Tracking Changes in Age Distribution of Head and Neck Cancer in the U.S. from 1975-2016

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May 15, 2020

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Abstract

Introduction There is currently a lack of available data clearly addressing whether the proportion of young patients diagnosed with head and neck cancer (HNC) within the U.S. has increased over the last several decades in comparison to other age cohorts. This study attempts to elucidate any trends in oral cavity, oropharynx, larynx and hypopharynx cancer age distribution in the United States population from 1975-2016. Unlike previous studies, this paper does not track incidence, but rather reports proportional changes of prevalence within age cohorts over time. Methods This is a retrospective chart review centered on data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). Each decade interval from 1975-2016 displays the proportion of HNC patients, classified by primary tumor subsite, within each age cohort. Results Mean age at diagnosis increased for three of the four HNC evaluated. Oropharyngeal cancer was the only subsite to demonstrate an overall proportional increase, mainly in middle age (40-59 years) patients. Cancers of the oral cavity were the only subset to show a true increase in the proportion of young (0-39 years) patients. When stratifying by gender, the proportion of young patients in female HNC cases is higher than the proportion of young male HNC cases. Conclusion Overall, this study demonstrates an increased proportion of older HNC patients that is consistent with the aging population. Oral cavity is the only cancer to demonstrate a true increase in the proportion of young patients, likely from the increased incidence of young women diagnosed with this cancer. Case reports citing more young patients becoming diagnosed with other types of HNC are not currently supported by the data. Lastly, the increased proportion of middle-age patients with oropharyngeal cancer likely reflects the increase in HPV-related cancers.

Title: Tracking Changes in Age Distribution of Head and Neck Cancer in the U.S. from 1975-2016

Running Title: A SEER Database Retrospective Chart Review

Data availability statement: All data used for this study is publicly available within the SEER database of the NCI.

Abstract

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Methods

This is a retrospective chart review centered on data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). Each decade interval from 1975-2016 displays the proportion of HNC patients, classified by primary tumor subsite, within each age cohort.

Results

Mean age at diagnosis increased for three of the four HNC evaluated. Oropharyngeal cancer was the only subsite to demonstrate an overall proportional increase, mainly in middle age (40-59 years) patients. Cancers of the oral cavity were the only subset to show a true increase in the proportion of young (0-39 years) patients. When stratifying by gender, the proportion of young patients in female HNC cases is higher than the proportion of young male HNC cases.

Conclusion

Overall, this study demonstrates an increased proportion of older HNC patients that is consistent with the aging population. Oral cavity is the only cancer to demonstrate a true increase in the proportion of young patients, likely from the increased incidence of young women diagnosed with this cancer. Case reports citing more young patients becoming diagnosed with other types of HNC are not currently supported by the data.Lastly, the increased proportion of middle-age patients with oropharyngeal cancer likely reflects the increase in HPV-related cancers.

Keywords: head and neck cancer, proportional changes, age at diagnosis, age distribution

Level of Evidence: 3 Retrospective Cohort Study

Introduction

On a global scale, head and neck cancers (HNC) account for 650,000 new cancer cases and 330,000 deaths annually (1,2). In the United States, HNC encompasses three percent of all cancers and accounts for 53,000 new cases and 10,800 deaths annually (1,3). Recent case reports have suggested that the age at diagnosis may be getting younger for many of the HNC subsites (12-18). However, there is no large scale study in the literature evaluating this possibility. Although there is substantial data documenting risk factors, genetic markers of HNC and trends of HNC epidemiology, we have been unable to find published data that clearly identifies whether there has been a true increase or decrease in the proportion of young patients diagnosed with HNC. This study is different from the published literature and unique in that it tracks the relative change in prevalence between HNC age cohorts to highlight proportional changes amongst age groups over time. We show the proportion of patients within age-cohorts diagnosed with HNC, stratified by primary tumor site subtype, throughout the last few decades. Evaluated HNC subtypes include oral cavity, larynx, oropharynx and hypopharynx. The purpose of this study is to determine whether HNC patients are truly "becoming younger".

Currently, the incidence of HNC is decreasing in the United States (4,5). This is attributed to reduction of tobacco use in the general population (6,7,8). However, the incidence of oropharyngeal squamous cell carcinoma, a subset of HNC, has increased over the last few decades (4,5,9,10). This has been linked to higher prevalence of HPV infection of the upper airway (4,5,10,11). There is currently contradicting data on the trends of other subsets of HNC. Population studies show that incidence of all subsets of HNSCC, besides OPSCC, is actually decreasing (4,5), but several independent studies report an alarming increase of patients younger than 40 being diagnosed with squamous cell carcinoma of the larynx and oral cavity (12-18). This is our primary point of interest – to determine whether a larger proportion of young patients are being diagnosed with HNC than before, even though overall HNC incidence is decreasing.

With the reduction of tobacco use and increase of upper airway HPV infection in the U.S. in recent decades, the risk factors for HNC have changed dramatically. This study breaks down, over time, HNC subtypes by age cohorts to clarify whether there are significant changes in the . Any possible changes in the age

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distribution of HNC could help uncover underlying risk factors. Further, this could guide physicians and researchers to develop more age-specific prevention and intervention methods.

Methods

The data for this review was obtained from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). SEER contains data for 34.6% of the United States population obtained from population-based cancer registries (19). SEER data is de-identified and contains information on patient demographics, primary tumor site, tumor morphology, stage at diagnosis, treatment and relevant comorbidities (19). Comprehensive patient data from 1975-2016 was requested from SEER 18 Regs Research Incidence Data and analyzed by a statistician. For patients with multiple HNC malignant tumors, their first primary tumor was chosen as the record to analyze.

HNC incidence data was obtained dating back to 1975 for the following areas: San Francisco-Oakland SMSA, Connecticut, metropolitan Detroit, Hawaii, Iowa, New Mexico, Utah, metropolitan Atlanta. Data dating back to 1992 was obtained for the following areas: San Jose-Monterey, Los Angeles, Alaska, rural Georgia. Data dating back to 2000 was obtained for California, Kentucky, Louisiana, New Jersey and greater Georgia. All data contributes to the proportion of patients with HNC in subsites of interest. Data was broken down into respective U.S. regions including West, Northeast, Midwest, Southwest and Southeast in order to visualize regional differences in cancer prevalence. Additional demographic factors such as gender and race were also included.

Primary head and neck tumor data was organized into cancers of the oral cavity, oropharynx, larynx and hypopharynx. **Oral cavity** cancers include primary tumors of the external upper lip, external lower lip, external lip not otherwise specified (NOS), mucosa of upper lip, mucosa of lower lip, mucosa of lip NOS, commissure of lip, overlapping lesion of lip, lip NOS, skin of lip NOS, dorsal surface of tongue, border of tongue, ventral surface of tongue, anterior 2/3 of tongue, overlapping lesion of tongue, tongue NOS, upper gum, lower gum, gum NOS, anterior floor of mouth, lateral floor of mouth, overlapping lesion of floor of mouth, floor of mouth NOS, hard palate, overlapping lesion of palate, palate NOS, cheek mucosa, vestibule of mouth, overlapping lesion of other/unspecified mouth. Cancers of the **oropharynx** encompass primary tumors of the base of tongue, lingual tonsil, soft palate, uvula, retromolar area, tonsillar fossa, tonsillar pillar, overlapping lesion of tonsil, tonsil NOS, vallecula, lateral wall of oropharynx, posterior wall of oropharynx, overlapping lesion of oropharynx, oropharynx NOS. Cancers of the **larynx** encompass primary tumors of the anterior surface of the epiglottis, glottis, supraglottis, subglottis, laryngeal cartilage, overlapping lesion of larynx, larynx NOS. Cancers of the **hypopharynx** encompass primary tumors of pyriform sinus, postcricoid region, aryepiglottic fold, posterior wall of hypopharynx, overlapping lesion of hypopharynx, hypopharynx NOS, pharynx NOS, waldeyer's ring and overlapping lesion of lip/oral cavity/ pharynx.

HNC data dates as far back as 1975 in the SEER database. HNC incidence was broken down into 10-year intervals from 1975-1984, 1985-1994, 1995-2004 and 2005-2016. Specific age cohort data was recorded for the last four decades for individuals 0-39, 40-59 and 60+ years of age. For study purposes, patients 0-39 years old were considered "young", patients ranging from 40-59 years of age were considered "middle-aged" and patients in the 60+ age group were considered "elderly". Data was broken down by decade and age cohort for each primary tumor site. Data for primary tumor site and mean/median age of diagnosis were also included for each decade. Additional data for the incidence of each of the four HNC subsites over time was also collected.

Data Analysis

Patients with HNC were extracted from the SEER*STAT case listing session. Patients' demographics were summarized across four different time intervals and as a whole population. Patients' age at HNC onset were treated as both continuous variable and categorical variable and were summarized by tumor site groups and different time groups. Similar analysis was done for age at HNC onset stratified by gender.

Results

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Demographics

A total of 273,352 cases were analyzed, 199,484 male and 73,868 female. The proportion of HNC patients went from 73.9% to 73.6% and the proportion of female patients went from 26.1% to 26.4% from 1975-2016 (Table 1). In total, white patients constituted 84.2%, black patients constituted 10.7%, American Indian/Alaska Native patients constituted 0.5%, and Asian or Pacific Islander patients constituted 3.9% of HNC patients from 1975-2016 (Table 1). Race was unknown in 0.6% of patients (Table 1).

f the four HNC subsets of focus from 1975-2016, 32.2% of primary tumors were in the oral cavity, 31.8% were in the oropharynx, 28.2% were in the larynx, and 7.8% were in the hypopharynx. (Table 1).

Age at Diagnosis

Site-based mean and median age of diagnosis for each decade is displayed in Table 2. The mean age at diagnosis for primary tumors of the oral cavity was 64.2 years, oropharynx was 61.1 years, larynx was 64.6 years and hypopharynx was 64.5 years. Mean age at diagnosis increased for all subsites except for cancers of the oropharynx. Oropharyngeal cancers exhibit a decrease in the mean age at diagnosis over the last four decades from 61.5 years in 1975-1984 to 61.2 years in 2005-2016 (Table 2). Of the four subsites combined, mean age at diagnosis has increased from 62.8 years to 63.6 years (Table 2).

Age at Diagnosis by Decade of Life

Age at diagnosis was evaluated by decade of life to ensure that the mean and median results were not obscuring shifts within the population.

Oral Cavity

From 1975 to 2016, the proportion of patients diagnosed at 0-39 years old has increased, while the proportion of patients diagnosed at 40-59 has decreased, and the proportion diagnosed at 60+ has not changed (Table 3).

Oropharynx

The proportion of patients diagnosed at 0-39 years of age has decreased, 40-59 has increased, and 60+ has decreased (Table 3).

Larynx

The proportion of patients diagnosed at 0-39 years of age decreased, 40-59 decreased, and 60+ has increased.

Hypopharynx

he proportion of patients diagnosed at 0-39 years of age decreased, 40-59 decreased and 60+ increased (Table 3).

Overall

When looking at age breakdown for all subsites combined, there is a decrease of 0.1% in the proportion of patients diagnosed 0-39 years of age (Table 3). There is a proportional increase in patients diagnosed at 40-59 years of age, and there is a proportional decrease in patients diagnosed at 60+ years of age (Table 3).

Proportional Trends by Subsite

Out of the four HNC subsets, cancers of the oropharynx have proportionally increased, specifically in the middle-aged population from 1975 to 2016, while cancers of the larynx, oral cavity and hypopharynx have proportionally decreased in the same time-frame (Table 1). Additionally, regional data showed similar trends in all four subsites throughout each region (West, Northeast, Midwest, Southwest and Southeast). No significant deviations were noted in any region (Table 1).

Age at Diagnosis by Gender

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In the last four decades,199,484 men and 73,868 women have been diagnosed with oral cavity, larynx, oropharynx and hypopharynx cancers (Table 1, 4). When assessing age at diagnosis, it was found that women were diagnosed proportionally higher in the young (0-39 years) age range (4.1% women vs. 3.0% men; Table 4). However, men are diagnosed with HNC at a rate about three times higher than women.

Discussion

Our study evaluated age-related trends in HNC (oral cavity, pharynx, oropharynx, hypopharynx) from 1975 to 2016. This was done in order to visualize proportional changes in young (0-39 years old), middle-aged (40-59 years old) and elderly (60+ years) patients. The results demonstrated that the mean age at diagnosis of the four HNC subsites combined has increased in the last four decades and similar trends can be seen within every subsite of HNC, with the exception of oropharyngeal cancer. The increased age at diagnosis reflects similar trends in the aging of the United States population (20,21,22). Individuals in the U.S. are living longer (21,21,22), and this is likely a contributing factor to the increasing age of cancer patients.

In the context of oral cavity cancers, there is an increase of mostly young patients and a decrease in middle-aged patients (Table 3). The oral cavity is the only HNC subsite exhibiting a true proportional increase in young patients (Table 3). Cancers of the oral cavity have encompassed a smaller proportion of HNC over time and exhibit a decreasing incidence over the last 40 years (Table 1). From the 1950s to the 1980s, the incidence of oral cavity cancer increased significantly in young white males, which was attributed to tobacco usage (23,24,25). However, when looking specifically at the female population, the incidence of oral cavity cancers has steadily increased from 2008 and onwards. These results support similar findings of increased incidence of oral cavity cancers in women in recent years (13,14) and case reports of very young patients presenting with oral cavity tumors (15,16).

In the context of oropharyngeal cancers, there is an increase in middle-aged patients and a decrease in young and elderly patients (Table 3). Additionally, we found that oropharyngeal cancer is the only subset of HNC that exhibits an increase in incidence in both males and females. These findings are echoed in many other studies (4,5,9,10). This increase in incidence has been attributed to the rising HPV epidemic and oral sex practices in the United States (4,5,8,10,11). When observing statistics from HPV-induced cervical cancers, infection is usually acquired between 20-30 years of age (26), and incidence of cervical cancer peaks around 20-30 years after beginning sexual activity (27). This places peak incidence of cancer at 40-60 years of age. Similar results are seen when evaluating for HPV-induced oropharyngeal cancer. A Canadian study by Claudie *et al* . (28) found that most individuals within the study began oral sex practices between the ages of 17-30, and that risk of oropharyngeal cancers increased significantly 30 years after this time. This places the highest risk of HPV-induced oropharyngeal cancer at above 47 years of age, which is confirmed by our results of higher proportions of middle-aged individuals acquiring oropharyngeal cancer (Table 3).

When assessing laryngeal cancers, there is an increase in elderly patients, and a decrease in middle-aged and young patients (Table 3). hese results are contradictory to previous case reports (17,18) and do not support the concerns that this cancer is occurring at younger ages. The proportion of young people diagnosed with laryngeal cancer has decreased in the last 40 years and laryngeal cancer patients are actually getting older at the time of diagnosis (Table 3). A Lithuanian study by Jaseviciene*et al* . (29) echoes these findings and quantifies the aging of the laryngeal cancer population. They report that the mean age at diagnosis of laryngeal cancer is increasing annually by 0.1566 years for men and 0.0602 years for women in Lithuania (29).

A higher proportion of elderly patients is also being diagnosed with hypopharyngeal cancer (Table 3), and hypopharyngeal cancer encompasses a smaller proportion of HNC cases now than in 1975 (Table 1). Another U.S. population study by Kuo*et al* . reports similar findings (30). However, hypopharyngeal cancer incidence has been noted to increase in France and some Asian countries This has been attributed to increased tobacco use (31).

Aside from age, an interesting trend observed in our gender-stratified HNC analysis was that the percentage of young (0-39 years) HNC patients is much higher in females than males (4.1% women vs. 3.0% men; Table

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4). However, overall cases of HNC are approximately three times higher in men than in women. In other words, men are more likely than women to present with HNC, but the women with HNC are more likely than men to present with the cancer at a young age.

Previous studies have addressed epidemiological trends of HNC, but they did not clearly identify proportional changes amongst age cohorts over time, leaving us to wonder if HNC patients are truly becoming younger. Bean et al. utilized the SEER database to evaluate differences in survival between small cell and squamous cell HNC. Although the study does show a breakdown of HNC age and subsite separately, it does not show age cohorts within the subsites, nor does it demonstrate temporality as does ours (32). A 2015 study by Gillison et al. touched on our primary question of age and HNC, but is restricted to oropharyngeal cancer and focuses on incidence, not proportional change of age cohorts over time (33). Mourad et al. similarly touched on HNC and age, but they focused on incidence, not proportional age prevalence, within a single decade and do not show subsites (4). While these studies, and many others, highlight interesting trends of HNC epidemiology, the primary question of whether patients are becoming younger or older has not been clearly addressed. Our study directly examines the relative change of prevalence between age cohorts over several decades. Our study also has the virtue of looking at multiple HNC subsites over the entire history of the SEER registry.

Conclusion

The mean age at diagnosis has increased in the last 40 years for three of the four HNC evaluated in this study, which is consistent with the aging U.S. population. Oropharyngeal cancer was the only subsite to have an increase in incidence in both males and females with a proportional increase in middle age (40-59 year) patients Cancers of the oral cavity were the only subset of HNC to show a true increase in the proportion of young (0-39 year) patients. Case reports citing more young patients becoming diagnosed with other types of HNC are not currently supported by the data. When stratifying by gender, the proportion of young patients in female HNC cases is much higher than the proportion of young patients in male HNC cases.

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22. Table 1. Resident population, by age, sex, race, and Hispanic origin: United States, selected years 1950–2016. (2017). Retrieved from https://www.cdc.gov/nchs/data/hus/2017/001.pdf
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Tables:

Table 1. Demographics and Tumor Site Comparisons Among the Four Diagnosis Time Groups

Table 1. De

	Time Group 1975-1984 (N
Gender, n (%)	

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Table 1. Demographics and Tumor Site Comparisons Among the Four Diagnosis Time Groups	Table 1. De
Male	23063 (73.9%
Female	8136 (26.1%)
Race (W, B, AI, API), n (%)	
White	27296 (87.5%
Black	3075 (9.9%)
American Indian/Alaska Native	43 (0.1%)
Asian or Pacific Islander	710 (2.3%)
Unknown	75 (0.2%)
Location, n (%)	
Northeast	5450 (17.5%)
Southeast	2233 (7.2%)
Midwest	10511 (33.7%
West	11638 (37.3%
Southwest	1367 (4.4%)
Site, n (%)	
Oral Cavity	11517 (36.9%
Oropharynx	6651 (21.3%)
Larynx	9905 (31.7%)
Hypopharynx	3126 (10.0%)

Table 2. Age at Diagnosis by Time Period Stratified by Tumor Site	Table 2. Age at Diagnosis by Time Pe
Site	**Statistics**
Oral Cavity	Mean(SD), Total N
	Median(Quartiles)
Oropharynx	Mean(SD), Total N
	Median(Quartiles)
Larynx	Mean(SD), Total N
	Median(Quartiles)
Hypopharynx	Mean(SD), Total N
	Median(Quartiles)
Total Combined	Mean(SD), Total N
	Median(Quartiles)

Table 3. Age Group at Diagnosis Compared By Time Period Stratified By Tumor Site and Overall	*Table 3. Age Group at*
	1975-1984
Oral Cavity	**Oral Cavity**
Age Group, n (%)	**N=11517**
0-39	479 (4.2%)
40-59	3736 (32.4%)
60+	7302 (63.4%)
Orpharynx	
Age Group, n (%)	**N=6651**
0-39	207 (3.1%)
40-59	2602 (39.1%)
60+	3842 (57.8%)
Larynx	

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Table 3. Age Group at Diagnosis Compared By Time Period Stratified By Tumor Site and Overall	*Table 3. Age Group at*
Age Group, n (%)	**N=9905**
0-39	146 (1.5%)
40-59	3693 (37.3%)
60+	6066 (61.2%)
Hypopharynx	
Age Group, n (%)	**N=3126**
0-39	37 (1.2%)
40-59	1110 (35.5%)
60+	1979 (63.3%)
Overall Combined	
Age Group, n (%)	**N=31199**
0-39	869 (2.8%)
40-59	11141 (35.7%)
60+	19189 (61.5%)

Table 4. Age at Diagnosis by Gender and By Time Period (All 4 Sites Combined)	**Table 4. Age at Diagnc**
	1975-1984
Males (All Tumors Combined)	**Males (All Tumors Cor**
	N=23063
Age at diagnosis	
Mean (SD)	62.7 (11.5)
Median (IQR)	63 (55, 70)
Range	0.0, 103.0
Age Group, n (%)	
0-39	588 (2.5%)
40-59	8276 (35.9%)
60+	14199 (61.6%)
Females(All Tumors Combined)	**Females(All Tumors Co**
	N=8136
Age at diagnosis	
Mean (SD)	63.1 (12.8)
Median (IQR)	63 (55, 71)
Range	0.0, 102.0
Age Group, n (%)	
0-39	281 (3.5%)
40-59	2865 (35.2%)
60+	4990 (61.3%)

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