 7.5% whereas the median age at diagnosis for tongue cancer is 61 years of age [21]. The other most involved sites are the lips (17%) and the floor of the mouth (14%). Lip cancer, especially the lower lip, is typically observed in people who are exposed to sunlight (e.g., fishermen, farmers, skiers and windsurfers) [22].

Risk factors

Major risk factors

Tobacco and Alcohol

The major risk factors associated with OC are tobacco use, in any available forms, and heavy alcohol consumption (people who drink five to eight drinks per day with one drink containing 1.5 oz or 10-15 g of alcohol) [23, 24]. The combined effects of alcohol and tobacco smoking have been shown to be synergistic. Of interest, a recent study showed that drinking is inversely associated with OC in non-smoking betel quid non-chewing individuals [25].

The risk for developing OC is five to nine times greater for smokers than non-smokers [26, 27]. The mechanisms of oral carcinogenesis is induced by the tobacco smoking constituents [28]. In particular the polymorphic variability in the enzymes involved in biotransformation of tobacco-related pro-carcinogens plays an important role in modulating oral cancer susceptibility [29]. Alcohol consumption is correlated to oral cancer because many chemical carcinogens derived from alcohol degradation are metabolized into active forms that have deleterious effects on organisms. Ethanol is
oxidized to acetaldehyde, a suspected carcinogen \[30\].

**Areca-nut and betel-quid**

Another common risk factor is betel-quid and areca-nut chewing. Betel-quid and areca-nut chewing are common social and cultural habits in many parts of Asia. Betel-quid consists of betel leaf, areca nut and slaked lime to which tobacco is often added. Frequent areca nut chewing is carcinogenic to humans \[31\]; arecoline, an alkaloid present in areca nut, causes cell death, apoptosis, and cell cycle arrest of epithelial cells contributing to the pathogenesis of oral carcinogenesis \[32, 33\].

**Age and family history of cancer**

Age indicates a temporal component in the biochemical and biophysical processes of cells that allow malignant transformation or the reduction of the immune system competence \[2\]. Specifically, the long-term exposure to risk factors may affect the gene products that control epithelial cell proliferation and death resulting in an uncontrolled malignant proliferation of cells \[22\]. Also, family history of oral cancer plays an important role and is considered a risk factor. However, more studies are necessary to elucidate which molecules and genes are responsible for oral cancer susceptibility in families. Family history of OC is mostly associated with an onset of the disease at an early age (about 45 years old) \[34\]. OC is also seen in family members without habits such as tobacco chewing, smoking or alcohol consumption \[35\].

**HPV infection**

Although the association between HPV infection and oropharyngeal cancer is now well established, it is still unclear whether HPV infection may lead to OC as well. Several studies suggest an association between human papillomavirus (HPV) infection and oropharyngeal cancers \[36\], particularly HPV 16 (90-95% of HPV-positive tumors). In the US there has been a recent increasing incidence of cancer of the oropharynx due to persistent HPV infection, especially among young white men \[37\]. HPV oncoproteins E6 and E7 inactivate the retinoblastoma RB pathway, cause TP53 degradation and P16 upregulation leading to HPV-associated squamous cell carcinoma of the oropharynx. Of interest, the 3-year survival of these cancers is significantly better than for conventional squamous cell carcinoma (82.4% vs. 57.1%); the prognosis may also be improved if the tumor is p16 positive regardless of HPV status.

The role of the protective effect of HPV vaccines against oropharyngeal cancer remains unclear \[38\]. However, a recent randomized controlled trial has shown that the prevalence of oral HPV four years after vaccination is lower when compared to women who did not receive the vaccine. This suggests that the vaccine may have potentially important implications for prevention of increasingly common HPV-associated oropharyngeal cancers \[39\].

**Immunosuppression**

Immunosuppressed subjects individuals are at increased risk for malignant tumor of the oral cavity and elsewhere in the body \[40\]. In particular HIV-infected individuals may develop OC, non-Hodgkin lymphoma and Kaposi sarcoma. Also transplant patients are at risk for multiple malignancies including OC \[41\].

**UV light and others**

A higher incidence of lip cancer, compared to the one of the labial mucosa, confirms the role of sun exposure in the carcinogenesis rather than tobacco smoking \[42\]. Finally, individuals affected by Plummer-Vinson syndrome (iron deficiency anemia, atrophic glossitis and esophageal webs) are predisposed to OC, especially women \[43, 44\].

**Hereditary conditions associated with adolescent - onset OC**

Several syndromes caused by inherited defects in genes have been associated with the development of OCs.

Fanconi anemia is a rare autosomal recessive genetic disorder characterized by bone marrow failure and increased risk of cancers, especially head and neck cancers and OC \[45\]. Dyskeratosis congenita is characterized by the triad leukoplakia, cutaneous pigmentation and nails dystrophy. Dyskeratosis congenita is associated with premalignant lesions of the oral cavity \[46, 47\]. Some associations between epidermolysis bullosa or juvenile papillomatosis and OC have also been reported \[48\]. Xeroderma pigmentosum (XP) is an autosomal recessive genetic disorder of DNA repair characterized by photosensitivity, pigmenatry changes, premature skin ageing and malignant tumour development. There are a substantial number of people with XP who have oral cavity neoplasms, particularly OC of the tip of the tongue \[49-51\]. OC of the anterior third of the tongue occur especially in young patients with XP \[52\]. These associations have strongly highlighted the need to carry out examinations of the child's oral cavity, especially if a systemic predisposing diseases, such as Epidermolysis bullosa, Xeroderma pigmentosum, Juvenile papillomatosis and Fanconi's anemia, are present \[53\].
Finally, marijuana smoking may be a potential risk factor for oral cancer although this association is still controversial [65, 66].

Protective factors

Controversial data exists on the effect of coffee and tea consumption and OC. A study revealed that they may decrease the risk of OC through antioxidant components [67], while another showed that the long term exposure of molecules present in coffee and tea may affect the anticarcinogenic action of saliva [68].

High fruit and vegetable consumption have shown to have a protective effect on the development of OC due to the dietary antioxidants and folate [69,70]. Intake of fruit and vegetables may protect against oral cancer, especially the groups of leguminosae (beans and peas), rosaceae (apples, peach, nectarines, plums, pears and strawberries), solanaceae (peppers and tomatoes) and umbelliferae (carrots) [71].

Diagnosis

Clinical Features

The clinical appearance of OC is variable and requires an expert eye to recognize its features. Early lesions may appear as red oral mucosa failing to heal within two weeks, or as a persistent lump with spontaneous bleeding or ulceration [72]. Lesions may appear flat, raised, exophytic and neck cancer

Poor oral hygiene and candida albicans infection

It is unknown if poor dental hygiene, predisposes to OC (Figure 2). New trends like poor condition of the mouth, lack of toothbrush use emerged as possible risk factors for head and neck cancer [60, 61], also due to the relevant mutagenic interaction between saliva and polymicrobial supragingival plaque [62]. Candida albicans may play a role in the pathogenesis of OC due to the production of nitrosamine, a potent carcinogen [63]. Hyperplastic candidiasis may be associated with potentially malignant disorders; deep fungal infections have been demonstrated in some nodular leukoplakias, although the association with cancer development remains unclear.

Some old dentifrices may contain extracts derived from the common bloodroot plant Sanguinaria Canadensis; these have been linked to the development of leukoplakia, especially in the maxillary vestibule [64]. Although the risk of malignant transformation in these lesions is not certain, monitoring of patients who have used these products is recommended. Finally, marijuana smoking may be a potential risk factor for

Uncommon risk factors

Chronic graft-versus-host disease

Chronic graft-versus-host disease (cGVHD) remains a significant complication of allogeneic hematopoietic cell transplantation (HCT) and continues to be the leading cause of non-relapse mortality. The oral cavity is affected in around 80% of cases, with a wide variety of signs and symptoms that can result in significant short- and long-term complications. Patients affected by chronic oral GVHD are at increased risk for oral dysplastic lesions and cancer [54-58]. Follow-up of these patients and biopsy of any suspicious lesions is recommended [59].

Diagnostic techniques

Visual and tactile examination is the most common tool available for clinicians and may result in detection of oral cancers. The first step is the visual inspection of the entire oral mucosa with particular attention to the tongue, the floor of the mouth and the retromolar pads, evaluating any changes in color and texture [74]. The tactile examination on facial bones and soft tissues is useful to note asymmetries or masses, and also the relevance of lymphadenopathy [75].

In the last years, several adjunctive techniques emerged to facilitate the detection of oral premalignant and malignant lesions, however incisional biopsy remains the gold standard for the diagnosis of OC [76].
New diagnostic methods

Various researches evaluate the new techniques of diagnosis to improve the clinical examinations. However some articles show significant results for oral cancer examination [77, 78], others reveal that the detection rate is not significantly improved [79-81].

An important review recognizes the new diagnostic techniques, with some usefulness for the dentist daily practice [76].

- Tissue reflectance: a) Microlux DL (AdDent, Danbury, CT), using LED and a fiber optic light guide, enhances the visibility but does not help with the true diagnosis of the oral lesion [82]; b) ViziLite Plus (Zila Pharmaceuticals, Phoenix, AZ) is a chemiluminescent light detection system that may increase the visibility of mucosal lesions, but its detection effect alone is unknown [83].

- Tissue fluorescence: VELscope (LED Dental Inc, Vancouver, Canada) is a multiuse device detecting tissue fluorescence useful in assessing lesion margins in patients with oral malignancies [84].

- Vital tissue staining: toluidine blue is a metachromatic dye that may be useful in long-term surveillance of high risk mucosal lesions mainly as a tool to identify sites for biopsy [85].

- Brush cytology: OralCDx Brush Biopsy (CDx Laboratories, Suffren, NY) is a brush that collects transepithelial cellular samples, to assess dysplastic changes in clinically suspicious lesions [86]. Of note, there is insufficient data to assess usefulness in innocuous mucosal lesions.

The malignant progression

Normal cells transform into preneoplastic cells and then to cancer after a series of clinical and histopathological stages involving genetic and molecular changes. These stages are clinically represented by manifestations on oral mucosa, such as leukoplakia, erythroplakia or leukoerythroplakia, and they all represent a predictive factor of malignant transformation [87].

Molecular changes

The multi-step progression of cancer involves a combination of acquired and inherited alterations in the DNA sequence. Genetic changes in keratinocytes cause a progressive acquisition of a malignant phenotype from premalignant to cancer, characterized by invasion across the epithelial basement membrane and eventual metastasis. The overexpression of oncogenes causes a disruption in the cell cycle driving to abnormal cell proliferation [2], while the expression of the tumor suppressor genes, especially the proteins p53 and p16 in the dysplastic epithelium are significant markers to detect preneoplastic lesions in the oral cavity [88].

Risk factors can lead to genetic and epigenetic alterations; the most observed cases of mutation of these genes are present in people from Asia due to the tobacco chewing and betel quid [89, 90]. Furthermore, epigenetic may cause an alteration of gene expression through aberrant DNA methylation, histone modifications and expression of microRNAs [91].

Potentially malignant disorders

Potentially malignant disorders comprise leukoplakia, erythroplakia, oral lichen planus and oral submucous fibrosis. These lesions are characterized by sequential accumulation of molecular changes that can lead to dysplasia (mild, moderate or severe) and then to frank invasive carcinoma [92].

Oral Lichen Planus (OLP) is an immuno-mediated inflammatory condition of the oral mucosa [93]. It occurs in 1 to 2% of adults and may be idiopathic or associated with a variety of systemic and local conditions. OLP usually affects the buccal mucosa and tongue bilaterally, and can present with three distinct forms: reticular/keratotic (classic), erosive/erythematous, and ulcerative forms. Less than 1% of OLP evolve in OC [94, 95].

Leukoplakia is a white lesion that can affect any site of the oral cavity, and its diagnosis it is made by the exclusion of any known diseases. The malignant transformation rate of all leukoplakias is 9-37%. There are three clinical different types of leukoplakia (the homogeneous, non-homogeneous and verrucous type); the most aggressive form is the proliferative verrucous type (60-100% of proliferative leukoplakias develop carcinoma) [96].

According to the WHO definition oral erythroplakia is defined as “any lesion of the oral mucosa that presents as bright red velvety plaques which cannot be characterized clinically or pathologically as any other recognizable condition”. The risk of malignant transformation of erythroplakia is the highest between the others premalignant forms (90%). This lesion presents as red areas mainly affecting the floor of the mouth, the soft palate and the ventral tongue [97].
Table 1. The TNM staging for oral cancer (T: tumor; N: lymph nodes; M: metastasis) [101]

<table>
<thead>
<tr>
<th>Stages</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T1, T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1, N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>N0, N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Table 2. Definition of the TNM staging [101]

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor more than 2 cm but no more than 4 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 4 cm in greatest dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Invasive tumor</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional lymph nodes (N)</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in a single ipsilateral lymph node, more than 3 cm but no more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node more than 6 cm in greatest dimension</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Distant Metastasis (M)</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>MX</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

Oral submucous fibrosis is a condition characterized by a fibrous aspect, a significant morbidity with pain and reduced oral opening which may affect any site of the oral cavity [98]. It is associated with areca nut chewing especially in Southeast Asia and the reported risk of malignant transformation varies from 2.3-7.6% [99].

Staging and treatment

Treatment planning for OC requires a multidisciplinary approach with surgeons, radiation oncologists, medical oncologists, radiologists, speech/swallowing pathologists and dentists.

Treatment of OC depends on the OC staging. TNM staging is based on the anatomic extent of the primary tumor and tumor spread (tumor size T, lymph node involvement N, and metastasis to distant sites M) [100].

According to the American Joint Committee on Cancer the different OC stages and treatment options are (Table 1 and 2) [101]:

- Stage 0: the cancer is in situ (Tis) and there aren’t regional lymph node and regional metastasis (N0-M0)
- Stage 1: the cancer is less than 2 centimeters in size (T1) without metastasis. The treatment options are surgery and/or radiation therapy. Surgery is the preferential treatment, and its goal is to remove the entire malignant tissue reaching a negative surgical margin. Radiation therapy is performed if surgery is not realizable or as adjuvant therapy (if surgical margins are involved by cancer) [102].
- Stage 2: the cancer is more than 2 centimeters and less than 4 centimeters in size (T1, T2), and can have spread to only one lymph node (N1). Surgery and radiation therapy are used to treat deeply infiltrative lesions, but radiation therapy is preferable with T2 lesions with minimal infiltration. The intensity modulated radiation therapy is directed to the lesion to minimize damage to the surrounding tissue and other anatomical structures. The ionizing radiation destroys cells in the target area stopping the growth of cells. The dose prescribed depends on tumor size. For early stage disease, doses of 66-74 Gy (2.0 Gy/fraction; daily Monday-Friday in 7 weeks) are used [103-106].
- Stage 3: the cancer is more than 4 centimeters in size, or any size (T3, T4), and can have spread to more than one
lymph node (N2). In T2 and small T3 tumors surgery and radiation therapy represent the elective treatment options. The size and location of the tumor guide the techniques of both. Chemotherapy is appropriate in lesions where the surgical approach is not efficient (neoadjuvant treatment), and it is combined with radiotherapy for concomitant treatments. Radiation doses used are 66-74 Gy (2.0 Gy/fraction; daily Monday-Friday in 7 weeks) [105]. The advantage of chemotherapy is the ability to reach the metastatic cells of the cancer, because radiation and surgery have effect on localized areas only. Cisplatin, carboplatin, fluorouracil, and cetuximab represent the main agents used in chemotherapy protocols [1]. Chemotherapy may be used in combination with radiotherapy (concurrent chemotherapy) or before it (induction chemotherapy) [104]. Induction chemotherapy (common agents are: docetaxel, paclitaxel, cisplatin and fluorouracil) is given to shrink a primary tumor to reduce its bulkiness in preparation for future radiation therapy or surgery [106, 107].

- Stage 4: the cancer is any size and has spread to any lymph node. The cancer has spread to other parts of the body (M1). Surgical approaches (i.e. total glossectomy, mandibulectomy) are dependent on the size and location of the lesions and are followed by postoperative radiation therapy. Although surgery is highly debilitating for the patient, minimally invasive procedures and surgical techniques of reconstruction have improved in the last years [1]. Palliative radiation therapy or chemotherapy can be used in patients with metastatic disease.

More recently novel molecular target agents have been developed as treatment options. Until now, inhibitors of the epidermal growth factor (EGFR), such as Cetuximab, anti-VEGF (e.g., Bevacizumab), m-TOR inhibitors and other VEGF or EGFR kinase inhibitors and multi-kinase inhibitors represent a curative targeted therapy in combination with radiotherapy and/or chemotherapy [108].

Treatment related complications

Patients treated with chemoradiotherapy are exposed to related toxic effects. Oral complications may cause acute and late toxicities that may not be recognized and treated. The most common oral complications are mucositis, salivary gland dysfunction and pain. Late toxicity may include dysphagia, dehydration and dysgeusia [1, 109]. Radiation therapy can lead to xerostomia, rampant dental caries secondary to dry mouth, trismus and osteoradionecrosis [110].

Conclusions

OC is the most common malignant disorder of the oral cavity, with high incidence rates in several developed countries. It represents the eighth most common cancer worldwide. In United States the median age at diagnosis is 65 years old, and the tongue remains the most affected site. Tobacco and heavy alcohol consumption are the most common risk factors for OC, with betel-quid and areca-nut chewing in some Asian countries. The role of HPV in the oral cavity is still controversial. Of interest, new trends are emerging in younger patients with no known risk factors. New diagnostic techniques are available for early detection although their reliability and validity is still unclear. Incisional biopsy remains the gold standard along with visual and tactile examination. Oral cancer requires a multimodality approach together with the oral medicine specialist, the dentist, the surgeon, the radiotherapist and oncologist. Treatment planning depends on the TNM staging system. Physicians have multiple diagnostic options and multidisciplinary approaches for the treatment of oral cancer, however further research is needed to better understand the natural history of OC. Finally, clinicians should screen their patients to detect early lesions and educate them about the risk factors that can lead to cancer.

Conflicting interests

The authors have declared that no conflict of interests exist.

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Author contributions

G.D.C conception and drafting of the review, A.V. and A.T. analysis and interpretation of the data, A.G. critical revision and approval of the review.

Abbreviations

OC: oral cancer; HPV: human papillomavirus; XP: xeroderma pigmentosum; OLP: Oral Lichen Planus.

References


100. Patel SG, Shah J. TNM staging of cancers of the head and neck.


