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Decreased overall survival in black patients with HPV-associated oropharyngeal cancer

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Abstract

Purpose: Racial disparities for overall survival (OS) in head and neck cancer have been well described. However, the extent to which these disparities exist for HPV-associated oropharyngeal squamous cell carcinoma (OPSCC), and the contribution of demographic, clinical, and socioeconomic status (SES) variables, is unknown.

Materials and Methods: Patients were identified from the Carolina Head and Neck Cancer Epidemiology Study (CHANCE), a population-based study in North Carolina. Cox proportional hazards regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for OS in black versus white patients with sequential adjustment sets.

Results: A total of 157 HPV-associated OPSCC patients were identified. Of these, 93% were white and 7% were black. Black patients with HPV-associated OPSCC were more likely to be

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younger, have an income <$20,000, live farther away from clinic where biopsy was performed, and have advanced T stage at diagnosis. Black patients had worse OS in the unadjusted analysis (HR 4.9, 95% CI 2.2–11.1, p<0.0001). The racial disparity in OS slightly decreased when sequentially adjusting for demographic, clinical, and SES variables. However, HR for black race remained statistically elevated in the final adjustment set which controlled for age, sex, stage, smoking, alcohol use, and individual-level household income, insurance, and education level (HR 3.4, 95% CI 1.1–10.1, p=0.028).

Conclusion: This is the first population-based study that confirms persistence of racial disparities in HPV-associated OPSCC after controlling for demographic, clinical, and individual-level socioeconomic factors.

Keywords

Head and neck neoplasms; disparities; race; survival; human papillomavirus

1.1. Introduction

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer in the United States, affecting approximately 65,410 new patients in 2019.[1,2] Over the past three decades, HNSCC epidemiology has changed significantly due to the rapidly increasing incidence of oropharyngeal squamous cell carcinoma (OPSCC).[3] This is primarily driven by rising exposure to the human papillomavirus (HPV) infection, which now accounts for 60–70% of incident OPSCC cases.[4] Compared to HPV-negative OPSCC, the demographic profile of patients with HPV-positive OPSCC tends to be younger, male, white, and non-smokers.[4] It is estimated that there are 3,500 new cases of HPV-associated OPSCC diagnosed in women and 15,500 in men each year in the United States.[5] White patients with OPSCC in the United States are more likely than black patients to have HPV-positive tumors (67.6% vs. 42.3%, respectively; p<0.001).[6] Most studies evaluating the prognosis for patients with OPSCC have been composed of primarily of white patients. To date, there is limited information regarding the prognosis of black patients with HPV-associated OPSCC.

Racial disparities in HNSCC have been well described, but it is unknown if these findings translate to HPV-associated OPSCC, which is now recognized as a distinct clinicopathologic entity. Although black patients account for a minority of all HNSCC cases, they contribute disproportionately to the morbidity and mortality associated with this disease.[7,8] Black HNSCC patients are diagnosed at more advanced disease stage and have worse survival outcomes compared to white HNSCC patients.[9–11] Previous studies have suggested that lower socioeconomic status and differential access to care contribute to this disparity.[11–14] Some studies have shown that the racial disparities in HNSCC are largely driven by the OPSCC subsite, given that HPV-associated disease is more prevalent in white patients and has better prognosis.[15–18] However few studies have examined racial disparities in OPSCC while also assessing the relative influence of HPV-status.

We recently conducted a systematic review of studies assessing racial disparities in OS in OPSCC after adjusting for HPV-status.[18] There were only 5 studies in the current literature that examined survival disparities by race after adjusting for HPV-status in OPSCC,[19–23] and

none included measures of SES in the adjustment set. Furthermore, only one study included alcohol use in the adjustment set. Our findings suggested that HPV-status accounts for much of the racial disparity in OS for OPSCC, but our conclusions were limited by the small number of relevant studies and narrow adjustment sets.

To address this gap in current literature we examined racial differences in HPV-associated OPSCC outcomes using a population-based study with information on individual level-SES, as well as comprehensive demographic, clinical, and treatment variables. Previous studies examining racial disparities have relied either on single-institution data, clinical trial data, or cancer registry data in which this information was not available.

1.2. Methods

1.2.1. Study Population

Data for this analysis was obtained from the Carolina Head and Neck Cancer Epidemiology Study (CHANCE), a population-based study in North Carolina.[24] Eligible cases were diagnosed with their first primary squamous cell carcinoma of the oral cavity, pharynx, and larynx diagnosed between January 1st, 2002 and February 28th, 2006; were ages 20 to 80 years at diagnosis; and resided in a 46-county region in central North Carolina. Case ascertainment relied on rapid identification of newly diagnosed cancer cases through the North Carolina Central Cancer Registry (NCCCR). The cancer registrars of 54 hospitals in the study area were contacted monthly to identify potentially eligible cases. Potentially eligible study subjects were mailed a brochure describing the purpose of the study, and upon consent, a study nurse conducted an at-home in-person interview. There were 1381 cases of HNSCC in CHANCE. Our present analysis included only tumors that were p16+ and classified as oropharynx cancers (C01.9, C02.4, C05.1, C05.2, C09.0, C09.1, C09.8, C09.9, C10.0–C10.4, C10.8, and C10.9). Samples that failed p16 typing were not included. Staging classification was based on the American Joint Commission on Cancer (AJCC) 8th edition. This study was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

1.2.2. Questionnaire and Covariate measurement

Demographic, lifestyle, oral health, diet, and other common risk factor information were collected using a structured questionnaire during an in-home visit conducted by trained nurse-interviewers. Potential confounders were selected *a priori* based on their potential associated with survival. These included age, race, gender, education, annual income, smoking, and alcohol consumption. Covariates obtained from the questionnaire included age, sex, race; pack-years of cigarette smoking; ever-consumption of alcohol products; whether the subject was covered by health insurance on diagnosis date, what type of insurance the subject was covered by; household income, and highest attained education level. Race was self-reported from a list of the following options: white, black, American Indian, Alaskan Native, Asian/Pacific Islander, other, and don’t know. Given the low number of other and unknown race (n=28), we focused our analysis on patients who self-identified as white or black. Clinical information such as TNM stage and primary treatment were abstracted from the subjects’ medical record and reviewed by a pathologist and head neck

cancer surgeon. Tumor HPV-status was assessed using p16 immunohistochemistry, and the full protocol has been previously reported in detail.[25]

1.2.3. Survival Assessment

CHANCE data were linked to the National Death Index (NDI) based on name, social security number, date of birth, sex, race, and state of residence to identify deaths through December 31, 2013. The NDI is a national file of identified death record information, including cause of death compiled from computer files submitted by State Vital Statistics offices. Greater than 75% of the CHANCE cases were perfect or near-perfect NDI matches on social security number, date of birth, and sex. The remaining near-matches were confirmed by examining the United States Social Security Death Index and obituaries on newspaper websites. We chose 5-year overall survival as our endpoint for this study, as there is a decreased contribution by the tumor to overall survival after this timepoint. Disease-specific survival was not available for this analysis secondary to lack of data on specific cause of death for patients in CHANCE.

1.2.4. Statistical Analysis

Descriptive statistics were calculated, and bivariate testing methods included *t* and chi-squared tests. Overall survival (OS) was calculated as time from diagnosis to either date of death due to any cause or censoring on December 31st, 2013 for individuals who were still alive, whichever came first. Subjects who were still alive on December 31st, 2013 were censored on that date. Hazard ratios (HRs) and 95% confidence intervals (CI) for the independent effects of race on overall survival were estimated by Cox proportional hazards regression models. Sequential adjustment sets were used to examine the relative contribution of demographic, clinical and SES variables to the racial survival disparity. Variables that were missing >10% of observations were left out of the survival analysis, which was determined as an *a priori* threshold. These included rural/urban household designation (n=44 missing) and driving distance to clinic where biopsy was performed (n=49 missing). All variables were treated as categorical variables for the survival models. The proportional hazards assumption was met for all covariates and there was no evidence of multicollinearity on variance inflation factor testing. STATA 16 (StataCorp, College Station, TX) was used for all analyses.

1.3. Results

1.3.1. Baseline Characteristics

There were 157 patients diagnosed with HPV-positive OPSCC. Of these, 146 patients identified as white and 11 as black. Baseline characteristics are summarized (Table I). The majority of patients were male (82%) and between 50 to 65 years of age (53%). Forty-two percent of individuals in our sample had an education of high school or less. Eleven percent had no medical insurance, and 18% had a household income of less than $20,000. The majority of patients in our sample reported at least a 10 pack-year smoking history (57%) and reported drinking alcohol (83%). The most common treatment modality was chemoradiation (39%), followed by surgery with adjuvant chemoradiation (26%). Twenty-

nine percent of patients had advanced T stage at diagnosis. Interestingly, only 2 out of the 157 patients presented with distant metastases.

Compared to white patients, black patients with OPSCC were significantly more likely to be younger, have an income <$20,000, live farther away from clinic where biopsy was performed, and have advanced T stage at diagnosis. Black patients were more likely to have at least a 10 pack-year smoking history (82%) compared to white patients (56%), although this difference was not statistically significant (p=0.228). There were no significant differences by race in terms of treatment type (P=0.805) or number of treatment modalities received (P=0.472). No other baseline characteristics varied significantly by race.

1.3.2. 5-year Overall Survival Analysis

In the unadjusted survival analysis, black HPV-positive OPSCC patients had significantly worse 5-year OS compared to white patients (HR 4.9, 95% CI 2.2–11.1, p<0.0001). We next sequentially adjusted for demographic, clinical, and SES variables. First, after adjustment for age, sex, T stage, N disease, and distant metastases, the racial disparity in 5-year OS remained statistically significant (HR 4.6, 95% CI 1.8–12.0, p=0.002) (Table II). As expected, T4 disease was associated with significantly worse 5-year overall survival compared to T1 disease (HR 2.5, 95% CI 1.0–6.3). Nodal disease and the presence of distant metastases at diagnosis were associated with elevated but non-statistically significant risk of death.

Second, smoking and alcohol use were added to the previous adjustment set. The association between black race and worse 5-year overall survival persisted (HR 4.1, 95% CI 1.5–11.4, p=0.007) (Table III). Neither smoking (>10 pack-years) nor alcohol use was significantly associated with worse overall survival (HR 1.0, 95% CI 0.5–2.2 and HR 1.6, 95% CI 0.5–4.6, respectively).

Finally, individual-level education, household income, and insurance status were added to the previous adjustment set, and the racial disparity remained statistically significant (HR 3.4, 95% CI 1.1–10.1, p=0.028) (Table IV). Having no insurance (HR 3.0, 95% 0.9–9.8) and a household income <$20,000 (HR 1.9, 95% CI 0.5–6.6) were associated with non-significant trends towards worse overall survival in the fully adjusted model.

1.4. Discussion

This is the first population-based study that confirms worse HPV-associated OPSCC survival outcomes in black patients across a range of adjustment sets incorporating demographic, clinical, and individual-level SES variables. It has previously been documented that racial differences in SES and access to care are significant determinants of head and neck cancer disparities.[11–14,26,27] In OPSCC, racial differences in HPV tumor-status have been shown to contribute to the survival disparity.[18,28] However, the relative contribution of HPV-status, tobacco use, alcohol use, treatment, and SES to racial disparities in OPSCC has not been determined. Our analysis with sequential adjustment sets demonstrates that racial differences in SES contributes to some but not all of the disparity.

Our findings build upon the growing evidence in current literature for the presence of racial disparities in OPSCC. In a large database analysis of OPSCC stratified by HPV-status, Faraji et al. found that there was a weak but non-significant trend towards worse overall survival (OS) among black patients with HPV-associated OPSCC after adjusting for age, sex, race, year of diagnosis, insurance status, income, education, rural residence, facility region, TNM stage, Charlson Deyo score, and treatment.[29] A recent analysis of the SEER database found that among patients with HPV-associated OPSCC, black patients had significantly worse cancer-specific mortality than white patients even after adjusting for county-level indicators of SES.[30] In another study, no racial difference in OS was found when controlling for treatment received in the Veteran's Affairs medical system.[19] It is possible that the more homogenous care afforded by the VA system could have mitigated some of the racial disparity attributable to differences in SES and access to care.

There may be several explanations for the persistence of the racial disparity in OS after adjustment for clinical and socioeconomic factors. First, unmeasured confounders in socioeconomic factors, physician and system factors, and access to care may exist. We found that black patients were more likely to have a low income compared to white patients, but our sample lacked the power to adjust for other variables such as frequency of primary care visits or routine dental visits. Studies have found that patients lacking routine dental visits are diagnosed at more advanced stages of head and neck cancer,[31–33] although it is unknown if this pattern varies by race. In the past, racial disparities were largely attributed to genetic differences, but it is now recognized that race is a complex social construct and genetic factors are not likely to integrate with socially-defined racial groups as previously thought.[34]

Our study has several limitations. First, our study population had a small number of black patients with HPV-associated OPSCC. It should be noted that this is a limitation nationally, thereby limiting precise estimation of differences in this study population. Also, p16 testing was not routinely performed at the time of data collection for this study so our sample likely underestimates the true number of HPV-associated OPSCC patients in CHANCE. Given the small sample size of our study, it is important to recognize that some of the non-significant findings may be due to lack of statistical power rather than a true non-effect. Efforts are being undertaken to combine databases to increase the sample size of black patients with HPV-associated OPSCC for future validation studies. Another limitation is that the CHANCE database did not collect data on patient comorbidities, which may confound the relationship between race and OS. Disease specific mortality was not included in the analysis due to a lack of data on the specific cause of death for many of the CHANCE patients.

Our findings may have implications for cancer treatment and future research directions. There is strong evidence to support that patients with HPV-associated OPSCC have improved treatment response and survival outcomes compared to patients with HPV-negative disease.[35] These findings have led to efforts to de-intensify treatment with the goal of alleviating therapy-related morbidity and mortality. Our results suggest that black patients with HPV-associated OPSCC may have worse outcomes despite their HPV-positive tumor status, and therefore, may not receive the same benefits from treatment deintensification. It is important to note that in our sample, we found no differences by race with regards to

treatment type or number of treatments modalities received. Future de-intensification trials should closely monitor survival outcomes by race to ensure that this disparity is not being propagated.

Conclusions

There is a well-established correlation between race and survival outcomes in head and neck cancer. This population-based study demonstrated that the black versus white racial disparity in overall survival for HPV-associated OPSCC is only partially mediated by differences in SES. The persistence of the disparity after adjustment for demographic, clinical, and SES variables suggests the contribution of unmeasured confounders. Future research should seek to elucidate these determinants in order to fully address the racial disparity.

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References

1. El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. WHO Classification of Head and Neck Tumours. 4th edition. International Agency for Research on Cancer; 2017.
2. American Cancer Society. Cancer Facts & Figures 2019. ACS; 2019. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf
3. Marur S, Forastiere AA. Head and Neck Cancer: Changing Epidemiology, Diagnosis, and Treatment. Mayo Clinic Proceedings. 2008;83(4):489–501. doi:10.4065/83.4.489 [PubMed: 18380996]
4. Marur S, D'Souza G, Westra WH, Forastiere AA. HPV-associated head and neck cancer: a virus-related cancer epidemic. Lancet Oncol. 2010;11(8):781–789. doi:10.1016/S1470-2045(10)70017-6 [PubMed: 20451455]
5. Viens LJ, Henley SJ, Watson M, et al. Human Papillomavirus-Associated Cancers - United States, 2008–2012. MMWR Morb Mortal Wkly Rep. 2016;65(26):661–666. doi:10.15585/mmwr.mm6526a1 [PubMed: 27387669]
6. Liederbach E, Kyrillos A, Wang C-H, Liu JC, Sturgis EM, Bhayani MK. The national landscape of human papillomavirus-associated oropharynx squamous cell carcinoma. International Journal of Cancer. 2017;140(3). doi:10.1002/ijc.30442
7. Peterson CE, Khosla S, Chen LF, et al. Racial differences in head and neck squamous cell carcinomas among non-Hispanic black and white males identified through the National Cancer Database (1998–2012). J Cancer Res Clin Oncol. 2016;142(8):1715–1726. doi:10.1007/s00432-016-2182-8 [PubMed: 27251759]
8. Gourin CG, Podolsky RH. Racial disparities in patients with head and neck squamous cell carcinoma. Laryngoscope. 2006;116(7):1093–1106. doi:10.1097/01.mlg.0000224939.61503.83 [PubMed: 16826042]
9. Ragin CC, Langevin SM, Marzouk M, Grandis J, Taioli E. Determinants of head and neck cancer survival by race. Head Neck. 2011;33(8):1092–1098. doi:10.1002/hed.21584 [PubMed: 20967872]

10. Mahal BA, Inverso G, Aizer AA, Bruce Donoff R, Chuang S-K. Impact of African–American race on presentation, treatment, and survival of head and neck cancer. Oral Oncology. 2014;50(12):1177–1181. doi:10.1016/j.oraloncology.2014.09.004 [PubMed: 25261298]
11. Reitzel LR, Nguyen N, Zafereo ME, Li G, Wei Q, Sturgis EM. Neighborhood deprivation and clinical outcomes among head and neck cancer patients. Health Place. 2012;18(4):861–868. doi:10.1016/j.healthplace.2012.03.005 [PubMed: 22445028]
12. Molina MA, Cheung MC, Perez EA, et al. African American and poor patients have a dramatically worse prognosis for head and neck cancer: An examination of 20,915 patients. Cancer. 2008;113(10):2797–2806. doi:10.1002/cncr.23889 [PubMed: 18839393]
13. Shin JY, Yoon JK, Shin AK, Diaz AZ. The influence of insurance status on treatment and outcomes in oral cavity cancer: an analysis on 46,373 patients. International Journal of Oral and Maxillofacial Surgery 2018;47(10):1250–1257. doi:10.1016/j.ijom.2018.03.022 [PubMed: 29655817]
14. Kwok J, Langevin SM, Argiris A, Grandis JR, Gooding WE, Taioli E. The impact of health insurance status on the survival of patients with head and neck cancer. Cancer. 2010;116(2):476–485. doi:10.1002/cncr.24774 [PubMed: 19937673]
15. Zandberg DP, Liu S, Goloubeva O, et al. Oropharyngeal cancer as a driver of racial outcome disparities in squamous cell carcinoma of the head and neck: 10-year experience at the University of Maryland Greenebaum Cancer Center. Head Neck 2016;38(4):564–572. doi:10.1002/hed.23933 [PubMed: 25488341]
16. Schrank TP, Han Y, Weiss H, Resto VA. Case-matching analysis of head and neck squamous cell carcinoma in racial and ethnic minorities in the United States--possible role for human papillomavirus in survival disparities. Head Neck. 2011;33(1):45–53. doi:10.1002/hed.21398 [PubMed: 20848419]
17. Settle K, Posner MR, Schumaker LM, et al. Racial survival disparity in head and neck cancer results from low prevalence of human papillomavirus infection in black oropharyngeal cancer patients. Cancer Prev Res (Phila). 2009;2(9):776–781. doi:10.1158/1940-6207.CAPR-09-0149 [PubMed: 19641042]
18. Lenze NR, Farquhar DR, Mazul AL, Masood MM, Zevallos JP. Racial disparities and human papillomavirus status in oropharyngeal cancer: A systematic review and meta-analysis. Head Neck Published online December 18, 2018. doi:10.1002/hed.25414
19. Zevallos JP, Sandulache VC, Hamblin J, et al. Impact of race on oropharyngeal squamous cell carcinoma presentation and outcomes among veterans. Head Neck. 2016;38(1):44–50. doi:10.1002/hed.23836 [PubMed: 24992520]
20. Goodman MT, Saraiya M, Thompson TD, et al. Human papillomavirus genotype and oropharynx cancer survival in the United States of America. Eur J Cancer. 2015;51(18):2759–2767. doi:10.1016/j.ejca.2015.09.005 [PubMed: 26602016]
21. Fakhry C, Westra WH, Wang SJ, et al. The prognostic role of sex, race, and human papillomavirus in oropharyngeal and nonoropharyngeal head and neck squamous cell cancer. Cancer. 2017;123(9):1566–1575. doi:10.1002/cncr.30353 [PubMed: 28241096]
22. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med. 2010;363(1):24–35. doi:10.1056/NEJMoa0912217 [PubMed: 20530316]
23. Isayeva T, Xu J, Dai Q, et al. African Americans with oropharyngeal carcinoma have significantly poorer outcomes despite similar rates of human papillomavirus-mediated carcinogenesis. Hum Pathol. 2014;45(2):310–319. doi:10.1016/j.humpath.2013.09.006 [PubMed: 24355195]
24. Divaris K, Olshan AF, Smith J, et al. Oral health and risk for head and neck squamous cell carcinoma: the Carolina Head and Neck Cancer Study. Cancer Causes Control. 2010;21(4):567–575. doi:10.1007/s10552-009-9486-9 [PubMed: 20049634]
25. D'Souza G, Anantharaman D, Gheit T, et al. Effect of HPV on head and neck cancer patient survival, by region and tumor site: A comparison of 1362 cases across three continents. Oral Oncol 2016;62:20–27. doi:10.1016/j.oraloncology.2016.09.005 [PubMed: 27865368]

26. Chu KP, Habbous S, Kuang Q, et al. Socioeconomic status, human papillomavirus, and overall survival in head and neck squamous cell carcinomas in Toronto, Canada. Cancer Epidemiology 2016;40:102–112. doi:10.1016/j.canep.2015.11.010 [PubMed: 26706365]
27. Arbes SJ, Olshan AF, Caplan DJ, Schoenbach VJ, Slade GD, Symons MJ. Factors contributing to the poorer survival of black Americans diagnosed with oral cancer (United States). Cancer Causes Control 1999;10(6):513–523. [PubMed: 10616821]
28. Stein E, Lenze NR, Yarbrough WG, Hayes DN, Mazul A, Sheth S. Systematic review and meta-analysis of racial survival disparities among oropharyngeal cancer cases by HPV status. Head & Neck Published online July 7, 2020:hed.26328. doi:10.1002/hed.26328
29. Faraji F, Rettig EM, Tsai H-L, et al. The prevalence of human papillomavirus in oropharyngeal cancer is increasing regardless of sex or race, and the influence of sex and race on survival is modified by human papillomavirus tumor status. Cancer. 2019;125(5):761–769. doi:10.1002/cncr.31841 [PubMed: 30521092]
30. Pike LRG, Royce TJ, Mahal AR, et al. Outcomes of HPV-Associated Squamous Cell Carcinoma of the Head and Neck: Impact of Race and Socioeconomic Status. J Natl Compr Canc Netw. 2020;18(2):177–184. doi:10.6004/jnccn.2019.7356 [PubMed: 32023531]
31. Langevin SM, Michaud DS, Eliot M, Peters ES, McClean MD, Kelsey KT. Regular dental visits are associated with earlier stage at diagnosis for oral and pharyngeal cancer. Cancer Causes Control. 2012;23(11):1821–1829. doi:10.1007/s10552-012-0061-4 [PubMed: 22961100]
32. Groome PA, Rohland SL, Hall SF, Irish J, Mackillop WJ, O'Sullivan B. A population-based study of factors associated with early versus late stage oral cavity cancer diagnoses. Oral Oncol. 2011;47(7):642–647. doi:10.1016/j.oraloncology.2011.04.018 [PubMed: 21612975]
33. Gupta B, Kumar N, Johnson NW. Evidence of past dental visits and incidence of head and neck cancers: a systematic review and meta-analysis. Syst Rev 2019;8(1):43. doi:10.1186/s13643-019-0949-0 [PubMed: 30717784]
34. American Association of Physical Anthropologists. AAPA Statement on Race & Racism.; 2019. Accessed October 25, 2019. https://physanth.org/about/position-statements/aapa-statement-race-and-racism-2019/
35. Wierzbicka M, Szyfter K, Milecki P, Składowski K, Ramlau R. The rationale for HPV-related oropharyngeal cancer de-escalation treatment strategies. Contemp Oncol (Pozn). 2015;19(4):313–322. doi:10.5114/wo.2015.54389 [PubMed: 26557780]

Table I:

Baseline characteristics in HPV-associated OPSCC stratified by race

Race	White		Black		
	No.	%	No.	%	P-value
Age					P=0.008
Age < 50 (n=52)	49	34%	3	27%	
Age 50 – 65 (n=84)	76	52%	8	73%	
Age 65+ (n=21)	21	14%	0	0%	
	146	100%	11	100%	
Sex					P = 0.997
Male (n=129)	120	82%	9	82%	
Female (n=28)	26	18%	2	18%	
	146	100%	11	100%	
Education					P = 0.086
Less than high school (n=25)	22	15%	3	27%	
High school graduate (n=41)	35	24%	6	55%	
Education past high school (n=91)	89	61%	2	18%	
	146	100%	11	100%	
Insurance (relative to private)					P = 0.118
Private insurance (n=93)	90	62%	3	27%	
Medicaid/Medicare (n=24)	21	14%	3	27%	
No insurance (n=18)	15	10%	3	27%	
Other insurance (n=22)	20	14%	2	18%	
	146	100%	11	100%	
Income					P=0.001
Income > $50,000 (n=75)	75	53%	0	0%	
Income $20,000 – $50,000 (n=49)	45	32%	4	36%	
Income < $20,000 (n=29)	22	15%	7	64%	
	142	100%	11	100%	
Rural/Urban Household					P=0.536
Metropolitan (n=90)	85	81%	5	62%	
Micropolitan (n=11)	10	10%	1	12%	
Rural (n=12)	10	10%	2	25%	
	105	100%	8	100%	
Driving Time to clinic where biopsy was performed (1st quartile as baseline)					P=0.049
1st quartile (n=20)	20	20%	0	0%	
2nd quartile (n=31)	30	30%	1	14%	
3rd quartile (n=27)	26	26%	1	14%	
4th quartile (n=30)	25	25%	5	71%	
	101	100%	7	100%	
Smoking (>10 pack-years)					P=0.228
< 10 Pack Years (n=66)	64	44%	2	18%	

Race	White		Black		
	No.	%	No.	%	P-value
> 10 Pack Years (n=90)	81	56%	9	82%	
	145	100%	11	100%	
Alcohol use					P=0.087
None (n=25)	24	17%	1	10%	
Any (n=130)	121	83%	9	90%	
	145	100%	10	100%	
T Stage					P=0.173
T1 (n=43)	41	28%	2	18%	
T2 (n=68)	66	45%	2	18%	
T3 (n=24)	20	14%	4	36%	
T4 (n=22)	19	13%	3	27%	
	146	100%	11	100%	
Early (1–2) vs. Advanced T Stage (3–4)					P=0.027
Early T Stage (n=111)	107	73%	4	36%	
Advanced T Stage (n=46)	39	27%	7	64%	
	146	100%	11	100%	
N stage					P=0.857
N0 (n=29)	26	18%	3	27%	
N1 (n=93)	88	60%	5	45%	
N2 (n=20)	18	12%	2	18%	
N3 (n=15)	14	10%	1	9%	
	146	100%	11	100%	
M Stage					P=0.889
M0 (n=155)	144	99%	11	100%	
M1 (n=2)	2	1%	0	0%	
	146	100%	11	100%	
Treatment Category					P=0.805
Chemotherapy Only (n=1)	1	1%	0	0%	
Radiation Only (n=11)	10	7%	1	9%	
Surgery Only (n=7)	7	5%	0	0%	
Radiation + Chemotherapy (n=61)	54	37%	7	64%	
Surgery + Radiation (n=36)	34	23%	2	18%	
Surgery +	40	27%	1	9%	
Chemoradiation (n=41)	146	100%	11	100%	
Number of Treatment Modalities					0.472
1 (n=19)	18	12%	1	9%	
2 (n=97)	88	60%	9	82%	
3 (n=41)	40	27%	1	9%	
	146	100%	11	100%	

Table II:

5-year Overall Survival in HPV-associated OPSCC adjusted for demographics and stage

	Adjustment with Demographics and Stage*		
	Hazard Ratio	**95% CI**	**P-Value**
Black (vs. white)	4.6	1.8 – 12.0	0.002
Age Category (Relative to < 50)			
50–65	0.8	0.4 – 1.7	0.607
65+	1.3	0.5 – 3.5	0.577
Female sex (relative to male)	0.8	0.3 – 2.0	0.653
T Stage (relative to T1)			
T2	0.7	0.3 – 1.8	0.464
T3	1.6	0.6 – 4.2	0.321
T4	2.5	1.0 – 6.3	0.047
Nodal disease (relative to N0)	1.7	0.7 – 4.2	0.253
Distant Metastases (relative to M0)	5.2	0.7 – 41.7	0.117

*Model adjusted for race, age, sex, T stage, nodal disease, and distant metastases

Table III:

5-year Overall Survival in HPV-associated OPSCC adjusted for demographics, stage, tobacco, and alcohol

	Addition of tobacco and alcohol use*		
	Hazard Ratio	**95% CI**	**P-Value**
Black (vs. white)	4.1	1.5 – 11.4	0.007
Age Category (Relative to < 50)			
50–65	0.9	0.4 – 2.0	0.773
65+	1.4	0.5 – 3.9	0.531
Female sex (relative to male)	0.8	0.3 – 2.0	0.694
T Stage (relative to T1)			
T2	0.8	0.3 – 1.9	0.546
T3	1.5	0.6 – 4.0	0.400
T4	2.5	1.0 – 6.3	0.053
Nodal disease (relative to N0)	1.7	0.7 – 4.2	0.267
Distant Metastases (relative to M0)	4.6	0.6 – 36.5	0.154
Smoking (> 10 pack-years)	1.0	0.5 – 2.2	0.903
Alcohol use (any vs. none)	1.6	0.5 – 4.6	0.403

*Model adjusted for race, age, sex, T stage, nodal disease, distant metastases, smoking, and alcohol use

Table IV:

5-year Overall Survival in HPV-associated OPSCC adjusted for demographics, stage, tobacco, alcohol and SES

	Addition of SES Variables*		
	Hazard Ratio	**95% CI**	**P-Value**
Black (vs. white)	3.4	1.1 – 10.1	0.028
Age Category (Relative to < 50)			
50–65	0.8	0.4 – 1.9	0.698
65+	1.2	0.4 – 3.8	0.817
Female sex (relative to male)	0.5	0.2 – 1.5	0.223
T Stage (relative to T1)			
T2	1.0	0.4 – 2.6	0.985
T3	2.2	0.8 – 6.3	0.131
T4	2.4	0.9 – 6.3	0.081
Nodal disease (relative to N0)	1.2	0.5 – 3.1	0.705
Distant Metastases (relative to M0)	11.4	1.2 – 103.4	0.031
Smoking (> 10 pack-years)	0.6	0.3 – 1.4	0.221
Alcohol use (any vs. none)	1.3	0.4 – 4.0	0.672
Education (relative to less than high school)			
High school graduate	1.0	0.3 – 3.0	0.973
Additional education past high school	0.8	0.3 – 2.1	0.600
Insurance (relative to private insurance)			
Medicaid/Medicare	4.3	1.2 – 15.9	0.028
None	3.0	0.9 – 9.8	0.071
Other	2.5	0.8 – 7.6	0.118
Income (relative to > 50 K)			
Income $20,000 – $50,000	0.8	0.3 – 2.2	0.683
Income < $20,000	1.9	0.5 – 6.6	0.313

*Model adjusted for race, age, sex, T stage, nodal disease, distant metastases, smoking, alcohol use, education, insurance status, and income