Outcomes of HPV-Associated Squamous Cell Carcinoma of the Head and Neck: Impact of Race and Socioeconomic Status

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ABSTRACT

Background: Socioeconomic factors affecting outcomes of HPV-associated squamous cell carcinoma of the head and neck (SCCHN) are poorly characterized. **Methods:** A custom SEER database identified adult patients with primary nonmetastatic SCCHN and known HPV status diagnosed in 2013 through 2014. Multivariable logistic regression defined associations between patient characteristics and HPV status, with adjusted odds ratios (aORs) and 95% confidence intervals reported. Fine-Gray competing risks regression estimated adjusted hazard ratios (aHRs) and 95% confidence intervals for cancer-specific mortality (CSM), including a disease subsite * HPV status * race interaction term. **Results:** A total of 4,735 patients with nonmetastatic SCCHN and known HPV status were identified. HPV-associated SCCHN was positively associated with an oropharyngeal primary, male sex, and higher education, and negatively associated with uninsured status, single marital status, and nonwhite race ($P \leq .01$ for all). For HPV-positive oropharyngeal SCCHN, white race was associated with lower CSM (aHR, 0.55; 95% CI, 0.34–0.88; $P=.01$) and uninsured status was associated with higher CSM (aHR, 3.12; 95% CI, 1.19–8.13; $P=.02$). These associations were not observed in HPV-negative or nonoropharynx SCCHN. Accordingly, there was a statistically significant disease subsite * HPV status * race interaction ($P_{interaction}<.001$). **Conclusions:** Nonwhite race and uninsured status were associated with worse CSM in HPV-positive oropharyngeal SCCHN, whereas no such associations were observed in HPV-negative or nonoropharyngeal SCCHN. These results suggest that despite having clinically favorable disease, nonwhite patients with HPV-positive oropharyngeal SCCHN have worse outcomes than their white peers. Further work is needed to understand and reduce socioeconomic disparities in SCCHN.

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Background

Squamous cell carcinomas of the head and neck (SCCHNs) are increasing in incidence worldwide.[1,2] Contemporary reports have identified HPV infection as a leading risk factor for development of SCCHN, particularly in oropharyngeal carcinoma.[3,4] Although the incidence of HPV-negative oropharyngeal carcinoma in the United States has been declining because of decreased smoking, HPV-positive disease is increasing.[5]

Social determinants of health for HPV-positive and HPV-negative SCCHN are poorly characterized—available data are limited to case reports or retrospective analyses of prospective trials.[5–15] It has been suggested that HPV-negative SCCHN is more common among nonwhite, urban, and poorly insured individuals due to higher smoking rates in these populations.[7,14] Furthermore, the inferior outcomes observed in patients of lower socioeconomic status (SES) with SCCHN have largely been attributed to a predominance of HPV-negative disease.[7,14] However, these hypotheses have not been tested in the prospective setting, given that clinical trials tend to include a disproportionate number of patients who are white and of higher SES.[16] Furthermore, no large population-based studies have examined the burden of HPV-associated disease and cancer-related survival as affected by socioeconomic factors.

Therefore, we sought to characterize the interplay between HPV status, race, socioeconomic factors, and outcomes in SCCHN.

Methods

Study Cohort

We used the custom SEER Head and Neck with HPV Status Database to identify 4,735 adult patients (aged >18 years) with primary nonmetastatic (M0) SCCHN and known HPV status diagnosed in 2013 through 2014.[17] These data are not yet public; we obtained access via a proposal to the SEER custom data group, where the a priori analyses described were determined to be appropriate use of the data. The study inclusion period of 2013 through 2014 represents the years in which HPV status was collected and reviewed for quality assurance.

Table 1. Baseline Patient Characteristics

Characteristic	HPV-Positive SCCHN n (%)	HPV-Negative SCCHN n (%)	Odds of HPV-Positive SCCHN aOR (95% CI)	*P* Value
Total, n	3,262	1,473		
SCCHN subsite				
Nonoropharynx	199 (6.1)	400 (27.2)	Ref	
Oropharynx	3,063 (93.9)	1,073 (72.8)	1.90 (1.62–2.24)	<.001
Tumor stage				
T1	806 (24.7)	298 (20.2)	Ref	
T2	1,183 (36.3)	397 (27.0)	1.14 (0.94–1.37)	.18
T3	507 (15.5)	294 (20.0)	0.80 (0.64–0.99)	.04
T4	403 (12.4)	305 (20.7)	0.68 (0.54–0.85)	.001
Unknown	345 (10.6)	176 (11.9)	0.91 (0.69–1.20)	.502
Nodal stage				
N0	407 (12.5)	306 (20.8)	Ref	
N1	595 (18.2)	300 (20.4)	1.39 (1.11–1.73)	.004
N2a	374 (11.5)	93 (6.3)	2.16 (1.61–2.88)	<.001
N2b	1,139 (34.9)	369 (25.1)	1.82 (1.48–2.23)	<.001
N2c	450 (13.8)	178 (12.1)	1.70 (1.32–2.18)	<.001
N2 NOS	54 (1.7)	71 (4.8)	1.29 (0.83–2.01)	.254
N3	163 (5.0)	82 (5.6)	1.62 (1.16–2.27)	.004
Unknown	80 (2.5)	74 (5.0)	2.10 (1.32–3.34)	.002
Initial definitive treatment[a]				
None	124 (3.8)	116 (7.9)	N/A (not patient-level characteristic)	
Surgery	969 (29.7)	299 (20.3)		
Radiotherapy	2,959 (90.7)	1,248 (84.7)		
Chemotherapy	2,375 (72.8)	1,009 (68.5)		
Age at diagnosis,[b] median (IQR)	N/A		0.92 (0.98–0.99)	<.001
Race				
White	2,774 (85.0)	990 (67.2)	Ref	
Nonwhite	518 (15.9)	483 (32.8)	0.40 (0.31–0.52)	<.001
Sex				
Female	428 (13.1)	338 (22.9)	Ref	
Male	2,834 (86.9)	1,135 (77.1)	1.59 (1.33–1.89)	<.001
Insurance status				
Private or other insurance	2,835 (86.9)	1,091 (74.1)	Ref	
Uninsured	79 (2.4)	70 (4.8)	0.53 (0.37–0.77)	.001
Medicaid	302 (9.3)	286 (19.4)	0.58 (0.47–0.71)	<.001
Unknown	46 (1.4)	26 (1.8)	0.74 (0.43–1.28)	.28

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SEER cancer registries code primary cancer site and histology based on ICD-O-3. Squamous cell carcinoma histology of the head and neck was identified using the following ICD-O-3 histologic type codes: 8050, 8051, 8054, 8070 through 8076, 8083, and 8094. TNM staging was determined using the 7th edition of the *AJCC Cancer Staging Manual*, as provided by SEER (8th edition staging is not yet reported by the database). Race was classified as non-Hispanic white versus nonwhite/Hispanic. Small-area estimates for percent ever-smoker were linked to SEER via estimates developed from the Behavioral Risk Factor Surveillance System (BRFSS) and the National Health Interview Survey (NHIS).

Table 1. Baseline Patient Characteristics (cont.)

Characteristic	HPV-Positive SCCHN n (%)	HPV-Negative SCCHN n (%)	Odds of HPV-Positive SCCHN aOR (95% CI)	*P* Value
Smoking propensity[c]	N/A		1.00 (0.99–1.00)	.72
Percent high school education[d]	N/A		1.02 (1.00–1.03)	.01
Household income,[d] median (IQR)	N/A		1.00 (1.00–1.00)	.22
Marital status				
Married	2,013 (61.7)	723 (52.6)	Ref	
Single	532 (16.3)	354 (25.8)	0.67 (0.56–0.80)	<.001
Divorced/Widowed/Separated	571 (17.5)	312 (22.7)	0.83 (0.69–0.99)	.04
Unknown	146 (4.5)	84 (6.1)	0.78 (0.57–1.07)	.13

Abbreviations: aOR, adjusted odds ratio; HPV, human papillomavirus; IQR, interquartile range; N/A, not applicable; NOS, not otherwise specified; OR, odds ratio; SCCHN, squamous cell carcinoma of the head and neck.
[a]Percentages do not add up to 100 due to receipt of multiple treatments.
[b]When age at diagnosis was treated as a categorical variable (ages 60–64 years vs all other ages ≥15 years [ref]), ages 60–64 years were associated with an increased odds of HPV-positive SCCHN (aOR, 1.22; 95% CI, 1.02–1.45; *P*=.33).
[c]Smoking propensity determined by small area estimates, linked to SEER via estimates developed from the Behavioral Risk Factor Surveillance System (BRFSS) and the National Health Interview Survey (NHIS).
[d]County attribute data, linked to SEER population data by state-county Federal Information Processing Standards codes.

Statistical Analyses

Comparison of Baseline Patient Characteristics by HPV Status

The Wilcoxon rank-sum and Mantel-Haenszel chi-square tests compared distributions of continuous and categorical covariates, stratified by HPV status among patients with M0 disease (N=4,735). Multivariable logistic regression defined adjusted odds ratios (aORs) and 95% confidence intervals (CIs) between patient characteristics and HPV status.

aORs for Presentation With Advanced Disease

Table 1 shows baseline patient characteristics. In addition, we performed multivariable logistic regressions to calculate the aORs of presenting with HPV-positive disease. The following variables pertaining to SES were included in the model: race (white [referent] or nonwhite), insurance status (private or other insurance [referent], uninsured, Medicaid, unknown), and marital status (married [referent], single, divorced/widowed/separated, unknown). Demographic and clinical variables included in the model were age at diagnosis (continuous), sex (female [referent], male), tumor stage (T1 [referent], T2, T3, T4, unknown), nodal stage (N0 [referent], N2a, N2b, N2c, N2 not otherwise specified [NOS], N3, unknown), oropharynx versus nonoropharynx SCCHN subsite (nonoropharynx included nasopharynx, hypopharynx, and other pharyngeal SCCHN), smoking propensity, household income (continuous county variable), education level (continuous county variable), and initial definitive treatment (none [referent], surgery, radiotherapy, chemotherapy). In the SEER database, smoking propensity, education level, and household income are population-level variables abstracted from county data. In Table 2, multivariable logistic regressions defined aORs and associated 95% CIs for odds of presenting with advanced disease (defined as T3–T4 or N2–N3). Given that advanced stage was the outcome of interest in this analysis, T and N characteristics were not included in the model separately.

Cancer-Specific Mortality Estimates by HPV Status, Tumor, and SES Characteristics

STATA/SE, version 14.2 (StataCorp LLP) was used for survival analyses of patients with M0 disease with at least 1 month of follow-up (n=4,476), in which the primary endpoint was cancer-specific mortality (CSM). Patients were stratified into the following 4 subgroups: HPV-positive oropharynx, HPV-negative oropharynx, HPV-positive nonoropharynx, and HPV-negative nonoropharynx. For each of these subgroups, multivariable Fine-Gray competing risks regression was used to estimate hazard ratios for the socioeconomic and clinical factors described earlier.

To ascertain whether there was a differential prognosis of race by HPV status and disease site, a Fine-Gray competing risks regression model for CSM included a race (nonwhite vs white) * disease subsite (nonoropharynx vs oropharynx) * HPV status (positive vs negative) interaction term. Once it was established that this interaction was statistically significant, we performed further multivariable analyses of the 4 individual subgroups that included the original factors in the model, excluding the interaction term, HPV status, and disease subsite.

Using the defined subgroups of HPV status and disease subsite, cumulative incidence plots for CSM were generated for the purposes of illustration along with estimation of 20-month CSM for each subgroup. Adjusted hazard ratios (aHRs) with associated 95% CIs and *P* values were calculated

Table 2. Multivariable aOR of Presenting With Advanced Disease (T3–T4 or N2–N3)

Characteristic	Early Stage n (%)	Advanced Stage n (%)	Odds of Advanced Stage	
			aOR (95% CI)	*P* Value
Total, n	1,246	3,489		
SCCHN subsite				
Nonoropharynx	248 (19.9)	351 (10.1)	Ref	
Oropharynx	998 (80.1)	3,138 (89.9)	2.31 (1.91–2.80)	<.001
HPV status				
Negative	452 (36.3)	1,021 (29.3)	Ref	
Positive	794 (63.7)	2,468 (70.7)	1.22 (1.05–1.42)	.10
Race				
Nonwhite	229 (18.3)	772 (20.8)	Ref	
White	1,017 (81.7)	2,947 (79.2)	0.68 (0.57–0.81)	<.001
Age at diagnosis, median (IQR)	60 (54–67)	59 (53–66)	0.99 (0.99–1.00)	.024
Sex				
Female	258 (20.7)	508 (14.6)	Ref	
Male	988 (79.3)	2,981 (85.4)	1.50 (1.26–1.78)	<.001
Insurance status				
Private or other insurance	1,055 (84.7)	2,871 (82.3)	Ref	
Uninsured	33 (2.6)	116 (3.3)	1.18 (0.79–1.78)	.42
Medicaid	127 (10.2)	461 (13.2)	1.33 (1.06–1.66)	.01
Unknown	31 (2.5)	41 (1.2)	0.44 (0.26–0.72)	.001
Smoking propensity,[a] median (IQR)	40.4 (33.5–44.9)	40 (33.3–44.6)	0.99 (0.98–1.00)	.19
Percent high school education,[b] median (IQR)	87.0 (82.3–89.7)	87.0 (83.1–89.8)	1.01 (1.00–1.06)	.18
Household income,[b] median (IQR), $USD	56,600 (48,700–71,380)	59,740 (50,310–71,020)	1.00 (1.00–1.00)	.94
Marital status				
Married	770 (61.8)	1,966 (56.3)	Ref	
Single	201 (16.1)	685 (19.6)	1.28 (1.06–1.54)	.01
Divorced/Widowed/Separated	210 (16.9)	673 (19.3)	1.38 (1.15–1.66)	.001
Unknown	65 (5.2)	165 (4.7)	1.16 (0.84–1.60)	.36

Abbreviations: aOR, adjusted odds ratio; HPV, human papillomavirus; IQR, interquartile range; SCCHN, squamous cell carcinoma of the head and neck.
[a]Smoking propensity determined by small area estimates, linked to SEER via estimates developed from the Behavioral Risk Factor Surveillance System and the National Health Interview Survey.
[b]County attribute data, linked to SEER population data by state-county Federal Information Processing Standards codes.

for all covariates. Statistical testing was 2-sided, with level of significance set at *P*=.05. The Dana-Farber/Harvard Cancer Center Institutional Review Board approved this study.

Results

Comparison of Baseline Patient Characteristics by HPV Status

As shown in Table 1, there were significant clinical and socioeconomic differences between HPV-positive and HPV-negative subgroups of patients with SCCHN. An oropharyngeal primary (aOR, 1.90; 95% CI, 1.62–2.24; *P*<.001), nodal involvement (aOR, 1.62; 95% CI, 1.16–2.27; *P*=.004 for N3 vs N0), male sex (aOR, 1.59; 95% CI, 1.33–1.89; *P*<.01), and higher education (aOR, 1.02; 95% CI, 1.00–1.03; *P*=.01) were associated with greater odds of having HPV-positive SCCHN. In contrast, bulky primary tumors (aOR, 0.68; 95% CI, 0.54–0.85; *P*=.001 for T4 vs T1), older age at diagnosis (aOR, 0.92; 95% CI, 0.98–0.99; *P*<.001), no health insurance (aOR, 0.53; 95% CI, 0.37–0.77; *P*=.001 for uninsured vs private/other insurance), single marital status (aOR, 0.67; 95% CI, 0.56–0.80; *P*<.001), and nonwhite race (aOR, 0.40; 95% CI, 0.31–0.52; *P*=.01) were associated with higher odds of having HPV-negative SCCHN.

aOR for Presentation With Advanced Disease

Associations between patient characteristics and advanced stage at presentation are shown in Table 2. On multivariable analysis, advanced stage at presentation was positively associated with oropharyngeal subsite (aOR, 2.31; 95% CI,

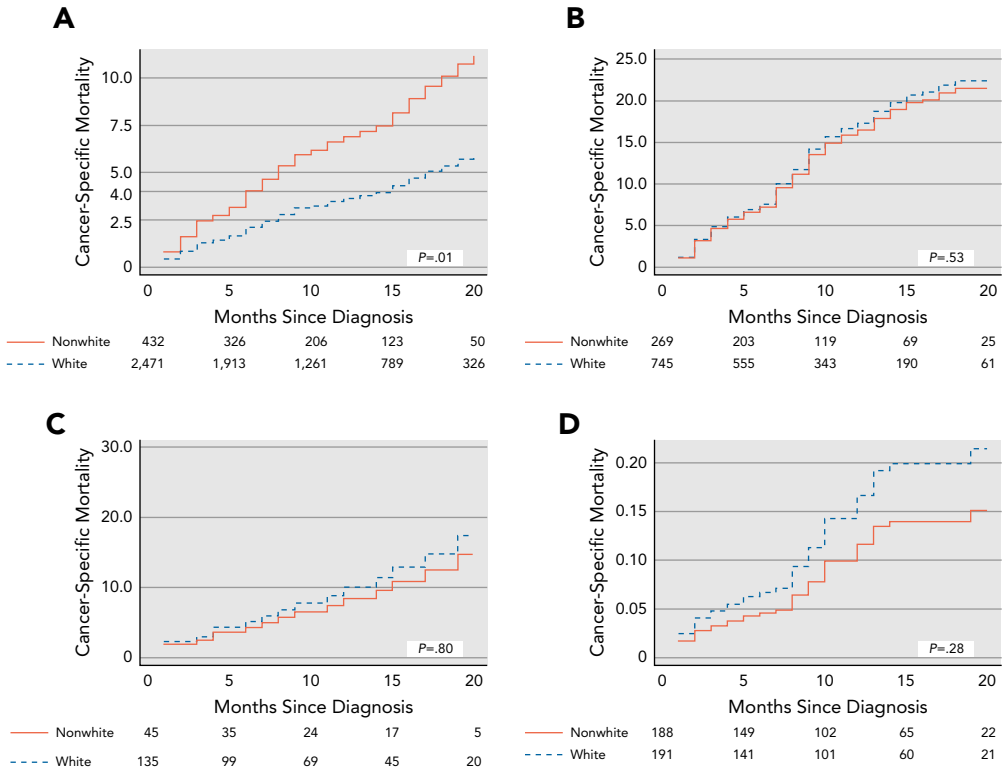

Figure 1. Kaplan-Meier cancer-specific survival curves comparing white and nonwhite patients with (A) HPV-positive oropharyngeal, (B) HPV-negative oropharyngeal, (C) HPV-positive nonoropharyngeal, and (D) HPV-negative nonoropharyngeal squamous cell carcinoma of the head and neck.

1.91–2.80; $P<.01$), male sex (aOR, 1.50; 95% CI, 1.26–1.78; $P<.01$), Medicaid insurance (aOR, 1.33; 95% CI, 1.06–1.66; $P=.01$), single marital status (aOR, 1.28; 95% CI, 1.06–1.54; $P=.01$), and divorced/widowed/separated marital status (aOR, 1.38; 95% CI, 1.15–1.66; $P=.001$), and was negatively associated with white race (aOR, 0.68; 95% CI, 0.57–0.81; $P<.001$).

CSM Estimates by HPV Status, Tumor, and SES Characteristics

After a median follow-up of 10 months, there were 339 cancer-related deaths and 109 competing deaths. White patients with HPV-positive oropharyngeal SCCHN had a significantly lower risk of CSM compared with their nonwhite peers (aHR, 0.55; 95% CI, 0.34–0.88; 20-month CSM, 5.6% vs 11.2%; $P=.01$; Figure 1A). Among those with HPV-negative oropharyngeal SCCHN, no statistically significant difference in CSM was seen between white and nonwhite patients (aHR, 1.11; 95% CI, 0.74–1.67; 20-month CSM, 22.9% vs 20.9%; $P=.60$; Figure 1B). Similarly, there were no significant differences in CSM between white and nonwhite patients for nonoropharyngeal SCCHN, regardless of HPV status (Figure 1C and D, Table 3). Accordingly, there was a significant interaction between race, disease subsite, and HPV status ($P_{interaction}<.001$; see Table 3).

In addition to risk of CSM based on race, uninsured patients with HPV-positive oropharyngeal SCCHN had a higher risk of CSM compared with their privately insured peers (aHR, 3.12; 95% CI, 1.19–8.13; $P=.02$); notably, such differences were not seen in other HPV-negative or nonoropharyngeal subgroups. Marital status did not have a significant effect on CSM in patients with HPV-positive oropharyngeal SCCHN, but among patients with HPV-negative oropharyngeal SCCHN, those who were single had a worse risk for CSM (aHR, 1.66; 95% CI, 1.04–2.65; $P=.04$).

Discussion

This report is, to our knowledge, the largest population-based analysis of the socioeconomic factors affecting outcomes in HPV-associated SCCHN. We found that nonwhite patients with HPV-positive oropharyngeal SCCHN were at higher risk of CSM than white patients, whereas both white and nonwhite patients with HPV-negative or nonoropharyngeal HPV-positive SCCHN had similarly poor outcomes ($P_{interaction}<.001$). In addition, uninsured patients with HPV-positive oropharyngeal SCCHN had an increased risk of CSM compared with their privately insured peers.

These findings are significant in that they contradict earlier reports and hypotheses suggesting that the worse CSM seen in nonwhite populations with SCCHN is driven by a higher likelihood of HPV-negative disease among

Table 3. Multivariable aHR for CSM Among Patients With M0 SCCHN and at Least 1 Month of Follow-Up (N=4,476)

Characteristic	Number of Patients/Cancer-Deaths/ Competing Deaths	CSM	
		aHR (95% CI)	*P* Value
Race * HPV status * disease subsite[a]	4,476/323/98	0.33 (0.24–0.45)	<.001
HPV-positive SCCHN, oropharynx	2,903/110/49		
White	2,471/83/43	Ref	
Nonwhite	432/27/6	1.82 (1.14–2.94)	.01
Private or other insurance	2,541/81/42	Ref	
Uninsured	73/7/2	3.12 (1.19–8.13)	.02
Medicaid	255/15/5	1.73 (0.91–3.27)	.09
Unknown insurance	34/7/0	3.62 (1.56–8.42)	.003
Married	1741/54/27	Ref	
Single	501/21/10	1.05 (0.57–1.95)	.88
Divorced/Widowed/Separated	527/28/11	1.08 (0.62–1.87)	.80
Unknown marital status	134/7/1	1.18 (0.52–2.67)	.69
HPV-negative SCCHN, oropharynx	1,014/148/34		
White	745/110/22	Ref	
Nonwhite	269/38/12	1.11 (0.74–1.67)	.60
Private or other insurance	771/104/21	Ref	
Uninsured	46/7/5	0.85 (0.36–2.05)	.72
Medicaid	178/33/4	1.13 (0.73–1.75)	.59
Unknown insurance	19/4/4	1.00 (0.22–4.73)	.99
Married	465/53/1	Ref	
Single	247/45/7	1.66 (1.04–2.65)	.04
Divorced/Widowed/Separated	236/42/17	1.30 (0.85–1.99)	.23
Unknown marital status	66/8/9	0.86 (0.33–2.21)	.75
HPV-positive SCCHN, nonoropharynx	180/19/3		
White	135/15/3	Ref	
Nonwhite	45/4/0	1.26 (0.18–8.75)	.82
Private or other insurance	146/12/3	Ref	
Uninsured	3/2/0	87.48 (5.02–1,524.14)	.002
Medicaid	29/4/0	1.51 (0.15–15.52)	.73
Unknown insurance	2/1/0	139.5 (5.53–3,520.18)	.003
Married	93/7/2	Ref	
Single	31/4/0	2.73 (0.60–12.47)	.20
Divorced/Widowed/Separated	44/5/1	1.83 (0.47–7.19)	.39
Unknown marital status	12/3/0	1.05 (0.08–13.29)	.97
HPV-negative SCCHN, nonoropharynx	379/46/12		
White	191/27/4	Ref	
Nonwhite	188/19/8	1.39 (0.73–2.62)	.31
Private or other insurance	269/28/9	Ref	
Uninsured	20/3/0	1.81 (0.50–6.51)	.37
Medicaid	86/15/3	1.30 (0.60–2.81)	.50
Unknown insurance	4/0/0		
Married	178/17/5	Ref	
Single	107/16/3	1.16 (0.57–2.36)	.69
Divorced/Widowed/Separated	76/11/3	0.72 (0.26–1.96)	.52
Unknown marital status	18/2/1	1.49 (0.42–5.28)	.54

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Table 3. Multivariable aHR for CSM Among Patients With M0 SCCHN and at Least 1 Month of Follow-Up (N=4,476) (cont.)

Characteristic	Number of Patients/Cancer-Deaths/ Competing Deaths	CSM	
		aHR (95% CI)	*P* Value
Age at diagnosis (per year increase)	4,476/323/98	1.04 (1.03–1.05)	<.001
Sex			
Female	727/76/13	Ref	
Male	3,749/247/85	0.67 (0.51–0.87)	.003
Smoking propensity (per 10% increase)	4,476/323/98	1.01 (0.99–1.03)	.38
High school education (per 10% increase)	4,476/323/98	1.02 (1.00–1.05)	.13
Median household income (per $10,000/y increase)	4,476/323/98	1.00 (1.00–1.00)	.03
Tumor stage			
T1	1,041/32/11	Ref	
T2	1,512/60/24	1.37 (0.88–2.12)	.16
T3	764/71/21	3.10 (1.99–4.84)	<.001
T4	654/125/30	5.30 (3.47–8.10)	<.001
Unknown	486/35/12	1.81 (1.06–3.11)	.03
Nodal stage			
N0	675/54/14	Ref	
N1	838/61/11	1.17 (0.79–1.73)	.44
N2a	444/11/7	0.69 (0.36–1.31)	.27
N2b	1,439/84/36	1.18 (0.80–1.72)	.41
N2c	589/64/15	1.23 (0.80–1.89)	.35
N2 NOS	116/11/4	1.64 (0.84–3.17)	.15
N3	233/25/5	1.81 (1.10–2.97)	.02
Unknown	142/13/7	0.93 (0.44–1.99)	.86
Definitive treatment			
None	204/67/10	Ref	
Surgery	1,215/35/12	0.40 (0.27–0.60)	<.001
Radiotherapy	4,001/221/80	0.22 (0.18–0.30)	<.001
Chemotherapy	3,223/197/62	0.80 (0.59–1.08)	.14

Abbreviations: aHR, adjusted hazard ratio; CSM, cancer-specific mortality; HPV, human papillomavirus; NOS, not otherwise specified; SCCHN, squamous cell carcinoma of the head and neck.
[a]Interaction term was tested in multivariable analysis with HPV status, disease subsite, race, smoking propensity, high school education, median household income, tumor stage, nodal stage, and definitive treatment. Following the identification of a statistically significant interaction among these variables, the HPV status/disease status subgroups (HPV-positive, oropharynx; HPV-negative, oropharynx; HPV-positive, nonoropharynx; HPV-negative, nonoropharynx) were examined in separate models, excluding the aforementioned interaction term, to examine the effect of race on cancer-specific survival in each subgroup.

this subgroup[6] or that nonwhite patients with HPV-negative disease and lower SES have disproportionately worse outcomes.[14,18] Differences in CSM between white and nonwhite populations with HPV-associated oropharyngeal SCCHN persisted even after adjusting for relevant potential socioeconomic confounders, such as insurance status, age, sex, smoking propensity, education level, and household income. As such, these results raise concern that nonwhite patients may not be achieving the full potential for improved outcomes seen in HPV-associated SCCHN in the modern era. Similar concerns exist regarding patients without insurance coverage.

A plausible explanation for these findings is that nonwhite and uninsured patients may have inferior access to care, such as supportive therapies during intensive treatment of SCCHN. Others have hypothesized that worse outcomes in SCCHN may result in part from insufficient access to screening programs that allow detection of cancer at earlier and more treatable stages.[19,20] Indeed, earlier work has demonstrated that African Americans are less likely to receive definitive treatment, with a consequent increased risk of CSM.[19] Finally, there may be undescribed genomic differences that result in worse outcomes in nonwhite patients with HPV-associated SCCHN. On the other hand, known HPV status may itself be an indicator of access to appropriate cancer care and good healthcare delivery.

Interestingly, despite the known association between sexual activity and HPV infection, married patients in this study were more likely than single patients to present with HPV-positive SCCHN. We hypothesize that

these differences may result from HPV coinfection among couples or, alternatively, from uncaptured risk factors, such as smoking and alcohol consumption, that may increase the likelihood of HPV-negative disease in single patients. We also found that single patients with HPV-negative SCCHN had a higher risk of CSM than married patients with HPV-negative SCCHN, which is consistent with findings of prior studies.[20–22]

Because of the retrospective nature of SEER, with incompletely captured data on smoking habits and the use of county-level indexes to estimate economic and educational factors, caution should be taken when interpreting these results. In particular, given the well-established effect of smoking status on outcome among patients with oropharyngeal cancers, the lack of individual-level patient data on smoking in the SEER database poses an ongoing challenge. Nonetheless, this study represents the first large report describing the effect of socioeconomic factors on HPV-associated SCCHN and CSM for those patients. Prior studies have relied on small case series of patients from academic centers and retrospective reviews of prospective studies, which are not representative of the general population.[16,23] By contrast, SEER registries capture a wider cross-section of the population, including a more representative racial and economic balance from both academic and community medical centers in urban and rural areas.[17]

Conclusions

This study highlights the socioeconomic differences between patients with HPV-positive and HPV-negative SCCHN and identifies striking racial disparities among individuals with HPV-positive oropharyngeal SCCHN. This work suggests a potentially missed opportunity for cure among nonwhite and uninsured populations with HPV-positive oropharyngeal SCCHN and an unmet need for access to high-quality cancer care. Further work is urgently needed to reduce socioeconomic disparities in SCCHN.

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