

Increasing Incidence of Oral Cancer in Hong Kong – Who, Where...and Why?

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Abstract

Background: Oral squamous cell carcinoma (SCC) is a lethal and deforming disease of rising incidence and global significance; 600,000 new cases are seen each year, including 40,000 in China. Despite advances in management, 50% of patients die within 5 years of diagnosis. Cancer is the leading cause of death in Hong Kong, with the Hong Kong Cancer Registry (HKCR) confirming a 2% increase in new cases each year, and oral SCC the tenth leading cause of cancer death in males. Strategies to improve clinical outcome require identification and early intervention in the 'high-risk' population. Unfortunately, demographic information is limited in HKCR making it difficult to undertake accurate population-based studies. This study aimed to profile contemporaneous demographics of oral cancer within the Hong Kong population.

Methods: Following local ethical approval, the Hong Kong Hospital Authority (HA) database was accessed to identify new cases of oral SCC diagnosed and treated during an 18-year period (January 2000 to December 2017).

Results: 6,706 oral cavity SCC cases were identified: 4,291 male and 2,415 female patients (with a mean age of 64.14 years). A trend for increasing number of cases each year was seen, with most patients presenting to hospitals on the Kowloon peninsula and Hong Kong Island. The tongue was the most commonly affected oral site in 3,168 patients, with tonsil (863), buccal mucosa (539) and floor of mouth (409) less common. Mean survival time between initial diagnosis and death was 1.95 years; patients with hard palate and oropharyngeal SCC survived the shortest period, whilst labio-buccal and vestibular cases exhibited significantly longer survival (p<0.0001).

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Conclusion: Whilst useful HA data are available regarding age, sex, site and outcome, there is need for further improvement in demographic profiling to characterise the 'high risk' oral cancer population in Hong Kong and to facilitate targeted early therapeutic intervention.

Keywords: Oral Cancer, Hong Kong, Population Studies

1. Introduction

Hong Kong, officially the Hong Kong Special Administrative Region (HKSAR) of the People's Republic of China, is an autonomous legislative city-state located to the south-east of mainland China comprising the iconic Hong Kong Island, the peninsula region of Kowloon, the New Territories and around 200 outlying islands. Accommodating nearly 7.5 million people, it is the fourth-most densely populated region in the World; Table 1. Largely a homogeneous society, with around 92% of the population Chinese (ethnically Han Chinese), Hong Kong has one of the World's longest life expectancies, 81.3 years for males and 83.7 years for females, and benefits from an extensive network of public and private healthcare systems¹.

The Hong Kong Department of Health (DH) is responsible for health care policies and, via the Hospital Authority (HA), administers subsidised services to citizens through a network of over 43 hospitals and clinics. The latter are organised into 7 geographically determined clusters (2 in Hong Kong Island, 3 in Kowloon and 2 in the New Territories) that offer comprehensive continuums of acute and community-based care, providing more than 90% of all medical services to the territory².

As a disease that particularly affects the ageing population, it is unsurprising that cancer is the leading cause of death in Hong Kong with the number of new malignancy cases increasing by around 2% each year³. The Hong Kong Cancer Registry (HKCR), an official member of the International Association of Cancer Registries, was established in 1963 as a population-based registry responsible for collating patient demographic data, cancer site and histopathological diagnoses for all medical institutions in Hong Kong. Unfortunately, detailed demographic information, risk factor behaviour (including smoking and alcohol consumption), treatment modality and survival are not currently recorded, resulting in rather limited information that is difficult to access³⁻⁵.

Oral cancer, predominantly squamous cell carcinoma (SCC) arising from mucosal lining tissue, comprises tumours of the lip, oral cavity and oropharynx. These are lethal and deforming cancers of rising incidence and global significance, with over 600,000 new cases reported each year worldwide, including nearly 40,000 in China alone^{6,7}. Even though the early signs of oral SCC are readily detectable by clinical examination, 5-year survival rates have remained around 50% because patients present late with advanced stage disease. In Hong Kong, oral SCC is the tenth most common cause of cancer mortality but few details are known regarding contemporary epidemiology, patient demographics, geographic distribution and treatment centres rendering population-based studies and public health care initiatives difficult^{6,7}.

The objective of this study, therefore, was to utilise HA data from public hospital records to construct a detailed clinico-pathological profile of patients diagnosed with oral cancer, with the ultimate aim of characterising the demographic profile of the 'high-risk' Hong Kong population who may benefit most from targeted screening and early interventional management.

2. Methods

2.1 Study Population and Clinical Database

All Hong Kong residents receiving a diagnosis of lip, oral cavity or oropharyngeal SCC during the 18-year period November 1st 1999 –October 31st 2018 were identified from the Clinical Data Analysis and Reporting System (CDARS). This is a computerized database of patient records managed and maintained by the Hong Kong HA. The database contains clinical information, including patient demographics, disease diagnoses and investigations carried out in all public health system hospitals. Following appropriate ethical approval, the CDARS database is available for individual epidemiological studies in Hong Kong.

2.2 Data Extraction

Anonymized clinical information, including patient sex, age at presentation, tumour diagnoses and mortality outcomes were noted. Relevant disease categories were accessed using codes 140 to 149.9 from the International Classification of Diseases, 9th Revision (https://www.cdc.gov/nchs/icd/icd9.htm), until quite recently the ICD version preferred by the HA, specifically identifying malignant neoplasms of lip, oral cavity and pharynx.

2.3 Statistical Analysis

Descriptive statistics were used and reported as mean, standard deviation (SD), standard error (SEM), 95% confidence intervals (95% C.I) and percentages. Analysis of Variance (ANOVA) was performed to compare differences in incidence between sexes at each individual cancer site. Mean survival time from initial diagnosis to death was investigated using Kaplan-Meier Survival Functions. SPSS for Windows version 24.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 7.0 (GraphPad Software Inc.) were used to perform the statistical analyses.

3. Results

A total of 6,706 patients with oral SCC (4,290 males and 2,416 females, with an M:F ratio of 1.77:1) were identified from the CDARS database. The mean age at diagnosis was 64.14 years (SD 14.34), with 3,820 patients (57%) recorded as deceased at 31st October 2018. The number of new cases increased from 315 per year in 2000 to 470 in 2017, as illustrated in Figure 1, although the age at diagnosis and overall mortality remained relatively consistent throughout the 18-year period, as shown in Figure 2.

Whilst Figure 3 illustrates the geographic location of newly presenting oral SCC patients, Table 2 summarizes the hospital locations and clinical specialties available at each site to receive patient referrals. Served by 9 hospitals, the highest concentration of cases (2,689 out of 6,706 or 40%) was seen on the Kowloon peninsula, 7 hospitals on Hong Kong Island saw a further 2,106 cases (31%), whilst the New Territories had the lowest concentration of patients (1,911 or 29%) collated around 6 hospitals. In general, hospitals served by oral and maxillofacial surgery, ENT and/or head and neck surgical specialties received the highest number of patient referrals.

Table 3 details tumour sites together with patient sex, age and clinical outcome data. Overall, the most common primary site was the tongue (3,168), followed by the tonsillar region (863), buccal mucosa (539), gingiva (435) and floor of mouth (409); other sites were less frequently involved. ANOVA analysis showed no statistical differences for sex or patient age at diagnosis at each individual cancer site. Chi-square analysis, however, revealed a significantly higher number of male patients developed SCC at the tonsillar region (p<0.0001), floor of mouth (p<0.0001), oropharynx (p<0.0001), retromolar region (p = 0.0154), and soft palate (p<0.0001).

Mean survival time between initial diagnosis and death was 1.95 years (SEM 0.06), with shortest survival for oropharyngeal tumours (0.97 years) and longest for labio-buccal and vestibule mucosal sites (2.64 to 3.0 years); Table 3. In order to analyze the influence of tumour site on clinical outcome more fully, individual sites were combined into 5 anatomical and pathologically related zones: tongue and floor of mouth (3,577), oropharynx, tonsil, soft palate, uvula and retromolar (1,598), labial commissure, buccal, vestibule and unspecified mouth (736), gingiva (435), and hard palate (360). Log rank (Mantel-Cox) analysis confirmed a significant difference (p<0.0001) between survival times: patients with tumours arising at labial commissure, buccal, vestibule and oropharyngeal tumours the shortest. These data are presented graphically as a Kaplan-Meier survival plot (Figure 4).

4. Discussion

4.1 Who?

This is the first study to attempt detailed clinico-pathological profiling of the oral cancer population in Hong Kong. It is difficult to compare these results with other data because pre-existing, accurate demographic information for cases within Hong Kong is surprisingly lacking, both in official statistics from the HKCR and in contemporaneous literature. The characteristic oral cancer patient seen in this study was most likely to be male, in the 6th decade of life, to reside within the urban districts of Kowloon or Hong Kong Island, and to present with tongue cancer. The male to female ratio for subjects in this study was 1.77 to 1, which is similar to previously reported statistics from mainland China⁸. Although not statistically significant, Table 3 shows a trend for female patients to present at a slightly older age than male counter-parts.

Ushida et al⁹ previously collated age and gender data for 5,888 oral cancer cases recorded by the HKCR over a 25-year period (1986-2010) and postulated a cohort effect on incidence due to advancing age and cumulative risk factor behaviour. Patient data from this study, however, not only revealed an increase in the overall number of patients (6,706 cases over 18 years) but also little change in either age at presentation or at death suggesting that the 'at risk' population remains remarkably consistent. Such findings may be pertinent in designing targeted oral health screening programmes in the future.

Whilst the overall burden of oral cancer in Hong Kong may not be numerically great, compared with more common cancers such as colorectal or lung (5,437 and 4,936 cases, respectively, registered during 2016 for example)⁶, the

implications for the affected individual can be catastrophic: 57% of our study population died. Whilst the specific cause of death was not always evident in the CDARS database, this alarming statistic is consistent with previously raised concerns regarding the high mortality of established, invasive oral SCC¹⁰.

4.2 Where?

Despite the numerically larger population that resides within the New Territories, 71% of new oral cancer cases presented to hospitals in Kowloon and Hong Kong Island. In mainland China, incidence rates were also noted to be higher for patients living in urban as opposed to rural areas raising interesting questions regarding aetiology⁸.

It is probably unsurprising, however, that the majority of patients cluster around large teaching hospitals, such as the Queen Mary or Princess Margaret, as they host clinical departments of oral and maxillofacial surgery, ENT and head and neck surgery; as shown in Table 2. Following primary care consultation for oral disease, patients are often referred by medical practitioners to ENT or head and neck services, whilst dental practitioners usually request oral and maxillofacial surgical care.

Overall, the provision of services for patients with oral cancer is not particularly well coordinated and it is unfortunate that there are few, truly multi-disciplinary head and neck cancer services in Hong Kong appropriately linked with oncology care. Patients may receive surgical treatment in one hospital and are then transferred to another establishment for post-operative radiotherapy; this means it can be difficult to follow individual patient journeys to determine detailed clinical outcome data.

4.3 Why?

Globally, the number of new oral cancer cases is increasing each year and this study has confirmed a rising incidence within the Hong Kong population (Figure 1). A similar increase was reported by the HKCR: 482 in 2007, rising to 669 in 2016 (the most recent year for which data are available), although there are no consistent explanations why this is occurring.

Invasive oral SCC results from multi-factorial influences operating over prolonged periods, especially excessive consumption of tobacco products, alcohol misuse and betel quid habits, which act as external carcinogens targeting susceptible oral mucosal sites such as tongue, buccal mucosa and floor of mouth. It is recognised that genetic predisposition and exogenous influences vary significantly between populations and, whilst tobacco smoking, alcohol consumption and increased age are probably the principal risk factors in Hong Kong (betel chewing being exceedingly rare), other as yet unknown unknown factors may be equally relevant such as diet and nutrition, socio-economic status, and employment ⁹⁻¹¹.

Whilst a role for human papillomavirus (HPV) infection is recognised, this seems uniquely associated with a rise in a less frequent sub-type of oropharyngeal, tonsil and tongue base cancer that affects younger patients, involves a postulated sexually transmitted aetiology, and exhibits more favourable response rates to chemo-radiotherapy. The precise role of HPV in the Hong Kong population is unknown, and evidence of HPV-status is lacking in the HA database. The poor survival outcome demonstrated for oropharyngeal cancer in this study population, however, suggests that HPV-related cancers are uncommon, although this may be an important are for further study^{11,12}.

4.4 Implications for Treatment Intervention

It is concerning that 57% of our study population were deceased at the time of data census. It is well known that early diagnosis can substantially improve both clinical outcome and long-term survival, especially by early recognition and eradication of potentially malignant conditions that precede invasive oral SCC¹³. Guidelines and screening programmes for colorectal, cervical, ovarian, liver and nasopharyngeal cancer are already in place in Hong Kong but, despite their success, there are no protocols available to screen for oral cancer¹⁴. General population screening programmes are problematic, of course, due to considerable public ignorance of oral cancer, the reality that the population most 'at risk' rarely attends for examination, the potential for bias and over-interpretation of success, and the consequent dangers of over-diagnosis and over-treatment¹⁵⁻¹⁷.

As screening every individual is impractical, and very unlikely to improve overall outcome, a more pragmatic approach is to stratify risk in a patient population and to specifically identify and then target those groups deemed to be at greatest risk of cancer development¹⁸. The particular relevance of patient profiling in oral oncology is the realization that multiple tiers of preventive intervention are available, and may be marshalled early in an attempt to minimize both the morbidity and high mortality resulting from established oral SCC^{6,10}.

4.4 Study Limitations

This study has attempted to profile the oral cancer population in Hong Kong, although was limited by the retrospective nature of data collected from the CDARS database. Based upon multiple data-entry points and ascribing of diagnostic coding by non-specialists, there are inevitable risks of omission and/or inaccuracy. Use of non-specific terminology, such as the anatomical site 'mouth unspecified' for example (although only involving 179 cases in this study) is particularly unhelpful in this regard. Indeed, the overall quality of recorded information in CDARS and its precise application in disease-specific research have both been criticised previously¹⁹.

It is important to recognise that patients with oral SCC may also have been treated in Hong Kong's busy and complex private health care system, and therefore not recorded by CDARS, although it is likely that only a relatively small number of cases would have been managed in this way.

In terms of oncology research, however, it is disappointing that pertinent socio-demographic information including tobacco and alcohol use, diet and nutrition, and family history, were all missing from the data sets. Similarly, as cancer staging was not recorded, our ability to correlate lifestyle, biological and natural history of disease factors to the development and presentation of oral cancer in our study population was severely limited.

Nonetheless, demographic information has been collated for 6,706 oral cancer patients and a baseline profile of disease activity in 21st Century Hong Kong established for the first time. Previous research into these issues has been limited. With this in mind, a series of new prospective studies are planned to investigate oral SCC epidemiology and clinical management pathways in more detail and in particular to delineate and profile the 'high-risk' population.

5. Conclusions

This study has emphasized our limited understanding of contemporaneous oral cancer prevalence in Hong Kong and the need for improved epidemiological data, including detailed patient risk factor behaviour, accurate information on tumour site and staging at presentation, utilization of treatment modalities and long-term clinical outcome. As a relatively well-defined geopolitical entity, Hong Kong provides a stable population in which cancer risk, socio-environmental issues and treatment interventions can be examined in considerable detail. Treatment outcomes will only improve with earlier cancer detection and effective intervention. For this reason, further research is

urgently needed into delineation of the 'high-risk' population and the application of preventive techniques in a structured, interventional management protocol.

Ethical Approval

Approval to conduct this retrospective study was granted by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (Reference number UW-18-250). All clinical data were anonymized by the CDARS, and all potential patient identifiers were removed upon return of database searches.

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FIGURES

Figure Legends

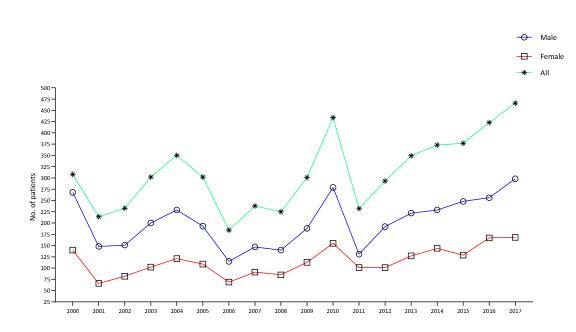
Figure 1: Trends in number of new oral SCC cases per year (2000 to 2017)

Figure 2: Trends in age at diagnosis and age at death per year (2000 to 2017)

Figure 3: Geographic distribution of patients diagnosed with oral cancer

Figure 4: Survival function - Years between diagnosis and death by tumour site







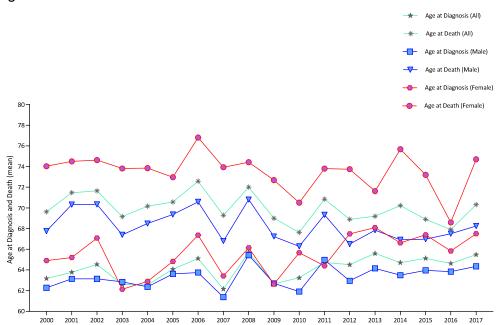


Figure 3

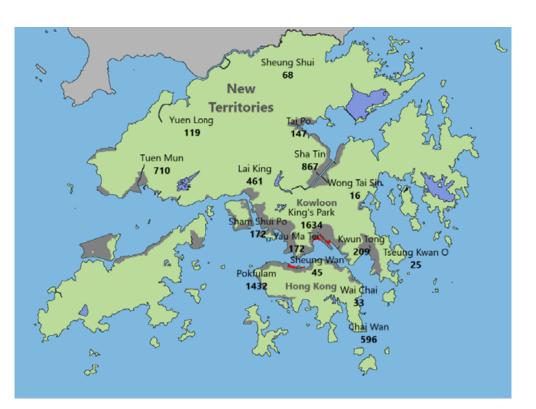


Figure 4

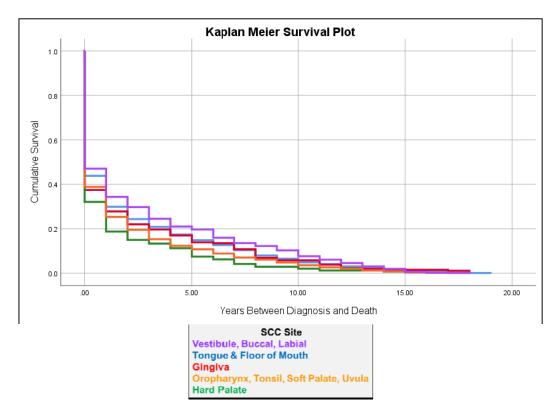


Table 1: Hong Kong Population Distribution (2014 Census Data)

Geographical Area	Population No. (million)	%
Hong Kong Island	1.27	17.5%
Kowloon	2.19	30.3%
New Territories	3.78	52.2%
Total	7.24	100.0%

Table 2: Geographical Area, Hospitals, Clinical Specialties & No of Oral Cancers Seen

Geographical Area	Hospital	OMFS	ENT	Head & Neck Surgery	No. of Oral SCC Cases
Hong Kong Island	Fung Yiu King	N	N	N	1
	Grantham	Ν	N	N	24
	Pamela Youde Nethersole	Ν	Y	Y	596
	Queen Mary	Y	Y	Y	1404
	Ruttonjee	Ν	Ν	N	33
	Tung Wah Eastern	Ν	Ν	N	3
	Tung Wah	Ν	Y	Y	45
Kowloon	Caritas Medical Centre	Y	Y	N	95
	Kwong Wah	Ν	Y	Y	172
	Our Lady of Maryknoll	Ν	Y	N	15
	Princess Margaret	Y	Ν	Y	461
	Queen Elizabeth	Ν	Y	Y	1634
	Tseung Kwan O	Ν	Y	N	25
	United Christian	Y	Y	N	209
	Wong Tai Sin	Ν	N	N	1
	Yan Chai	Ν	N	Y	77
New Territories	Alice Ho Nethersole	Y	Y	N	147
	North District	Y	Ν	N	68
	Pok Oi	Ν	N	N	119
	Prince of Wales	Y	Y	Y	855
	Shatin	Ν	N	N	12
	Tuen Mun	Y	Y	Y	710
Total	22	8	12	9	6706

Table 3: Patient Sex, Age at Diagnosis & Clinical Outcome according to Cancer Site

(C)

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Cancer Site	No. of patients	(No. Deceased	(% Deceased)	Mean Age in Years + (SD)	Mean Survival in Years + (SEM)
All sites (Total)	6706	3820	57.0	64.14 (14.34)	1.95 (0.06)
Males	4290	2599	60.6	63.31 (13.32)	1.89 (0.07)
Females	2416	1221	50.5	65.61 (15.9)	2.09 (0.11)
Tongue (Total)	3168	1644	51.9	62.21 (14.68)	2.066 (0.09)
Males	1879	1055	56.1	61.75 (13.83)	1.973 (0.11)
Females	1289	589	45.7	62.9 (15.83)	2.233 (0.16)
Tonsil (Total)	863	421	48.8	61.19 (12.66)	1.85 (0.18)
Males	684	342	50.0	61.07 (12.0)	1.74 (0.19)
Females	179	79	44.1	61.65 (14.95)	2.29 (0.47)
Buccal Mucosa (Total)	539	315	58.4	70.06 (13.27)	2.64 (0.24)
Males	283	178	62.9	68.64 (13.18)	2.82 (0.33)
Females	256	137	53.5	71.62 (13.22)	2.42 (0.33)
Gingiva (Total)	435	259	59.5	69.86 (12.87)	1.95 (0.23)
Males	234	144	61.5	68.00 (13.13)	1.88 (0.31)
Females	201	115	57.2	72.04 (12.22)	2.03 (0.34)
Floor of Mouth (Total)	409	273	66.7	63.69 (12.98)	2.13 (0.22)
Males	328	223	68.0	62.54 (11.4)	2.2 (0.24)
Females	81	50	61.7	68.35 (17.3)	1.8 (0.52)
Hard Palate (Total)	360	240	66.7	67.57 (15.56)	1.21 (0.17)
Males	199	142	71.4	65.72 (14.16)	1.0 (0.19)
Females	161	98	60.9	69.89 (16.9)	1.52 (0.31)
Oropharynx (Total)	338	254	75.1	65.75 (12.81)	0.97 (0.14)
Males	268	206	76.9	65.13 (12.05)	0.99 (0.16)
Females	70	48	68.6	67.99 (15.22)	0.88 (0.26)
Retromolar Region (Total)	209	137	65.6	66.31 (13.82)	1.72 (0.27)
Males	151	110	72.8	65.27 (12.86)	1.75 (0.3)
Females	58	27	46.6	69.01 (15.9)	1.59 (0.65)
Mouth Unspecified (Total)	179	133	74.3	68.34 (13.86)	2.26 (0.32)
Males	104	79	76.0	67.07 (12.44)	2.5 (0.42)
Females	75	54	72.0	70.11 (15.53)	1.91 (0.49)
Soft Palate (Total)	169	122	72.2	64.83 (14.51)	1.86 (0.26)
Males	135	104	77.0	66.20 (12.76)	1.76 (0.28)
Females	34	18	52.9	59.38 (19.31)	2.44 (0.7)
Uvula (Total)	19	13	68.4	67.53 (13.43)	2.62 (1.01)
Males	16	12	75.0	68.50 (12.11)	2.83 (1.07)
Females	3	1	33.3	62.33 (21.78)	2.42 (0.91)
Vestibule (Total)	11	7	63.6	66.45 (21.38)	2.86 (1.62)
Males	3	2	66.7	66.00 (13.53)	2.0 (2.0)

Females	8	5	62.5	66.63 (24.5)	3.2 (2.25)
Labial Commissure (Total)	7	1	16.7	58.67 (12.57)	3.0 (0.0)
Males	6	1	20.0	57.00 (13.29)	3.0 (0.0)
Females	1	0	0.0		