Racial Differences in Treatment and Survival among Veterans and Non-Veterans with Stage I NSCLC: An Evaluation of Veterans Affairs and SEER-Medicare Populations

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ABSTRACT

Background: Surgery is the preferred treatment for stage I non–small cell lung cancer (NSCLC), with radiation reserved for those not receiving surgery. Previous studies have shown lower rates of surgery among Blacks with stage I NSCLC than among Whites.

Methods: Black and White men ages ≥65 years with stage I NSCLC diagnosed between 2001 and 2009 were identified in the Surveillance, Epidemiology, and End Results (SEER)-Medicare database and Veterans Affairs (VA) cancer registry. Logistic regression and Cox proportional hazards models were used to examine associations between race, treatment, and survival.

Results: Among the patients in the VA (n = 7,895) and SEER (n = 8,744), the proportion of Blacks was 13% and 7%, respectively. Overall, 16.2% of SEER patients (15.4% of Whites, 26.0% of Blacks) and 24.5% of VA patients received no treatment (23.4% of Whites, 31.4% of Blacks). In both cohorts, Blacks were less likely to receive any treatment compared with Whites [ORadj = 0.57; 95% confidence interval (CI), 0.47–0.69 for SEER-Medicare; ORadj = 0.68; 95% CI, 0.58–0.79 for VA]. Among treated patients, Blacks were less likely than Whites to receive surgery only (ORadj = 0.57; 95% CI, 0.47–0.70 for SEER-Medicare; ORadj = 0.73; 95% CI, 0.62–0.86 for VA), but more likely to receive chemotherapy only and radiation only. There were no racial differences in survival.

Conclusions: Among VA and SEER-Medicare patients, Blacks were less likely to get surgical treatment. Blacks and Whites had similar survival outcomes when accounting for treatment.

Impact: This supports the hypothesis that equal treatment correlates with equal outcomes and emphasizes the need to understand multilevel predictors of lung cancer treatment disparities.

Introduction

Lung cancer is the second most commonly diagnosed malignancy among men in the United States, and the leading cause of cancer-related deaths. Non–small cell lung cancer (NSCLC) is the predominant subtype of lung cancer, accounting for 85% of lung cancer diagnoses. Although typically diagnosed at advanced stages, approximately one-third of NSCLC diagnoses are early-stage disease for which the standard of care is surgical resection. Surgical resection rates for early-stage NSCLC range from 50% to 80% (1), and is often the preferred treatment recommended for patients with stage I NSCLC. Studies continue to report that Blacks with localized NSCLC have lower surgical resection rates compared with Whites, and that this difference is associated with worse survival outcomes (2–4). It has also been observed that Black patients have higher rates of refusal or contraindications to surgery (5, 6); however the causes of these disparities are complex and often attributed to access to care and socioeconomic status.

Lung cancer disproportionately affects U.S. veterans due to the greater prevalence of smoking compared with the non-veteran U.S. population (7). There are about 8,000 new cases of lung cancer each year among patients receiving care in the Veterans Affairs (VA) health care system (8). Among patients with early-stage NSCLC in the VA, racial disparities in surgery decreased between 2001 and 2010 and were no longer apparent at the end of the study period (9) and increases in overall survival for stage I patients have been observed (10). What remains unclear is the extent of racial disparities in the various types of treatment among patients with stage I NSCLC and the impact of disparities in treatment on survival outcomes. The purpose of this study was to evaluate the extent of racial disparities in treatment and survival of elderly men with stage I NSCLC receiving care in the VA health care system and patients in the general U.S. population.

Materials and Methods

Data sources

Analyses for this study utilized data from the NCI’s 2014 Surveillance, Epidemiology, and End Results (SEER)-Medicare linkage and the Department of Veterans Affairs (VA) Central Cancer Registry (VACCR). The SEER (11) and VA cancer registries (12) have been described previously in detail and both adhere to guidelines of the North American Association of Central Cancer Registries. To summarize, SEER is a national registry documenting demographic, diagnostic, treatment, and survival characteristics for approximately 30%
of the United States (11). SEER data (Patient Entitlement and Diagnosis Summary File) were linked with Medicare data (i.e., Medicare Provider Analysis and Review) and claims from institutional (OUTPT) and noninstitutional (NCH) providers, thereby providing detailed claims data for patients over the age of 65 years or those under 65 years with a medical disability (13). The VACCR documents demographic, tumor, and primary treatment information for patients diagnosed and/or treated at any facility in the VA health care system, and captures approximately 90% of VA cancer cases (12). The VACCR was linked with the VA Corporate Data Warehouse and the National Death Index to capture vital status, date, and cause of death for VA patients. The study using SEER-Medicare (SM) data was considered exempt by the Icahn School of Medicine at Mount Sinai, because it relies on existing data without patient identifiers and the study utilizing VA cancer registry data was approved by the Durham VA Institutional Review Board (IRB #01543).

Patient population

Patients with a first or only primary cancer diagnosis of stage I NSCLC between 2001 and 2009 were selected in both SM and VA cohorts. The samples were limited to non-Hispanic Black or White men. The VA population is 97% male and the SM population is at least 65 years of age; therefore we further restricted both cohorts to males 65 years or older at diagnosis. For patients in SM, only those with continuous Part A and Part B, and no HMO coverage in the year prior to diagnosis, or the year after diagnosis (or until death) were included. Additional exclusions were applied to each cohort to facilitate comparisons (see Supplementary Fig. S1).

Construction of variables

Patient race was the predictor of interest and specifically compared non-Hispanic Blacks with non-Hispanic Whites. The primary outcomes were treatment received (surgery, radiotherapy, chemotherapy), if any, within 1 year of diagnosis and 5-year overall survival and lung cancer–specific survival. Patients were defined as receiving treatment if they received at least one of the above treatments, and further categorized as receiving surgery only, radiation only, chemotherapy only, or >1 treatment. Five-year survival was calculated from the date of diagnosis to the earliest of date of death or date of last follow-up. Patients who were alive as of those dates were censored. Age at diagnosis was categorized as 65–69, 70–74, 75–79, and ≥80 years, and marital status was categorized as single, married, prior marriage (separated, divorced, widowed), or unknown. Those with unknown marital status (2.4%) were excluded from the SM cohort. In both SM and VA cohorts, diagnostic codes identified within the 12 months prior to the lung cancer diagnosis were queried to calculate a Charlson comorbidity score for each patient (NCI: Charlson Comorbidity macro, 2014 version). Patients with a score ≥3 were combined into a single group. Histologic subtypes were classified as adenocarcinoma, large cell, squamous cell, and other, according to the International Agency for Research on Cancer (14). Within stage I, patients were categorized as IA, IB, or I (not otherwise specified, NOS).

Statistical analysis

All of the following analyses were conducted separately for each cohort. Demographic and tumor characteristics of Black and White patients were compared using χ² tests. Multivariable logistic regressions were conducted to examine associations between race and receipt of treatment overall (yes/no), and for each treatment category (yes/no). An adjusted multinomial logistic regression was also used to assess the odds of treatment type (radiation only, chemotherapy only, >1 treatment, no treatment), compared with surgery only. Overall and lung cancer–specific 5-year survival was assessed using univariate Kaplan–Meier curves, and adjusted Cox proportional hazards models. Models were stratified to assess survival among subgroups of patients (full cohort, surgery only, radiation only, chemotherapy only, >1 treatment, no treatment). All multivariable models were adjusted for age in years at diagnosis, marital status, Charlson comorbidity score, histology, stage, and year of diagnosis. An additional adjustment for treatment type was included in survival models where relevant. Statistical analysis was conducted using SAS software, version 9.4 (SAS Institute) for both SM and VA cohorts.

Results

Patient characteristics

Among the 8,744 patients identified in the SM cohort, the racial distribution was 7% Black and 93% White and the corresponding distribution in the VA cohort (n = 7,895) was 13% Black and 87% White (Table 1). Black patients were diagnosed significantly younger than White patients in the SM cohort (30.5% vs. 21.4% diagnosed between 65 and 69 years, respectively), but the age distribution in VA was not statistically different by race (P = 0.60). In the SM cohort, Black patients were less likely to be married (49.8% vs. 72.3%), but more likely to have a higher comorbidity score (14.3% with score ≥3, compared with 11.1%) and squamous cell carcinoma (47% vs. 39%), and be diagnosed with stage IB (40.2% vs. 37.7%) than White patients. Among VA patients, Blacks were less likely than Whites to be married (34% vs. 46%) and have squamous cell carcinoma (39% vs. 40%); however, Blacks and Whites had similar comorbidity status and stage distribution. Overall, 16.2% of SM patients did not receive treatment (15.4% of White patients, 26.0% of Black patients) and 24.5% of VA patients received no treatment (23.4% of White patients, 31.4% of Black patients). Approximately half of both cohorts received surgery only, and the White–Black difference in receipt of surgery only was 15% in SM and 7% in VA.

Receipt of treatment

In both cohorts, Black patients were significantly less likely to receive any treatment compared with Whites (ORadj = 0.57; 95% confidence intervals [CI], 0.47–0.69 for SM; ORadj = 0.68; 95% CI, 0.58–0.79 for VA; Fig. 1A). When evaluating the likelihood of being in a specific treatment group versus not, Blacks were less likely than Whites to receive surgery only (ORadj = 0.57; 95% CI, 0.47–0.70 for SM; ORadj = 0.73; 95% CI, 0.62–0.86 for VA), but more likely to receive chemotherapy only and radiotherapy only. This was the case in both cohorts, although the strength of association was greater in SM. Both VA and SM populations saw no racial difference in receipt of >1 treatment (Fig. 1A). When comparing each treatment category to the surgery only group, Black patients were more likely to receive no treatment, radiotherapy only, and chemotherapy only, compared with White patients. There was no significant racial difference in receipt of >1 treatment compared with surgery alone (ORadj = 1.07; 95% CI, 1.00–1.62 in SM; ORadj = 1.20; 95% CI, 0.93–1.56 in VA; Fig. 1B).

Survival

Among all patients with stage I NSCLC, Black patients had significantly worse 5-year overall survival in SM and VA (Fig. 2). Regarding lung cancer–specific survival, Blacks in the SM cohort had worse survival than Whites, but no racial difference was observed in the VA cohort (Fig. 2). After adjustment for demographic and clinical characteristics, Black patients had significantly worse 5-year overall survival.
survival compared with White patients (HRadj = 1.17; 95% CI, 1.06–1.3 for SM; HRadj = 1.08; 95% CI, 1.001–1.16 for VA), but when also adjusting for treatment, there was no significant racial difference in overall survival (HRadj = 0.99; 95% CI, 0.89–1.09 for SM; HRadj = 0.97; 95% CI, 0.91–1.05 for VA). Within each of the treatment groups, there was no significant association between race and overall survival in either cohort (Table 2A). Results were similar for lung cancer–specific 5-year survival, except that in the VA cohort, among those who received radiotherapy, Black patients had better survival, compared with White patients (HRadj = 0.81; 95% CI, 0.66–0.99; Table 2B).

### Discussion

This retrospective study assessed treatment and survival disparities among older male patients with stage I NSCLC in VA and SEER populations. In both cohorts, Blacks were less likely to get any treatment, particularly surgical treatment. However, there were no racial differences in overall survival or lung cancer–specific survival when accounting for the type of treatment received. These findings suggest that although the extent of treatment disparities vary between these two populations, the estimated effect size of race on receipt of treatment and survival are similar when adjusting for relevant demographic and clinical characteristics. To our knowledge, our study is the first report evaluating national-level VA and SEER populations of patients with stage I NSCLC, specifically among older Black and White men within these populations.

Racial disparities in lung cancer incidence, treatment, and survival have been documented for decades and some studies suggest they continue to exist. In particular, studies continue to report significantly lower surgery rates among Blacks compared with Whites for early-stage NSCLC (1–3, 15) and worse overall survival (4). In a recent study evaluating treatment trends for early-stage lung cancer, Shin and colleagues found that over an almost 30-year time period there has been an increasing proportion of older patients and patients receiving radiotherapy alone instead of surgery; however, overall survival has improved among early-stage NSCLC and race remains a prognostic factor (16). Although the landscape for treatment for stage I NSCLC may be changing due to increased utilization of stereotactic body radiotherapy (SBRT), it remains to be seen how this impacts treatment disparities. Furthermore, due to increases in life expectancy and adoption of lung cancer screening, the proportion of older patients with early-stage disease will continue to grow. Studies show that age is a strong predictor for receipt of surgery and that even among patients with minimal comorbidities older patients are less often recommended surgery (17). This emphasizes the importance of understanding disparities specifically among the older population of patients with stage I
NSCLC, as more early-stage disease patients will be detected via screening and potentially eligible for surgery. In a cohort of patients with stage I NSCLC in the National Cancer Database, the surgery rate was 8% less for Blacks than Whites, similar to the absolute difference observed in VA in this study (18). In addition, Blacks had greater rates of no treatment, as was the case in both VA and SM cohorts in our study. Interestingly, Whites were more likely to get SBRT while more Blacks got external beam radiation. Our study showed an increased likelihood of Blacks getting radiotherapy only compared with surgery, and chemotherapy only compared with surgery, and were more likely to get chemotherapy only compared with surgery than White subjects. Black and White subjects did not have significantly different odds of choosing >1 treatment compared with surgery only.

Studies continue to report that Blacks experience higher overall mortality than Whites for early-stage NSCLC (4, 20). Similar to our study findings, other studies have shown that when accounting for treatment and other covariates, Blacks and Whites have similar survival outcomes (21–24). For example, in previous analyses of SEER-Medicare patients, despite a 14% lower resection rate among Blacks, survival rates were equivalent for Blacks and Whites when adjusting for demographic and clinical characteristics (24). Moreover, Soneji and colleagues observed that although Blacks have worse overall mortality, this is mostly due to death from competing causes as there was no racial difference in lung cancer–specific deaths (4). In our study, we observed no racial difference in overall or lung cancer–specific survival when accounting for type of treatment (i.e., surgical or nonsurgical), if any, received. Together, these studies support the hypothesis that disparate outcomes are eliminated when comparable treatment is received.

An underlying factor related to health care disparities is access to health care. For this reason, it is assumed that disparities are mitigated or absent in health care systems providing universal access to services and that care and outcomes are improved where access to care issues are minimized. Several studies have compared care received and outcomes in the general U.S. population to those receiving care in U.S. integrated health care systems such as the Military Health System, Veterans Affairs Health Administration, and Kaiser Permanente (25–27). Lin and colleagues compared survival in the U.S. Military Health System (MHS) with the SEER population for patients with NSCLC and observed that those in the MHS were more likely to receive surgery for early-stage and radiation for advanced stage lung cancer compared with their SEER counterparts (25). Also, overall survival outcomes were better in the MHS overall and within all subgroups for age, race, and stage with...
the exception of stage II NSCLC. Similarly, Landrum and colleagues reported improved survival among patients with NSCLC in VA compared with SEER, although this was, in part, due to diagnosis at earlier stages in VA (28). Another VA versus SEER comparison was conducted in a single geographic location and found that patients with stage I/II NSCLC in SEER had higher surgical resection rates than VA overall, but not within the subgroup of patients ages 65 and older, and that stage I/II 5-year survival rates were significantly higher in SEER (26). Most recently, a study comparing Kaiser members and nonmembers with early-stage NSCLC in California found that the Black–White racial disparity in receipt of surgery was similar within and out of the Kaiser system (27). Our study specifically compared racial disparities in stage I treatment and survival and noted greater differences in receipt of treatment in SM than VA, but similar findings for the impact of race on both receipt of treatment and survival. One distinction to note is that significant estimates of effect were stronger in SM for the impact of race on receipt of treatment than in VA.

Few studies have attempted to assess the intersection of race and gender when explaining disparities in lung cancer treatment and outcomes. Among patients in the National Lung Screening Trial in which surgery rates were much higher overall (92%), the White–Black difference was 3% in women but 28% in men (3). In a population-based study examining the association of both race and sex on the receipt of lung cancer treatment in Medicare patients, the authors report significant interaction between race and sex (30). Specifically, the racial difference in the surgical resection rate for stage I/II NSCLC was 21.5% lower for Blacks than Whites, but only 10% lower for Black women versus White women. Our study focused solely on men, in part, because the surgical disparity is greater among men, but also because...

Figure 2.
Five-year overall survival and lung cancer–specific survival. Survival curves with log-rank test P-values for Black subjects (blue) and White subjects (red) in the SM and VA cohorts. A, Five-year overall survival curves for Black subjects and White subjects in the SM and VA cohorts with log-rank test P-values. These curves show that White subjects had significantly better 5-year overall survival outcomes than Black subjects in both cohorts. B, Five-year lung cancer–specific survival curves for Black subjects and White subjects in the SM and VA cohorts with log-rank test P-values. These curves show that White subjects had significantly better 5-year lung cancer–specific survival outcomes than Black subjects in the SM cohort. This relationship did not hold for the VA cohort, which did not have a significant difference in the lung cancer–specific survival outcomes between the two races.
Table 2. Adjusted hazard of death for Black vs. White (reference) patients for 5-year overall survival and lung cancer–specific survival.

<table>
<thead>
<tr>
<th>Model</th>
<th>SM cohort</th>
<th>VA cohort</th>
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<tbody>
<tr>
<td></td>
<td>HRadj* (95% CI)</td>
<td>HRadj* (95% CI)</td>
</tr>
<tr>
<td><strong>Overall 5-year survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>1.17 (1.06–1.30)</td>
<td>1.08 (1.00–1.16)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
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</tr>
<tr>
<td>None</td>
<td>0.99 (0.89–1.09)</td>
<td>0.97 (0.91–1.05)</td>
</tr>
<tr>
<td>Surgery only</td>
<td>1.11 (0.91–1.36)</td>
<td>1.08 (0.95–1.25)</td>
</tr>
<tr>
<td>RT only</td>
<td>1.01 (0.81–1.28)</td>
<td>0.86 (0.73–1.07)</td>
</tr>
<tr>
<td>Chemo only</td>
<td>1.04 (0.68–1.58)</td>
<td>0.79 (0.51–1.33)</td>
</tr>
<tr>
<td>&gt;1 treatment</td>
<td>0.89 (0.70–1.13)</td>
<td>1.04 (0.80–1.35)</td>
</tr>
<tr>
<td><strong>Lung cancer–specific 5-year survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>1.21 (1.07–1.37)</td>
<td>1.06 (0.96–1.17)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0.99 (0.79–1.24)</td>
<td>0.85 (0.73–1.00)</td>
</tr>
<tr>
<td>Surgery only</td>
<td>0.89 (0.66–1.20)</td>
<td>1.12 (0.94–1.34)</td>
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<tr>
<td>RT only</td>
<td>1.11 (0.85–1.46)</td>
<td>0.81 (0.66–0.99)</td>
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<tr>
<td>Chemo only</td>
<td>1.07 (0.67–1.70)</td>
<td>0.88 (0.54–1.45)</td>
</tr>
<tr>
<td>&gt;1 treatment</td>
<td>0.97 (0.75–1.26)</td>
<td>0.97 (0.71–1.33)</td>
</tr>
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Abbreviation: RT, radiotherapy.
*Adjusted for age at diagnosis, marital status, comorbidity score, histology, stage, and year of diagnosis.
Additional adjustment for treatment category.

the VA lung cancer population is 97% males. The racial difference among men in our study (15% in SM, 7% in VA) was much less than reported in other studies, most likely due to the longer timeframe for capturing receipt of treatment in our study (1 year). This suggests that disparities may be greater when assessing timeliness of care.

A number of factors contribute to the observed disparities including genetic, environmental, and behavioral factors (31, 32). Among these factors, comorbidity is likely the most relevant among older populations. In our study, over 50% of SEER patients had no comorbidities compared with less than 20% of VA patients, which likely explains the lower treatment rates in VA for both Blacks and Whites compared with SEER. We also noted higher rates of adenocarcinoma histology in SEER than in VA, and this has been reported in other studies (26, 33). Although we attempted to include potential confounders, there are likely others that were not incorporated because they were not available in both SM and VA datasets. For example, smoking history was unavailable in SM and tumor size was not available in the VA dataset, both of which are key factors to consider for lung cancer outcomes but that also may play a role in the association between race and lung cancer treatment and survival. In addition, a key limitation was that the data were not coloected and therefore we could not conduct a statistical comparison of the two cohorts. This inability to directly compare the two study populations in the analysis could have resulted in an over- or under-statement of similarities and distinctions in findings in the SEER and VA cohorts.

In conclusion, our results indicate the impact of race on receipt of any treatment, as well as each possible treatment category, is similar in both veteran and non-veteran male populations, suggesting that treatment disparities are mitigated but not absent in equal access health care systems. However, in both cohorts survival disparities do not exist when accounting for treatment.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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Conception and design: C.D. Williams, N. Alpert, A.J. Bullard, R.M. Flores, E. Taioli
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): C.D. Williams, A.J. Bullard, E. Taioli
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): C.D. Williams, N. Alpert, T.S. Redding IV, R.M. Flores
Writing, review, and/or revision of the manuscript: C.D. Williams, N. Alpert, T.S. Redding IV, A.J. Bullard, R.M. Flores, M.J. Kelley, E. Taioli
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): N. Alpert, T.S. Redding IV, A.J. Bullard, E. Taioli
Study supervision: C.D. Williams, E. Taioli

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