Racial Disparities Among Lung Cancer Patients Recommended Operative Therapy

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ABSTRACT

Hypothesis: Healthcare system/provider biases and differences in patient characteristics are thought to be prevailing factors underlying racial disparities. The influence of these factors on the receipt of care would likely be mitigated among patients recommended optimal therapy. We hypothesized that there would be no significant evidence of racial disparities among early-stage lung cancer patients recommended surgical therapy.

Design: Retrospective cohort study.

Patients and Setting: Patients within the Surveillance, Epidemiology, and End-Results-Medicare database diagnosed with stage I or II lung cancer between 1992 and 2002 (follow-up through 2005).

Main Outcome Measures: Receipt of lung resection and overall survival.

Results: Among 17,739 patients recommended surgical therapy—mean (SD) age 75 (5) years, 89% white, 6% black—blacks less frequently underwent resection compared to whites (69% versus 83%, $p<0.001$). After adjustment, black race was associated with a lower odds of receiving surgical therapy (OR 0.43, 99% CI 0.36-0.52). Unadjusted 5-year survival rates were lower for blacks compared to whites (36% versus 42%, $p<0.001$). After adjustment, there was no significant association between race and death (HR 1.03, 99% CI 0.92-1.14) despite a 14% difference in receipt of optimal therapy.

Conclusions: Even among patients recommend surgical therapy, blacks underwent lung resection less often then whites. Unexpectedly, racial differences in the receipt of optimal therapy did not appear to affect outcomes. These findings suggest that distrust, beliefs and perceptions about lung cancer and its treatment, and limited access to care (despite insurance) might have a more dominant role in perpetuating racial disparities than previously recognized.

INTRODUCTION

Lung cancer is the second most common malignancy in the US and is responsible for more deaths than any other cancer.[1] Pulmonary resection provides the best chance of cure for patients with early-stage disease.[2-4] Blacks with early-stage lung cancer have lower 5-year survival rates than whites, and this difference in outcome has been attributed to lower rates of resection among blacks.[5]

Barriers to the receipt of optimal cancer therapy are likely numerous and complex.[6] Several potential factors underlying racial differences in the receipt of surgical therapy include differences in pulmonary function[7], access to care[8], refusal of surgery[9], beliefs about tumor spread upon air exposure at the time of operation[10] and the possibility of cure without surgery[11], distrust of the health care system/physicians[12], suboptimal patterns of patient/physician communication[13], and health care system/provider biases.[14, 15] Differences in patient characteristics (i.e. lung function, performance status, severity of comorbidity) and healthcare system/provider bias are often argued to be significant factors underlying racial disparities.

To better understand the relationship between hypothesized factors and racial differences in care and outcomes, we conducted a cohort study using the Surveillance, Epidemiology, and End-Results (SEER)-Medicare database. Among patients recommended surgical therapy, the effects of healthcare system/provider biases on the receipt of optimal care might be mitigated, as might the potentially confounding effects of some measured and unmeasured patient characteristics. We hypothesized that resection and survival rates would not vary between whites and blacks among a cohort of early-stage lung cancer patients who were recommended surgical therapy.

METHODS

A retrospective cohort study was conducted of patients diagnosed with lung cancer between 1992 and 2002. The use of SEER-Medicare to investigate cancer care, and the quality and validity of variables therein, have been described extensively elsewhere.[16-22] The University of Washington Institutional Review Board approved this study, and waived consent because the investigation involved existing, de-identified data.

Among 221,208 patients diagnosed with lung cancer between 1992 and 2002, sequential exclusions were made for the following patients: advanced stage of disease or missing stage data (n=177,910), diagnosis at autopsy or death (n=134), age less than 66 years (n=9,284), diagnosis of a second malignancy up to 6 months after lung cancer diagnosis (n=1,333), partial fee-for-service Medicare coverage and/or concurrent enrollment in a health maintenance organization (n=10,389), or a histology code inconsistent with lung cancer (n=32). An additional 4,387 patients who were not recommended surgical therapy (19% of whites and 26% of blacks) were excluded from the analysis for a final cohort of 17,739 patients.

SEER data abstractors examined medical records to determine whether surgical therapy was recommended.[23] In this study, patients were considered to have been recommended surgical therapy if there was a documented recommendation in the medical records and/or if the patient underwent surgical therapy.

Race was the main predictor variable, ascertained using the Medicare Enrollment Database, and classified as white, black, or other based on a prior recommendation.[17] Income and education level were based on quartiles of median income and proportion of people with only a high-school education living in the patient's zip code at the time of diagnosis. Geography was determined by the location of the SEER registry. Residence refers to the size of the

population where the patient lived (metropolitan ≥ 250,000; urban 20,000-249,999, and rural <19,999). The previously validated Klabunde-modified Charlson comorbidity index was derived from Carrier and Outpatient claims in the year prior to diagnosis.[24] Stage was based on the 6th edition of the American Joint Committee on Cancer staging manual.

Outcomes included resection and overall survival. Resection, radiation therapy, and chemotherapy were ascertained up to 6 months after diagnosis using *The Healthcare Common Procedure Coding System*, *International Classification of Diseases* procedure codes, and Revenue Center Codes, as appropriate, in the Carrier Claim and Outpatient files (codes available upon request). Death information was available in the Medicare Enrollment Database with follow-up through 2005.

Differences in continuous and categorical variables between blacks and whites were tested using t-tests for independent samples and the chi-square, respectively. Logistic regression was used to evaluate whether an association existed between race and the receipt of resection after adjustment for potentially confounding factors. Unadjusted differences in overall survival were estimated using the Kaplan-Meier method. Cox proportional hazards (PH) models were used to evaluate the unadjusted and adjusted relationships between race and survival. Schoenfeld residuals were used to test the PH assumption and extended (stratified) Cox models were fitted if the PH assumption was violated. Survival time was defined by the interval between date of diagnosis and date of death or censoring. Robust variance estimators were used for all regression analyses. All regression analyses were case-complete analyses. Seven percent of patients had at least one missing covariate value. The proportion of patients with missing covariate data did not vary between blacks and whites (7% versus 7%, p=0.82), and patients with

missing covariate data did not have a lower 5-year survival rate compared to those with no missing data (42% versus 42%, p=0.46).

Several post-hoc sensitivity analyses were conducted. The relationship between race and receipt of surgical therapy would ideally be characterized in terms of relative risks or risk differences, but generalized linear models estimating relative risks and risk differences could not be fit. Results from the logistic regression analysis were re-examined after converting odds ratios to relative risks. When event rates are high, as was the case in this investigation (receipt of surgical therapy), an odds ratio tends to overestimate the risk ratio.[25] The relationship between race and receipt of surgical therapy was also re-evaluated in a time-to-event analysis censoring for deaths occurring among untreated patients within 6-months of diagnosis. If rates of death between diagnosis and treatment varied by race, then the results of the primary analysis might have been biased. Finally, all regression analyses were repeated after adjustment for clustering within SEER registry because practice patterns might have been highly correlated within a given SEER registry. Adjustment for clustering at the provider or institution level was not possible because not all patients underwent surgical therapy and some patients received no therapy at all.

STATA (Special Edition 9.2, Statacorp, College Station, Texas) was used for all statistical analyses. A two-sided p-value of <0.01 was considered statistically significant.

RESULTS

A total of 17,739 patients with stage I/II lung cancer—median (range) age 74 (66-103) years, 89% white, and 6% black—were recommended surgical therapy (Table 1). Compared to whites, blacks were more frequently men, in the lowest quartiles of income and education, not

married at the time of diagnosis, residing in a metropolitan area, and had comorbid conditions. Racial differences in the distributions of stage and histology were not significant .

Blacks underwent lung resection less frequently than whites (69% versus 83%, difference 14%, 99% CI 11-18%) despite both groups having been recommended surgical therapy (Table 2). Among those who did not undergo resection, there was no significant difference in the proportion of blacks versus whites who underwent medical management (36% vs. 40%, p=0.26). After accounting for the potential confounding effects of variables listed in Table 1, blacks had a 55% lower odds of having received a lung resection compared to whites (Table 3). This association persisted in all sensitivity analyses though the magnitude of the association was attenuated in some cases: odds ratios converted to relative risk (adjusted relative risk 0.83, 99% CI 0.78-0.88), censoring for early death (adjusted hazard ratio (HR) 0.67, 99% CI 0.60-0.75), adjustment for clustering within SEER registries (adjusted odds ratio (OR) 0.45, 99% CI 0.34-0.60).

Blacks had a lower unadjusted 5-year overall survival rate compared to whites (36% vs. 42%, $p<0.001$). After adjusting for patient and disease characteristics, only a small and non-significant association between black race and death was evident (Table 3), despite the fact that blacks underwent resection 14% less often than whites. This lack of association between race and death persisted in a sensitivity analysis adjusting for clustering within SEER registries (adjusted hazard ratio 1.03, 99% CI 0.93-1.13). In an exploratory analysis, treatment received (including no therapy) was added to the model to investigate whether race had an effect on death through a pathway unrelated to the receipt of therapy. Blacks had a 6% lower hazard of death compared to whites, though this association was not significant (adjusted HR 0.94, 99% 0.82-1.09). In another exploratory analysis, lung-cancer cause-specific survival rates were evaluated

though there was no racial variation in outcomes in the unadjusted (62% vs 64%, p=0.17) or adjusted (HR 1.01, 99% CI 0.88-1.17) analyses.

DISCUSSION

Multiple factors likely result in racial differences in care and outcomes among early-stage lung cancer patients, but the impact of any one factor(s) on overall differences is not well understood. Healthcare system/provider biases and differences in patient characteristics are often thought to be predominant factors underlying racial disparities. Accordingly, we hypothesized that the influence of these factors on the receipt of optimal therapy would be mitigated among patients recommended surgical therapy, and therefore we did not expect significant racial variation in lung resection or outcomes. This investigation is the first to describe care and outcomes among early-stage lung cancer patients recommended surgical therapy using a nationally representative database. Contrary to expectation, we observed a large (14%) difference between blacks and whites in the proportion of patients who actually underwent lung resection even though all patients were recommended surgical therapy. Another surprising finding was that this large difference in receipt of optimal therapy did not appear to affect long-term survival after adjustment for patient and disease characteristics. These findings suggest that reasons other than healthcare system/provider biases and patient characteristics may play a larger role in creating racial disparities than previously recognized.

There are several possible explanations for why large racial differences in care were observed among lung cancer patients recommended surgical therapy. Blacks have been shown to refuse surgical therapy more frequently than whites for reasons relating to beliefs about accelerated tumor spread at the time of operation[10], the possibility of cure without resection[11],

and distrust of the healthcare system and providers.[12] Though refusal rates have been reported as high as 18% among blacks[9], the generalizability of that finding is uncertain because the proportion of blacks in that study was higher than that reported in nationally representative cohorts (35% vs. 10%).[26] The current study could not determine why patients did not receive surgical therapy, but the findings are consistent with the notion that refusal rates among lung cancer patients may be high and higher among blacks. Another explanation for why blacks underwent lung resection less frequently than whites is limited access to care. All patients in this study had uniform health insurance and demonstrated the ability to utilize health services—as evidenced by a documented diagnosis and treatment recommendation—but not all patients may have had access to care facilities and/or providers able to provide optimal cancer therapy. Supporting that notion, a study of Medicare beneficiaries found that primary care physicians treating black patients had less access to high-quality sub-specialists compared to physicians treating white patients.[27] A third explanation for racial differences in care is that healthcare system/provider biases may exist even in a setting where optimal therapy is recommended. Studies evaluating patients with a diagnosis of lung cancer or a pulmonary nodule found that patients in racially discordant physician-patient pairs received less information and were less often prompted to actively participate in conversation compared to patients in racially concordant pairs.[13] Additionally, black patients trusted their physician less often than white patients after an initial visit with a surgeon or oncologist, and this distrust appeared to be linked to perceptions that physician communication was not supportive, partnering, or informative.[12] Finally, hypothesized factors not measured in the current study or previously investigated—such as racial variation in distance/travel or family/social support[6]—might also explain racial differences in the receipt of lung resection.

Despite large racial differences in the receipt of optimal therapy, there were no observable differences in survival between blacks and whites. This finding is seemingly implausible because it is contrary to conventional wisdom, practice guidelines, and empirical evidence. Among all SEER-Medicare patients with stage I/II lung cancer, stage-based survival rates were significantly higher for patients who received operative therapy compared those who did not (Stage I: 50% vs. 15%, $p<0.001$; Stage II (28% vs. 8%, $p<0.001$). Inadequate risk-adjustment provides one explanation for this unexpected finding. The relationship between race and survival may have been confounded by unmeasured patient selection factors. For instance, forced expiratory volume is strongly associated with both the receipt of surgical therapy and survival and may vary by race.[7] No racial difference in survival might be observed if operated white patients were at higher-risk (defined by poorer pulmonary function) for death compared to operated black patients—counterbalancing the effect of more lung resections among whites compared to blacks. Since SEER-Medicare does not record detailed information about patient selection, this study may not have provided adequate adjustment for all potential confounders—including forced expiratory volume, performance status, and severity of comorbid conditions. To the extent that this explanation is true, the issue of overuse and underuse of therapy is important to consider.[28] Surgical therapy may have been "overused" among whites or it may have been "underused" among blacks, although this determination cannot be made because practice guidelines recommendations are not based on risk-stratification.[2]

The major limitation of this study is concern over the accuracy and validity of the "recommended surgery" variable within SEER. Although SEER data is considered highly valid[22], there are no published third-party evaluations of the validity and accuracy of this variable. The face validity of this variable could be evaluated because the *recommendation* to undergo

surgical therapy and *receipt* of surgical therapy were ascertained by two independent sources—SEER and Medicare, respectively. While it is plausible that a patient who is recommended surgical therapy might or might not actually undergo resection, it is not likely that patients *not* recommended surgical therapy would undergo resection. Among patients *not* recommended surgical therapy, only 1% underwent resection and this proportion did not vary by race. One shortcoming of this variable is an inability to identify the type of provider (surgeon, oncologist, pulmonologist, etc.) who made the recommendation and/or the context (both clinical and cultural) in which the recommendation was made. Another limitation of this study is that our findings may only be generalizable to elderly, Medicare beneficiaries. However, given that the median age at diagnosis of lung cancer is 70 years old[26] and that Medicare provides health care coverage for over 97% of Americans over 65 years of age, this study might be considered to be representative of most lung cancer patients. Although evidence shows that other racial groups, such as Hispanics, have disparate care and outcomes[29], we were not able to evaluate other racial groups because prior studies indicate that SEER and/or Medicare only reliably measure black or white race.[17]

In conclusion, even among early-stage lung cancer patients recommended surgical therapy there was large racial variation in the receipt of optimal cancer treatment after adjustment and despite uniform healthcare coverage. While these findings do not refute the likely roles of healthcare system/provider biases and patient characteristics as important causal factors underlying health disparities, the findings do suggest that other factors (i.e. distrust, perceptions and beliefs about lung cancer and its treatment, and limited access to sub-specialty care) may have a more dominant role in causing disparities than previously recognized. The implication of these findings is that interventions designed to narrow gaps in healthcare should

target both structural aspects of care and providers, patients, and communities at risk for lung cancer and suboptimal care.

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Table 1. Patient Characteristics by Race

	White (n=15,726)	Black (n=1,096)	p-value
Age, No. (%), y			< 0.001
66-70	4,103 (26)	368 (34)	
71-75	5,223 (33)	366 (33)	
76-80	4,071 (26)	236 (22)	
81-85	1,789 (11)	103 (9)	
86+	540 (3)	23 (2)	
mean (SD)	75 (5)	74 (5)	< 0.001
Male, No. (%)	8,279 (53)	629 (57)	0.002
Income, No. (%)			< 0.001
Lowest Quartile	3,180 (20)	639 (58)	
Missing	593 (4)	28 (3)	
Education, No. (%)			< 0.001
Lowest Quartile	2,965 (19)	712 (65)	
Missing	589 (4)	27 (3)	

Table 1. Patient Characteristics by Race (continued)

	White (n=15,726)	Black (n=1,096)	p-value
Marital Status, No. (%)			< 0.001
Unmarried	6,051 (39)	580 (53)	
Missing	526 (3)	47 (4)	
Geography, No. (%)			< 0.001
West	6,839 (44)	331 (30)	
East	2,751 (18)	138 (13)	
Midwest	4,173 (27)	449 (41)	
South	1,963 (13)	178 (16)	
Residence, No. (%)			< 0.001
Metropolitan	13,399 (85)	1,059 (97)	
Urban	963 (6)	13 (1)	
Rural	1,364 (9)	24 (2)	
Prior Malignancy, No. (%)	3,783 (24)	262 (24)	0.91

Table 1. Patient Characteristics by Race (continued)

	White (n=15,726)	Black (n=1,096)	p-value
Comorbidity Index, No. (%)			< 0.001
0	8,758 (58)	544 (50)	
1	4,545 (29)	310 (28)	
2	1,572 (10)	143 (13)	
3+	851 (5)	99 (9)	
Stage, No. (%)			0.09
IA	6,550 (42)	450 (41)	
IB	6,335 (40)	475 (43)	
IIA	591 (4)	31 (3)	
IIB	2,250 (14)	140 (13)	
Histology, No. (%)			0.009
Non-Small Cell	14,136 (90)	993 (91)	
Small Cell	327 (2)	27 (3)	
Not-Otherwise-Specified	691 (4)	56 (5)	
Other*	572 (4)	20 (2)	

*Includes carcinoid tumors, sarcomas, and other rare histologic typ

Table 2. Racial Variation in Treatment and Outcomes Among Patients Recommended Surgical Therapy

	White (n=15,726)	Black (n=1,096)	p-value
Therapy, No. (%)			< 0.001
Resection	13,112 (83)	756 (69)	
Radiation Therapy	606 (4)	69 (6)	
Chemotherapy	150 (1)	26 (2)	
Chemoradiation Therapy	280 (2)	29 (3)	
None	1,578 (10)	216 (20)	
5-Year Survival, % (99% CI)			
Stage I	46 (45-47)	39 (35-43)	< 0.001
Stage II	25 (23-27)	18 (10-26)	0.21
Overall	41 (41-43)	36 (32-40)	< 0.001

Table 3. Multivariate Analyses of the Relationship Between Race, Treatment, and Outcomes Among Patients Recommended Surgical Therapy

	Lung Resection	Death
	Odds Ratio (99% CI)	Hazard Ratio (99% CI)
Black versus White		
Unadjusted	0.43 (0.36-0.52)	1.17 (1.06-1.29)
Add Patient Characteristics[a]	0.47 (0.38-0.57)	1.04 (0.94-1.16)
Add Cancer Characteristics[b]	0.45 (0.37-0.56)	1.03 (0.92-1.14)

[a]Adjusted for age, sex, income, education, marital status, geography, area of residence, prior malignancy, and comorbidity index

[b]Adjusted for histology and stage