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Matched-Pair Analysis of Race or Ethnicity in Outcomes of Head and Neck Cancer Patients Receiving Similar Multidisciplinary Care

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Abstract It is unknown whether population-level racial or ethnic disparities in mortality from squamous cell carcinoma of the head and neck (SCCHN) also occur in the setting of standardized multidisciplinary-team directed care. Therefore, we conducted a matched-pair study that controlled for several potentially confounding prognostic variables to assess whether a difference in survival exists for African American or Hispanic American compared with non-Hispanic white American SCCHN patients receiving similar care. Matched pairs were 81 African American case and 81 non-Hispanic white control patients and 100 Hispanic American cases and 100 matched non-Hispanic white controls selected from 1,833 patients of a prospective epidemiologic study of incident SCCHN within a single, large multidisciplinary cancer center. Matching variables included age (±10 years), sex, smoking status (never versus ever), site, tumor stage (T_{1-2} versus T_{3-4}), nodal status (negative versus positive), and treatment. Cases and controls were not significantly different in proportions of comorbidity score, alcohol use, subsite distribution, overall stage, or tumor grade. Matched-pair and log-rank analyses showed no significant differences between cases and controls in recurrence-free, disease-specific, or overall survival. Site-specific analyses suggested that more aggressive oropharyngeal cancers occurred more frequently in minority than in non-Hispanic white patients. We conclude that minority and non-Hispanic white SCCHN patients receiving similar multidisciplinary-team directed care at a tertiary cancer center have similar survival results overall. These results encourage reducing health disparities in SCCHN through public-health efforts to improve access to multidisciplinary oncologic care (and to preventive measures) and through individual clinician efforts to make the best multidisciplinary cancer treatment choices available for their minority patients. The subgroup finding suggests a biologically based racial/ethnic disparity among oropharyngeal patients and that prevention and treatment strategies should be tailored to different populations of these patients.

Head and neck cancers arise in the oral cavity, oropharynx, hypopharynx, and larynx and are overwhelmingly squamous cell carcinomas. In several independent analyses of National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) data, the incidence of these cancers is higher in African Americans than in their white counterparts (1–4). SEER data from the past 30 years also indicate that 5-year relative survival rates for minority patients fall in the bottom of the overall ranges for cancers of the oral cavity and pharynx (range, 52-62%) and larynx (range, 62-71%; ref. 1). Indeed, laryngeal cancer mortality in African American men is more than double that in white men and ranks second only to prostate cancer mortality in magnitude of disparity (1, 2). This pattern of results is echoed in several other population- and hospital-based studies (5–16). Although survival disparities between African American and non-minority patients receive substantial attention, studies of survival among Hispanic American head and neck cancer patients are scarce (17, 18).

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Table 1. Matched and other demographic and exposure characteristics of minority American cases and non-Hispanic white American controls with head and neck cancer

Variable	African Americans (*n* = 81), *n* (%)	Non-Hispanic whites (*n* = 81), *n* (%)	*P*
Age category (y)*,†			0.618
<50	5 (6.2)	7 (8.6)	
50-69	69 (85.2)	64 (79.0)	
≥70	7 (8.6)	10 (12.4)	
Sex*			1.0
Male	68 (84.0)	68 (84.0)	
Female	13 (16.0)	13 (16.0)	
Comorbidity score			0.803
None-mild	73 (90.1)	71 (87.7)	
Moderate-severe	8 (9.9)	10 (12.3)	
Smoking status*,‡			0.621
Current	55 (67.9)	50 (61.7)	
Former	15 (18.5)	20 (24.7)	
Never	11 (13.6)	11 (13.6)	
Alcohol drinking status			0.647
Current	45 (55.5)	48 (59.3)	
Former	22 (27.2)	17 (21.0)	
Never	14 (17.3)	16 (19.7)	
Variable	**Hispanic Americans (*n* = 100), *n* (%)**	**Non-Hispanic whites (*n* = 100), *n* (%)**	
Age category*,†			0.598
<50	26 (26.0)	20 (20.0)	
50-69	57 (57.0)	61 (61.0)	
≥70	17 (17.0)	19 (19.0)	
Sex*			1.0
Male	81 (81.0)	81 (81.0)	
Female	19 (19.0)	19 (19.0)	
Comorbidity score			0.435
None-mild	94 (94.0)	90 (90.0)	
Moderate-severe	6 (6.0)	10 (10.0)	
Smoking status*,‡			0.511
Current	33 (33.0)	40 (40.0)	
Former	40 (40.0)	33 (33.0)	
Never	27 (27.0)	27 (27.0)	
Alcohol drinking status			0.174
Current	42 (42.0)	54 (54.0)	
Former	27 (27.0)	25 (25.0)	
Never	31 (31.0)	21 (21.0)	

*Matched variables.
†Age was matched to within ± 10 y.
‡Smoking was matched by ever and never.

It is not known whether race/ethnicity is an independent prognostic factor or a surrogate for other known prognostic factors, such as differences in stage at presentation, etiologic exposures, and comorbid conditions, among patients with squamous cell carcinoma of the head and neck (SCCHN). Differences in treatment also could account for reported racial/ethnic disparities in SCCHN mortality, but no prior studies known to us have substantially clarified this factor. A better understanding of disparity-associated factors would encourage better treatment and prevention choices for minority patients and would help in focusing public-health interventions designed to control SCCHN among minority populations.

Therefore, we conducted a matched-pair study to determine whether a difference in survival exists for African American or Hispanic American SCCHN patients compared with non-Hispanic white American SCCHN patients treated at a single, large, multidisciplinary cancer center. To our knowledge, this is the first study to use a matched-pair design to control for variables of known prognostic significance (including smoking status and treatment) in patients at a single hospital undergoing the same approach of multidisciplinary care. Finding a lack of racial disparities in this setting would support improving minority access to multidisciplinary care (in addition to enhanced prevention) to reduce population-wide disparities

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in SCCHN survival in the United States. The finding that racial disparities persist even in this tertiary multidisciplinary setting, however, would increase the complexity of addressing the U.S. population-wide disparities in SCCHN survival.

Patients and Methods

Patients

Our matched-pair study patients were selected from a prospective epidemiologic study of newly diagnosed, previously untreated SCCHN patients enrolled at The University of Texas M.D. Anderson Cancer Center between May 1995 and March 2008. This study was approved by the Institutional Review Board. It included patients with incident cases of pathologically confirmed SCCHN and excluded patients with salivary gland, nasopharyngeal, or lip carcinoma, as well as patients with a prior malignancy (excluding nonmelanoma skin cancers). All participants were required to be U.S. residents.

After providing informed consent, all participants prospectively completed a self-administered epidemiologic questionnaire at presentation that covered demographic and exposure information. Patients classified their own race/ethnicity using investigator-defined options: "Black (African American)"; "Spanish origin (Hispanic)";

Table 2. Matched and other tumor-specific characteristics of African American cases and non-Hispanic white American controls with head and neck cancer

Variable	African Americans (n = 81), n (%)	Non-Hispanic whites (n = 81), n (%)	P
Site*,†			1.0
Oral cavity	30 (37.0)	30 (37.0)	
Oral tongue/floor of mouth	16	17	
Gingivobuccal	14	13	
Oropharynx	25 (30.9)	25 (30.9)	
Tonsil	14	15	
Other oropharynx	11	10	
Larynx	20 (24.7)	20 (24.7)	
Supraglottic	12	13	
Glottic	8	7	
Hypopharynx	6 (7.4)	6 (7.4)	
Tumor stage*,‡			1.0
T_1	9 (11.1)	9 (11.1)	
T_2	15 (18.5)	15 (18.5)	
T_3	23 (28.4)	23 (28.4)	
T_4	34 (42.0)	34 (42.0)	
Nodal stage*,§			0.157
N_0	29 (35.8)	29 (35.8)	
N_1	12 (14.8)	12 (14.8)	
N_2	35 (43.2)	40 (49.4)	
N_3	5 (6.2)	0 (0)	
Overall stage			1.0
I	7 (8.6)	7 (8.6)	
II	6 (7.4)	6 (7.4)	
III	12 (14.8)	11 (13.6)	
IV	56 (69.2)	57 (70.4)	
Grade‖			0.616
Well differentiated	8 (11.0)	5 (6.8)	
Moderately differentiated	46 (63.0)	51 (68.9)	
Poorly differentiated	19 (26.0)	18 (24.3)	
Treatment*			1.0
Surgery alone	11 (13.6)	11 (13.6)	
Surgery + radiotherapy	23 (28.4)	23 (28.4)	
Surgery + chemoradiotherapy	8 (9.9)	8 (9.9)	
Radiotherapy alone	11 (13.6)	11 (13.6)	
Chemoradiotherapy	28 (34.5)	28 (34.5)	

*Matched variables.
†Site was matched by oral cavity, oropharynx, hypopharynx, or larynx.
‡Tumor stage was matched by T_1-T_2 or T_3-T_4.
§Nodal stage was matched by N_0 or $N_{1\text{-}3}$.
‖Grade was not recorded in 8 African Americans and 7 non-Hispanic whites.

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Table 3. Matched and other tumor-specific characteristics of Hispanic American cases and non-Hispanic white American controls with head and neck cancer

Variable	Hispanic Americans (*n* = 100), *n* (%)	Non-Hispanic whites (*n* = 100), *n* (%)	*P*
Site*,†			1.0
Oral cavity	41 (41.0)	41 (41.0)	
Oral tongue/floor of mouth	27	27	
Gingivobuccal	14	14	
Oropharynx	35 (35.0)	35 (35.0)	
Tonsil	20	18	
Other oropharynx	15	17	
Larynx	20 (20.0)	20 (20.0)	
Supraglottic	15	15	
Glottic	5	5	
Hypopharynx	3 (3.0)	3 (3.0)	
Oropharynx + hypopharynx	1 (1.0)	1 (1.0)	
Tumor stage*,‡			1.0
T_1	19 (19.0)	19 (19.0)	
T_2	39 (39.0)	39 (39.0)	
T_3	23 (23.0)	23 (23.0)	
T_4	19 (19.0)	19 (19.0)	
Nodal stage*,§			0.744
N_0	39 (39.0)	39 (39.0)	
N_1	10 (10.0)	13 (13.0)	
N_2	45 (45.0)	45 (45.0)	
N_3	6 (6.0)	3 (3.0)	
Overall stage			0.861
I	11 (11.0)	11 (11.0)	
II	18 (18.0)	18 (18.0)	
III	11 (11.0)	15 (15.0)	
IV	60 (60.0)	56 (56.0)	
Grade‖			0.481
Well differentiated	12 (13.8)	10 (12.3)	
Moderately differentiated	47 (54.0)	51 (63.0)	
Poorly differentiated	28 (32.2)	20 (24.7)	
Treatment*			1.0
Surgery alone	21 (21.0)	21 (21.0)	
Surgery + radiotherapy	15 (15.0)	15 (15.0)	
Surgery + chemoradiotherapy	5 (5.0)	5 (5.0)	
Radiotherapy alone	24 (24.0)	24 (24.0)	
Chemoradiotherapy	35 (35.0)	35 (35.0)	

*Matched variables.
†Site was matched by oral cavity, oropharynx, hypopharynx or larynx.
‡Tumor stage was matched by $T_{1\text{-}2}$ or $T_{3\text{-}4}$.
§Nodal stage was matched by N_0 or $N_{1\text{-}3}$.
‖Grade was not recorded in 13 Hispanic Americans and 19 non-Hispanic whites.

"White, Anglo, Caucasian"; "American Indian"; "Asian"; or "Other." "Former smokers" were defined as smokers who had quit at least 1 y and were grouped with current smokers as "ever-smokers." "Never-smokers" were patients who had smoked fewer than 100 cigarettes in their lifetime. "Drinkers" were patients who had consumed at least one alcoholic drink per week for at least 1 y, whereas "former drinkers" were those who had quit this pattern of drinking for at least 1 y.

Medical records were reviewed for primary disease site and subsite, clinical stage, treatment, histology, outcome measures and dates, and medical comorbidities. Medical comorbidities were classified according to a modification of the Kaplan-Feinstein comorbidity index (Adult Comorbidity Evaluation 27), which reflects the presence of related comorbidities as none to mild, moderate, or severe (19). This comorbidity index has been shown as an independent prognostic factor in SCCHN (19, 20). Tumor grade was classified according to the original histologic description at our institution, and if results were available from more than one histologic biopsy or specimen at the beginning of treatment, the more advanced grade was chosen. Tumors previously classified as "moderately well" or "moderately poorly"

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differentiated were considered moderately differentiated for this study. Patients underwent multidisciplinary-team directed care and treatment at the University of Texas M.D. Anderson Cancer Center, where a team of head and neck medical, radiation, and surgical oncologists evaluate and prospectively choose a treatment plan for such patients based on a conference discussion among the three services.

Statistical methods

Each minority case patient was matched with one non-Hispanic white control patient in a fashion blinded to patient outcomes. Matching variables were age (±10 y), sex, smoking status (never or ever), site of primary tumor (oral cavity, oropharynx, hypopharynx, or larynx), tumor stage (T_{1-2} or T_{3-4}), pathologic nodal status (N_0 or N_{1-3}), and treatment (surgery, radiotherapy, surgery and radiotherapy, chemoradiotherapy, or surgery and chemoradiotherapy). To detect any significant differences between the two minority groups and the non-Hispanic white groups, the frequencies of factors not included in the matching criteria were compared using the Pearson χ^2 test. For comparisons in which one or more cells of the contingency table had fewer than 10 observations, Fisher's exact test was used. Student's *t* test (with adjustment for unequal variances where necessary) was used to compare ages and follow-up times between groups. All tests were two-sided and $P < 0.05$ was preset as the cutoff for significance. Recurrence-free, disease-specific, and overall survival for both minority groups were compared with those of non-Hispanic whites using Kaplan-Meier estimates and the log-rank test for equality of survival curves. Calculations were completed using Statistical Analysis System software (version 9.1, SAS Institute, Inc.). Analysis was completed for time from first appointment, using recurrence and death as censoring variables. Death was categorized as death due to SCCHN or overall death (any cause). In matched-pair analysis, the crude risk for recurrence and death with 95% confidence intervals (95% CI) associated with the minority group was calculated with McNemar's χ^2 test using STATA software (version 7.0, STATA Corporation). Power calculations were done using PS software (version 2.1.31, Vanderbilt University Department of Biostatistics, Nashville, TN).

Results

Demographics

The parent study involved 1,833 patients with a newly diagnosed/previously untreated SCCHN (127 African Americans, 134 Hispanic Americans, 1,551 non-Hispanic whites, 21 other ethnicities). In this group, 106 African American, 120 Hispanic American, and 1,388 non-Hispanic white patients had received definitive treatment for cure at our institution and were available for matching. Of this group, 81 African American and 100 Hispanic American patient cases could be matched one to one with non-Hispanic white patient controls. The characteristics of minority and matched non-Hispanic white patients are listed in Table 1. As expected, we did not observe any significant differences between the groups with respect to the matched variables, even when age was trichotomized or smoking status was more detailed. The mean age was 59.6 ± 8.0 years (median, 59; range, 39-81) for the African Americans and 59.3 ± 8.4 years (median, 58; range, 43-83; $P = 0.816$) for their non-Hispanic white controls. The mean age was 58.6 ± 11.8 years (median, 58.5; range, 31-86) for the Hispanic Americans and 58.7 ± 11.3 years (median, 58.5; range, 30-83, $P = 0.951$) for their non-Hispanic white controls. Furthermore, the groups did not have significant differences in comorbidity score or alcohol status (Table 1).

As shown by the tumor characteristics in Table 2 (African Americans and their matched non-Hispanic white controls) and Table 3 (Hispanic Americans and their non-Hispanic white controls), both minority groups were identical across matched variables with their controls and did not have significant differences from controls when tumor and nodal stage were further detailed. Furthermore, we did not observe significant differences between case and control

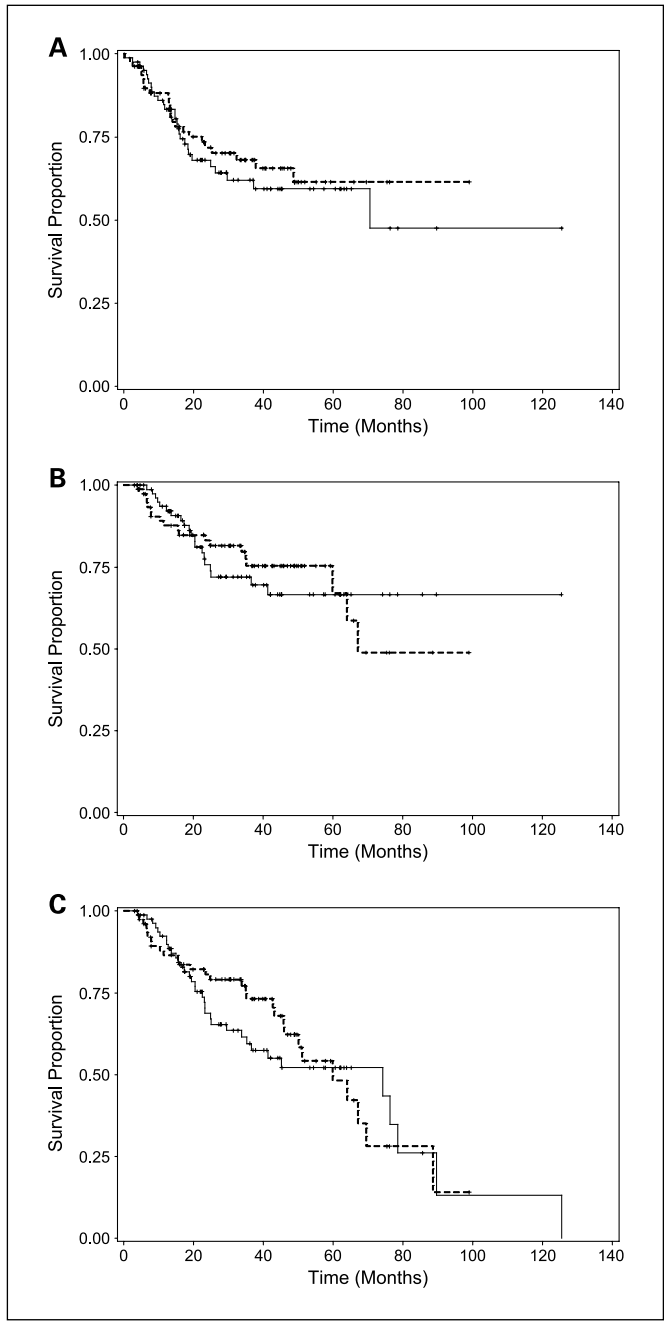

Fig. 1. Survival of African American case and matched non-Hispanic white control patients with SCCHN. The case group is represented by solid lines, the control group by dashed lines. *A*, recurrence-free survival ($P = 0.569$); *B*, disease-specific survival ($P = 0.826$); *C*, overall survival ($P = 0.536$).

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Table 4. Matched-pair analysis of risk for death or recurrence for African and Hispanic American patients

Matched pairs			Risk of recurrence or death associated with minority (95% CI)	*P*
Minority group	Non-Hispanic whites			
	Recurrence or death	No event		
African Americans				
No recurrence	16	37		
Recurrence	8	20	1.25 (0.62-2.58)	0.618
Alive	16	45		
Death from cancer	3	17	1.06 (0.50-2.25)	1.0
Alive	16	34		
Death any cause	8	23	1.44 (0.73-2.91)	0.337
Hispanic Americans				
No recurrence	15	61		
Recurrence	9	15	1.00 (0.46-2.20)	1.0
Alive	10	70		
Death from cancer	8	12	1.20 (0.48-3.10)	0.832
Alive	14	57		
Death any cause	14	15	1.07 (0.48-2.40)	0.853
AA and HA combined				
No recurrence	31	98		
Recurrence	17	35	1.13 (0.68-1.89)	0.712
Alive	26	115		
Death from cancer	11	29	1.12 (0.63-1.97)	0.788
Alive	30	91		
Death any cause	22	38	1.27 (0.76-2.12)	0.396

Abbreviations: AA, African Americans; HA, Hispanic Americans.

groups in disease subsite, overall stage, or grade distributions. The most common primary tumor sites in African Americans were the oral cavity (37% overall; 3 oral tongue, 13 floor of mouth, and 14 gingivobuccal) and oropharynx (31% overall; 14 tonsil, 9 base of tongue, and 2 soft palate). Oral cavity subsites in the non-Hispanic white controls included 9 oral tongue, 8 floor of mouth, and 13 gingivobuccal; oropharynx subsites in non-Hispanic white controls included 15 tonsil and 10 base of tongue. The most common primary tumor sites in Hispanic Americans were the oral cavity (41% overall; 19 oral tongue, 8 floor of mouth, and 14 gingivobuccal) and oropharynx (35% overall; 20 tonsil and 15 base of tongue). Oral cavity subsites in non-Hispanic white controls included 22 oral tongue, 5 floor of mouth, and 14 gingivobuccal; oropharynx subsites in non-Hispanic white controls included 18 tonsil, 16 base of tongue, and 1 soft palate. One Hispanic American and the corresponding non-Hispanic white control had simultaneous primary tumors of the oropharynx and the contralateral hypopharynx.

Survival analysis

African Americans. The mean follow-up times were 34.9 months both for African American (median, 32.0 months; range, 4.7-85.6 months) and non-Hispanic white (median, 34.7 months; 3.1-99.0 months; $P = 1.0$) patients alive at last contact. Twenty-eight African Americans and 24 non-Hispanic whites experienced disease recurrence, and the Kaplan-Meier recurrence-free survival curves for these two groups were very similar (Fig. 1A; log-rank $P = 0.569$). Twenty African Americans and 19 non-Hispanic whites died of SCCHN (Fig. 1B; log-rank $P = 0.826$), and 31 African Americans and 24 non-Hispanic whites died of any cause (Fig. 1C; log-rank $P = 0.536$). Second primary malignancies developed in 8 African American patients (6 at tobacco-associated sites) and in 4 non-Hispanic white control patients (2 at tobacco-associated sites).

Thirty-seven concordant pairs, or matched pairs in which the African American and the non-Hispanic white patient had a concordant outcome, experienced no recurrence; 8 concordant pairs experienced disease recurrence (Table 4). Of the 36 discordant pairs (in which the case and matched control had discordant outcomes of recurrence in one not in the other), the African American patient had recurrence in 20 pairs and the non-Hispanic white patient had recurrence in 16 pairs. In crude matched-pair analysis, African American patients did not have a significantly elevated risk of disease recurrence [odds ratio (OR), 1.25; 95% CI, 0.62-2.58; $P = 0.618$] or a significantly elevated risk of death from SCCHN (OR, 1.06; 95% CI, 0.50-2.25; $P = 1.0$) or from any cause (OR, 1.44; 95% CI, 0.73-2.91; $P = 0.337$).

Hispanic Americans. The mean follow-up times were 37.9 months for Hispanic American (median, 35.3 months; range, 2.0-134.3 months) and 35.0 months for non-Hispanic white (median, 30.7 months; range, 1.6-102.1 months; $P = 0.468$) patients alive at last contact. Twenty-four Hispanic Americans

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and 24 non-Hispanic whites recurred, and the Kaplan-Meier recurrence-free survival curves for these two groups were very similar (Fig. 2A; log-rank $P = 0.954$). Twenty Hispanic Americans and 18 non-Hispanic whites died of SCCHN (Fig. 2B; log-rank $P = 0.873$), and 29 Hispanic Americans and 28 non-Hispanic whites died of any cause (Fig. 2C; log-rank $P = 0.844$). Second primary malignancies developed in 7 Hispanic American patients (4 at tobacco-associated sites) and 4 non-Hispanic white control patients (4 at tobacco-associated sites).

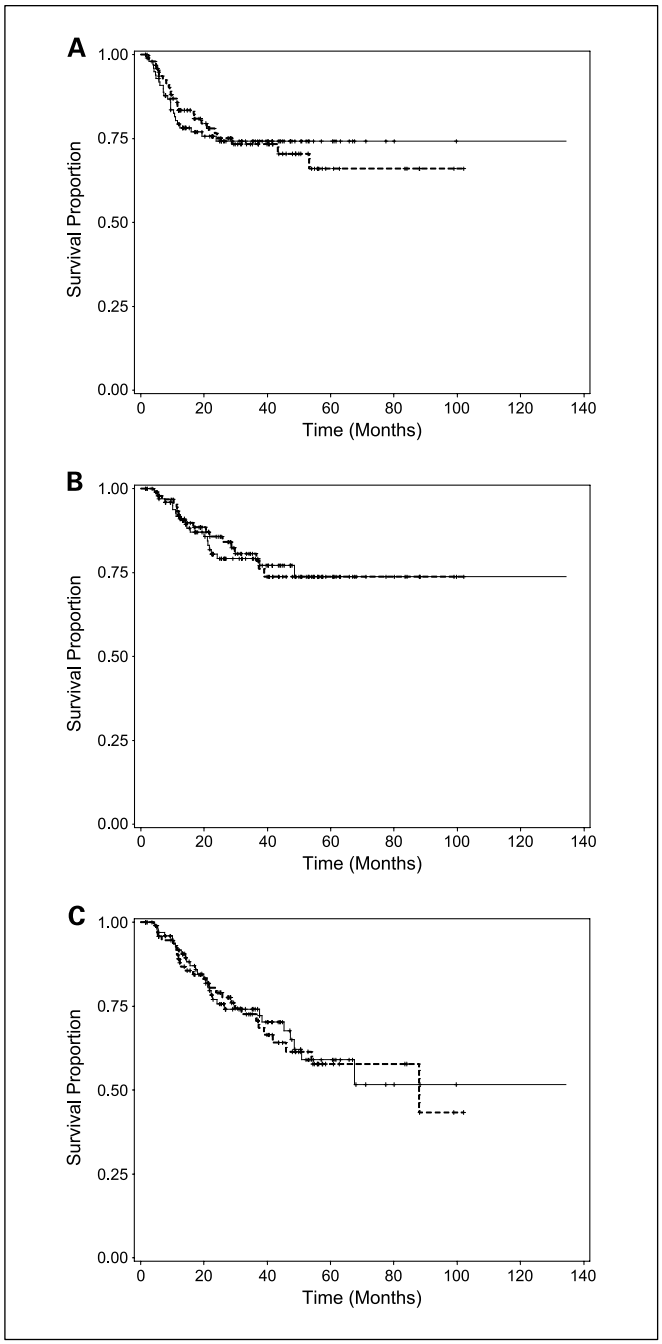

Fig. 2. Survival of Hispanic American case and matched non-Hispanic white control patients with SCCHN. The case group is represented by solid lines, the control group by dashed lines. *A,* recurrence-free survival ($P = 0.954$); *B,* disease-specific survival ($P = 0.873$); *C,* overall survival ($P = 0.844$).

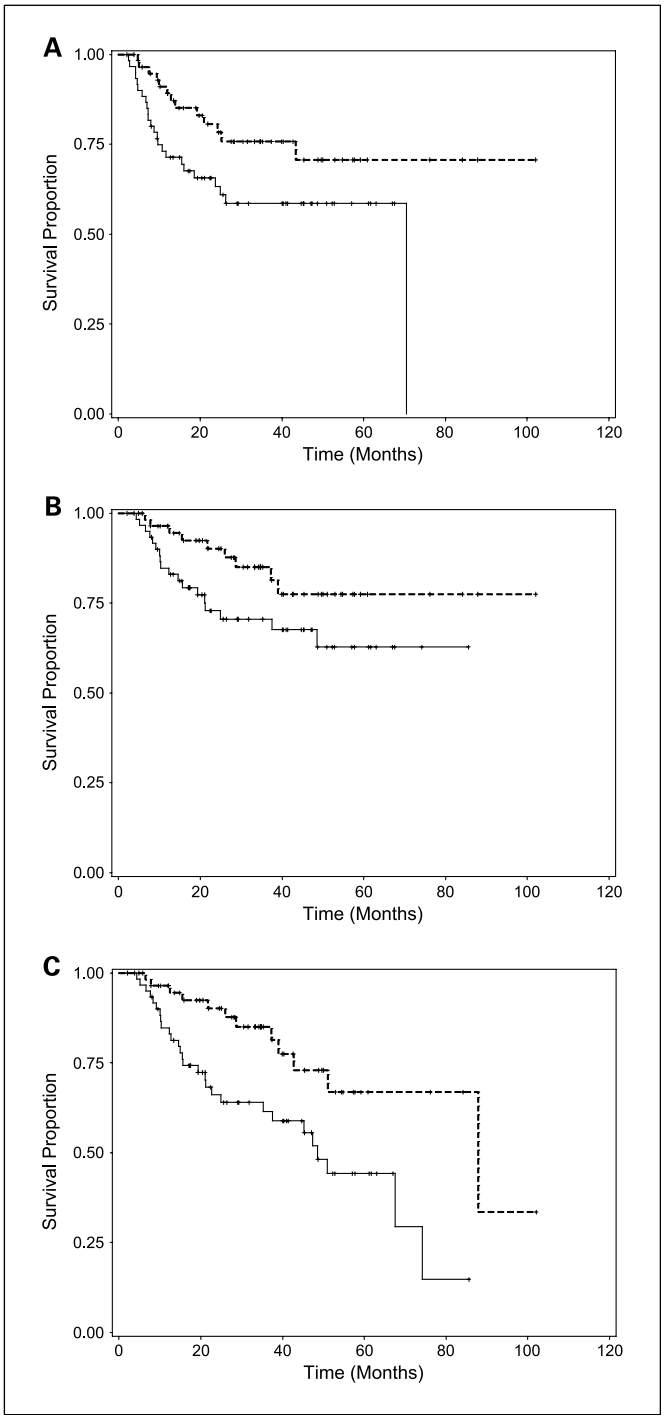

Fig. 3. Survival of minority case and matched non-Hispanic white control patients with oropharyngeal cancer. The case group is represented by solid lines, the control group by dashed lines. *A,* recurrence-free survival ($P = 0.028$); *B,* disease-specific survival ($P = 0.067$); *C,* overall survival ($P = 0.004$).

Both the Hispanic American and non-Hispanic white patients had no recurrence in 61 concordant pairs and had recurrence in 9 concordant pairs (Table 4). The recurring patient was Hispanic American in half and non-Hispanic white in half of the 30 discordant pairs. In crude matched-pair analysis,

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Hispanic American patients did not have a significantly elevated risk of disease recurrence (OR, 1.00; 95% CI, 0.46-2.20; $P = 1.0$) or a significantly elevated risk of death from SCCHN (OR, 1.20; 95% CI, 0.48-3.10; $P = 0.832$) or from any cause (OR, 1.07; 95% CI, 0.48-2.40; $P = 0.853$).

Site-specific comparisons. In head and neck site-specific analyses, the oropharynx provided the only evidence of disparities in recurrence-free (Fig. 3A), disease-specific (Fig. 3B), and overall (Fig. 3C) survival for minority patients. Disparities for oropharyngeal cancer patients had similar patterns for the overall minority group (Table 5; Fig. 3) and (albeit generally with weaker log-rank *P* values) for the African American or Hispanic American group (Table 5) of oropharyngeal cancer patients. In general, however, the disparities were stronger for African Americans than for Hispanic Americans.

The minority case and non-Hispanic white control experienced no oropharyngeal cancer recurrence in 31 concordant pairs and oropharyngeal cancer recurrence in 8 concordant pairs (Table 6). In more than 75% of the 21 discordant pairs, the minority patient recurred. In crude matched-pair analyses, minority patients had a significantly elevated risk of oropharyngeal cancer recurrence (OR, 3.20; 95% CI, 1.12-11.17; $P = 0.027$) and death from oropharyngeal cancer (OR, 3.25; 95% CI, 1.00-13.68; $P = 0.049$) or from any cause (OR, 5.67; 95% CI, 1.64-30.18; $P = 0.003$). Although limited in sample size, similar patterns of elevated risk were found in specific African American or Hispanic American comparisons with controls for oropharyngeal cancer recurrence, death from oropharyngeal cancer, and death from any cause. Similar to the results in the preceding paragraph, the risk disparities were generally stronger in African Americans than in Hispanic Americans.

Discussion

We found no evidence of disparities in survival for either African American or Hispanic American patients with SCCHN compared with similar non-Hispanic white patients who received similar multidisciplinary-team directed treatment at a tertiary cancer center. Kaplan-Meier survival analysis showed no statistical difference across all end points, and matched-pair analyses showed no significantly elevated risk of recurrence or death for either of the two minorities. These results suggest that not adequately controlling for confounding variables (including smoking and treatment) may account for much of the racial disparity reported for SCCHN survival in the literature. The site-specific disparity we found among oropharyngeal cancer patients despite careful matching on smoking and treatment is consistent with a recent report of an unmatched single-institution study (worse disease-free and overall survival for African American oropharyngeal cancer patients; ref. 21) and suggests that a biology-based factor underlies this site-specific disparity.

Several groups have explored racial survival disparities within population-based databases providing much less control than our present study had for confounding factors. Although the SEER population-based database provides a large sample, using it for survival analyses and comparisons comes with limitations. For example, population-based studies only allow limited matching, and the detailed staging, grading, and treatment data needed to appropriately control for confounding variables are not available from SEER. Also unavailable are data on comorbidities, smoking status, and alcohol use, which increasingly are recognized as important prognostic variables.

Even more important, because significant geographic and institutional differences exist between minority and majority populations, dramatic differences in treatment standards and quality of care are inherent within the samples of population-based studies. For example, data on the majority of African American patients in SEER come from geographic areas where minority care often is provided by institutions with relatively limited resources and clinical technology (11). One population-based study has suggested that racial differences may affect treatment decisions (9). It is certainly possible that significant regional and institutional variations in treatment standards, quality of care, and access to care confound survival analyses and underlie mortality disparities at the population level.

Studies of statewide cancer registries also have shown elevated hazard ratios for mortality and other survival disparities for African American compared with non-Hispanic white patients; confounding factors in these studies, however, are similar to those in national-database studies (11–13). Although single-institution studies have produced findings similar to those of the larger-database studies, they often suffer methodologic weaknesses including small numbers and consequently limited power (10, 15, 22).

A major strength of the present study is that all patients received multidisciplinary-team directed care at a single tertiary cancer center, thus limiting variations in the choice and quality

Table 5. Racial and ethnic disparities in outcomes among oropharyngeal cancer patients

Oropharyngeal subgroup	Recurrence (*n*)	*P**	Mortality			
			Oropharyngeal cancer (N)	*P**	All-cause (*n*)	*P**
African Americans	13		7		10	
Non-Hispanic white controls	5	0.023	3	0.174	4	0.049
Hispanic Americans	11		11		15	
Non-Hispanic white controls	8	0.445	6	0.257	7	0.045
AA and HA Combined	24		18		25	
Non-Hispanic white controls	13	0.028	9	0.067	11	0.004

**P* values are log-rank test.

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Table 6. Matched-pair analysis of risk for death or recurrence for African and Hispanic American patients restricted to oropharyngeal cancer patients only

Matched pairs			Risk of recurrence or death associated with minority (95% CI)	*P*
Minority group	Non-Hispanic whites			
	Recurrence or death	No event		
African Americans				
No recurrence	2	10		
Recurrence	3	10	5.00 (1.07-46.93)	0.039
Alive	2	16		
Death from cancer	1	6	3.00 (0.54-30.39)	0.289
Alive	1	14		
Death any cause	3	7	7.00 (0.90-315.60)	0.070
Hispanic Americans				
No recurrence	3	21		
Recurrence	5	6	2.00 (0.43-12.36)	0.508
Alive	2	22		
Death from cancer	4	7	3.50 (0.67-34.53)	0.180
Alive	2	18		
Death any cause	5	10	5.00 (1.07-46.93)	0.039
AA and HA combined				
No recurrence	5	31		
Recurrence	8	16	3.20 (1.12-11.17)	0.027
Alive	4	38		
Death from cancer	5	13	3.25 (1.00-13.68)	0.049
Alive	3	32		
Death any cause	8	17	5.67 (1.64-30.18)	0.003

of treatment. Furthermore, we used very close matching on smoking status, treatment, and other factors to ensure that case and control groups were very similar. No other study we know of has adjusted for or matched on smoking status. SCCHN has a better prognosis in never-smokers than in smokers, in part because never-smoking is a surrogate for oncogenic human papillomavirus (HPV), which is associated with improved outcome, and because smoking is linked to medical comorbidities (20, 23–26). In addition to HPV positivity, never-smoker SCCHN patients tend to have wild-type p53 and lower expression of the epidermal growth factor receptor, both of which seem to be biomarkers of less aggressive disease (25, 27).

Historically, the overwhelming majority of SCCHN in the United States has been attributed to cigarette and alcohol use, and these factors have a higher prevalence in African Americans than in non-Hispanic whites (28, 29). Such disparities in consumption and disease risk factors may lead to a significant confounding of survival analyses. If we had not included smoking status in the match criteria for this study, the proportion of smokers and related medical comorbidities likely would have been higher in the African American patient group, and the proportion of never-smokers, and thus less aggressive SCCHN, likely would have been higher in the non-Hispanic white patient group. Therefore, with absent matching on smoking status, our results probably would have produced misleading evidence of survival disparities, which actually would have been based on differences in the distribution of aggressive disease. Matching on smoking status, an increasingly recognized marker of disease aggressiveness, avoided this limitation.

Despite this careful matching on smoking, we did observe site-specific minority disparities in recurrence and survival among oropharyngeal cancer patients. Of all head and neck subsite cancers, oropharyngeal cancer is the most strongly associated with oncogenic HPV with regard to both etiology and treatment outcomes, and this association is integrally linked to sexual activity (24, 30). We had very limited data on HPV in our cohort of patients and could not adequately investigate the role of HPV in the oropharyngeal disparity we observed.

Potential limitations of our study included its sample size, referral or other biases, and potential prognostic variables we did not include. Our relatively small sample size of 81 African American pairs and 100 Hispanic American pairs was limited, as expected, by the smaller numbers of African American and Hispanic American versus non-Hispanic white patients treated at our institution. Nevertheless, given the overall survival and follow-up times of our non-Hispanic white control patients, we had 80% power with a two-sided α of 0.05 for detecting a modestly (1.5-fold) increased risk of SCCHN recurrence or death in our minority patient groups. Furthermore, these power calculations do not include the additional statistical precision provided by our extensive matching process. Referral or other biases may have limited how well our minority groups represent the broader U.S. population of minority SCCHN patients. For example, we excluded patients

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who did not receive definitive treatment or who received it outside of our institution (17% of African American, 10% of Hispanic American, and 11% of non-Hispanic white patients within the parent epidemiologic study of 1,833 patients). In our study, however, African American patients were similar to those in the broader population in having a relatively high likelihood of presenting with advanced disease, further pointing out the importance of our careful matching on stage (5, 7–9). In addition, the ineligibility of patients with distant metastases may have reduced the proportion of minority patients in the parent study. Regarding absent prognostic factors, we did not have data for these and thus were unable to include socioeconomic status, social support, and access to earlier diagnosis or treatment. Our future plans include studying the impact of these factors on survival of SCCHN patients treated in our tertiary multidisciplinary setting.

In conclusion, our findings show an overall lack of racial disparity in SCCHN survival when similar patients receive similar, multidisciplinary-team directed care at a single large cancer center. We are encouraged that these findings point to opportunities for improving population-level disparities that include much greater public-health efforts to prevent SCCHN and improve its prognosis by reducing tobacco and alcohol use in minority populations and to increase earlier presentation by improving access to care (both preventive and therapeutic). These findings also encourage clinicians in academia and the community to make the best multidisciplinary treatment choices available for their minority SCCHN patients. Despite matching for never smoking, we did observe worse survival outcomes for minority (especially African American) oropharyngeal cancer patients. These findings raise important questions about the potential etiologic and prognostic roles of HPV in racial oropharyngeal disparity and raise further prevention-related questions about the role of sexual behavior in this disparity (30, 31).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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Matched-Pair Analysis of Race or Ethnicity in Outcomes of Head and Neck Cancer Patients Receiving Similar Multidisciplinary Care

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