ORIGINAL ARTICLE

Racial Disparities in Lung Cancer Survival: The Contribution of Stage, Treatment, and Ancestry

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ABSTRACT

Introduction: Lung cancer is a leading cause of cancer-related death worldwide. Racial disparities in lung cancer survival exist between blacks and whites, yet they are limited by categorical definitions of race. We sought to examine the impact of African ancestry on overall survival among blacks and whites with NSCLC cases.

Methods: Incident cases of NSCLC in blacks and whites from the prospective Southern Community Cohort Study (N = 425) were identified through linkage with state cancer registries in 12 southern states. Vital status was determined by linkage with the National Death Index and Social Security Administration. We evaluated the impact of African ancestry (as estimated by using genome-wide ancestry-informative markers) on overall survival by calculating the time-dependent area under the curve (AUC) for Cox proportional hazards models, adjusting for relevant covariates such as stage and treatment. We replicated our findings in an independent population of NSCLC cases in blacks.

Results: Global African ancestry was not significantly associated with overall survival among NSCLC cases. There was no change in model performance when Cox proportional hazards models with and without African ancestry were compared (AUC = 0.79 for each model). Removal of stage and treatment reduced the average time-dependent AUC from 0.79 to 0.65. Similar findings were observed in our replication study.

Conclusions: Stage and treatment are more important predictors of survival than African ancestry is. These findings suggest that racial disparities in lung cancer survival may disappear with similar early detection efforts for blacks and whites.

Keywords: Lung cancer; Genetic ancestry; Survival; Race; Disparities

Introduction

Lung cancer is the leading cause of cancer death among both men and women in the United States, with a 5-year relative survival rate of 18%.[1,2] Although lung cancer mortality has decreased in recent years (in large part because of greater smoking cessation efforts), a racial disparity exists such that blacks experience poorer survival than whites do.[1,3–5] Specifically, the national 5-year survival rate is 18% among whites and 15% among

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blacks.[2] In blacks the disease is diagnosed at a late stage more frequently than in whites, and blacks are less likely to receive the recommended course of treatment based on disease stage.[2,6–8] Several recent studies have suggested that controlling for differential access to health care results in no difference in survival outcomes among blacks and whites.[9–11] We and others have demonstrated that blacks and whites experience no difference in lung cancer survival after controlling for stage and socioeconomic factors.[12,13] A recent analysis of Surveillance, Epidemiology, and End Results (SEER) program data also suggests that blacks have lung cancer survival similar to that of whites.[14] However, blacks are an admixed population with varying proportions of African ancestry[15,16] and self-identified whites can carry African ancestry.[17] Identification of ancestry-informative markers, which are genetic variants that differ in frequency between ancestral populations, allows us to distinguish individual-level ancestral origins at the genetic level (i.e., genetic ancestry). Prior studies have shown important associations between genetic ancestry and biomedical phenotypes[18–20] such as lung function[21–23] and breast cancer risk[24,25]; however, the association between genetic ancestry and survival after a diagnosis of lung cancer has yet to be examined. We examined the effect of African ancestry on lung cancer survival in blacks and whites with NSCLC in the Southern Community Cohort Study (SCCS), which is the cohort with the largest representation of blacks in the United States. Black and white SCCS participants were primarily recruited from community health centers across the Southeast and thus have similar access to health care. Analyses were replicated in a population of black individuals with lung cancer that was ascertained from the population-based Metropolitan Detroit Cancer Surveillance System.

Methods

Study Population

Study participants were selected from the SCCS, which is a prospective cohort study of approximately 86,000 adults age 40 to 79 years. Participants were enrolled between March 2002 and September 2009 from a 12-state region across the southeastern United States (Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Virginia, and West Virginia). Approximately 15% of participants were recruited through mail-in questionnaires that were sent to a random subset of adults across the 12-state region. The remaining 85% of participants were enrolled at community health centers throughout the region. Individuals were eligible to participate if they were between the ages of 40 and 79 years. Demographic characteristics, family history of disease, insurance coverage, tobacco use, and other information were collected through in-person interviews by a trained interviewer upon enrollment at the health centers and by completion of the same questionnaire for the recruits from the general population. Individuals self-reported race/ethnicity by selecting any of the following investigator-defined racial/ethnic groups: white, black/African American, Hispanic/Latino, Asian or Pacific Islander, American Indian or Alaska Native, or other racial or ethnic group. Approximately two-thirds of participants self-identified as black/African American. Upon enrollment, all individuals were asked to donate a biologic specimen (blood, urine, saliva, or buccal cell), to which approximately 90% of participants agreed. A detailed description of the study design and recruitment has been previously published.[26,27] The SCCS was approved by institutional review boards at Vanderbilt University and Meharry Medical College. Written informed consent was obtained from all participants.

Case Identification and Mortality Assessment

All incident NSCLC cases occurring within the SCCS between 2002 and 2010 were identified through linkage with the 12 state cancer registries. Individuals with a diagnosis of lung cancer before study enrollment were excluded. Histologic type, stage at diagnosis, and treatment information were obtained from the individual state cancer registries. Stage was derived by using the American Joint Committee on Cancer TNM System staging guidelines (sixth and seventh editions). Because of the small sample size, we combined individuals with stage II and III disease. For individuals missing stage information, we used the SEER Summary Stage guidelines, assuming that local disease was equivalent to stage I, regional disease was equivalent to stage II/III, and distant disease was equivalent to stage IV. Treatment information describing the administration of chemotherapy, radiation therapy, hormone therapy, immunotherapy, surgery, or other cancer-directed treatment was summarized into a design variable with five levels: no treatment, chemotherapy only, radiation only, surgery only, and multimodality treatment (patients receiving any combination of the aforementioned treatment options). Participants were followed for all-cause mortality. Vital status was determined at the end of follow-up (December 31, 2011) through linkage with the Social Security Administration or the National Death Index. Survival time was defined as the time from the date of diagnosis to the date of death, loss to follow-up, or censoring.

Genotyping and Quality Control

Individuals in the SCCS were genotyped with the Illumina HumanExome BeadChip v1.1 (Illumina, San