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Racial disparities in oropharyngeal cancer survival

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ABSTRACT

Background: Oropharyngeal cancer is an important cause of mortality and morbidity. Several studies have revealed racial disparities in head and neck cancer outcomes. The goal of our study was to evaluate the impact of race on survival in patients with oropharyngeal cancer, using a large population-based cancer database.

Materials and methods: This was a retrospective cohort study. Data were extracted from the Surveillance, Epidemiology, and End Results (SEER) 18 Database of the National Cancer Institute. The study cohort included patients diagnosed with oropharyngeal squamous cell carcinoma between 2004 and 2012. The outcomes of interest were overall survival (OS) and disease-specific survival (DSS).

Results: After adjusting for age, sex, marital status, tumor site, and year of diagnosis, black race was associated with worse OS (HR 1.67, $p < 0.0001$) and DSS (HR 1.67, $p < 0.0001$).

Conclusion: Black race is associated with worse survival in patients with oropharyngeal cancer. Further research is needed to elucidate the mechanism by which race impacts survival in oropharyngeal cancer. This may reveal potential areas of opportunity for public health interventions aimed at addressing disparities in cancer outcomes.

Introduction

Oropharyngeal cancer accounts for 10–12% of all upper aerodigestive tract cancers [1]. The incidence of oropharyngeal cancer is rising [2]; approximately 14,000 cases were diagnosed in the United States in 2013, accounting for 2400 deaths [3]. Traditionally, the major risk factors for oropharyngeal cancer are tobacco use and alcohol consumption [4]. More recently, Human Papilloma Virus (HPV) infection has been recognized as a major risk factor for oropharyngeal cancer, and is associated with better prognosis [5–8]. Oropharyngeal cancer is a major cause of mortality, with a 5-year relative survival rate of approximately 50% [9].

Several studies have revealed racial disparities in head and neck cancer outcomes. Black patients have worse survival outcomes than other racial groups for cancers of the oral cavity, larynx, and salivary glands [10–13]. However, it is unclear if this is the case specifically for oropharyngeal cancer. Although African Americans have lower incidence of oropharyngeal cancer compared to whites, some authors have suggested that disparities in head and neck cancer may be the driven by racial differences in HPV positive oropharyngeal cancer [12,14,15]. The goal of our study was to evaluate the impact of race on survival in patients with oropharyngeal cancer, using a large population-based cancer database. We hypothesized that black patients have worse survival than other racial groups.

Materials and methods

Data were extracted from the Surveillance, Epidemiology, and End Results (SEER) 18 Database of the National Cancer Institute, which includes data obtained from 18 population-based cancer registries in the United States. The study cohort included patients diagnosed with oropharyngeal squamous cell carcinoma between 2004 and 2012. The following International Classification of Diseases for Oncology codes were included: C01.9 (Base of tongue, NOS), C02.4 (Lingual tonsil), C05.1 (Soft palate, NOS), C05.2 (Uvula), C09.0 (Tonsillar fossa), C09.1 (Tonsillar pillar), C09.8 (Overlapping lesion of tonsil), C09.9 (Tonsil, NOS), C10.0 (Vallecula), C10.2 (Lateral wall of oropharynx), C10.3 (Posterior wall of oropharynx), (C10.8-Overlapping lesion of oropharynx), and C10.9 (Oropharynx, NOS). Exclusion criteria included multiple primary tumors, cases in which race was recorded as "Unknown," cases in which the mode of therapy was unknown, and cases without any cancer-directed therapy.

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Race was recorded in the SEER database as "White"; "Black"; "Other: American Indian, Alaska Native, Asian/Pacific Islander"; or "Unknown." For analysis, race was dichotomized to "Black," and "White/Other." Marital status was grouped as "married" (including common law) or "single" (single-never married, divorced, widowed). Tumor site was grouped as "base of tongue," "soft palate," "tonsil," "pharyngeal wall," and "Other." Unresectable tumor was defined as T4b or N3 tumor. All cases were coded using AJCC staging 6th edition [16].

The SEER computer software (SEER*Stat version 8.3.2; National Cancer Institute, Bethesda, Maryland, USA; Information Management Services, Inc., Calverton, Maryland, USA) was used to extract data from the SEER database. The statistical analysis was performed using SAS system, version 9.4 (SAS Institute, Inc., Cary, NC, USA). Candidate covariates for the analysis included demographic characteristics (race, age and gender), marital status, year of diagnosis, subsite, AJCC stage group, presence of distant metastasis, presence of unresectable tumor, histologic grade, surgical resection of primary site, treatment with neck dissection, and radiation therapy. The primary outcome variable was overall cumulative survival OS. The secondary outcome variable was disease-specific cumulative survival DSS. Survival analysis was performed using Kaplan-Meier analysis. Sensitivity analysis was performed by repeating the analysis after excluding patients with distant metastasis and unresectable tumor. Cox proportional hazard regression model was used for multivariable analysis. Race, age, sex, marital status, year of diagnosis, site, AJCC stage group, presence of distant metastasis, presence of unresectable tumor, histologic grade, surgical resection of primary site, treatment with neck dissection, and radiation therapy were entered a priori into the model. Missing values were handled by performing multiple imputation using Markov chain Monte Carlo method. Twenty repetitions were used to yield about 99% efficiency. An estimate was considered statistically significant at $\alpha = 0.05$. This study was exempt from review by the Stanford University School of Medicine Institutional Review Board because it was conducted using de-identified public data.

Results

Univariable analysis

From 2004 to 2012, the SEER database identified 13,434 patients meeting the inclusion criteria. The patients' characteristics are displayed in Table 1. Oropharyngeal subsite varied according to race with 19.2% of tumors occurring in subsites other than the tonsil and base of tongue, compared with 9.5% in non-black patients ($p < 0.0001$). Race was not associated with early (Stages I or II) vs. advanced (Stages III or IV) AJCC stage at presentation. However, black patients were more likely to present with distant metastasis and unresectable tumors. Black patients were less likely to have poorly differentiated tumors.

Table 1
Patient characteristics.

Variable	Black	White/Other	P value
Mean Age (SD)	57.5 (9.9)	58.9 (10.4)	<0.0001
Female	292 (21%)	2034 (16.9%)	<0.0001
Married	425 (30.6%)	7033 (58.4%)	<0.0001
Site			<0.0001
Tongue base	490 (35.3%)	4938 (41%)	
Soft Palate	109 (7.9%)	461 (3.8%)	
Tonsil	631 (45.5%)	5964 (49.5%)	
Pharyngeal Wall	30 (2.2%)	168 (1.4%)	
Other	128 (9.2%)	515 (4.3%)	
Advanced AJCC Stage	1219 (87.8%)	10,426 (86.6%)	0.186
Distant Metastasis	80 (5.8%)	300 (2.5%)	<0.0001
Unresectable Tumor	264 (19%)	1187 (9.9%)	<0.0001
Poorly Differentiated	432 (31.1%)	4690 (38.9%)	<0.0001
Surgical Resection	392 (28.2%)	4683 (38.9%)	<0.0001
Radiation Therapy	1239 (89.3%)	10,855 (90.1%)	0.003
Neck Dissection	206 (14.8%)	2789 (23.2%)	<0.0001

The results of the univariable analysis are shown in Table 2. Black patients had worse overall survival (OS) and disease-specific survival (DSS), compared with other racial groups ($p < 0.0001$) (Fig. 1). The difference in OS between racial groups remained after stratifying by AJCC stage group ($p = 0.0038$ for early stage, $p < 0.0001$ for advanced stage), T stage ($p < 0.0001$), and nodal metastasis ($p < 0.0001$). The difference in DSS between racial groups remained after stratifying by AJCC stage group ($p = 0.0038$ for early stage, $p < 0.0001$ for advanced stage), T stage ($p < 0.0001$), and nodal metastasis ($p < 0.0001$).

A subset analysis was performed, excluding patients with distant metastasis and unresectable tumors. Black patients still had worse OS than other racial groups (5-year OS 51.0% vs. 73.5%, $p < 0.0001$). Black patients also had worse DSS, compared with other racial groups (5-year DSS 61.4% vs. 79.8%, $p < 0.0001$).

Multivariable analysis

The results of the multivariable analysis for overall survival (OS) are shown in Table 3. Black race was associated with worse OS (HR 1.67, $p < 0.0001$), after adjusting for age, sex, marital status, year of diagnosis, site, AJCC stage group, presence of distant metastasis, presence of unresectable tumor, histologic grade, and modes of therapy. Married status was associated with improved OS (HR 0.59, $p < 0.0001$). Sex was not associated with OS (HR 1.04, $p = 0.32$).

The results of the multivariable analysis for disease-specific survival (DSS) are shown in Table 4. Black race was associated with worse DSS (HR 1.67, $p < 0.0001$), after adjusting for age, sex, marital status, year of diagnosis, site, AJCC stage group, presence of distant metastasis, presence of unresectable tumor, histologic grade, and modes of therapy. Married status was associated with improved DSS (HR 0.60, $p < 0.0001$). Female sex was associated with worse DSS (HR 1.10, $p = 0.03$).

Discussion

The results of our study show that race is associated with survival in oropharyngeal cancer. Black patients were more likely to present with distant metastasis and unresectable tumors. Black patients had worse OS and DSS than other racial groups, even after adjusting for age, sex, marital status, year of diagnosis, site, AJCC stage group, presence of distant metastasis, presence of unresectable tumor, histologic grade, and modes of therapy. Married status was associated with improved OS and DSS. Female sex was associated with slightly worse DSS, but had no impact on OS.

Few studies have examined racial disparities in oropharyngeal cancer. Weatherspoon et al. examined oral cavity and oropharyngeal cancer incidence trends and disparities, using the SEER database [14]. They found that whites had higher incidence risk compared with all other race/ethnicity groups. Zandberg et al. assessed racial disparities in 1318 patients with oral cavity, oropharyngeal, hypopharyngeal, or laryngeal tumors treated at their institution [12]. They found that black race was associated with worse survival in head and neck cancer patients. Similar to our study, they found that black race was associated with worse overall survival for oropharyngeal cancer patients specifically. However, race did not impact survival for patients with oral cavity cancer. Similar to our study, they also found that sex was not associated with OS. Unlike our study, they did not assess DSS. They also