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## Oral Cancer: The Silent Killer



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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

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 HNSCC s 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**, 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.

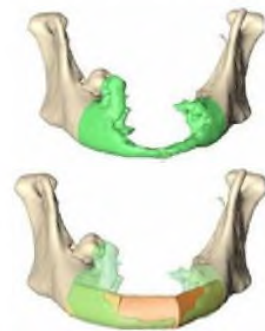
#### Management

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/forim-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.