Original Article

Racial Parities in Outcomes After Radiotherapy for Head and Neck Cancer

Gene-Fu F. Liu, MD[1]; Mark C. Ranck, MD[1]; Abhishek A. Solanki, MD[1]; Hongyuan Cao, PhD[2]; Antonia Kolokythas, DDS[3]; Barry L. Wenig, MD[4]; Lucy Chen, MD[5]; Stephanie Ard, RN[6]; Ralph R. Weichselbaum, MD[1,6]; Howard Halpern, MD, PhD[1,6]; and Michael T. Spiotto, MD, PhD[1,6]

BACKGROUND: Although black patients experience worse outcomes after treatment for squamous cell carcinoma of the head and neck (HNSCC), these conclusions were based on populations in which blacks comprised a minority of patients. The objective of the current study was to determine the impact of race on outcomes in patients with HNSCC who received radiotherapy at an institution in which blacks comprised the majority of patients. **METHODS:** In this retrospective cohort study, the authors reviewed 366 black patients and 236 white patients who had nonmetastatic HNSCC for which they received radiotherapy between 1990 and 2012. The primary study outcome measures were locoregional control, freedom from distant metastasis, progression-free survival, and overall survival. **RESULTS:** The median follow-up was 18.3 months for all patients. The 2-year locoregional control rate was 71.9% for black patients compared with 64.2% for white patients (hazard ratio, 0.72; $P = .03$). There was no difference between blacks and whites regarding 2-year freedom from distant metastasis, progression-free survival, or overall survival. Among the patients who had stage III through IVB disease, blacks and whites had similar outcomes. On multivariate analysis, race was not statistically significant for locoregional control, freedom from distant metastasis, progression-free survival, or overall survival. Despite these similar outcomes, black patients had worse socioeconomic factors and increased comorbidities but had similar treatment compliance compared with white patients. **CONCLUSIONS:** With more adverse prognostic factors, black patients experienced oncologic outcomes similar to the outcomes of white patients after receiving radiotherapy for HNSCC. The current data suggest that centers that treat large percentages of minority patients who receive radiotherapy for HNSCCs may overcome existing health care disparities through improved treatment compliance. ***Cancer*** **2014;120:244–52**. © *2013 American Cancer Society*.

KEYWORDS: radiotherapy, head and neck neoplasms, minority health, outcomes assessment, minority groups.

INTRODUCTION

In the United States, racial disparities persist across multiple diseases and grow in importance as the country becomes increasingly diverse. This disparity also pervades oncology, in which black race has been correlated with worse 5-year overall survival (OS) rates compared with white race within almost every cancer subtype, including pediatric malignancies.[1,2] A recent Surveillance, Epidemiology, and End Results (SEER) report indicated that black race predicted for increased head and neck squamous cell carcinoma (HNSCC)-specific and noncancer mortality.[3] Similarly, single-institution series from the University of Florida, the University of Maryland, and The University of Texas MD Anderson Cancer Center demonstrated that OS rates among black patients with HNSCC approached half the rates of white patients.[4-6] The difference also extended to decreased disease-free survival, cause-specific survival, and freedom from distant metastases (FFDM). Thus, black race often predicted for worse oncologic outcomes in many cancer patients, including those with HNSCCs.

However, the current literature is limited by the relative and absolute number of black patients analyzed. First, black patients comprised approximately 10% to 15% of the study sample in most series.[3-5,7-9] Second, the absolute number of black patients in individual institutional studies was low, often ranging from 50 to 100 patients.[6,10,11] Third, for multiinstitutional studies, such as the SEER database, many patient and tumor variables were unknown and complicated the

Corresponding author: Michael T. Spiotto, MD, PhD, Department of Radiation and Cellular Oncology, The University of Chicago, KCBD 6142, 900 East 57th Street, Chicago, IL 60637; Fax: (773) 702-1968; mspiotto@radonc.uchicago.edu

[1]Department of Radiation and Cellular Oncology, University of Chicago Medical Center, Chicago, Illinois; [2]Department of Health Studies, University of Chicago, Chicago, Illinois; [3]Department of Oral and Maxillofacial Surgery, University of Illinois Hospital and Health Sciences System, Chicago, Illinois; [4]Department of Otolaryngology-Head and Neck Surgery, University of Illinois Hospital and Health Sciences System, Chicago, Illinois; [5]Section of Hematology and Oncology, University of Illinois Hospital and Health Sciences System, Chicago, Illinois; [6]Department of Radiation Oncology, University of Illinois Hospital and Health Sciences System, Chicago, Illinois.

The first two authors contributed equally to this work.

DOI: 10.1002/cncr.28417, **Received:** July 10, 2013; **Revised:** July 20, 2013; **Accepted:** August 26, 2013, **Published online** October 10, 2013 in Wiley Online Library (wileyonlinelibrary.com)

analyses. Finally, in all studies, blacks had other confounding factors, such as increased alcohol consumption, smoking, and lower socioeconomic status. Thus, studying patient cohorts with greater black representation may help better characterize the impact of race on oncologic outcomes in HNSCC.

The University of Illinois at Chicago features a unique patient demographic in which blacks comprise the majority of patients treated. To this end, we sought to determine the extent of racial disparities in the outcomes of patients with HNSCC in which blacks comprise a large proportion of the population.

MATERIALS AND METHODS

Eligible Study Population

Between 1990 and 2012, we identified 694 patients with nonmetastatic HNSCC who received radiotherapy (RT) at the University of Illinois Medical Center. We excluded 3 patients who had inadequate treatment information, 20 Asian patients, and 69 patients for whom race was not documented, resulting in 366 black patients and 236 white patients who were eligible for analysis. Data were collected in accordance with The University of Illinois at Chicago Institutional Review Board guidelines (protocol 2011-1075). A single attending physician (M.T.S.) collected all patient data from available physical and electronic medical records. Before treatment, patients were discussed at a multidisciplinary conference and underwent oncologic workup, which included history and physical examination, endoscopic evaluation of the primary tumor, and imaging. Gastrostomy and tracheostomy tubes were placed in patients at the discretion of the treating physician. All patients received RT as a component of their care. Patients were evaluated by a physician at least once weekly while receiving RT, during which acute toxicities were documented. After treatment completion, patients were followed by providers within otolaryngology and/or medical and radiation oncology, and follow-up data were acquired from visits within any department at the University of Illinois Medical Center. Patients underwent routine follow-up starting 1 month after RT and were followed every 2 months for 2 years, every 4 to 6 months during years 3 through 5, and yearly thereafter. Workup of potentially recurrent disease was ordered at the discretion of the treating physician.

Measures

Documentation of race was based on patients' self-reporting on clinic or hospital intake sheets. Patient comorbidity burden was approximated using the Charlson comorbidity index.[12] Performance status was assessed using the Karnofsky performance status (KPS).[13] Patients were staged according to the American Joint Committee on Cancer staging system at the time of diagnosis. Median income data were captured by cross-referencing patient-reported zip codes with proprietary data accessed from the US Census Bureau and the Office of Management and Budget.[14] Alcohol history was defined as $\geq$2 or $<$2 alcoholic drinks per day. Smoking was defined as $\geq$10 or $<$10 pack-years. A truncated RT course was defined as 1 shortened by more than 5 treatment fractions because of patient noncompliance. We defined RT delays as RT courses that were completed 5 days or longer than the anticipated completion based on the initial start date. The expected timeframe of RT was based on the radiation dose prescribed and, thus, was independent of the definitive or postoperative RT course.

Acute toxicity was scored according to the Radiation Therapy Oncology Group common toxicity criteria. Events for locoregional control (LRC), FFDM, progression-free survival (PFS), and OS were calculated from the last day of RT. Patterns of local, regional, or distant failure were documented as sites of first failure. LRC and FFDM were calculated as the time to locoregional or distant disease recurrence, respectively. PFS was calculated as the time to any failure or death from any cause. OS was calculated as the time to death from any cause.

Statistical Analysis

All patients were included in the analysis regardless of treatment compliance. Statistical analysis was performed using the JMP statistical software package (version 9; SAS Institute Inc., Cary, NC). All tests of statistical significance were 2-sided, and significance was defined as a P value $< .05$. The chi-square test was used to compare differences between discrete variables, and the t test was used to compare continuous variables. Differences between medians were assessed using the Wilcoxon test. Survival analysis was performed for all patients and also in a separate analysis stratified only for patients with stage III through IVB disease to minimize treatment bias, because this population often is treated more homogeneously than patients with early stage HNSCC. Survival curves were plotted based on the Kaplan-Meier method, and comparisons between categorical risk factors were conducted using the log-rank test. Censoring was considered noninformative. For univariate analysis, we selected factors with a known impact on oncologic outcomes as well as patient and treatment characteristics that were different between black patients and white patients. We used a Cox

TABLE 1. Patient Characteristics, n = 602

Characteristic	No. of Patients (%)		*P*
	Black Patients, n = 366	White Patients, n = 236	
Age: Median [IQR], y	57.7 [49.3-64.8]	57.5 [48.9-63.2]	.83
Follow-up: Median [IQR], mo	21.5 [7.3-59.0]	15.4 [6.3-46.3]	.05
Sex			
Men	270 (73.8)	185 (78.4)	.20
Women	96 (26.2)	51 (21.6)	
Karnofsky performance status			
≥70	305 (83.3)	184 (78)	.18
<70	25 (6.8)	9 (3.8)	
Not stated	36 (9.8)	43 (18.2)	
Comorbidity index			
Medium	245 (66.9)	180 (76.3)	.03
High	105 (28.7)	51 (21.6)	
Very high	16 (4.4)	5 (2.1)	
Stage			
I	33 (9)	12 (5.1)	.08
II	31 (8.5)	32 (13.6)	
III	64 (17.5)	50 (21.2)	
IVA	193 (52.7)	113 (47.9)	
IVB	45 (12.3)	29 (12.3)	
Stage grouping			
Early disease: Stage I-II	64 (17.5)	44 (18.6)	.72
Advanced disease: Stage III-IVB	302 (82.5)	192 (81.4)	
Household income: Median [IQR], US$	28,203 [25,143-36,334]	42,774 [36,670-55,301]	< .0001
Relationship status			
Divorced	22 (6)	28 (11.8)	< .0001
Married or remarried	91 (24.8)	90 (38.1)	
Single	189 (51.6)	75 (31.8)	
Widowed	25 (6.8)	16 (6.8)	
Not stated	39 (10.7)	27 (11.4)	
Living situation			
Lives alone	150 (41)	81 (34.3)	< .0001
Lives alone, with assistance	78 (21.3)	29 (12.3)	
Lives with others	93 (25.4)	96 (40.7)	
Not stated	45 (12.3)	30 (12.7)	
Alcohol history			
≥2 Drinks/d	232 (63.4)	118 (50)	.02
<2 Drinks/d	73 (19.9)	60 (25.4)	
Not stated	62 (16.9)	58 (24.6)	
Tobacco history			
Yes	306 (83.6)	180 (76.2)	.01
No	40 (10.9)	43 (18.2)	
Not stated	20 (5.5)	13 (5.5)	
Illicit drug use			.01
Yes	56 (15.3)	20 (8.5)	
No	310 (84.7)	216 (91.5)	
Primary site			
Hypopharynx	35 (9.8)	19 (8.3)	< .0001
Larynx	121 (34)	45 (19.7)	
Nasal cavity	1 (0.3)	5 (2.2)	
Nasopharynx	16 (4.5)	4 (1.8)	
Oral cavity	60 (16.9)	77 (33.6)	
Oropharynx	100 (28.1)	57 (24.9)	
Other	4 (1.1)	4 (1.8)	
Paranasal sinus	6 (1.7)	5 (2.2)	
Major salivary gland	2 (0.6)	4 (1.8)	
Unknown primary	11 (3.1)	9 (3.9)	
Lymph node levels IV/V/SCV involved			
Yes	86 (23.5)	30 (12.7)	.0008
No	280 (76.5)	206 (87.3)	

Abbreviations: IQR, interquartile range; SCV, supraclavicular fossa.

TABLE 2. Treatment Characteristics, n = 602

Characteristic	No. of Patients (%)		
	Black Patients, n = 366	White Patients, n = 236	*P*
RT timing			
Postoperative	115 (31.4)	93 (39.4)	.05
Definitive	251 (68.6)	143 (60.5)	
Induction chemotherapy			
Yes	108 (29.5)	57 (24.2)	.15
No	258 (70.5)	179 (75.8)	
Concurrent chemotherapy			
Yes	221 (60.3)	139 (58.9)	.72
No	139 (38)	97 (41.1)	
Not stated	6 (1.6)	0 (0)	
Intensity-modulated RT			
Yes	160 (43.7)	119 (50.4)	.11
No	206 (56.3)	117 (49.6)	
RT delay			
Yes	97 (26.5)	56 (23.7)	.70
No	257 (70.2)	160 (67.8)	
Not stated	12 (3.3)	20 (8.5)	
Truncated RT course			
Yes	12 (3.3)	19 (8.1)	.01
No	354 (96.7)	216 (91.9)	
Era of RT			
1990-1997	66 (18)	49 (20.7)	.63
1998-2004	162 (44.3)	97 (41.1)	
2005-2012	38 (37.7)	90 (38.1)	

Abbreviation: RT, radiotherapy.

proportional hazards model to examine the effects of these different risk factors on event outcomes for LRC, FFDM, PFS, and OS. Cox multivariate analysis was performed to adjust for explanatory confounding variables on univariate analysis. Nominal logistic regression was used to adjust for explanatory confounding variables for truncated treatment courses and toxicity measures. Patient characteristics that were not recorded were not included in the statistical analysis.

RESULTS

Population and Tumor Characteristics

The median follow-up for the entire group was 18.3 months overall but was longer for black patients (21.5 months vs 15.4 months; $P = .05$) (Table 1). Black and white patients presented with similar disease stages, age, sex, and KPS. Compared with white patients, black patients had a higher burden of high or very high medical comorbidities, had lower median incomes, and were more likely to be single. Black patients had more alcohol consumption, more frequently had $\geq$10 pack-years of cigarette smoking, and had more illicit drug use. Black patients had more laryngeal primaries, and white patients had more oral cavity primaries. When accounting for smoking, alcohol use, and other socioeconomic factors, black race still accounted for a higher risk of laryngeal primaries (odds ratio [OR], 3.43; 95% confidence interval [CI], 1.76-6.89; $P = .0002$). Black patients presented more frequently with lymphatic involvement of level IV, level V, or the supraclavicular fossa (23.5% vs 12.7%; $P = .0008$).

Treatment Characteristics

White patients were more likely than black patients to undergo surgery before they received RT (39.4% vs 31.4%; $P = .05$) (Table 2). When primary oral cavity tumors, which often are treated with initial surgery, were excluded, there was no difference in postoperative RT between black and white patients (29.1% vs 31.5%, respectively; $P = .60$). Similar proportions of black and white patients received chemotherapy with regard to both induction and concurrent chemotherapy. RT technique was similar between black and white patients in terms of the receipt of intensity-modulated RT and the frequency of RT delays. Although black and white patients shared a similar frequency of RT delays, fewer black patients experienced a truncated RT course (3.3% vs 8.1%; $P = .01$). When adjusting for comorbidities and postoperative RT, black patients still had fewer truncated RT courses (OR, 0.36; 95% CI, 0.16-0.75; $P = .007$). Similar percentages of black patients and white patients were treated at distinct times during the study.

Outcomes

The 2-year LRC rate was 71.9% for black patients compared with 64.2% for white patients, and blacks had better LRC on univariate analysis (HR, 0.72; 95% CI, 0.54-0.96; $P = .03$) (Table 3). On multivariate analysis, race did not predict for LRC, and only postoperative RT predicted for improved LRC (HR, 0.73; 95% CI, 0.52-1.05; $P = .09$). Although black patients had increased lower neck lymph node involvement, there was no difference in FFDM between black patients and white patients. Multivariate analysis indicated that a history of consuming $\geq$2 alcoholic drinks daily, stage III or IV disease, a truncated RT course, era of RT and lower neck lymph node involvement independently predicted for worse FFDM.

There was no difference in PFS or OS between blacks and whites (PFS, $P = .32$; OS, $P = .21$) (Fig. 1). The 2-year PFS rate was 57.4% for black patients compared with 55.2% for white patients, and the 2-year OS rate was 76.2% for black patients compared with 77.7% for white patients. On univariate analysis, race did not impact PFS (HR, 0.89; 95% CI, 0.79-1.12; $P = .32$) (Table 3) or OS (HR, 1.21; 95% CI, 0.87-1.69; $P = .24$).

TABLE 3. Univariate Analysis of Outcomes in Black Patients and White Patients, n = 602

	HR (95% CI)			
Variable	Locoregional Control	Freedom from DM	PFS	OS
Black race	0.72 (0.54-0.96)	1.32 (0.87-2.03)	0.89 (0.79-1.12)	1.21 (0.87-1.69)
P	.03	.19	.32	.24
KPS ≥70	0.75 (0.42-1.53)	1.00 (0.42-3.28)	0.62 (0.40-1.05)	0.52 (0.29-1.03)
P	.40	.99	.07	.06
High/very high comorbidity	0.98 (0.89-1.43)	0.79 (0.48-1.32)	0.97 0.74-1.24)	1.0 (0.71-1.41)
P	.89	.31	.79	.97
Advanced disease: Stage III-IV	1.42 (0.96-2.18)	5.11×10^9 (12.8-?)	1.98 (1.40-2.90)	2.78 (1.67-5.05)
P	.08	< .0001	< .0001	< .0001
Income ≤$35,000	0.99 (0.74-1.32)	1.10 (0.75-1.65)	1.04 (0.84-1.32)	1.12 (0.83-1.53)
P	.92	.60	.68	.45
Lives with others	1.0 (0.72-1.39)	1.14 (0.93-2.32)	1.00 (0.78-1.30)	1.09 (0.78-1.53)
P	.99	.11	.96	.63
Primary site				
Oropharynx: Referent				
Hypopharynx	0.88 (0.46-1.60)	1.87 (0.96-3.56)	1.22 (0.78-1.85)	1.45 (0.84-2.45)
Larynx	1.06 (0.70-1.61)	0.95 (0.53-1.69)	0.97 (0.70-1.34)	0.86 (0.56-1.32)
Oral cavity	1.43 (0.95-2.57)	1.24 (0.70-2.21)	1.30 (0.94-1.80)	1.09 (0.70-1.69)
Other	1.55 (0.94-2.52)	1.56 (0.78-3.00)	1.56 (1.05-2.27)	1.51 (0.91-2.47)
P	.15	.19	.07	.15
Alcohol: ≥2 drinks/d	1.49 (1.01-2.27)	2.76 (1.53-5.49)	1.44 (1.07-1.99)	2.07 (1.33-3.40)
P	.04	.0004	.02	.0009
Smoking: >10 pack-years	1.16 (0.48-1.83)	0.95 (0.57-1.67)	1.14 (0.82-1.62)	1.77 (1.09-3.10)
P	.48	.84	.43	.02
Illicit drug use	1.21 (0.79-1.78)	1.15 (0.64-1.93)	1.17 (0.84-1.60)	1.31 (0.84-1.95)
P	.36	.62	.33	.21
Lymph node levels IV/V/SCV involved	1.31 (0.90-1.85)	2.27 (1.47-3.44)	1.58 (1.20-2.05)	1.97 (1.38-2.76)
P	.15	.0003	.001	.0003
Postoperative RT	0.53 (0.37-0.73)	0.76 (0.50-1.15)	0.64 (0.50-0.82)	0.68 (0.48-0.94)
P	.0001	.20	.0003	.02
RT delay >5 d	1.48 (1.06-2.03)	0.96 (0.59-1.52)	1.39 (1.07-1.78)	1.49 (1.06-2.08)
P	.02	.89	.01	.02
Truncated RT course	4.16 (2.39-6.75)	3.71 (1.56-7.44)	3.70 (2.34-5.55)	4.52 (2.53-7.50)
P	< .0001	.005	< .0001	< .0001
Intensity-modulated RT	1.24 (0.92-1.67)	1.21 (0.81-1.79)	1.42 (1.12 −1.80)	1.48 (1.07-2.03)
P	.15	.35	.004	.02
Era of RT				
1990-1997: Referent				
1998-2004	1.28 (0.86-1.93)	2.35 (1.33-4.49)	1.44 (1.06-2.00)	1.46 (0.96-2.28)
P	.23	.003	.02	.07
2005-2012	1.54 (1.02-2.39)	2.23 (1.18-4.45)	2.07 (1.47-2.94)	2.15 (1.36-3.47)
P	.04	.01	< .0001	.0009

Abbreviations: CI, confidence interval; DM, distant metastasis; KPS, Karnofsky performance status; OS, overall survival; PFS, progression-free survival; RT, radiotherapy; SCV, supraclavicular fossa.

The log cumulative hazard function plots for OS and PFS were parallel, and the global test failed to reject the proportional hazards assumptions with *P* values of .41 and .23, respectively, indicating that the proportional hazards assumption held for OS and PFS (data not shown). On multivariate analysis, definitive RT, stage III and IV disease, and increased alcohol history were associated with decreased PFS and OS (Table 4).

Toxicity

Compared with white patients, black patients experienced significantly less grade ≥3 acute mucositis (21.3% vs 27.1%; *P* = .001) but had similar rates of acute dermatitis, weight loss, and feeding-tube placement during RT as well as long-term dependence on feeding-tubes and tracheostomies. On multivariate analysis, black patients still experienced significantly less grade ≥3 mucositis during therapy (OR, 0.50; 95% CI, 0.29-0.84; *P* = .009) (Table 5). Feeding tube placement during RT was associated with increased stage, smoking history, concurrent chemotherapy and conformal RT use.

DISCUSSION

In this study, we observed similar outcomes between black patients and white patients who received RT for HNSCC.

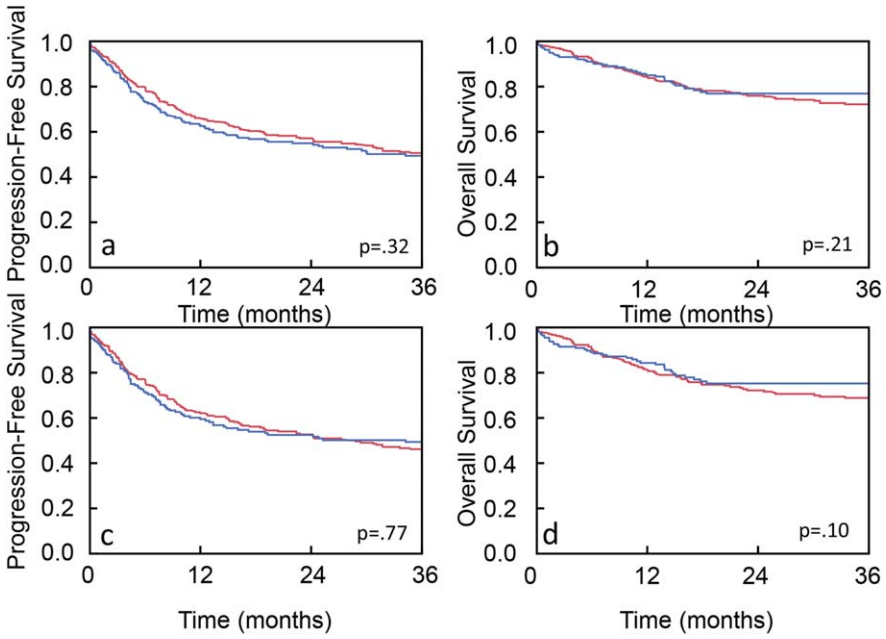

Figure 1. These Kaplan-Meier curves illustrate the outcomes of black patients (red lines) and white patients (blue lines) with head and neck squamous cell carcinoma (HNSCC) in terms of (a) progression-free survival (PFS) and (b) overall survival (OS) for all patients with HNSCC who received radiotherapy. (c) PFS and (d) OS are illustrated for patients with stage III and IV HNSCC who received radiotherapy. The log-rank test was used to assess for differences in OS and PFS.

The absence of racial disparity was not because of worse than expected outcomes in the white cohort, and the 2-year OS and PFS were similar to those reported in other studies that examined racial disparities.[4,6,7] Conversely, the outcomes of black patients in our study were similar to those historically reported for white patients.[6,7] Because the outcomes of blacks and whites were similar after RT, analyzing our results may enable us to determine how to overcome health care disparities in oncology and, potentially, in other diseases.

Many reports have suggested that patient-specific socioeconomic factors drive outcome disparities in HNSCC.[3,7,15] In our data set, blacks had lower median incomes as well as higher rates of comorbidities, unmarried status, and alcohol, tobacco, and illicit drug use. Other studies also have demonstrated that patient-specific socioeconomic factors offer an incomplete explanation.[3,4,6,7] When controlled for race, unmarried status, and socioeconomic status, a recent SEER analysis of 34,568 patients in which 12.4% of patients were black demonstrated that black race remained independently predictive of increased HNSCC-specific mortality.[3] In addition, a study of 20,915 patients in which 8.4% were black demonstrated that, for all levels of poverty, the median OS for black patients remained less than that for white patients.[7] By contrast, the black cohort in our study had oncologic outcomes similar to those of whites despite adverse factors. Taken together, our data suggest that traditional socioeconomic factors may inadequately explain racial disparities.

One possible explanation for the lack of racial disparities in our study may be the lower incidence of oropharyngeal primaries associated with human papillomavirus (HPV). Specifically, white patients have higher rates of favorable prognosis, HPV-positive HNSCCs, which approach half of all HNSCCs treated and, consequently, result in improved OS rates compared with black patients.[16-18] Some studies have reported racial disparities in outcomes that were likely because of divergent outcomes in oropharyngeal primaries among races, suggesting an impact of HPV-positive cancers on racial disparities.[6,15] By contrast, in other series, black patients still had worse outcomes for tumor subsites in which HPV does not impact prognosis.[8,15] Since 2009, 9 of 105 patients with HNSCC in our series tested positive for the HPV biomarker p16, and most of those were white patients who had oropharyngeal primaries (15.4% white patients vs 4.6% black patients; $P = .06$). Although we cannot account for HPV-positive cancers in the current series, our results indicate equivalent outcomes for black

TABLE 4. Multivariate Analysis of Outcomes in Black Patients and White Patients, n = 602

	HR (95% CI)			
	Local Control	Freedom From Distant Metastasis	PFS	OS
Black race	0.73 (0.52-1.05)	0.90 (0.66-1.83)	0.90 (0.80-1.52)	1.11 (0.71-1.77)
P	.09	.68	.52	.66
Tumor stage III-IV	1.59 (0.99-2.70)	4.43×10^{9} ($7.54\text{-}7.79 \times 10^{41}$)	2.37 (1.48-4.03)	2.87 (1.47-6.34)
P	.05	< .0001	.0002	.001
Alcohol: ≥2 drinks/d	1.30 (0.87-1.99)	3.53 (1.77-8.12)	1.46 (1.03-2.10)	1.77 (1.08-3.06)
P	.20	.0001	.03	.02
RT delay >5 d	1.41 (0.96-2.02)	NA	1.27 (0.92-1.73)	1.31 (0.84-1.98)
P	.08		.15	.23
Postoperative RT	0.55 (0.36-0.81)	NA	0.64 (0.46-0.89)	0.62 (0.39-0.96)
P	.003		.007	.03
Era of RT				
1990-1997: Referent				
1998-2004	0.93 (0.59-1.51)	2.19 (1.03-5.41)	1.17 (0.76-1.84)	1.53 (0.81-3.08)
P	.76	.04	.48	.20
2005-2012	1.23 (0.76-2.03)	2.69 (1.19-6.91)	1.68 (096-2.97)	2.12 (0.96-4.87)
P	.41	.02	.07	.06
Truncated RT course	NA	4.08 (1.40-9.53)	ND	ND
P		.01		
Lymph node levels IV/V/SCV involved	NA	1.79 (1.05-2.98)	1.42 (0.98-2.03)	1.31 (0.80-2.48)
P		.03	.06	.27
KPS ≥70	NA	1.17 (0.48-3.89)	0.90 (0.53-1.65)	1.02 (0.49-2.48)
P		.76	.71	.97
Intensity-modulated RT	NA	NA	1.06 (0.73-1.57)	1.15 (0.69-1.90)
P			.73	0.59
Smoking: >10 pack-years	NA	NA	NA	1.36 (0.60-3.93)
P				.49

Abbreviations: CI, confidence interval; HR, hazard ratio; KPS, Karnofsky performance status; NA, not applicable (because the *P* value was > .1 on univariate analysis); ND, not determined (because there were too few events for analysis); OS, overall survival; PFS, progression-free survival; RT, radiotherapy; SCV, supraclavicular fossa.

patients and white patients with non-HPV-positive HNSCCs who received RT.

The large, relative, and absolute representation of blacks in our series may explain similar observations regarding the lack of health care disparity between black and white patients. Whereas most previous single-institutional studies reported on cohorts in which blacks comprised only 10% to 15% of the total population[3-5,7-9] and/or less than 100 patients in total,[6,10,11] our observations were based on 366 black patients who comprised 61% of the total population. In a patient population in which 47% were black, Connell et al demonstrated that blacks and whites achieved statistically equivalent biochemical control after RT for prostate cancer.[19] In addition, when blacks represented 55% to 60% of patients, 2 separate studies on women with breast cancer demonstrated that race did not have an impact on outcomes.[20,21] Thus, we reason that black patients may experience less disparate outcomes when they comprise a larger proportion of the treated population.

We postulate several reasons that may account for how the percentage of blacks in the patient population impacts outcomes. One reason may be that the small sample sizes of blacks in previous studies were more prone to random variations, which may have complicated the analyses. Another possibility may rely on more effective communication between the health care provider and the patient. Black patients have described their health care visits as less informative, supportive, and partnering, and this may translate into inferior treatment compliance and outcomes.[22] Because effective communication between health care providers and patients may improve treatment compliance, we observed that blacks and whites had similar rates of completing the intended RT course. Furthermore, effective communication resulting in improved treatment compliance may have improved outcomes, because we observed that those who experienced truncations or delays in treatment had worse 2-year PFS and OS. In contrast to the racial variations in treatment delivery,[23] in our series, white patients and black patients

TABLE 5. Multivariate Analysis of Toxicity, n = 602

	OR (95% CI)					
	Acute Toxicity				Late Toxicity	
Variable	Grade ≥3 Mucositis	Grade ≥3 Dermatitis	Feeding Tube During RT	≥10% Weight Loss	Feeding Tube at Failure or Last Follow-Up	Tracheostomy at Failure or Last Follow-Up
Black race	0.50 (0.29-0.84)	0.90 (0.50-166)	0.69 (0.42-1.12)	0.63 (0.20-2.07)	0.64 (0.39-1.06)	1.34 (0.78-2.52)
P	.0009	.74	.14	.43	.09	.29
Tumor stage III-IV	1.67 (0.75-3.99)	5.72 (2.00-19.58)	26.82 (9.01-116.3)	6.28×10^6 (0.75-?)	42.30 (8.58-767.4)	11.06 (3.11-70.84)
P	.21	.007	< .001	.06	< .0001	< .0001
Alcohol: ≥2 drinks/d	0.77 (0.44-1.37)	2.07 (1.02-4.46)	1.46 (0.85-2.52)	1.58 (0.38-10.7)	2.11 (1.17-3.91)	1.90 (1.00-3.83)
P	.38	.04	.17	.56	.01	.05
Smoking: >10 pack-years	1.49 (0.56-4.40)	7.30 (1.36-136.2)	3.37 (1.40-8.79)	1.00 (0.16-19.2)	6.35 (2.03-28.21)	4.97 (1.37-32.07)
P	.44	.02	.006	.99	.0008	.01
High comorbidity	0.71 (0.39-1.26)	1.20 (0.64-2.25)	1.24 (0.73-2.11)	0.28 (0.01-1.56)	1.34 (0.77-2.31)	1.36 (0.76-2.41)
P	.24	.57	.43	.17	.30	.30
Very high comorbidity	3.37 (0.88-13.71)	1.21 (0.16-6.28)	0.66 (0.15-2.73)	2.51×10^{-7} (0-15.7)	0.83 (0.16-3.53)	1.87 (0.36-7.79)
P	.08	.83	.57	.53	.81	.42
KPS ≥70	1.03 (0.37-3.19)	1.32 (0.44-4.56)	1.04 (0.38-2.75)	8.75×10^6 (0.32-?)	1.27 (0.48-3.47)	1.38 (0.49-4.56)
P	.95	.63	.94	.23	0.63	0.56
Postoperative RT	0.59 (0.32-1.06)	0.34 (0.16-0.70)	0.84 (0.49-.43)	0.94 (0.22-3.47)	0.57 (0.32-0.99)	1.40 (0.78-2.52)
P	.08	.003	.52	.93	.05	0.26
Concurrent chemotherapy	1.89 (0.96-3.83)	1.17 (0.55-2.51)	2.80 (1.49-5.39)	1.92 (0.43-10.8)	3.02 (1.58-5.94)	2.38 (1.22-2.52)
P	.07	.68	.001	.40	.0007	.01
Intensity-modulated RT	0.76 (0.44-1.30)	0.25 (0.13-0.45)	0.26 (0.15-0.44)	0.49 (0.13-1.74)	0.33 (0.19-0.56)	0.23 (0.13-0.41)
P	.32	< .001	< .001	.27	< .0001	< .0001

Abbreviations: CI, confidence interval; KPS, Karnofsky performance status; OR, odds ratio; RT, radiotherapy.

received similar treatments with respect to surgery, chemotherapy, and RT. Thus, the similar types of treatment regimens and rates of compliance may be viewed as a surrogate for effective communication between health care providers and patients.

In addition, we observed that the incidence of oral cavity and laryngeal primaries differed between white patients and black patients, whereas the incidence of oropharyngeal primaries did not. Although some groups have not reported racial differences in primary sites,[4,7] other groups have reported increased percentages of oropharyngeal and oral cavity primaries in whites.[6,15] These racial differences in tumor incidence may be explained by the referral patterns at our institution, because we have lower rates of HPV-positive cancers than would be expected. Nevertheless, it will require further study to determine whether factors unique to our institutional demographics or biologic factors account for the differences in primary sites between races.

Our results are limited, like any retrospective review. First, our study relied on a relatively small number of patients over a 22-year time frame. Nevertheless, the number of black patients in this study approximates as many black patients as were accrued in a multi-institutional study involving 100 centers.[9,24] Second, greater than 80% of our patients had locally advanced disease, which may reflect both the lower socioeconomic status of our patients and the referral patterns at our institution. Yet, our rate of advanced disease is similar to other reports documenting racial disparities in HNSCC.[4,5] Third, we restricted our analysis to patients who received RT and, thus, cannot comment on the racial disparities in patients who received only surgery or chemotherapy. Although race may not have an impact on outcomes after RT, our results are still applicable to the majority of patients, as demonstrated in a recent SEER analysis in which 79.7% of patients with HNSCC received RT as a component of their care.[25] Finally, the lack of disparity in our series may be because of a larger proportion of disadvantaged patients regardless of race. Still, white patients in our population had significantly better socioeconomic factors than black patients. Furthermore, the OS and LRC rates for black patients in our series were as good or better than the rates for white patients

and were on par with the outcomes of white patients reported in multiple other series.[4-7,15] Therefore, despite the worse socioeconomic factors among black patients, we observed similar outcomes in black and white patients who received RT for HNSCC.

Thus, we conclude that race does not predict outcomes in patients with HNSCC when minorities comprise a large proportion of the patient population. It is likely that biologic and patient-specific socioeconomic factors cannot adequately explain racial differences in outcomes among patients with HNSCC. We propose that centers caring for a greater percentage of minority patients may have unique patient-health care provider relationships to overcome racial disparities in health care. Thus, these results may be applicable to other cancers and other nonmalignant diseases.

FUNDING SUPPORT

Michael T. Spiotto is supported by a Burroughs Wellcome Career Award for Medical Scientists.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

REFERENCES

1. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin.* 2011;61:212-236.
2. Carroll WL. Race and outcome in childhood acute lymphoblastic leukemia. *JAMA.* 2003;290:2061-2063.
3. Rose BS, Jeong JH, Nath SK, Lu SM, Mell LK. Population-based study of competing mortality in head and neck cancer. *J Clin Oncol.* 2011;29:3503-3509.
4. Al-Othman MO, Morris CG, Logan HL, Hinerman RW, Amdur RJ, Mendenhall WM. Impact of race on outcome after definitive radiotherapy for squamous cell carcinoma of the head and neck. *Cancer.* 2003;98:2467-2472.
5. Moore RJ, Doherty DA, Do KA, Chamberlain RM, Khuri FR. Racial disparity in survival of patients with squamous cell carcinoma of the oral cavity and pharynx. *Ethn Health.* 2001;6:165-177.
6. Settle K, Taylor R, Wolf J, et al. Race impacts outcome in stage III/IV squamous cell carcinomas of the head and neck after concurrent chemoradiation therapy. *Cancer.* 2009;115:1744-1752.
7. 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;113:2797-2806.
8. Nichols AC, Bhattacharyya N. Racial differences in stage and survival in head and neck squamous cell carcinoma. *Laryngoscope.* 2007;117:770-775.
9. Wong SJ, Harari PM, Garden AS, et al. Longitudinal Oncology Registry of Head and Neck Carcinoma (LORHAN): analysis of chemoradiation treatment approaches in the United States. *Cancer.* 2011;117:1679-1686.
10. Murdock JM, Gluckman JL. African-American and white head and neck carcinoma patients in a university medical center setting. Are treatments provided and are outcomes similar or disparate? *Cancer.* 2001;91(1 suppl):279-283.
11. Chen LM, Li G, Reitzel LR, et al. Matched-pair analysis of race or ethnicity in outcomes of head and neck cancer patients receiving similar multidisciplinary care. *Cancer Prev Res (Phila).* 2009;2:782-791.
12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373-383.
13. Karnofsky DA, Burchenal J. The Clinical Evaluation of Chemotherapeutic Agents in Cancer: New York: Columbia University Press; 1949.
14. Datasheer LLC.2012 Zip code database. Available at: http://www.zip-codes.com/zip-code-database.asp. Accessed April 8, 2012.
15. Gourin CG, Podolsky RH. Racial disparities in patients with head and neck squamous cell carcinoma. *Laryngoscope.* 2006;116:1093-1106.
16. Chernock RD, Zhang Q, El-Mofty SK, Thorstad WL, Lewis JS Jr. Human papillomavirus-related squamous cell carcinoma of the oropharynx: a comparative study in whites and African Americans. *Arch Otolaryngol Head Neck Surg.* 2011;137:163-169.
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;2:776-781.
18. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med.* 2010;363:24-35.
19. Connell PP, Ignacio L, Haraf D, et al. Equivalent racial outcome after conformal radiotherapy for prostate cancer: a single departmental experience. *J Clin Oncol.* 2001;19:54-61.
20. Chu QD, Smith MH, Williams M, et al. Race/ethnicity has no effect on outcome for breast cancer patients treated at an academic center with a public hospital. *Cancer Epidemiol Biomarkers Prev.* 2009;18:2157-2161.
21. Komenaka IK, Martinez ME, Pennington RE Jr, et al. Race and ethnicity and breast cancer outcomes in an underinsured population. *J Natl Cancer Inst.* 2010;102:1178-1187.
22. Gordon HS, Street RL Jr, Sharf BF, Kelly PA, Souchek J. Racial differences in trust and lung cancer patients'; perceptions of physician communication. *J Clin Oncol.* 2006;24:904-909.
23. Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. *J Natl Cancer Inst.* 2002;94:334-357.
24. Ang KK, Chen A, Curran WJ Jr, et al. Head and neck carcinoma in the United States: first comprehensive report of the Longitudinal Oncology Registry of Head and Neck Carcinoma (LORHAN). *Cancer.* 2012;118:5783-5792.
25. Dansky Ullmann C, Harlan LC, Shavers VL, Stevens JL. A population-based study of therapy and survival for patients with head and neck cancer treated in the community. *Cancer.* 2012;118:4452-4461.