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Head and Neck Cancer in Canada: Trends 1992 to 2007

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Abstract

Objectives. The objective of this study was to investigate the changes in the epidemiology (incidence, age at diagnosis, and survival) of head and neck cancers (HNCs) in Canada in the past decade.

Study Design. Analysis of a national cancer data registry.

Setting. All Canadian hospital institutions treating head and neck cancer.

Subjects and Methods. Using Canadian Cancer Registry data (1992-2007), the authors categorized HNCs into 3 groups according to their possible association with human papillomavirus (HPV): oropharynx (highly associated), oral cavity (moderate association), and "other" (hypopharynx, larynx, and nasopharynx), which are not HPV related. They calculated age-adjusted incidence, median age at diagnosis, and survival for each category.

Results. Oropharynx tumors increased in incidence over the study time period (annual percent change: 1.50% men, 0.8% women), whereas oral cavity tumors decreased (2.10% men, 0.4% women), as did other HNCs (decreased by 3.0% for men and 1.9% for women). The median age at diagnosis for oropharynx cancer decreased by an average of 0.23 years/y. There was no change for oral cavity tumors but an increase for other HNCs of 0.12 years/y. Survival for patients with oropharynx cancer increased by 1.5%/y but was significant for men only. Survival for patients with oral cavity and other HNCs also increased in men only by 0.9%/y and 0.25%/y, respectively.

Conclusion. Oropharynx cancer, which is highly correlated with HPV infection, is increasing in incidence in Canada, with a decreasing age at diagnosis and an improvement in survival. This could have implications for screening strategies and treatment for oropharyngeal cancers in Canada.

Keywords

head and neck cancer, oropharynx cancer, human papillomavirus, incidence, age at diagnosis, survival

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Up until the past 15 years, the incidence, distribution of subsites, and etiology of head and neck cancers (HNCs) have been relatively stable. The most common subsites were the larynx and oral cavity, and the most common etiologic factors consisted of tobacco and alcohol consumption. Recently, the emergence of human papillomavirus (HPV) as an etiologic factor for HNCs (especially oropharynx) has changed not only the risk factor profile for this disease but also the epidemiology and survival. Oropharynx cancer is now thought to be attributable to HPV infection in about 80% of cases.[1,2] This is in contrast to oral cavity cancers, of which approximately 20% are HPV related, and larynx and other HNCs, which are largely not attributable to HPV infection.[1,2] Oropharynx cancers are as common, if not more common, than oral cavity and larynx cancers.[1-3] Patients are being diagnosed at earlier ages, there are more women diagnosed, and the survival of HPV-related HNCs is greater compared with non-HPV-related cancers.[1-3]

Several countries have taken the initiative to evaluate the aforementioned changes in HNC epidemiology. The Survival Epidemiology and End Result (SEER) database in the United States has been a particularly useful tool for evaluating these changes. Chaturvedi et al[1] examined the incidence and age at diagnosis of oral and oropharyngeal squamous cell carcinomas from 1973 to 2004. They found an increased incidence of HPV-related tumors (annual percent change of 0.80%) and a decreased age at diagnosis (61 vs 63.8 years). Pulte and Brenner[2] also used the SEER database but instead examined changes in survival over the period from 1982 to 2006. They found an improvement in

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survival for HPV-related tumors, which was most dramatic with tonsil cancer (survival increase of 22.2%). For oral cavity cancers, they found an improved survival of 11.8%. For larynx cancer, which is usually not HPV related, they found virtually no improvement in survival (1.9%).[2]

In Europe, Karim-Kos et al[3] did a comprehensive review of the changing epidemiology for 17 different cancer sites (including oral cavity and oropharynx) in 21 European countries from 1995 to 2000 using the various national Cancer Registry data. They too found an increased incidence and improved survival for HPV-related HNCs (oropharynx and oral cavity). These results have been supported by other studies in France,[4] Scandinavia,[5] and Italy.[6]

In Canada, there have been 2 small studies examining the recent trends in incidence and survival of oropharyngeal cancer. In first of these studies, Auluck et al[7] examined the age-adjusted incidence of oral cavity and oropharyngeal cancers using provincial (British Columbia) Cancer Registry data. These authors found an increase in the incidence of oropharyngeal cancers and a decrease in the incidence of oral cavity cancers during the study period (1980-2006). Gupta et al[8] used provincial (Ontario) Cancer Registry data and compared these with the incidence and survival rates in the SEER database over the period 1984 to 2001. They found no change in the incidence of oropharynx cancer over the study period. They did, however, find an improved survival for both oropharyngeal cancers and oral cavity cancers of 23% and 10%, respectively.

To our knowledge, there has not been a comprehensive Canadian study, using nationwide Cancer Registry data, to examine the incidence, age at diagnosis, and survival for HNCs. Thus, the aim of this study was to evaluate whether there have been similar changes in the incidence, age at diagnosis, and survival for HNCs in Canada using National Cancer Registry data over the period 1992 to 2007.

Methods

The data were drawn from the Canadian Cancer Registry (CCR) data file that contains patient demographic and tumor specific data on each tumor recorded in provincial and territorial cancer registries from 1992 to 2007, inclusive. The CCR file was provided to the University of New Brunswick (UNB) Research Data Centre (RDC) as part of a pilot program to evaluate and revise disclosure rules for working with the CCR data in the RDC network. Names and personal identification numbers were removed and replaced with unique identifiers prior to the data being sent to the RDC. All analysis was conducted within the UNB-RDC, and all output was vetted for release using enhanced vetting methods required by Statistics Canada. Ethics approval was obtained by Statistics Canada directly prior to the distribution of data.

Statistics Canada has updated and harmonized reporting across provinces so that every incidence of cancer has the relevant *International Classification of Diseases for Oncology, Second/Third Edition* (*ICD-O-2/3*) code associated with it for specific cancer site. Using these codes, we classified HNCs into 3 groups based on the probability of being HPV related as guided by the published research reviewed in the earlier section. The first group consisted of oropharynx cancer, which is highly correlated with HPV infection (n = 10,860 males, n = 4002 females). This included ICD-O-2/3 codes C019, C024, C051, C052, C090-103, C108-109, C140, and C142. The second group was oral cavity cancer, which has a moderate (20%-25% chance) of being HPV related (n = 9775 males, n = 6250 females). The relevant codes were C003-4, C020-C023, C029-C031, C039-C041, C049-C050, C059-C062, and C069. Finally, the remaining types of HNC were grouped together. These included all other head and neck mucosal tumors, which are considered as a group to have a very low probability (<5%) of being HPV related (n = 23,922 males, n = 6732 females). The relevant codes were C110-C139, C300, and C310-C329.

To compute age-adjusted incidence, raw numbers of cases were aggregated by 5-year age group and gender, for each calendar year by each HNC subsite, beginning with the 20- to 24-year-old age cohort. HNC among individuals younger than 40 years is very rare, and as a sensitivity check, we reran all of the estimations for adults aged 40 and older, and the results were very similar to what is reported here. Next, annual population counts by age group and gender were obtained from publicly available data compiled by Statistics Canada and used to compute annual age/gender-specific incidence rates (cases per 100,000) for each type of HNC. These figures were then weighted according to the 2006 Census of Population and compiled to yield age-adjusted incidence of each HNC cancer type by year and gender. Annual incidence rates were regressed on a constant and time trend using ordinary least squares regression (OLS), the trend taking a value 1 in 1992, 2 in 1993, and so on. Given the form of the estimation, it was also possible to test that any observed trends in incidence for particular cancer types were also significantly different from each other, as well as significantly different from zero. For the regression analysis, incidence rates were converted into logarithmic form so that the interpretation of the estimated OLS regression coefficient on the time trend is the average annual proportional change in the incidence rate over the sample period 1992 to 2007. As an alternative, Poisson regression models were estimated on the incidence of cases of each type of cancer by gender-age-year cells, with the corresponding adult population in each cell as the exposure. Regression models included controls for age group and gender as well as a time trend variable as defined above.

For the same underlying population, mean and median age at diagnosis were computed for individuals aged 20 or older, by gender, year, and HNC type according to the classification above. Ordinary least squares regression analysis was used to identify whether there was any significant trend over time in median or mean age at diagnosis.

The third dimension considered was whether there were any differences over time in the 5-year survival rates for each type of HNC cancer. Vital statistics, including date of death, are part of the Statistics Canada CCR file for any

Table 1. Changes in Incidence for Head and Neck Cancers in Canada, 1992 to 2006

	% Change in Incidence/y	% Change in Total Incidence	*P* Value
Oropharynx			
Women	+0.8	+13.7	.038
Men	+1.50	+27.1	.000
Oral cavity			
Women	−0.4	*NS*	.341
Men	−2.1	−39.9	.000
Other sites			
Women	−1.9	−35.5	.000
Men	−3.0	−61.6	.000

Abbreviation: *NS*, not significant.

Table 2. Changes in Age at Diagnosis for Head and Neck Cancers in Canada, 1992 to 2006

	Change in Median Age at Diagnosis/y	Total Change in Age at Diagnosis	*P* Value
Oropharynx			
Women	−0.22	−3.52	.004
Men	−0.23	−3.68	.000
Oral cavity			
Women	+0.09	*NS*	.190
Men	+0.05	*NS*	.217
Other sites			
Women	+0.13	+2.08	.029
Men	+0.12	+1.92	.011

Abbreviation: *NS*, not significant.

tumor included in the registry prior to the end of 2006, with the exception of tumors diagnosed and registered in Quebec. Thus, this part of the analysis excluded Quebec and used incidence data over the period 1992 to 2001 inclusive so that a full 5 years following diagnosis could be observed. The analysis was also limited to those aged 40 to 89 years owing to small numbers of cases in certain age groups when decomposed by gender, year of diagnosis, and cancer type. Three separate measures were computed: (1) raw survival rates (the proportion of people diagnosed in a particular year who survived at least 5 years), (2) age-adjusted survival rates, and (3) relative age-adjusted survival rates, where the survival rate for each age cohort was first divided by the all-cause 5-year survival rate for that cohort drawn from Statistics Canada life tables and applied prior to the construction of the age-adjusted measure. Each series (by gender and cancer type) was then regressed on a trend using OLS to assess the statistical significance of any time trends in the data over the sample period. As an alternative approach, a person-specific indicator variable was defined that took a value 1 if the individual was still alive 5 years after diagnosis and zero if the person was deceased within the 5-year period. This measure was then regressed on a set of indicator variables for age at diagnosis (in 5-year intervals) and time trend using a logistic regression analysis applied to a person-level data set.[1] This regression was run separately by gender and cancer type, and the significance of any differences in the incidence of survival over time by cancer type was evaluated.

Results

The change in incidence of HNCs in Canada varied by subsite (**Table 1**). Oropharyngeal cancers in men increased at an annual percent change of 1.50%/y, for a total increase of 27.1% over the study period 1992 to 2007. Oropharyngeal cancers in women increased at an annual percent change of 0.8%/y, for a total increase of 13.7% over the same time period. These increases were both statistically significant. Oral cavity cancers in men decreased at an annual percent change of 2.1%/y, for a total decrease of 39.9% over the study period, whereas oral cavity cancers in women decreased by only 0.4%/y. Only the former decrease was statistically significant. Finally, the remaining other HNCs (larynx, hypopharynx, and nasopharynx) decreased dramatically in both men and women. The annual decrease was 3.0% in men and 1.9% in women, for a total decrease in incidence over the study period of 61.6% and 35.5%, respectively. These decreases were both statistically significant. In addition, the estimate of the rate of increase for oropharynx cancers is significantly different from the rate of change of other cancers, for both men and women. Poisson regression estimates are qualitatively similar and are available on request from the authors.

The trends in age at diagnosis are illustrated in **Table 2**. For oropharynx cancers, the median age at diagnosis decreased by 0.23 years/y in men and 0.22 years/y in women, for a total decrease of 3.68 years and 3.52 years, respectively, over the study period. These decreases were statistically significant. There was no statistically significant difference in the age at diagnosis for oral cavity tumors in either men or women, with an average increase in age at diagnosis of only 0.05 years/y in men and 0.09 years/y in women. Finally, the remaining HNC tumors saw an increase in age at diagnosis in both men and women. In men, age at diagnosis increased by 0.12 years/y over the study period, whereas the age at diagnosis for women increased by 0.13 years/y. This resulted in a total increase in the age at diagnosis of 1.92 years for men and 2.08 years for women. These increases were both statistically significant.

The trends for survival of HNCs in Canada over the study period 1992 to 2001 are demonstrated in **Table 3**. As mentioned previously, this study period was shorter to allow for 5-year follow-up of all cases. The survival for oropharyngeal cancer in men increased at an annual percent change of 1.5%, for a total increase of 13.5% in the study period. This was statistically significant. No significant increase in survival for oropharyngeal cancer in women was identified, with an annual increase in survival of only 0.4% in that

Table 3. Changes in Survival for Head and Neck Cancers in Canada Diagnosed 1992 to 2001

	% Increase in Survival/y	% Total Increase Survival	*P* Value
Oropharynx			
Women	+0.4	*NS*	.278
Men	+1.5	+13.5	.000
Oral cavity			
Women	+0.4	*NS*	.143
Men	+0.9	+8.1	.001
Other sites			
Women	+0.3	*NS*	.311
Men	+0.2	+1.8	.002

Abbreviation: *NS*, not significant.

group. For oral cavity cancer, there was a statistically significant increase in survival for men over the study period (0.9%/y, total increase in survival 8.1%) but no statistically significant increase in survival for women (0.4%/y). Finally, there was a small but statistically significant increase in survival for men in all other HNCs (0.2%/y, total 1.8%) but no statistically significant increase for women (0.3%/y). It should be noted that the sample sizes for women were always smaller than those for men and that the sample size for the survival calculation was smaller than for the incidence and age at diagnosis calculation. The logistic regression results (available on request) yielded comparable results.

Discussion

Our study is to our knowledge the first of its kind to review the changes in incidence, age at diagnosis, and survival at a Canadian national level. We found dramatic changes in the incidence for HNCs in Canada from 1992 to 2007, particularly when divided by subsite. Oropharynx cancer was the only subsite in which there was an increase in incidence (1.5%/y in men and 0.8%/y in women). This is similar to the increase identified in the United States by Chaturvedi et al[1] using the SEER database (annual percent change increase of 0.80). Oral cavity cancers decreased significantly over their study period in men (2.1%/y). All other subsites decreased dramatically (3.0%/y in men, 1.9%/y in women).[1] Our results confirm those reported in the United States and Europe that there is an increase in the incidence of HPV-related HNCs compared with those that are not HPV related.[1-6]

The age at diagnosis for oropharyngeal cancers in Canada dropped over the study period by approximately 3.5 years for both men and women. This was similar to the decrease of 2.8 years identified by Chaturvedi et al[1] in the United States. The decrease in age at diagnosis for oropharyngeal cancers was accompanied by an increase in age at diagnosis for nonoropharynx, non–oral cavity cancers. The decrease in age at diagnosis has many implications, including the need for altered awareness of oropharyngeal cancers in young people by family doctors and dentists. Also, there are societal and economic implications due to time away from work for younger patients and cost to the health care system for possible long-term complications in these patients.

There were significantly different changes in the survival of HNCs for men over the study period in Canada. The largest improvement in survival was found in oropharyngeal cancers (13.5%), with a smaller but still significant improvement seen for oral cavity cancers (8.1%). All other cancers had small increases in survival (1.8%). No statistically significant differences were seen in the survival for any cancers in women. This may be at least partly due to the smaller sample size in women. The results of the survival calculation were likely influenced by the necessity of waiting 5 years after diagnosis to assess survival. This meant that the last year of diagnosis included in the survival calculation was 2001. When we consider that other authors have identified a significant increase in the prevalence of HPV-related tumors since 2001, this fact may significantly underestimate the improvement in survival of HPV-related tumors over this time period. Quite possibly, later studies using this same data set may demonstrate more improvement in survival, especially for oropharyngeal tumors.

Changes of this magnitude in incidence, age at diagnosis, and survival for HNCs at various subsites have had and will continue to have dramatic implications for patients and oncologists in Canada, as they have in the United States. The most commonly accepted treatment for oropharynx cancer is chemoradiotherapy. With the increased incidence of oropharynx cancers, there has been a proportionately larger number of HNC patients treated using chemoradiotherapy. As a result, there is likely to be an increased incidence in the complications of this treatment method, which is magnified by the fact that the patients being treated are younger and have more time to accumulate late complications.

Patients with HPV-related cancers have a significantly improved survival compared with those that are not HPV related. This appears to be the case regardless of the treatment they receive.[9] This begs the question as to whether these patients should receive less aggressive treatment. De-escalation of treatment for HPV-related oropharynx cancers is the subject of much discussion among head and neck surgeons. This is a very difficult question to address, as the survival of HPV-related oropharynx cancers is so good that it would take a huge number of patients over a very long study period to address this question appropriately. Also, there are ethical implications of offering patients less, rather than more, aggressive treatment. Some centers are attempting to address this question in a retrospective fashion (unpublished results), but there are inherent biases associated with using retrospective data.

Our results show gender differences in the incidence, age at diagnosis, and survival. These differences for most oral cavity cancers and for other HNCs (larynx and hypopharynx) reflect known gender differences in smoking practices. For oropharynx cancers, the difference is less clear. The

main risk factor for these cancers is HPV exposure, and thus both genders should be affected by exposure to the virus.

The main limitation of our study is the fact that there are no HPV data available for patients available in the Cancer Registry. As a result, we are inferring that the changes in incidence, age at diagnosis, and survival for oropharyngeal cancers are related to HPV etiology, but this cannot be confirmed. Human papillomavirus testing is now standard in most Canadian centers, so potentially a follow-up study will be able to address this point.

Conclusion

Oropharyngeal cancers have had a significant increase in incidence, a significant decrease in age at diagnosis from 1992 to 2007, and, in men, a significant increase in survival in Canada from 1992 to 2001. Oral cavity cancers demonstrated a moderate decrease in incidence and a moderate increase in survival for men in Canada over the same time period. All other HNCs demonstrated a significant decrease in incidence, a significant increase in age at diagnosis, and a very small increase in survival over the same time period.

These findings confirm that the changing demographics for HNC identified in the United States and Europe are occurring in a very similar magnitude in Canada.

Author Contributions

Stephanie Johnson-Obaseki, study design, manuscript, and American Academy of Otolaryngology presentation; **James Ted McDonald**, study design, data acquisition and analysis; **Martin Corsten**, study design and manuscript; **Ryan Rourke**, study design and manuscript.

Disclosures

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