Incidence and survival trends of lip, intra-oral cavity and tongue base cancers in south-east England

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Abstract

Background Oral cavity cancers are on the increase in the UK. Understanding site-specific epidemiological trends is important for cancer control measures.

This study demonstrates the changing epidemiological trends in lip, intra-oral cavity and tongue base cancers in south-east England from 1987 to 2006.

Aim:

Methods This was a retrospective study using anonymised data obtained from the Thames Cancer Registry (TCR) London. Data were analysed using SPSS v.17 and survival analyses with Kaplan-Meier and Cox regression. Age standardisation of the incidence rates was performed. It was conducted in south-east England, which has an average population of 12 million. The study analysed 9,318 cases (ICD-10 code C00–C06, C14). Kent Research Ethics Committee UK granted ethical approval.

Results Oral cancers were more common in men, with male: female ratio of 1.6:1. Tongue cancers had the highest frequency at 3,088 (33.1%).

Incidence varied with each cancer type. Mean incidence (per 1,000,000) ranged from 2.3 (lip cancer) to 13.8 (tongue cancer). There has been a statistically significant increase in incidence for cancers of the tongue base, other parts of tongue, gum and palate ($p < 0.001$).

Median survival time varied by sub-site, with lip cancer having the best median survival time (11.09 years) compared with tongue base cancer (2.42 years). Survival analyses showed worse prognosis for men, older age at diagnosis, and presence of synchronous tumours ($p < 0.001$).

Conclusion There is a rising incidence of tongue and tongue base, gum and palate cancers in south-east England with wide variability in survival. Oral cancer awareness and screening programmes should be encouraged.

KEYWORDS

Oral cavity cancer – tongue base cancer – lip cancer

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Introduction

There has been a worldwide change in the incidence and survival trends of head and neck cancers. Oral cancers are on the increase in most parts of the world, with an annual estimated incidence of around 275,000.¹ There is also a wide geographic variation; areas characterised with high incidence rates include south and south-east Asia (Sri Lanka, India, Pakistan, Taiwan), parts of western (France) and eastern Europe (Hungary Slovakia, Slovenia), parts of Latin America and the Caribbean (Brazil, Uruguay, Puerto Rico) and in pacific regions (Papua New Guinea and Melanesia).² Oral cancer is the most common cancer in men in

some high-risk countries. This raises significant public health concern.

The epidemiology of lip, intra-oral cavity and tongue base cancers has changed in the UK in the last 30 years. There has been an increase in the incidence of oral cavity cancer among young adults in the UK³ and age has been suggested as a strong independent predictor of survival, with longer survival time for age group <45 years. Regional differences have been reported between England and Scotland in both incidence and mortality trends of oral and pharyngeal cancers as recorded in the WHO and IARC databases.⁴ Scotland had a higher incidence rate of oral

cancer in both men and women compared with England from 1987 to 2006. There has, however, been an increasing incidence trend in both countries for oral cancers. Mortality from oral cancer has increased in Scotland in men, compared with no significant increase in men in England. In women, Scotland has had no significant change in mortality compared with a decreasing mortality trend in women in England.⁴

The aetiology of oral cancers appears to be multifactorial. However, established risk factors include smoking, chewing tobacco or betel quid, alcohol excess, and snuff dipping, while sunlight exposure has been associated with lip cancer. Recent evidence strongly suggests virally-mediated carcinogenesis, in particular HPV-associated oropharyngeal cancer.

Documenting these recent trends is of immense value to cancer control measures, monitoring policies, improving clinical outcomes, resource allocation and stimulating research.

Aims and objectives

To demonstrate the changing epidemiological trends in lip, intra-oral cavity and tongue base cancers in south-east England from 1987 to 2006, along the following domains:

- > Site-specific frequencies
- > Incidence
- > Survival trends.

Methods

Study design

A retrospective, quantitative study using secondary anonymised data obtained from the Thames Cancer Registry (TCR) London.

Setting

South-east England comprising of London, Kent, Surrey and Sussex counties, with an average population of 12 million. This population increased from 10.7 million to 11.8 million between 1987 and 2006 (a 10% increase).

Participants

All cases of lip, intra-oral cavity and tongue base cancers in south-east England were registered with the TCR (ICD-10 code C00 – C06, C14) between 1987 and 2006. A total of 9,318 cases were analysed. Data were analysed using SPSS v.17 and survival analyses with Kaplan-Meier and Cox regression. Age standardisation of the incidence rates was performed, as well as trend tests of the graphs.

Ethical Considerations

Ethical approval was granted by the Kent Research Ethics Committee UK. The data obtained from the TCR were anonymised without any patient-identifiable information, and received as an encrypted file. The data were stored on a password-protected NHS computer in a secure, locked research room at the William Harvey hospital Ashford with access available only to the lead researcher. Data protection and confidentiality procedures were strictly adhered to throughout the period of this study, with password-protected

encrypted files used for statistical analysis on a secure computer in the study statistician's office at the University of Kent.

Results

These heterogeneous cancers differ by anatomical site and nature, and as such we have presented the results in the following separate groups: C00 (lip cancer), C01 (tongue base cancer), C02, C03, C04, C05, C06 (oral cavity cancers) and C14 (ill-defined sites in lip, oral cavity and pharynx)

Background population

It is pertinent to note that in the 20-year period, the population of south-east England increased from 10.7 million to 11.8 million (10% increase). Inter-regional and international migrations are the main components of this population change.⁵ Data from the 2011 census show that London is the most ethnically and socially diverse region of the UK, and also had the greatest proportional changes since the 2001 census.^{6,7} Across the English regions and Wales, London had the highest proportion of ethnic-minority groups, including African (7%), Indian (6.6%), Caribbean (4.2%), any 'other' white group (12.6%) and the lowest proportion of the White-British group at 44.9%.⁶ The effects of immigration, economic activities and a multi-cultural denominator should be considered when interpreting the observed trends.

Demographics

Over the 20-year period, the most common cancers of the 9,318 cases had the following frequencies in decreasing magnitude:

- > C02 (other parts of tongue): 3,088 (33.1%)
- > C06 (other and unspecified mouth): 1,253 (13.4%)
- > C04 (floor of mouth): 1,251 (13.4%)
- > C03 (gum): 879 (9.4%)
- > C05 (palate): 810 (8.7%)
- > C01 (tongue base): 778 (8.3%)
- > C14 (ill-defined sites in lip, oral cavity and pharynx): 746 (8.0%)
- > C00 (lip): 515 (5.5%)

These cancers were more common in men, having a male: female ratio of 1.6:1.

Incidence

Incidence varied over the study period with each cancer type. Mean incidence (per 1,000,000) for each cancer subsite over the 20 years were as follows (Tab 1):

- > Other parts of tongue: 13.8
- > Floor of mouth: 5.6
- > Other and unspecified parts of mouth: 5.6
- > Gum: 3.9
- > Palate: 3.6
- > Tongue base: 3.5
- > Other ill-defined sites of lip, oral cavity and pharynx: 3.4
- > Lip: 2.3

Table 1 Cancer sub-site specific incidences (per 1,000,000) in south-east England

Year	C00 Lip	C01 Tongue base	C02 Tongue	C03 Gum	C04 Floor of mouth	C05 Palate	C06 Unspecified mouth	C14 ill-defined
1987	3.55	1.4	10.75	2.9	3.74	2.43	4.39	2.9
1988	2.8	1.87	12.06	3.18	5.61	3.18	4.49	3.55
1989	2.05	1.68	10.36	3.27	6.16	2.8	4.57	2.33
1990	2.42	2.6	10.88	3.44	5.67	2.7	4.09	3.63
1991	1.57	2.32	13.34	1.67	4.91	3.7	4.45	3.61
1992	2.5	2.5	12.2	2.77	6.01	2.5	5.73	2.4
1993	2.22	2.86	12.93	2.4	6.74	2.77	4.52	2.95
1994	2.12	2.39	12.71	3.96	5.52	3.77	5.16	3.22
1995	2.2	3.12	9.63	3.39	4.86	4.13	6.14	3.12
1996	2.1	3.37	15.69	3.37	5.75	3.65	5.11	2.55
1997	2.18	3.36	14.69	3.9	4.63	4.17	5.71	2.99
1998	1.89	3.25	12.53	4.24	6.94	3.07	6.58	4.24
1999	2.23	4.02	16.88	5.18	5.36	4.11	6.16	3.39
2000	2.12	4.34	14.43	5.31	6.02	3.81	6.11	3.54
2001	2.28	4.83	15.18	4.83	5.79	3.86	7.28	4.3
2002	2.43	5.91	14.07	3.47	4.95	3.04	6.17	4.34
2003	3.12	4.59	17.86	5.81	6.76	3.81	6.33	3.55
2004	2.16	4.66	16.06	5.7	5.44	4.66	7.16	3.54
2005	2.06	4.8	15.59	5.82	6.51	5.05	6.17	4.11
2006	2.21	5.44	18.96	4	5.19	5.36	6.04	2.72

Table 2 Survival analysis by cancer subtypes

Cancer Type	Mean incidence (per 1,000,000)	Median survival time (in years)	Median survival 95% confidence intervals
Tongue cancer	13.8	4.07	3.47–4.67
Other and unspecified parts of mouth cancer	5.6	3.80	3.13–4.47
Floor of mouth cancer	5.6	3.65	3.06–4.24
Gum cancer	3.9	2.72	1.92–3.52
Palate cancer	3.6	5.90	4.71–7.08
Tongue base cancer	3.5	2.42	1.98–2.85
Other ill-defined sites of lip, oral cavity and pharynx cancer	3.4	0.09	0.78–1.12
Lip cancer	2.3	11.09	9.25–12.93

The range of incidence also varied, eg 1.40–5.91 per 1,000,000 for tongue base cancer compared with 9.63–18.96 per 1,000,000 for other parts of tongue cancers.

There was a statistically significant increase in incidence for C01 (tongue base cancer), C02 (other parts of tongue cancer), C03 (gum) and C05 (palate cancer); each $p < 0.001$ on trend test for graphs (Fig 1, Fig 2).

Survival

Cox-regression analysis showed that gender had a significant impact on survival, with women having a better prognosis; $p < 0.001$. Median survival time varied depending on the sub-site, with lip cancer having the best median survival time (11.09 years), followed by palate cancer (5.9 years), other parts of tongue cancer (4.07 years), other and

Figure 1 Increasing incidence trend of tongue cancer, tongue base cancer and palate cancers in south-east England

unspecified parts of mouth cancer (3.8 years), floor of mouth cancer (3.65 years), gum cancer (2.72 years) and tongue base cancer (2.42 years) (Tab 2).

The ill-defined-sites cancers had the worst prognosis (median survival time 0.09 years, 0.78–1.12), with 60% of patients dying within the first year of diagnosis. This may be due to late presentation, more aggressive disease or a lack of clear management pathways for this group. ‘Ill-defined’ refers to specimens taken from the lip, oral cavity or pharynx that have not been assigned the standard pathological codes, either because of their location or lack of clarity on pathological orientation or origin, and had to be registered on the TCR database, as is standard practice using ICD 10 Code C14.

Survival analysis using Cox regression and Kaplan-Meier showed worse prognosis for men, older age at diagnosis, and presence of synchronous tumours ($p < 0.001$).

Discussion

Incidence

Intra-oral and tongue base cancers have increased in incidence over the last 20 years in this study. These findings are consistent with other similar studies in south-east England,⁸ England and Wales,⁹ Scotland,¹⁰ Europe¹¹ and the US.^{12,13}

Incidence of oral cavity cancer in England has risen by nearly 30% from 1997 to 2007, while the incidence of

palate cancer has increased by 66%.⁹ It is unclear if the rise in palate cancer is mainly from the soft palate, thus matching the increase in oropharyngeal cancers.

The age-standardised incidence rate of oral cavity cancers in England from 2002 to 2006 as reported by the National Cancer Intelligence Network was 3.02 per 100,000 (95% CI: 2.95–3.08). The total number of cases was 8834, with 1766.8 cases per year. The highest rates nationally were recorded in London at 3.64 per 100,000.⁹ In this same population, a significant increase in tonsil cancer incidence has previously been reported.¹⁴ There is an increase in oropharyngeal cancers, with current evidence suggesting HPV as the driver in a unique subset of these cancers.

The incidence of oral cancer among young people in the UK has been increasing since the 1970s. In south-east England, age has been suggested as a strong independent predictor of survival, with 5-year relative survival higher in the younger age group (<45 years) compared with the older age group (>45 years).¹⁵ An increasing incidence of oral carcinoma among young patients has also been reported in Europe and the US.¹⁵

Hypotheses for the rising incidence

Intra-oral and tongue base cancers are strongly associated with cigarette smoking^{16,17} or betel nut chewing¹⁸ (more common among immigrants from the Indian subcontinent).⁹ There is also a strong association with excessive

alcohol consumption, which has a synergistic effect with tobacco consumption.¹⁹ Increasing alcohol consumption was associated with an increased risk of cancers of the oral cavity and pharynx in a study of over 1.2 million UK women (increase per 10/d = 29%, CI: 14%–45%, $p < 0.001$).²⁰

Several recent studies have demonstrated HPV as a driving aetiology, particularly for oropharyngeal cancers.^{21–26} These cancers include the tonsils, tongue base, soft palate and posterior pharyngeal wall. The incidence of oropharyngeal cancers in the UK has more than doubled in the last 10 years²⁷ with a recent meta-analysis showing a dramatic rise across Europe from 40% to 70% over the same period.²⁸ The stratification by HPV status and smoking has implications for survival, as this subset of HPV-positive cancers have a better survival.²⁹

The evolution of clinical practice with improved referral pathways and diagnostic modalities for head and neck cancers in the UK may have contributed to the increased cancer pick-up rates, as has the improved cancer registration data quality available from the cancer registries.

Survival

Mortality from oral cancer appears to remain static (despite an increasing incidence) in England and Wales.⁹ This may be due to changes at the stage at presentation.

The one-year relative survival for patients diagnosed with oral cavity cancer in England between 1990–1992 and 2005–2007 has increased from 74% to 78% for men and from 74% to 80% for women. The three-year relative survival has also improved between 1990–1992 and 2003–2005, rising from 55% to 60% for men diagnosed and from 58% to 68% for women.³⁰

The five-year relative survival for the most recently diagnosed cases of oral cavity cancer nationally is 56%⁹ while one- and five-year relative survival for palate cancer remains unchanged, with the five-year relative survival for the most recently diagnosed cases being 60%.

Social deprivation also appears to impact on survival, with worse outcomes in the more deprived groups.³⁰ This may also explain significant regional disparity in both incidence and mortality rates observed, with higher rates in Scotland compared with the rest of England and Wales.

Study limitations

This study does not include tumour stage information, which would have been useful as it impacts survival depending on the tumour site. The higher the tumour stage, the worse the survival outcomes.^{8,9,12} The lack of sufficient tumour staging data at the TCR has been a recognised shortfall in data collection and quality for most cancers, including head and neck cancers, over the years.⁸

The reasons for this are multifactorial, including the submission of incomplete cancer data by the hospital cancer multidisciplinary teams and networks for both pre-treatment/clinical staging and pathological staging. In June 2013, the TCR published their findings on the completeness of MDT staging data received³¹ and there remains wide variability in the compliance of various NHS Trusts, albeit with noticeable improvements. Improving cancer data quality has increasingly been addressed by the surgeons, pathologists and registry teams over recent years.

Conclusion

Intra-oral cavity cancers are common in south-east England, with a current rising incidence of tongue, tongue base, gum and palate cancers. Current evidence suggests HPV as a contributing aetiology in the oropharyngeal group (including tongue base, tonsil, soft palate, and pharynx) along with the traditional risk factors of cigarette smoking and alcohol consumption.

There is wide variability in survival depending on tumour type, but worse prognosis for men, the elderly and those with synchronous tumours. Increasing awareness of the signs and symptoms of oral cavity cancers amongst the general population is advocated. Oral cancer risk-awareness programmes should be encouraged. Further studies are required to explain these trends.

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