

Oral Cancer: The Silent Killer



Written by Dr Kumara Ekanayake
MBBCh, BAO, FRCS, FRCS
(OMFS), MS, BDS, FDSRCS,
FDSRCS, MSc

Consultant Surgeon,
National Unit for Maxillofacial
Surgery, St James's Hospital

September 15th is the mouth cancer awareness day in Ireland. Cancer of the mouth is the sixth most common malignancy in the world. Around 300 000 people worldwide are affected by oral cancer annually and it is ranked tenth among the number of mortalities due to malignancies. In Ireland, roughly 300 new cases are diagnosed every year, according to the Irish cancer Society. Yet the public awareness is considerably less when compared to other cancers like breast, prostate, skin and bowel. To put this into perspective, more people die in Ireland due to oral cancer than from skin melanoma.

Squamous cell carcinomas comprise more than 95% of all oral cancers. Although most patients are males over 40 years, it is also rarely seen in young children below 15 years. It is now apparent that this disease is affecting more and more young people who have little or no risk factors. Their disease progression is aggressive, and the outcome is generally poor.

This cancer can result in significant suffering if untreated. Facial disfigurement and functional disabilities lead to psycho-social isolation. Early diagnosis will result in proper management leading to complete cure in most cases. The overall 5-year survival rate has not improved much over the past decades which is about 55%.

Apart from squamous cell carcinoma (SCC), the oral cavity can be affected by other malignancies. Salivary gland tumours, lymphomas and melanomas are not uncommon. Various sarcomas, such as osteogenic and chondrosarcomas are seen rarely.

Oral cancer can affect the lips, tongue, gingivae, buccal mucosa, hard and soft palate and the floor of mouth. The oropharyngeal cancer involves the soft palate, oropharynx, base of the tongue and tonsil.



Advanced oral cancer with metastasis in the neck nodes



Squamous cell carcinoma of lower lip

Aetiology

Smoking and tobacco use

It is well known that smoking is associated with the development of many malignancies. Any type of tobacco consumption is harmful. Research has proved that oral tobacco products such as snuff, dip, spit, chew, or dissolvable tobacco increase the risk. Many people in south Asian and southeast Asian countries use betel quid also known as pan, which consist of tobacco, lime, betel leaf and areca nut.

Areca nut contains arecoline, a parasympathomimetic alkaloid stimulant. This alkaloid causes oral sub mucous fibrosis, which is a potentially malignant condition with a very high transformation rate to oral squamous cell carcinoma. Gutka is another chewable tobacco product. They tend to keep the tobacco quid in the buccal sulcus and therefore the incidence of buccal SCC is very high in these countries. In contrast, the buccal SCC is almost unheard of in countries where chewing tobacco is not widely practiced. In Ireland and in most European/North American countries, the SCC is common in the floor of the mouth and the lateral border of the tongue.

Alcohol

Alcohol increases the risk of oral SCC. Heavy drinkers are at a higher risk. Drinking alcohol and smoking together multiplies the risk. Simultaneous smoking and alcohol use is the most consistent factor found in the majority of patients with oral cancer. The risk is about 30 times higher.

Infective agents

Human Papilloma Virus (HPV) is associated with the development of pharyngeal and tongue base SCC. HPV 16 and 18 have been implicated in head and neck squamous cell carcinomas (HNSCC). HPV is mainly transmitted to the oral cavity through oral sex. Patients with HPV positive HNSCCs have a better prognosis than those with HPV negative HNSCCs. Tumour suppressor gene P53 associated mutations are also less frequent in these patients. Oral candidiasis is believed to have an association in the aetiology of certain lesions.

UV exposure

Lip cancer behaves differently, although it is also a Squamous Cell carcinoma. It behaves less aggressively, and the neck node metastasis is seen somewhat later. The main predisposing factors are the excessive exposure to UV light and tobacco usage. Fair skinned people are at a higher risk.

Genetic factors

It is believed that some people are inherently susceptible, and they are unable to metabolise carcinogens or procarcinogens. Their ability to repair the DNA damage is also impaired. Individuals with Fanconi Anaemia and Dyskeratosis Congenita are

more susceptible to develop oral malignancies. They can develop multiple synchronous lesions.

Immunodeficiency, poor diet, poor oral health, and male gender are some of the other observations associated with oral cancer. Nevertheless, many patients develop oral cancer without having any known risk factors.

Potentially Malignant Disorder (PMD)

These lesions carry a higher risk of malignant transformation compared to the normal oral mucosa. Research has established that almost all oral malignancies are preceded by clinically visible lesion. PMDs exhibit various degree of dysplasia on histopathological examination.

Majority of the PMDs present as a white patch (leukoplakia), white patch with red areas (erythroleukoplakia) or as a red patch (erythroplakia). It is usually seen in the buccal mucosa in patients who use betel quid, and in the floor of mouth, or lateral border of tongue in heavy smokers and drinkers. Other conditions like oral lichen planus, oral sub mucous fibrosis actinic cheilitis, proliferative verrucous leukoplakia, oral lichenoid lesions and discoid lupus have all been implicated to a varying degree.



Multiple synchronous tongue lesions; Leukoplakia of right side of tongue, and early SCC on left side in a tobacco chewer

Various presentations of oral cancer

- Non healing ulcer in the mouth
- White or red patch or mixture of white and red area inside the mouth
- Dark or pigmented patch
- A lump/raised area in the mouth or neck
- Difficulty in mouth opening, chewing or swallowing
- Numbness of the lower lip, tongue, or face

- Impaired tongue mobility
- Wasting of one half of the tongue
- A persistent sore throat and hoarseness
- Unexplained bleeding, mobile teeth, dental pain or pain radiating to the ear
- Ill-fitting denture
- Pathological fracture of mandible

Behaviour of the oral Squamous cell carcinoma

As this is an epithelial tumour, it originates in the oral mucosa and locally invades slowly. Then spreads to the ipsilateral cervical lymph nodes. Tongue and floor of mouth tumours tend to spread bilaterally at an early stage. If left untreated, the tumour can metastasise to lung and other regions such as bones and skin. Lymphangitis carcinomatosa is rarely seen.

Diagnosis

The diagnosis is established with an incisional biopsy. A CT/MRI/PET scans will help to identify the extent and staging of the disease. TNM classification based on the tumour size/depth, nodal state and the presence or absence of metastasis will be used to stage the disease. Spread to the cervical nodes decreases the overall survival by 50%. Occult node metastasis is about 20-30% in patients with clinically negative neck nodes. Therefore, sentinel node biopsy is being used in some centres to detect any occult metastasis in early oral cancer. A recent systematic review and meta-analysis has shown a high specificity of sentinel node biopsies in patients with clinical tumour stage CT 1-2 and clinically negative nodes.

Prognostic Indicators

The outcome of the oral cancer may depend on various factors. The site and size of the lesion, age, gender, certain pathological findings such as the depth of invasion, histological grade, the pattern of invasion, perineural invasion, lymphovascular invasion, lymphoid response, tumour budding, tumour clearance margins and extra capsular spread have been implicated.

Management

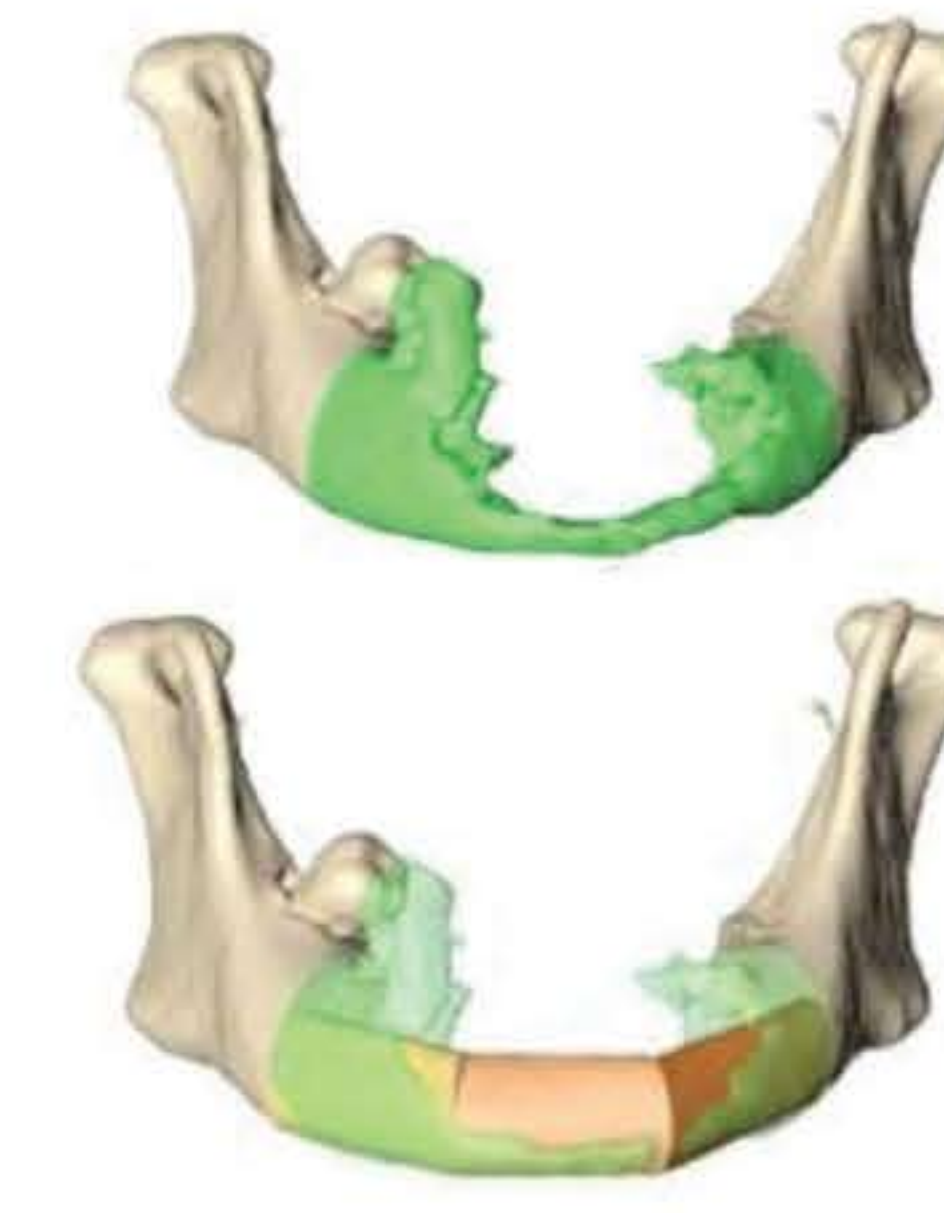
Once the diagnosis is established, each patient is discussed at a multi disciplinary tumour (MDT) conference involving surgeons, radiation oncologists, medical oncologists, pathologists, prosthodontists, speech therapists etc. A decision of how to

manage the disease is decided at this conference. Surgery is the mainstay of management in oral SCC. However, depending on the stage of the disease and the histopathology, it may be necessary to use neo adjuvant/ adjuvant chemotherapy. Most patients presenting with late disease will receive radiotherapy post operatively.

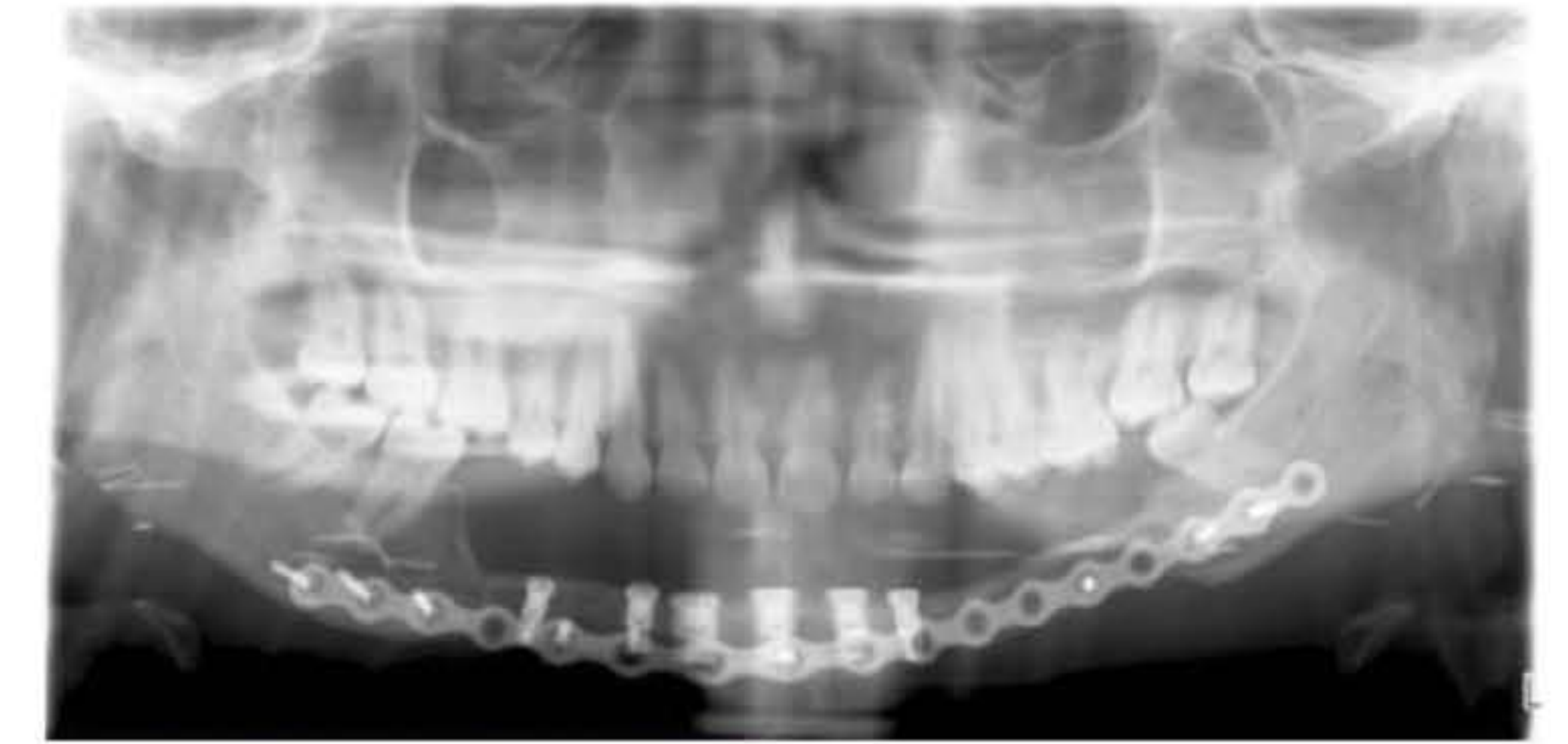
Early lesions can be surgically excised with a minimum of 1 cm margin in most cases leading to complete excision with a pathologically proven safe margin. For these patients, the 5-year survival rate is almost 100%. However, larger lesions will need wider excisions causing much morbidity due to the removal of highly specific oral tissues such as tongue, soft palate, lips, buccal mucosa, and teeth bearing mandible or maxilla. Therefore, the disfigurement and loss of speech, swallowing, oral seal, and taste causes much suffering to the patient. Microvascular reconstruction techniques have improved the re-establishment of much of the lost form and function.

These surgical procedures are very technically demanding, and it is necessary to have the participation of two surgical teams. Some surgeries could take eight to ten hours depending on the complexity of the resection and reconstruction. Therefore, preoperative optimisation of the patient is mandatory to address any co morbidities. Reconstructive methods have evolved significantly, and computer aided design and computer aided manufacturing (CAD-CAM) method is the best available technique at present.

Many patients will require a unilateral or bilateral neck dissection to address the cervical nodes. This will depend on the TNM stage of the disease.



CAD CAM reconstruction of mandible (Adapted from <http://dx.doi.org/10.21037/fomm-2020-mr-03>)



Mandibular resection reconstructed with a fibula free flap and dental implants

“As most cancers in the mouth are preceded by a recognisable potentially malignant lesion, self-examination and being aware of the various presentations may help in alerting the person. A visit to the dental practitioner every six months is vital...”

Immunotherapy with PD-1 inhibitors has shown some benefit in certain studies and there is hope that neoadjuvant or adjuvant treatment with them will bring more hope to these patients in the future.

Follow up in the outpatient department is mandatory for at least five years after treatment. Patient education and habit intervention is vital for prevention/development of further lesions. Many patients revert to the old lifestyle after a short period of abstinence from bad habits as they feel that they are out of the woods.

Prevention

As most cancers in the mouth are preceded by a recognisable potentially malignant lesion, self-examination and being aware of the various presentations may help in alerting the person. A visit to the dental practitioner every six months is vital as the dentist is the best person trained to identify these lesions. In case of any suspicion, a visit to the GP or the dentist is the first step, as they will refer the patient to a specialist without delay.

Following measures will help in prevention of oral cancer.

- Stop smoking

- Cut down on alcohol consumption
- Self-examination of the mouth
- Attend the dentist at six monthly intervals
- Vaccinate children with HPV vaccine
- Use a lip balm and skin protection from sun exposure
- Keep healthy by having a well-balanced diet rich in vegetables and fruits

Oral cancer is a deadly disease once it is well established. Surgery is the best hope for these patients. Unfortunately, the survival rate has not improved significantly despite the advancing knowledge into the aetiology and new interventions. However, due to the recent advances in surgical techniques and reconstructive methods, a reasonable quality of life can be expected after even extensive ablative surgeries. Any unexplained symptom persisting for more than two weeks needs investigating. Early lesions can be diagnosed and treated easily, and most lesions precede by a clinically recognisable lesion in the oral cavity. Therefore, regular oral cavity examination as a surveillance/screening method cannot be over emphasised.