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Oral cancer in Hong Kong: identifying and managing the 'high-risk' population

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How research can help identify those most at risk of oral carcinogenesis.

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In the April 2018 issue of the *FDJ*, we outlined the structure and organisation of oral and maxillofacial surgery (OMFS) services in Hong Kong, and the role of the academic discipline within the Faculty of Dentistry at Hong Kong University.[1] This article explores the important issues of oral cancer diagnosis and clinical management in the region, with special reference to research and development as well as the need to both identify and profile the local population most 'at risk' of oral carcinogenesis.

A British colony for more than 150 years until the official transfer of sovereignty to the People's Republic of China in 1997, Hong Kong has one of the world's longest life expectancies. Following rapid population growth after the Second World War, approximately 7.5 million people now live here, making it the fourth most densely populated region in the world. Largely a homogeneous society, around 92% of the population is Chinese (ethnically Han Chinese), with another 580,000 non-Chinese people including Filipino, Indonesian, Asian, European and North American residents. Many of the latter groups are non-permanent residents based in Hong Kong for work purposes only.

Hong Kong cancer statistics

Cancer is a major health problem in most developed countries and, particularly as a disease afflicting the ageing population, it is the leading cause of death in Hong Kong, followed by pneumonia, cardiovascular disease and accidents.[2] Significantly, the number of new cancer cases in Hong Kong appears to be increasing by around 2% each year.[2] The Hong Kong Cancer Registry was established in 1963 as a population-based registry responsible for collating patient demographic data, cancer site and histopathological diagnoses for both public and private medical institutions in Hong Kong – although detailed demographic information remains limited and difficult to access.[3]

In 2015 (the most recent year for which complete data are available) 30,318 new cancer cases were recorded in the Hong Kong Cancer Registry, primarily in people aged 60 or older – with colorectal, lung and breast tumours the most frequent (Table 1).[3] Approximately half of all cancer deaths were caused by lung, colorectal and liver tumours.

Head and neck cancer

A total of 1,692 new cancers arose in the head and neck region in Hong Kong in 2015 (approximately 5% of the total) (Table 2).[3] Accounting for 876 of these cases, nasopharyngeal cancer was the most frequent (and the tenth most common cancer overall). In young men aged between 20 and 44 years, it was the most common malignancy (124 out of 740 cancers in this age range). More common in southern parts of China than in western populations, nasopharyngeal cancer exhibits distinct epidemiological features including a particularly high incidence in Han Chinese and significant familial aggregation affecting first-degree relatives.

Rank	Site	Number	Percentage
1	Colorectal	5,036	16.6%
2	Lung	4,748	15.7%
3	Breast	3,920	12.9%
4	Prostate	1,831	6.0%
5	Liver	1,791	5.9%
6	Stomach	1,167	3.8%
7	Skin	1,018	3.4%
8	Uterus	978	3.2%
9	Lymphoma	976	3.2%
10	Nasopharynx	876	2.9%

Table 1 The ten most frequent cancers in Hong Kong in 2015[3]

Rank	Site	Number	Percentage
1	Nasopharynx	876	2.9%
2	Tongue	235	0.8%
3	Larynx	188	0.6%
4	Oral cavity	144	0.5%
5	Tonsil/oropharynx	86	0.3%
6	Salivary glands	78	0.3%
7	Hypopharynx	74	0.2%
8	Lip	9	0.03%
9	Other	2	0.007%

Table 2 Head and neck cancers in Hong Kong in 2015[3]

OSCC is now the 10th leading cause of cancer death in male patients in Hong Kong

High level of tobacco and alcohol consumption
Diet low in fruit and vegetables
Poor oral hygiene and irregular dental care
Male of short stature
Low socioeconomic status and material deprivation
Limited educational attainment
Manual occupation or long-term unemployment

Table 3 Profile of patients at 'high risk' of oral carcinogenesis[9]

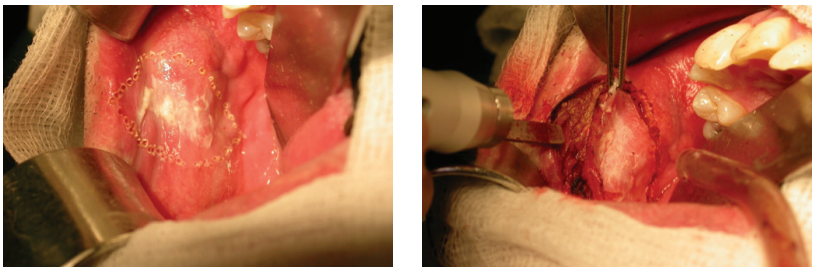

Figure 1 Secondary prevention: Carbon dioxide laser excision of a newly presenting and incision biopsy confirmed, moderately dysplastic leukoplakia in a 59-year-old European man. Histopathological examination of the excision specimen revealed an unexpected microinvasive oral squamous cell carcinoma, which was completely excised. The patient required no further treatment and has remained disease-free since the intervention.

Figure 2 Tertiary prevention: Treatment in a 35-year-old Chinese man who had undergone right lateral tongue oral squamous cell carcinoma treatment 5 years previously. Biopsy-proven mildly dysplastic leukoplakia is seen arising anterior to the existing partial glossectomy scar (A) and healing by secondary intention is evident at three weeks following carbon dioxide laser excision (B) with no residual leukoplakia and clear excision margins on histopathological examination. The patient remains under close follow-up.

Primary prevention	Avoidance of tobacco use and excessive alcohol consumption Attention to healthy diet and nutrition Awareness of all risk factor behaviours
Secondary prevention	Identification and treatment of potentially malignant disorders Early identification and treatment of oral squamous cell carcinoma
Tertiary prevention	Reduce risk of oral squamous cell carcinoma recurrence Early identification and treatment of new disease

Table 4 Preventive strategies in oral cancer management

Although the precise aetiological interactions between Epstein–Barr virus infection, smoking, high consumption of pickled food, and population migration remain obscure, secondary preventive techniques to facilitate screening, early diagnosis and intervention (primarily radiotherapy) in high-risk populations have evolved as definitive and effective treatment modalities.[4] Other head and neck cancers are much less common in the Hong Kong population (Table 2).[3]

Oral cancer

Oral squamous cell carcinoma (OSCC) is, of course, a lethal and deforming disease of rising incidence and global significance, with more than 300,000 new cases reported each year worldwide, including nearly 40,000 in China alone.[5] Even though the early signs of OSCC are readily detectable by oral examination, 5-year survival rates have remained around 50% because patients characteristically present late with advanced-stage disease requiring complex and combined surgical and chemoradiotherapy treatment. OSCC in the oral cavity and tongue accounted for 379 new cancer cases in Hong Kong in 2015, with 343 of these found in patients aged 45 or older; OSCC is now the 10th leading cause of cancer death in male patients in Hong Kong.[3] Unfortunately, it is difficult to delineate precisely either the geographic distribution or the treatment centre for these cases, rendering meaningful population-based studies problematic.

Ushida *et al* reviewed 5,888 oral cavity cancers recorded by the Hong Kong Cancer Registry for a 25-year period (1986–2010) and noted a particularly increased incidence in those aged 45–64 years.[6] Interestingly, age-specific incidence rates appeared to decline slightly in men, whereas rates among women demonstrated a significant upward trend (146% in this age group), especially from 2000 onwards.

Although similar to those reported worldwide, these observations clearly emphasise our limited understanding of contemporaneous disease prevalence in Hong Kong and the need for much better epidemiological data, including detailed patient risk factor behaviour, tumour site and staging at presentation, use of treatment modalities and clinical outcome. Current data and research in these issues in Hong Kong are limited and, in view of the difficulties in determining individual patient journeys within the complex healthcare system, a series of new studies are planned to detail OSCC epidemiology and clinical management pathways – and to delineate and profile the 'high risk' population.

Potentially malignant disorders

OSCCs may be preceded by potentially malignant disorders (PMDs), clinically recognisable and non-invasive mucosal lesions such as leukoplakia, erythroplakia and erythroleukoplakia or more widespread disorders such as proliferative verrucous leukoplakia.[7] Although the natural history of PMDs remains poorly understood, the overall risk of cancer development

may be in excess of 12%.[7] The efficacy of early diagnosis and interventional management in PMD treatment has been demonstrated previously in a Northern European population, with a resultant reduction in malignant transformation risk.[8–10] Application of a minimal morbidity treatment, such as carbon dioxide laser excision surgery, to suspicious oral mucosal lesions offers a therapeutic window of opportunity to halt the process of carcinogenesis.[10]

There are, unfortunately, very few data available on PMD distribution in Hong Kong, nor are there any reliable treatment studies. Corbet *et al* observed an 0.8% prevalence of leukoplakia (the most common PMD) in a population of 537 elderly Hong Kong residents (aged between 65 and 74 years), although frictional hyperkeratosis and denture-induced lesions were actually the predominant diagnoses.[11] A similar study in the adjacent Guangdong province of mainland China showed a 1.3% prevalence of leukoplakia.[12] However, a more recent study from Shanghai in eastern China found only a 0.22% prevalence.[13] Wang *et al* have usefully highlighted the lack of available and consistent national population data regarding PMD.[14] Although elderly age, tobacco smoking and alcohol are consistently identified as frequent population risk factors, it is likely that the demography of PMD in Hong Kong is complex, and now requires formal investigation and documentation.

Identifying the 'high-risk' population

General population screening may be unsuccessful in improving oral cancer diagnosis and management but there is little doubt that the ability to stratify risk in patient populations and subsequently target interventional management to 'high-risk' groups can be of proven therapeutic benefit.[4,9] Using a series of European-based population studies, a profile for patients at 'high risk' of oral carcinogenesis has been suggested previously.[9] Although the more salient features are summarised in Table 3, there is clearly a need to attempt detailed profiling of the 'at-risk' population in Hong Kong.

Clinical intervention and 'preventive' therapy

Early diagnosis and effective intervention in a targeted 'at-risk' population has now been demonstrated in the management of nasopharyngeal carcinoma.[4] The particular relevance of such patient profiling in oral oncology is the realisation that multiple tiers of preventive intervention are available, and may be marshalled early in an attempt to minimise both treatment morbidity and resultant mortality from unexpected or neglected OSCC;[8,9] long-term clinical outcome is demonstrably improved following early interventional management.[7]

Table 4 lists preventive approaches applicable to PMD and OSCC management. Although primary prevention is appropriate and beneficial for all patients, Figure 1 illustrates a specific clinical example of a secondary preventive intervention in which carbon dioxide laser excision of a buccal mucosal leukoplakia lesion effectively identified and treated an unexpected, pre-existing OSCC. In Figure 2, the efficacy of tertiary prevention is demonstrated by laser excision of a newly presenting dysplastic PMD in a patient with a history of previous tongue OSCC. Fundamental to all such 'preventive' interventions, however, is our ability to precisely identify and target the population deemed to be most 'at risk'.

Conclusions

OSCC is a disease of multifactorial origin, with varying risk factor behaviour in different population groups. Although the overall burden of OSCC in Hong Kong may not be numerically great, compared with other more common cancers, the implications for the affected individual can be catastrophic. Clinical outcomes will improve only with earlier OSCC detection and effective treatment of precursor lesions with malignant potential.[10] As a relatively well-defined geopolitical entity, Hong Kong provides a stable population in which cancer risk, socioenvironmental issues and treatment interventions can be examined in considerable detail.[6] Further research is now urgently needed into the delineation of 'high-risk' groups and the appropriate application of preventive techniques in a structured interventional management protocol.

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