Racial Differences in Waiting List Outcomes in Chronic Obstructive Pulmonary Disease

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Rationale: Blacks with chronic illness have poorer outcomes than whites in the United States. The health outcomes of minorities with chronic obstructive pulmonary disease (COPD) on the lung transplant waiting list have not been studied.

Objectives: To compare outcomes of black and white patients with COPD after listing for lung transplantation in the United States.

Methods: Retrospective cohort study of all 280 non-Hispanic black and 5,272 non-Hispanic white adults 40 years and older with COPD listed for lung transplantation in the United States between 1995 and 2004.

Measurements and Main Results: Blacks with COPD were more likely to have pulmonary hypertension, obesity, and diabetes; to lack private health insurance; and to live in poorer neighborhoods than whites. Blacks were less likely to undergo transplantation after listing compared with whites, despite adjustment for age, lung function, pulmonary hypertension, cardiovascular risk factors, insurance coverage, and poverty level (adjusted hazard ratio, 0.83; 95% confidence interval, 0.70–0.98; $P = 0.03$). This was accompanied by a greater risk of dying or being removed from the list among blacks (unadjusted hazard ratio, 1.31; 95% confidence interval, 1.05–1.63; $P = 0.02$).

Conclusions: After listing for lung transplantation, black patients with COPD were less likely to undergo transplantation and more likely to die or be removed from the list compared with white patients. Unequal access to care may have contributed to these differences.

Keywords: racial disparities; lung transplantation; survival; competing risks; black or African American

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the United States (1). In 2000, more than 10 million Americans carried a diagnosis of COPD, a 43% increase in prevalence since 1980 (2). The mortality rate from COPD increased by 74% among blacks compared with 65% among whites during the same 20-year period, despite a slightly lower prevalence of COPD among blacks compared with whites (2). In addition, blacks have an almost twofold increased rate of

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

The mortality rate for blacks with chronic obstructive pulmonary disease (COPD) is rising faster than that of whites in the United States. The waiting list outcomes of blacks with COPD have not been studied.

What This Study Adds to the Field

Blacks with COPD on the waiting list for lung transplantation are less likely to undergo transplantation than whites with COPD in the United States.

emergency room visits for COPD and are more likely to be hospitalized for COPD than whites (2).

Poorer access to subspecialist care may contribute to the worse health outcomes of blacks with pulmonary disease in the United States. For example, race-based differences in access to surgical care contribute to the higher mortality rate of blacks with early-stage non-small cell lung cancer (3). In addition, blacks with pulmonary fibrosis and pulmonary hypertension have higher mortality rates than whites with these diseases (4–6). For patients with advanced COPD, lung transplantation is a therapy that, although not necessarily improving survival, does treat the dyspnea and functional impairment that accompany this devastating disease (7, 8). Although racial disparities exist in access to kidney and liver transplantation, it is not known whether blacks and whites have equal access to lung transplantation (9, 10).

We hypothesized that, after listing for lung transplantation, blacks with COPD would be less likely to undergo transplantation and more likely to die or be removed from the waiting list than whites in the United States. We also hypothesized that differences in socioeconomic status and health insurance coverage would explain these disparities.

METHODS

Study Design and Subjects

We performed a retrospective cohort study of all non-Hispanic black and white adults 40 years or older with a diagnosis of COPD/emphysema who were placed on the United Network for Organ Sharing (UNOS) waiting list for lung transplantation in the United States between January 1, 1995, and December 31, 2004. Hispanics with COPD were examined in a secondary post hoc analysis. We excluded those with a physician-reported diagnosis of α_1 -antitrypsin deficiency. The Columbia University Medical Center Institutional Review Board approved the study.

(Received in original form August 25, 2007; accepted in final form November 14, 2007)

Supported by the National Institutes of Health grants RR024157 (D.J.L.), HL077612 and HL075476 (R.G.B.), and HL082895 and HL086719 (S.M.K.). Also supported in part by Health Resources and Services Administration contract 234-2005-370011C.

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Am J Respir Crit Care Med Vol 177, pp 450–454, 2008

Originally Published in Press as DOI: 10.1164/rccm.200708-1260OC on November 15, 2007
Internet address: www.atsjournals.org

Data Collection

Demographic, clinical, and administrative data at the time of listing were collected at 78 U.S. transplant centers using the UNOS Adult Lung Transplant Candidate registration worksheet (11) and obtained from a Standard Transplant Analysis and Research file based on Organ Procurement and Transplantation Network data as of January 11, 2007.

Clinical staff at each transplant center coded race and ethnicity in one or more of the following categories in accordance with the Office of Management and Budget directive: white, black or African American, Hispanic/Latino, Asian, American Indian or Alaskan Native, or Native Hawaiian or other Pacific Islander (12). Multiracial patients were excluded from our analysis. Cigarette smoking was defined as greater than 20 pack-years for those listed from 1995 to October 24, 1999; greater than 10 pack-years for those listed from October 25, 1999, to June 2004; and any cigarette use from July 2004 to December 2004. Physiologic data included percent-predicted FVC (FVC%), percent-predicted FEV₁ (FEV₁%), and pulmonary hemodynamics. Spirometric testing and reference equations were not standardized across sites. We defined pulmonary hypertension as a mean pulmonary artery pressure greater than 25 mm Hg. The distance walked in 6 minutes was recorded as a dichotomous variable (>150 ft or <150 ft). Measures of gas exchange were not available. Using 2000 U.S. Census data, we included the percentage of families living below the federal poverty line in each study subject's residential zip code as a measure of neighborhood-level socioeconomic status (13, 14).

Outcomes

Dates of transplantation and removal from the list were obtained from the UNOS file. Deaths were determined using the Social Security Death Master File and the UNOS dataset (15). Study subjects who died after removal from the list were considered to have died on the date provided by the Social Security file. Study subjects who were placed on the waiting list more than once during the study period were followed continuously from their first waiting list registration to their last recorded status, including any time spent off the waiting list. Subjects who did not experience an endpoint (transplantation, removal, or death) were censored as alive on the last follow-up date reported to UNOS.

Statistical Analysis

Continuous variables were summarized by mean $\pm$ standard deviation or median (interquartile range [IQR]) and compared with *t* tests or Wilcoxon rank sum tests, as appropriate. Categorical variables were summarized by frequency and percentage and compared using χ^2 tests or Fisher's exact tests.

Patients on the waiting list for transplantation can experience one of three competing events: transplantation, removal from the list, or death. Standard survival analyses, such as the Kaplan-Meier method and Cox proportional hazards modeling, typically examine the time to one of these events, censoring subjects at the time of one of the other two events. However, these models assume that these censoring events are not related to the probability of occurrence of the event of interest (noninformative censoring). This assumption may not hold true in a cohort awaiting transplantation. For example, those who are censored upon transplantation may have had a different risk of death if they had not been censored (i.e., if they had not undergone transplantation) compared with those remaining on the list (i.e., informative censoring).

We therefore used a competing risk survival method that avoids this bias to estimate the cumulative incidences of these events: transplantation and the combined event of death or removal from the waiting list (16–18). We modeled outcomes as a three-state Markov chain (19). The initial state was alive on the waiting list. Transplantation and the combined event of death or removal from the list were absorbing states. We compared cumulative incidences of each of these outcomes between racial groups using Gray's test (20) and constructed proportional hazards models for the subdistribution of each competing risk as described by Fine and Gray (21). We sequentially included purposefully selected covariates: age, sex, measures of disease severity (FVC%, FEV₁%, six-minute-walk distance, pulmonary hypertension), cardiovascular risk factors (diabetes, hypertension, and body mass index), private insurance, community poverty level, and transplant center volume. Multiple imputation was used for missing covariate values in

multivariate models. *P* values less than 0.05 were considered statistically significant. Statistical analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC) and R 2.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

During the study period, 280 black and 5,272 white patients with COPD who were 40 years or older were listed for lung transplantation and comprised the study cohort. Cohort characteristics are presented in Table 1. Blacks were somewhat younger than whites and were more likely to be obese. Although FEV₁% was similar between blacks and whites, blacks had a lower FVC%. Blacks were more likely to have pulmonary hypertension and to have a lower six-minute-walk distance than whites. Blacks were also more likely to have diabetes mellitus and hypertension, to lack private health insurance coverage, and to live in neighborhoods of greater poverty than whites.

After listing, 171 blacks (61%) and 3,580 whites (68%) received lung transplants, 47 blacks (17%) and 804 whites (15%) died on the waiting list, and 39 blacks (14%) and 500 whites (9%) were removed from the waiting list. Of those removed from the list, 13 of 39 blacks and 229 of 500 whites subsequently died. At the conclusion of the study period, 23 blacks (8%) and 388 whites (7%) remained on the waiting list. Among the 539 subjects removed from the list, the most common reasons for removal were "too sick to transplant" (11 blacks and 145 whites) and "other" (12 blacks and 131 whites). The median time on the waiting list for those experiencing an event (transplantation, death, or removal) was 400 days (IQR, 185–714 d) for blacks and 407 days for whites (IQR, 167–738 d; Wilcoxon rank sum test, *P* = 0.74).

Blacks were less likely to undergo lung transplantation than whites (Figure 1; Table 2; unadjusted hazard ratio [HR], 0.84; 95% confidence interval [CI], 0.72–0.97; *P* = 0.02). The 1- and 5-year cumulative incidences of transplantation were 31 and 62% for blacks and 36 and 68% for whites, respectively. The median time to transplantation among those undergoing transplantation during the study period was 361 days (IQR, 170–622 d) for blacks and 335 days (IQR, 139–643 d) for whites (Wilcoxon rank sum test, *P* = 0.54). After adjustment for possible confounders, blacks still had a lower transplantation rate compared with that of whites (Table 2; adjusted HR, 0.83, 95% CI, 0.70–0.98; *P* = 0.03). Additional adjustment for ABO blood type did not change these findings (data not shown). For those who were transplanted, post-transplant survival time did not vary by race (HR for blacks vs. whites, 0.98; 95% CI, 0.78–1.24; *P* = 0.88).

Blacks were more likely to die or be removed from the waiting list than whites (Figure 1 and Table 2; unadjusted HR, 1.31; 95% CI, 1.05–1.63; *P* = 0.02). The 1- and 5-year cumulative incidences of death or removal from the list were 11 and 28% for blacks and 7 and 23% for whites, respectively. Adjustment for measures of disease severity did not meaningfully change the association between race and the risk of death or removal (model 2 in Table 2). However, adjustment for cardiovascular risk factors (model 3) and access to care factors (model 4; adjusted HR, 1.19; 95% CI, 0.94–1.50; *P* = 0.14) reduced the HR of blacks versus whites for death or removal from the list. This indicates that these factors confounded (or accounted for) the higher rate of death or removal among blacks. Notably, the absence of private insurance was associated with a slightly lower FVC% (age- and sex-adjusted mean difference, –1.4%; 95% CI, –0.4 to –2.4%; *P* = 0.007) and FEV₁% (age- and sex-adjusted mean difference, –0.9%; 95% CI, –0.3 to –1.4%; *P* = 0.004) compared with those with private insurance.

The associations between race and outcome did not vary significantly by insurance coverage or by poverty level (all

TABLE 1. COHORT CHARACTERISTICS AT THE TIME OF LISTING FOR TRANSPLANTATION

Variable	Black (n = 280)	White (n = 5,272)	P Value
Age, yr	54 ± 6	56 ± 6	<0.001
Male sex	120/280 (43%)	2,377/5,272 (45%)	0.46
Body mass index (n = 5,505)	24 ± 5	24 ± 5	0.20
Obese (body mass index ≥ 30 kg/m ²)	40/276 (14%)	534/5,229 (10%)	0.009
Year of listing			0.74
1995–1999	137/280 (49%)	2,633/5,270 (50%)	
2000–2004	143/280 (51%)	2,639/5,270 (50%)	
FVC, % predicted (n = 5,378)	51 ± 16	54 ± 17	0.003
FEV ₁ , % predicted (n = 5,386)	22 ± 9	22 ± 10	0.63
Mean pulmonary artery pressure, mm Hg (n = 4,454)	29 ± 9	25 ± 7	<0.001
Pulmonary capillary wedge pressure, mm Hg (n = 4,615)	13 ± 6	12 ± 5	0.01
Transpulmonary gradient, mm Hg (n = 4,315)	16 ± 9	13 ± 7	<0.001
Pulmonary hypertension*			<0.001
Pulmonary hypertension with PCWP < 15	66/219 (30%)	894/4,176 (21%)	
Pulmonary hypertension with PCWP ≥ 15	59/219 (27%)	751/4,176 (18%)	
No pulmonary hypertension	94/219 (43%)	2,531/4,176 (61%)	
Six-minute-walk distance < 150 ft	35/243 (14%)	391/4,515 (9%)	0.002
Diabetes mellitus	29/276 (11%)	152/5,208 (3%)	<0.001
Hypertension	91/271 (34%)	982/5,127 (19%)	<0.001
Smoking history	241/268 (90%)	4,681/5,083 (92%)	0.20
Health insurance			
Private	168/279 (60%)	3,811/5,258 (72%)	<0.01
Medicaid	66/279 (24%)	631/5,258 (12%)	<0.01
Medicare	103/279 (37%)	1,766/5,258 (34%)	0.25
Families living in poverty†, % (n = 5,347)	17 (8–25)	9 (5–14)	<0.001

Definition of abbreviation: PCWP = pulmonary capillary wedge pressure.

Data are number/total number (%), mean ± SD, and median (interquartile range).

* Those with pulmonary hypertension and missing PCWP were not included.

† Median (interquartile range) of the percentage of families living below the federal poverty line in each study subject's zip code.

P values for interaction ≥ 0.13). However, among those without private insurance, there was a lower transplantation rate among blacks compared with whites (age- and sex-adjusted HR, 0.75; 95% CI, 0.59–0.98; *P* = 0.03), whereas among those with private insurance, blacks and whites had similar transplantation rates (age- and sex-adjusted HR, 0.96; 95% CI, 0.78–1.16; *P* = 0.65).

On May 4, 2005, UNOS instituted a new lung allocation system that prioritizes transplant candidates based on the risks of death before and after transplantation (in contrast to the previous system in which organs were allocated based on waiting time). Forty-eight blacks and 807 whites from the study cohort remained on the waiting list on May 4, 2005. Under the new system, 4 blacks (8%) and 120 whites (15%) died, 12 blacks (25%) and 204 whites (25%) underwent transplantation, and 9 blacks (19%) and 95 whites (12%) were removed from the waiting list.

From 1995 to 2004, only 64 Hispanics with COPD were placed on the lung transplant waiting list in the United States. Compared with non-Hispanic whites, Hispanics had a nonsignificantly lower rate of transplantation (age- and sex-adjusted HR, 0.79; 95% CI, 0.57–1.10; *P* = 0.16) and an increased rate of death or removal from the list (age- and sex-adjusted HR, 1.55; 95% CI, 1.03–2.32; *P* = 0.02).

DISCUSSION

We have shown that black patients with COPD were less likely to undergo lung transplantation after listing than white patients in the United States during the late 1990s and early 2000s. This finding was independent of important potential confounders, such as age, lung function, pulmonary hypertension, cardiovascular risk factors, transplant center volume, type of health insurance coverage, and neighborhood poverty level. We also observed a higher risk of death or removal from the waiting list among blacks compared with whites (despite similar lung function at the time of listing), possibly explained in part by

the following: (1) differences in health insurance coverage and neighborhood poverty level, two factors that may reflect access to health care, and (2) a higher prevalence of cardiovascular risk factors. These disparities are consistent with those observed among patients awaiting kidney and liver transplantation and among patients with other advanced lung diseases, such as pulmonary hypertension and pulmonary fibrosis (4–6, 9, 10).

The lung transplant waiting list comprises patients who have not only successfully accessed care at a transplant center but who have also demonstrated physical fitness, medical need, and socioeconomic resources sufficient to allow listing for lung transplantation. It may therefore be surprising that differences

Figure 1. Cumulative incidences of transplantation and death or removal from the waiting list for blacks and whites.

TABLE 2. PROPORTIONAL HAZARDS COMPETING RISK MODELS

	Transplantation		Death or Removal from the List	
	HR for Blacks Compared with Whites (95% CI)	P Value	HR for Blacks Compared with Whites (95% CI)	P Value
Unadjusted	0.84 (0.72–0.97)	0.02	1.31 (1.05–1.63)	0.02
Model 1*	0.83 (0.70–0.97)	0.02	1.33 (1.07–1.65)	0.02
Model 2†	0.81 (0.69–0.95)	0.009	1.31 (1.05–1.64)	0.02
Model 3‡	0.83 (0.71–0.97)	0.02	1.26 (1.00–1.57)	0.046
Model 4§	0.83 (0.70–0.98)	0.03	1.19 (0.94–1.50)	0.14

Definition of abbreviations: CI = confidence interval; HR = hazard ratio.

* Adjusted for age, sex, and transplant center volume.

† Model 1 plus adjustment for FVC%, FEV₁%, pulmonary hypertension, six-minute-walk distance.

‡ Model 2 plus adjustment for diabetes, hypertension, and body mass index.

§ Model 3 plus adjustment for private insurance and poverty level.

in health insurance coverage seemed to explain at least some of the increased risk among blacks. Although the somewhat lower FEV₁% among those without private insurance in our study suggests that the absence of private health care coverage may have contributed to delays in referral, evaluation, and listing for transplantation, differences in disease severity alone did not explain our findings. Public health insurance coverage, such as Medicaid, facilitates access to health care services but possibly not to the same degree that private insurance does (22). Perhaps private insurance permits continued access to medical care for those already listed. Alternatively, waiting list candidates without private insurance may have had worse outcomes due to more severe comorbidities that led to death or transplant ineligibility.

Differences in community poverty level between blacks and whites also explained some of the higher risk of death or removal from the list among blacks. Our results add COPD to the growing list of diseases in which lower socioeconomic status is a predictor of poorer health status (23, 24). Because we included only a single measure of community-level socioeconomic status (14), it is possible that unmeasured individual- or community-level socioeconomic factors might explain some or all of the association between race and death or removal from the list. Additional studies with attention to individual level data may help identify specific socioeconomic or access factors that explain the racial disparities we observed.

We found higher prevalences of hypertension, diabetes mellitus, and obesity among blacks, differences that may have also contributed to a higher risk of death or removal from the list for this group. This finding is consistent with previous reports of high prevalences of cardiovascular comorbidities in those with COPD (25, 26) and corresponds to other studies of health differences between racial groups (27). Ours is the first study to demonstrate that such racial differences exist among waiting list candidates with COPD.

Unlike the allocation system in place during the study period, the current allocation system prioritizes lung transplant candidates based on the expected survival benefit of transplantation (28). Inasmuch as cardiovascular risk factors lead to an increased risk of mortality, blacks with COPD (who may be sicker at the time of listing) may be helped by the new allocation system. However, the effects of poor insurance and poverty will likely still place blacks at increased risk for removal from the list or death, as these factors are not taken into account by the new allocation system. The association between race and waiting list outcomes should again be investigated after sufficient experience under the new system has accrued.

We are unaware of any previous published reports of a higher prevalence of pulmonary hypertension among blacks compared with whites with COPD awaiting lung transplantation. Blacks had higher prevalences of pulmonary hypertension both with

and without elevated pulmonary capillary wedge pressure. Elevated pulmonary capillary wedge pressure appears to be common in those with emphysema and may be an important determinant of pulmonary artery pressure in these patients (29). We cannot determine the cause of these higher left-sided filling pressures from our data, but the greater burden of systemic hypertension among blacks in our study suggests that left-sided heart disease may have contributed to this finding. Some have suggested that abnormal lung mechanics may increase pulmonary capillary wedge pressure in patients with emphysema as well (30, 31).

The white:black ratio of self-reported, physician-diagnosed lifetime emphysema or chronic bronchitis has ranged from 9:1 to 11:1 (2). In this cohort of lung transplant candidates with COPD, the white:black ratio was 19:1. Although confounding factors, reporting or misclassification bias, and random variation might explain this finding, the most concerning possible explanation is that blacks with COPD may not have accessed the lung transplantation waiting list as readily as whites during the study period. As in other diseases, many factors might impact on this barrier to accessing the list, including differences in age, comorbidities, social support, health beliefs, physician attitudes and competencies, and socioeconomic status (23, 24, 32–34). Delays in referral, evaluation, and listing of blacks with COPD in our study could explain the greater pulmonary hypertension, lower exercise capacity, and higher risks of death or removal from the list in this group. Impediments to specialty care for black patients with COPD could also have important implications in terms of smoking cessation, long-term oxygen therapy, pulmonary rehabilitation, or lung volume reduction surgery.

We found that only 64 Hispanics with COPD were placed on the waiting list during the 10-year study period and displayed similar waiting list outcomes to non-Hispanic blacks. Although preliminary, these findings should prompt additional studies focusing on outcomes of Hispanics as well as the clinical and social characteristics of Hispanic Americans with COPD.

Our study had several limitations. First, we studied patients already on the waiting list for lung transplantation, preventing examination of the factors that might contribute to race-based disparities in access to evaluation and wait listing. Whether medical, psychiatric, social, geographic, and financial barriers prevent listing of blacks to a greater extent than whites is unclear. Second, reference equations used to calculate percent-predicted measures of lung function varied by center and may or may not have accounted for known differences in lung volumes between healthy blacks and whites (35). Third, there was likely some misclassification of race in the cohort. However, racial classification before the outcomes of interest occurred, making misclassification of this exposure by outcome and bias away from the null unlikely. Finally, there were missing

data for some variables. We used a principled approach (multiple imputation) to account for these data.

In summary, after listing for lung transplantation, blacks with COPD have had a lower likelihood of transplantation and a higher risk of death or removal from the waiting list than whites in the United States since 1995. Differences in insurance coverage, socioeconomic status, and cardiovascular risk factors explained some but not all of the higher risk of death or removal from the waiting list. Although it is controversial whether transplantation improves the long-term survival of those with COPD (7), these findings should alert primary care physicians and pulmonologists to consider referral of black patients with COPD for transplantation at the earliest signs of advanced disease, such as worsening hypoxemia or hypercapnia, declining lung function or functional status, or severe or recurrent exacerbations. Transplant pulmonologists and surgeons may want to list black patients with COPD at the earliest appropriate time, as the likelihood of transplantation for black patients with COPD is lower than that of whites. Treatment of cardiovascular risk factors for those awaiting lung transplantation should follow current guidelines. Future studies of the etiology of racial disparities in lung transplantation, the role of the lung allocation system, and effective interventions are required to ensure equal outcomes for all patients with COPD.

Conflict of Interest Statement: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

Acknowledgment: The authors thank Katarina Anderson, Ph.D., and Jennifer Wainright, Ph.D., for their assistance with data collection.

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