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Diverging incidence trends for larynx and tonsil cancer in low socioeconomic regions of the US☆

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ABSTRACT

Objective: Oropharynx cancer incidence trends in low socioeconomic (SES) regions of the United States (US) have not been well described. Our objective was to describe tonsil cancer incidence trends in low SES regions, and compare observed trends with those for larynx cancer.

Materials and methods: Age-adjusted incidence rates and trends for tonsil and larynx squamous cell carcinomas (2000–14) from Surveillance, Epidemiology, and End Results (SEER 18) were evaluated using SEER*Stat and Joinpoint 4.5.0.1. Annual percentage changes (APCs) were compared between low and high SES counties. The laryngeal cancer cohort was included as a comparator reflecting a tobacco-related malignancy.

Results: Tonsil cancer incidence trends increased at least as much in low SES as in high SES counties (APC/AAPC 4.4, 95%CI 2.4–6.4 versus APC/AAPC 2.9, 95%CI 2.4–3.3). Pairwise comparison confirmed no differences between incidence trends across SES quintiles for tonsil cancer incidence rates. In contrast, age-adjusted incidence rates of larynx cancer decreased in high SES counties (APC/AAPC −2.4, 95%CI −2.4 to −2.0, $p < 0.001$) and were stable in low SES counties (APC/AAPC −0.9, 95%CI −1.9 to 0.2, $p = 0.10$). Compared with larynx cancer patients, tonsil cancer patients in low SES regions were significantly more likely to be younger and white.

Conclusion: In low SES US counties, tonsil cancer incidence rates increased from 2000 to 2014, while larynx cancer rates did not change, reflecting diverging trends for larynx and tonsil cancers. Tonsil cancer incidence rates are increasing in most US regions regardless of regional socioeconomic status. Prevention efforts should take these findings into account.

Introduction

Oropharynx carcinoma incidence rates have been increasing, primarily due to an increase in the frequency of cancer attributed to the human papilloma virus (HPV) [1,2]. Studies from Canada and New Zealand have reported significantly higher rates of oropharyngeal cancer in more socially deprived groups [3]. Significantly, incidence rates increased to a greater extent in regions with low-income populations [4]. Incidence rates for other types of cancer caused by HPV are greater in low-income than high-income populations [5,6]. While numerous studies have described increases in incidence rates for oropharynx cancer both in the US and abroad [1–4,7–11], no studies to date have examined whether tonsil cancer incidence trends in the US are increasing in lower socioeconomic (SES) populations. The largest population-based study to investigate incidence trends for HPV-related oropharyngeal cancers in the United States uses data from SEER registries that included exclusively high-SES geographies [8]. Studies of HPV in low SES populations are limited by the lack of population-based datasets that include specific markers for HPV or individual smoking history. Therefore, the objective of this study was to describe tonsil cancer incidence trends in low SES regions, and compare observed trends with those for larynx cancer. The laryngeal cancer cohort was included as a comparator reflecting a tobacco-related malignancy since the SEER database does not report individual smoking or HPV status. Such studies may be helpful in anticipating cancer trends and facilitate targeting oropharynx prevention efforts to areas where they are most needed.

Materials and methods

Data was obtained from the Surveillance, Epidemiology, and End Results (SEER 18) public-use database which collects cancer incidence

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Table 1
Selection criteria for SEER case records.

Inclusion
Malignant Behavior, Known Age, Cases in Research Database, first matching record for each person
Year of diagnosis 2000–2014
Tumor Site:
Tonsil or Larynx
Histology:
8070/3: Squamous cell carcinoma, NOS through
8077/3: Squamous cell carcinoma, grade III or
8082/3: Lymphoepithelial carcinoma or
8083/3: Basaloid squamous cell carcinoma
Exclusion
Death certificate only
Alaska Registry

and survival data from 18 population-based cancer registries in distinct geographic areas. Data from patients who were diagnosed with tonsil squamous cell carcinoma or larynx squamous cell carcinoma between January 1, 2000 to December 31, 2014 were recorded. Case listing from the Surveillance Research Program, National Cancer Institute SEER*Stat software version 8.3.5 was used to generate a database of tonsil and larynx squamous cell carcinoma cases between January 1, 2000 to December 31, 2014. Cases from Alaska were excluded due to inadequate county level information. Selection criteria are listed in Table 1. Age-adjusted incidence rates for tonsil and larynx cancer were obtained from SEER*Stat using the same selection criteria. Incidence rates were reported as per 100,000 and adjusted to the 2000 US standard distribution with 19 age groups. Ninety-five percent confidence intervals were generated using the Tiwari modification [12]. A p-value of $p < 0.05$ was used for statistical significance testing. The SEER database does not distinguish between oropharynx cancers caused by HPV from those associated with smoking. Tonsil subsite was selected for inclusion in the study based on the greater association of HPV with this oropharyngeal subsite [13]. Larynx site was selected for inclusion as a means of comparison due to the strong association of larynx cancer with smoking. Changes in tonsil and larynx cancer incidence rates were compared over the study period.

A composite socioeconomic status (SES) index was used to categorize patients into SES groups based on county unemployment and poverty rates, income levels, neighborhood house values, home/car/telephone ownership, and living crowdedness, as well as population occupation and education based on the Yost index as described previously [14]. Time-dependent county attributes, divided into three-year intervals (2000, 2003, 2006, 2009, 2012) reflected year-specific area-based characteristics. Low socioeconomic status was defined as the lowest quintile and high socioeconomic status included all other SES quintiles. Patients were assigned to the SES quintile based on county Yost index value in the year of diagnosis.

The patient count, stratified by SES, year of diagnosis, and patient age, was then imported into the Joinpoint Program (4.5.0.1) to determine county age-adjusted incidence rates, annual percentage changes (APCs) and average annual percentage changes (AAPCs) for tonsil and larynx squamous cell carcinomas during this period. Cancer rates were assumed to change at a constant percentage of the rate of the previous year. The AAPC summarized trends, using the underlying Joinpoint model to compute a summary measure over the entire interval. Trends were analyzed for statistically significant changes over time using permutation testing. Pairwise comparisons evaluated differences in trends across geographic regions based on SES quintile [15]. The study was approved by the Fox Chase Cancer Center Institutional Review Board.

Results

Selection criteria for squamous cell carcinoma patients of the tonsil or larynx diagnosed from 2000 through 2014 are listed in Table 1. Of patients diagnosed during this period, 33,759 patients with larynx cancer and 22,206 with tonsil cancer were included.

Table 2
Incidence trends for tonsil and larynx cancer in low and high SES counties.

	County SES	Period	APC/AAPC	95%CI	p-Value
Tonsil cancer	Low SES	2000–14	4.4	(2.4–6.4)	$p < .001$
	High SES	2000–14	2.9	(2.4–3.3)	$p < .001$
Larynx cancer	Low SES	2000–14	−0.9	(-1.9–0.2)	$p = 0.1$
	High SES	2000–14	−2.4	(-2.8–2.0)	$p < .001$

Abbreviations: SES, socioeconomic status; APC, average percentage change; AAPC, average APC; CI, confidence interval.

Tonsil cancer and larynx cancer incidence trends in low SES counties, those in the lowest quintile of an SES index, were compared with those from higher SES SEER counties. For tonsil cancer, incidence trends increased during this time period at least as much in low SES counties as in high SES counties (APC/AAPC 4.4, 95% CI 2.4–6.4, $p < 0.001$, versus APC/AAPC 2.9, 95% CI 2.4 – 3.3, $p < 0.001$) (Table 2). Higher APCs and AAPCs were observed in low-income regions, but the confidence intervals in such areas overlapped with those in higher income regions. No joinpoints were identified suggesting constant increases in incidence rate over this period. Furthermore, APC and AAPC values were equivalent. Pairwise comparison confirmed no differences between incidence trends across SES quintiles for tonsil cancer incidence rates, suggesting that the magnitude of the increase in incidence trends for tonsil cancer was not significantly different across SES regions. In contrast, the age-adjusted incidence rates of larynx cancer decreased in high SES counties during the same period (APC/AAPC −2.4, 95% CI −2.4 to −2.0, $p < 0.001$). In low SES counties, larynx cancer rates were stable (APC/AAPC −0.9, 95% CI −1.9 to 0.2, $p = 0.10$). Thus, in low SES counties, tonsil cancer incidence rates increased while larynx cancer rates did not change (Table 2, Fig. 1).

Overall, incidence rates for larynx cancer were moderately to strongly correlated with lower SES indicators, while tonsil cancers incidence rates were not correlated with these factors (Table 3). Tonsil cancer incidence was weakly correlated with percent unemployed (Pearson correlation: 0.095, $p = .02$ at the $p < .05$ level). Counties with high tonsil cancer incidence rates were as likely to be situated in counties with low SES attributes as high SES attributes. In contrast, high county-level incidence rates for larynx cancer was strongly associated with both low median income and as well as high percentages of the

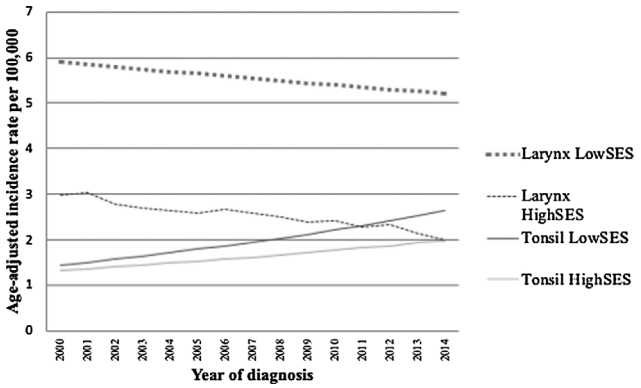

Fig. 1. Age-adjusted incidence rates of tonsil cancers are increasing in all regions regardless of socioeconomic status (SES) while the incidence of larynx cancer is stable or declining. Although greater increases in tonsil cancer incidence rates were observed in low SES regions than those in higher SES regions, differences did not reach statistical significance. Over this period, tonsil cancer incidence rates increased at least as much in low SES as in high SES regions.

Table 3
Correlations between age-adjusted incidence rates and county SES attributes.

	Larynx cancer		Tonsil cancer	
SES index	−0.336**	p = .0001	0.008	p = .844
Median household income	−0.317**	p = .0001	0.010	p = .814
Percent unemployed	0.150**	p = .0001	0.095*	p = .020
Percent with less than high school education	0.349**	p = .0001	0.036	p = .379
Percent working class	0.299**	p = .0001	0.010	p = .805
Percent below 150% poverty level	0.297**	p = .0001	−0.010	p = .807

** Pearson correlation significant at p = .01 level, (2-tailed).
* At the p < .05 level (2-tailed) for 612 counties.

population with less than a high school education (Table 3).

Comparisons of the clinical features of larynx and tonsil cancer patients from low SES counties diagnosed during this period are listed in Table 4. The age distribution of patients from low SES regions differed for tonsil cancer patients and larynx cancer patients (Fig. 2). The age distribution of the tonsil cancer patient cohort was significantly different from that of the larynx cancer cohort. Tonsil cancer patients were significantly more likely to be less than 50 years old while larynx cancer patients were significantly more likely to be greater than 65 years old (Table 4). Moreover, patients from low SES counties with tonsil cancers were more likely to be white than low SES larynx cancer patients. There was no significant difference in gender distribution between tonsil and larynx cancers in low SES regions.

Discussion

The incidence of oropharyngeal cancer has been increasing since the 1970s while incidence rates for cancer from non-oropharyngeal sites remained stable or declined during the same period [2,16]. These trends have been widely attributed to the increasing prevalence of HPV-related oropharynx cancer. The degree to which HPV-related disease contributes to oropharyngeal cancer in lower SES populations has not well been described and is limited by an absence of routine testing beyond histopathology in SEER registries. The largest population-based study to investigate incidence trends for HPV-related oropharyngeal cancers use data from SEER registries with exclusively higher-SES regions [8].

In this study, we compared changes in tonsil cancer incidence rates in high and low SES counties, and observed increasing age-adjusted incidence rates of tonsil cancer across all SES regions. In contrast,

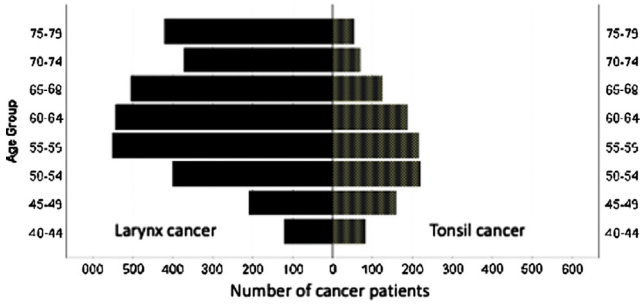

Fig. 2. The distribution of larynx and tonsil cancer patients by age group is compared for a cohort of patients residing in low SES counties. Tonsil cancer patients in low SES counties present at younger ages than larynx cancer patients.

larynx cancer incidence rates in the same counties remained stable or declined during the same period. These results suggest that since the incidence of tobacco-related head and neck malignancies is decreasing overall, the increasing tonsil cancer incidence trends in low SES regions may be attributable to HPV-mediated disease. The low SES group includes counties in the bottom quintile of a composite SES index, which corresponds to counties with high poverty rates, low median family incomes, and low education levels. Moreover, differences in demographic characteristics between tonsil and larynx cancer patients in the low SES cohorts resemble those described previously [17]. Tonsil cancer patients in low SES regions were significantly younger than larynx cancer patients from such regions. Tonsil cancer patients were also more likely to be white while larynx cancer patients were more likely to be African American, but no sex differences were observed. Racial differences have been noted by others [18] and may be related to sexual practices or susceptibility to latent HPV infection [19,20].

Increasing tonsil cancer incidence trends have been reported in low SES regions of other countries. Our findings are not inconsistent with those of Auluck et al, who described increasing oropharyngeal cancer incidence rates in lower SES regions in British Columbia [4]. However, in British Columbia, significantly greater increases in age-adjusted incidence rates were observed in the most deprived regions than the least deprived regions. Oropharynx cancer incidence trends increased significantly more in the lowest SES regions. In contrast, we observed greater increases in tonsil cancer incidence rates in low SES regions than other areas, but confidence intervals were wide and differences between trends were not statistically significant. The low population

Table 4
Clinicopathologic differences between tonsil and larynx cancer patients from lower SES counties.

		Larynx cancer		Tonsil cancer		p-Value
		Count	Percent	Count	Percent	
Age	< 50 years	332	10.6%	243	21.7%	p = .0001
	50–64 years	1497	47.9%	626	55.9%	
	65 or more years	1297	41.5%	251	22.4%	
Sex	Female	674	21.6%	249	22.2%	p = .640
	Male	2452	78.4%	871	77.8%	
Race	White	2429	77.7%	946	84.5%	p = .0001
	Black	681	21.8%	168	15.0%	
	Other	10	0.3%	4	0.4%	
	Unknown	6	0.2%	2	0.2%	
ICDO3 codes	8070/3: SCC, NOS	2497	79.9%	858	76.6%	p = .0001
	8071/3: SCC, keratinizing	522	16.7%	117	10.4%	
	8072/3: SCC, large cell, non-keratinizing	58	1.9%	98	8.8%	
	8074/3: SCC, spindle cell	22	0.7%	2	0.2%	
	8082/3: Lymphoepithelial carcinoma	3	0.1%	7	0.6%	
	8083/3: Basaloid SCC	24	0.8%	38	3.4%	

Abbreviations: SCC, squamous cell carcinoma.

density in the most deprived geographic areas likely limited statistical power to detect differences. We concluded that tonsil cancer incidence trends in such areas increased at least as much in low SES areas as in higher SES regions.

Our findings have implications for oropharynx cancer prevention. Lower SES status is a risk factor for cervical cancer, which is also caused by HPV. Screening for cervical premalignancy resulted in decreasing incidence and mortality rates from cervical cancer. Nevertheless, women from low income regions failed to benefit from preventative efforts due to lower participation rates. Consequently, cervical cancers are increasingly concentrated in lower socioeconomic areas [9,21,22]. Increasing awareness of the importance of HPV vaccination will likely lead to declining tonsil cancers incidence rates in the future. It is important that low income populations are not left behind.

As is inherent in all analyses using population-based registries, limitations exist regarding the clinical data that could be obtained. There is no documentation for lifestyle risk factors available in the SEER database. In addition, since SEER does not provide HPV status on individuals, increasing incidence rates in low income areas may not necessarily be attributable to HPV. The well-known association of smoking with head and neck squamous cell carcinoma, which is strongest for larynx cancer, remains a significant confounder in any analysis of oropharynx cancer incidence rates in lower SES populations. In order to address this concern, we chose to evaluate trends specifically for tonsil cancer rather than oropharynx cancer, since the former is more strongly associated with HPV-related malignancy [13]. Currently, it is estimated that HPV-related oropharynx cancers constitute as much as 70% of oropharynx cancers nationwide [8,23] and up to 60% in countries outside the United States [24]. In fact, Chaturvedi et al. [8] noted an increase in contribution of HPV to oropharynx cancer of 16.3% from 1984 to 1989 to 71.7% from 2000 to 2004.

In order to address limitations with respect to absence of HPV diagnostic confirmation and smoking history, trends in incidence of larynx cancer, which is closely associated with tobacco use were compared with tonsil cancer incidence trends during the same time period and in the same geographic regions. It seems implausible that incidence rates for tobacco-related oropharynx cancer would increase while larynx cancers decline. Prior studies have shown that tobacco-related cancers are more strongly associated with low income and education levels than HPV-related oropharynx cancers. However, no population-based studies of HPV-related cancers arising in low income areas has been conducted in the US. In this study, we found no association between low SES and tonsil cancer incidence rates. Thus, during the study period, tonsil cancers were equally likely to arise in low income as high-income counties. Moreover, tonsil cancer incidence rates increased in low SES counties. Even in regions characterized by significant poverty, in the lowest quintile of a composite SES index, the incidence of tonsil cancer increased at rates at least equal to those in other SES counties.

The study is limited in linking patients to SES status at the county level rather than the individual level. There may be significant socioeconomic heterogeneity in residents living in some regions. Nevertheless, neighborhood characteristics have previously been shown to be highly predictive of a variety of health-related outcomes [25]. The composite SES index used in this study is based on multiple SES-related factors. A composite time-dependent score that links several indicators distinct from income alone may more accurately reflect overall socioeconomic status than income alone [14].

Moreover, while the SEER database aims to capture as representative a sample of the US population as possible, the data from 18 cancer registries in distinct geographic regions may limit the generalizability of the data. Nevertheless, SEER is currently the only population-based database in the United States available to evaluate incidence rates and trends of cancers with SEER 18 capturing over one quarter of the US population.

Conclusion

From 2000 through 2014, the incidence of tonsil cancer increased equally in low SES counties and as in higher SES counties while incidence rates for larynx cancer declined or remained stable. Prevention efforts which currently involving education to promote awareness of the importance of HPV vaccination should include lower income populations.

Conflict of interest

The authors declared that there is no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2019.02.024.

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