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Treatment delays, race, and outcomes in head and neck cancer

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ABSTRACT

Purpose: Patient race has been shown to predict for differences in outcomes and has been attributed to socioeconomic factors such as social support and access to healthcare. In head and neck cancer (HNC), a disease without recommended screening, we sought to investigate the association between race, treatment delays and outcome.

Methods: Records of 1802 patients with non-metastatic squamous cell HNC treated between 1998 and 2013 were retrospectively assessed from an institutional database. Patient demographics, tumor and treatment characteristics, and patient outcomes were abstracted from the chart. Differences between groups were assessed via logistic regression multivariate analysis (MVA). Outcomes including locoregional control (LRC) and overall survival (OS) were then estimated via Kaplan-Meier and Cox-regression MVA.

Results: Median follow up was 34 months. Patient races included white (n = 1671, 93%), black (n = 80, 4%), Asian (n = 18, 1%), and other (n = 33, 2%). On logistic regression MVA, Black patients were less likely to be married (39% vs. 63%; OR 0.5 95%CI 0.30–0.83, p = 0.007) or be currently employed (43% vs. 61%; OR 0.44 95%CI 0.26–0.74, p = 0.002) when compared to non-blacks. Black patients were also younger (54 vs. 59 years, p = 0.001), more likely to present with advanced tumor stage (T4: 48% vs. 25%), and more often had >45 days elapsed from diagnosis to treatment initiation (DTI) (61% vs. 49%, p = 0.028). Delays in treatment, such as delayed diagnosis (advanced disease presentation) and delays in DTI > 45 days were also associated with marital and employment status.

Black patients were associated with a lower 3-year LRC rate (65% vs. 81%, $p < 0.001$) and OS rate (43% vs. 69%, $p < 0.001$), compared to non-black patients. Patients with >45 days DTI had a detriment in 3-year LRC (77% vs. 83%, p = 0.002) and OS (66% vs. 69%, p = 0.009). On Cox MVA, black race was independently prognostic for worse LRC (HR 1.62 95%CI 1.04–2.51, p = 0.033) and OS (HR 1.55 95%CI 1.15–2.08, p = 0.004) vs. non-blacks.

Conclusion: Black race is independently prognostic for LRC and OS. Delays in HNC treatment, such as more advanced tumor stage presentation and delays in treatment initiation, may be attributed to socioeconomic factors such as employment status and social support. Efforts to accommodate these factors may expedite treatment, in hopes of improving the race related outcome disparity in HNC.

1. Introduction

In the United States, head and neck cancer (HNC) accounts for 5% of newly diagnosed malignancies [1]. In HNC, the primary factors predictive of outcome include primary site, stage, tumor histology, tobacco use, and human papilloma virus (HPV) association [2]. Racial disparities have been described in multiple diseases, and are well recognized in HNC [3–10]. Although efforts have been made to identify and correct factors that lead to

Abbreviations: 95%CI, 95% confidence interval; AC, Academic Center; DTI, Diagnosis to Treatment Initiation; Gy, Gray; HNC, Head and Neck Cancer; HPV, Human Papillomavirus; IMRT, Intensity-Modulated Radiation Treatment; LRC, Locoregional Control; MVA, Multivariate analysis; N-AC, Non-Academic Center; NS, Not significant (P > 0.05); OR, Odds ratio; OS, Overall Survival; RT, Radiation Therapy; UVA, Univariate Analysis.

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differences in outcomes, black race is still associated with worse survival [3,4,6–10]. Previous studies have discussed several contributing factors to racial disparity, including: socioeconomic status and cultural barriers [8,11–14], social support [15,16], employment status [17], genetic factors [5,18,19], insurance status [20], differences in treatment [12,21], and other prognostic factors (i.e. tobacco use or HPV prevalence) [5,22]. The socioeconomic barriers and lack of social support may influence delays in treatment, treatment breaks, and the completion of treatment [15–17,23–25], which leads to differences in treatment efficacy [7]. Treatment delays can be described as delays in diagnosis (i.e. advanced disease presentation), delays in the initiation of treatment, and delays in the completion of treatment (i.e. extended RT duration) [26]. These delays can lead to disease progression, repopulation [27], and local control deficits [28,29].

Our institution is a member of Total Cancer Care (TCC), which provides a database of patients spanning multiple states, and provides a diverse cohort comparable to the general population [30]. The purpose of our study is to determine whether race is associated with treatment delays and a detriment in HNC outcome. Our goal is to identify factors that may contribute to this the racial disparity, so that methods can be developed to facilitate improved prognosis in this population.

2. Methods

2.1. Study design and setting

After Institutional Review Board approval, records of head and neck cancer (HNC) squamous cell carcinoma patients, treated at Moffitt Cancer center in Tampa (Fl) or at non-Moffitt affiliated consortium sites [30], were retrospectively reviewed from 1998 to 2013. This diverse population was treated over various states and hospitals, and was considered a broader patient sampling compared to a single institution study. Patient demographics, tumor and treatment characteristics, and patient outcomes were abstracted from the chart and institutional and consortium TCC database.

2.2. Participants

This is a cohort study. Patients eligible require pathologic diagnosis of squamous cell HNC, without evidence of distant metastatic disease at the time of diagnosis, treated with either definitive or adjuvant radiation therapy (RT). Patients with known race were included in this study, categorized as white, black, Asian or other. Patients with an unknown race status (n = 5) were excluded from this study.

2.3. Variables

Demographic, clinical, and treatment factors were analyzed. This includes location of RT treatment (academic center (AC) vs. outside non-academic center (N-AC)), and continuous variables such as age and year of diagnosis. Demographics such as employment status, tobacco use, age, household income of county, insurance status (government based: Medicaid/Medicare/other vs. private insurance vs. unknown), co-morbidities (diabetes, cardiovascular disease, pulmonary disease, or liver disease), and marriage status were defined at the time of diagnosis. Chemotherapy was either administered concurrently or sequentially. Sequential chemotherapy was defined as either starting >14 days prior to the start of radiation (induction chemotherapy) or after the completion of radiation.

Variables were grouped based on outcome, such as categorizing race as “black” vs. “non-black”. Marriage status was categorized as “married” if the patient was married or in a domestic partnership, and “not-married” if the patient was single, divorced, widowed, separated, or no known marital status. Patients with no known marital status only constituted a small portion (<3%) for each race. During the primary course of treatment, only 3 (<1%) patients received chemotherapy immediately after radiotherapy completion, and were grouped with induction chemotherapy patients, labeled as “induction/sequential”. Estimated household income was based on the patient’s county of residence, with the median abstracted from www.consensus.gov, and was categorized by the cohort’s median.

Advanced stage of diagnosis (advanced tumor (T3/T4) or nodal (N2/N3) stage), diagnosis to treatment initiation (DTI) >45 days, and RT duration >7 weeks were surrogate markers used to estimate delays in cancer diagnosis, treatment initiation, or completion of treatment, respectively.

2.4. Statistical methods

To determine independent predictors of black vs. non-black, non-overlapping factors were analyzed via logistic regression multivariate analysis (MVA). The association between pertinent demographic variables and factors associated with treatment delays (stage, DTI, RT duration) were compared via Pearson Chi-Square.

Time-to-event outcomes were defined from the date of first treatment. Locoregional control (LRC) was defined to the first local or regional recurrence or censored at last follow-up. Overall survival (OS) was defined to death or censored at last patient contact. LRC and OS distributions were estimated using Kaplan-Meier method compared via Log-rank test univariate analysis (UVA). Demographic, clinical, and treatment factors were included on multivariate analysis (MVA) via Cox proportional hazard regression analysis. Two-sided p-values and the level of significance of 0.05 were used for statistical analyses, with all analyses performed using SPSS v 22 (IBM, Armonk, NY).

3. Results

3.1. Population

There were a total of 1802 patients included in this study with a median follow up was 34 months. Patient races included white (n = 1671, 93%), black (n = 80, 4%), Asian (n = 18, 1%), and other (n = 33, 2%). Most patients had stage IV disease (67%), were married (62%), and were employed (60%) at time of diagnosis. Just under half of the cohort had oropharyngeal cancer (47%) and exhibited current tobacco use (43%). Majority of patients were treated with concurrent chemotherapy (58%). Cisplatin was the most common chemotherapy used (n = 868), and was utilized in 77% of the patients treated with systemic therapy (Table 1).

3.2. Factors associated with race

The patient characteristics between black and non-black patients are shown in Table 1. Factors independently predictive of race were determined by logistic regression multivariate analysis (Table 2). On multivariate analysis, Black patients were less likely to be married (39% vs. 63%; OR 0.5 95%CI 0.30–0.83, p = 0.007) or be currently employed (43% vs. 61%; OR 0.44 95%CI 0.26–0.74, p = 0.002), when compared to non-blacks. Black patients were also younger (54 vs. 59 years, p = 0.001), more likely to present with advanced tumor stage (T4: 48% vs. 25%, p = 0.001), reside in a county with median household income ≥ $48,000 (75% vs. 48%, p < 0.001), and more often had >45 days DTI (61% vs. 49%, p = 0.028). Black patients also had a different