ORIGINAL ARTICLE

Racial Disparities in Survival After Lung Transplantation

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Context: Racial disparities have not been comprehensively evaluated among recipients of lung transplantation.

Objectives: To describe the association between race and lung transplant survival and to determine whether racial disparities have changed in the modern (2001-2009) compared with the historical (1987-2000) transplant eras.

Design, Setting, and Patients: A retrospective cohort study of 16 875 adults who received primary lung transplants from October 16, 1987, to February 19, 2009, was conducted using data from the United Network of Organ Sharing.

Main Outcome Measures: We measured the risk of death after lung transplant for nonwhites compared with whites using time-to-event analysis.

Results: During the study period, 14 858 white and 2017 nonwhite patients underwent a lung transplant; they differed significantly at baseline. The percentage of nonwhite transplant recipients increased from 8.8% (before 1996) to 15.0% (2005-2009). In the historical era, 5-year survival was lower for nonwhites than whites (40.9% vs 46.9%). Nonwhites were at an increased risk of death independent of age, health and socioeconomic status, diagnosis, geographic region, donor organ characteristics, and operative factors (hazard ratio, 1.15; 95% confidence interval, 1.01-1.30). In subgroup analysis of the historical era, blacks had worsened 5-year survival compared with whites (39.0% vs 46.9%) and black women had worsened survival compared with white women (36.9% vs 48.9%). In the modern transplant era, survival improved for all patients. However, a greater improvement among nonwhites has eliminated the disparities in survival between the races (5-year survival, 52.5% vs 51.6%).

Conclusion: In contrast to the historical era, there was no significant difference in lung transplant survival in the modern era between whites and nonwhites.

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RACIAL DISPARITIES IN ACCESS to health care and survival have been well described for many medical conditions.[1-3] Establishing equity by eliminating these disparities, a goal of the Healthy People 2010 initiative,[4] has been proposed as a means of preventing tens of thousands of deaths each year.[5,6] Previous data, however, suggest that some racial disparities in health care have not changed, or perhaps have even worsened, with time.[2,7,8]

See Invited Critique at end of article

In solid organ transplantation—a field marked by medical complexity, high cost, and limited availability of donor organs—racial minority recipients of kidney, liver, and heart transplantation often have worse survival than white recipients.[9-15] Among patients with end-stage lung disease, blacks have worse survival than whites while on the lung transplant waiting list.[16,17] Recent reports,[17-19] however, suggest that they have similar survival after transplantation. No study has examined racial disparities in survival after lung transplant in a historical context.[12,14,20,21]

We studied the association between race and survival among all primary lung transplants in the United States since 1987. We analyzed data available through the United Network of Organ Sharing (UNOS) to evaluate whether racial disparities in survival were present among lung transplant recipients and to document how these disparities evolved between 1987 and 2009.

METHODS

STUDY DESIGN AND PARTICIPANTS

We performed a retrospective cohort study of American adults (≥18 years) who were registered to the lung transplant waiting list (N=32 328) since November 19, 1985. We focused on patients who underwent primary lung

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transplantation (n=16 879) between October 16, 1987, and February 19, 2009. Patients were excluded if they did not have race or ethnicity data (n=4). Patients who did not have follow-up data (n=152) were excluded from survival analysis. The median follow-up time was 816 days (range, 0-6579 days). The Stanford University Institutional Review Board approved the study.

DATA COLLECTION

Patient data (demographic and clinical) were collected at US transplant centers using standard UNOS worksheets.[22-24] The data were made available through a Standard Transplant Analysis and Research file based on Organ Procurement and Transplantation Network (OPTN) data as of May 1, 2009.

Clinical staff at each transplant center determined and coded race and ethnicity in the following categories in accordance with the directive from the Office of Management and Budget: white, black or African American, Hispanic or Latino, Asian, American Indian or Alaskan native, native Hawaiian or Pacific Islander, or multiracial.[25] There were 14 858 white (88.0%), 1170 black (6.9%), 620 Hispanic (3.7%), 136 Asian (0.8%), 46 American Indian or Alaskan native (0.3%), 11 native Hawaiian or Pacific Islander (0.1%), and 34 multiracial (0.2%) primary lung transplant recipients. All patients not coded as white were included in the nonwhite cohort. In subgroup analyses, Asians, American Indians or Alaskan natives, native Hawaiians or Pacific Islanders, and multiracial patients were collectively evaluated under the category termed *other*.

We divided the dates of transplantation into historical (1987-2000) and modern (2001-2009) eras based on empiric analysis and previous studies.[18,26] Among patients who received transplants before 1996, there was a higher frequency of missing data for specific variables, including educational level, creatinine level, history of diabetes mellitus and hypertension, corticosteroid use, and insurance type. We thus subdivided the historical era into 2 cohorts (1987-1995 and 1996-2000). We also subdivided the modern era into 2 cohorts (2001-2004 and 2005-2009) to account for changes resulting from implementation of the Lung Allocation Score in May 2005.[14,27] The Lung Allocation Score determines organ allocation based on a scoring algorithm that incorporates a patient's predicted waiting list survival and posttransplant survival rather than on their waiting list time accrued.[27]

In sensitivity analysis, we evaluated transplant eras by dividing all recipients into 4 equal cohorts based on date of transplantation. Cohorts were delineated as 1 (October 16, 1987-April 30, 1997), 2 (May 1, 1997-February 15, 2002), 3 (February 16, 2002-December 29, 2005), and 4 (December 30, 2005-Feburary 19, 2009).

Covariates for analysis were selected from the literature.[18] Diagnosis groups were classified according to Lung Allocation Score guidelines[27] and included groups A (primarily obstructive lung diseases, eg, chronic obstructive pulmonary disease), B (primarily pulmonary vascular diseases, eg, pulmonary hypertension), C (cystic fibrosis or immunodeficiency disorders), and D (primarily restrictive lung diseases, eg, idiopathic pulmonary fibrosis). Organ Procurement and Transplantation Network regions were categorized as 1 (Connecticut, Maine, Massachusetts, New Hampshire, and Rhode Island); 2 (Delaware; Maryland; New Jersey; Pennsylvania; Washington, DC; and West Virginia); 3 (Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, and Puerto Rico); 4 (Oklahoma and Texas); 5 (Arizona, California, Nevada, New Mexico, and Utah); 6 (Alaska, Hawaii, Idaho, Montana, Oregon, and Washington); 7 (Illinois, Minnesota, North Dakota, South Dakota, and Wisconsin); 8 (Colorado, Iowa, Kansas, Missouri, Nebraska, and Wyoming); 9 (New York and Vermont); 10 (Indiana, Michigan, and Ohio); and 11 (Kentucky, North Carolina, South Carolina, Tennessee, and Virginia). Donor cytomegalovirus status was defined by cytomegalovirus serologic test results at the time of organ donation. Health insurance type was categorized as either private or nonprivate (including Medicaid, Medicare, US Department of Veterans Affairs, self-pay, and donated or free care). To evaluate neighborhood-level socioeconomic status, we used 2000 US Census Bureau[28] data to obtain median household income in each patient's residential zip code.

In the final model, recipient age, donor age, creatinine level, zip code–based median household income, and body mass index were treated as continuous variables. Sex, long-term corticosteroid use, history of diabetes mellitus, hypertension under treatment, mechanical ventilation, procedure type (double/bilateral vs single lung transplant), graft ischemic time (≥6 hours vs <6 hours), donor cytomegalovirus status (positive vs negative), ABO group compatibility (identical vs nonidentical), educational level (college or higher vs high school or lower), US citizenship, and insurance type (private vs nonprivate) were included as dichotomous variables. Diagnosis group, medical condition at transplant (outpatient, inpatient intensive care unit, and inpatient non–intensive care unit), human leukocyte antigen mismatches (≤2, 3-4, or ≥5), transplant era, and OPTN region were treated as categorical variables.

OUTCOMES

Dates of transplantation, length of follow-up, and patient outcomes (coded as dead, alive, retransplanted, or lost) were obtained from the UNOS data set. Patients who did not die during follow-up were categorized as alive on the last date of follow-up reported to UNOS. Those who underwent retransplantation were categorized as alive at the end of follow-up before retransplantation. In secondary analysis, we evaluated the composite outcome of death or retransplantation as the primary event.

STATISTICAL ANALYSIS

Continuous variables were described as mean (SD) and were compared using *t* tests. Categorical variables were summarized using frequency and percentage and were compared using χ^2 tests. Time-to-event analysis was performed using Kaplan-Meier survival curves; differences between groups were assessed with log-rank tests. Survival estimates were obtained using Kaplan-Meier analysis. Cox proportional hazards regression analysis was used for multivariate survival analysis. Missing data for patients who received lung transplants after 1995 were imputed using multiple imputation with chained equations methods.[29] Patients who received their transplant before or during 1995 were excluded from multivariate analyses that included the nonrandom missing variables described in the "Data Collection" subsection of this section. Proportional hazards assumptions were tested using scaled Schoenfeld residuals. Variables that failed to meet the proportional hazards assumption were used to stratify the multivariate Cox proportional hazards regression analyses. In post hoc analysis, the risk of death among racial minority subgroups, also stratified by sex, was compared with the risk in whites using Cox proportional hazards regression analysis. $P \leq .05$ was considered significant. The study had 80% power to detect hazard ratio (HR) estimates of 1.14 or more. Statistical analyses were performed using Stata/IC 10.1 for Macintosh (Stata Corporation, College Station, Texas).

RESULTS

During the study period, 27 633 white (85.5%) and 4694 nonwhite (14.5%) patients were on the lung transplant

Table 1. Cohort Characteristics at the Time of Lung Transplantation[a]

Variable	No.	White (n=14 858)	Nonwhite (n=2017)	*P* Value[b]
Demographic				
Age, mean (SD), y	16 875	50 (13)	49 (12)	<.001
Female sex	16 875	6916 (46.6)	1099 (54.5)	<.001
Body mass index, mean (SD)	16 818	24.0 (7.7)	25.4 (7.3)	<.001
Health status				
Medical condition				
Not hospitalized	16 692	13 233 (90.0)	1770 (88.9)	.29
Hospitalized, non-ICU		842 (5.7)	125 (6.3)	
Hospitalized, ICU		626 (4.3)	96 (4.8)	
Receiving mechanical ventilation	16 879	418 (2.8)	62 (3.1)	.51
Creatinine level, mean (SD), mg/dL	14 755	0.9 (1.0)	0.9 (0.4)	.85
Long-term corticosteroid use	14 042	5928 (48.2)	1031 (58.8)	<.001
History of diabetes mellitus	14 237	1358 (10.9)	261 (14.5)	<.001
Hypertension treated by medication	11 870	1621 (15.5)	349 (24.6)	<.001
Diagnosis group				
A, eg, COPD	16 875	7783 (52.4)	739 (36.6)	<.001
B, eg, pulmonary hypertension		865 (5.8)	155 (7.7)	
C, eg, cystic fibrosis		2319 (15.6)	89 (4.4)	
D, eg, idiopathic pulmonary fibrosis		3891 (26.2)	1034 (51.3)	
Transplant era				
1987-1995	16 875	2944 (19.8)	285 (14.1)	<.001
1996-2000		3680 (24.8)	415 (20.6)	
2001-2004		3569 (24.0)	493 (24.4)	
2005-2009		4665 (31.4)	824 (40.9)	
Transplant factors				
Procedure type, double/bilateral lung	16 867	7219 (48.6)	1127 (55.9)	<.001
Donor age, mean (SD), y	16 875	32 (14)	32 (14)	.09
Graft ischemic time, mean (SD), h	14 856	4.7 (1.8)	4.7 (1.7)	.92
Blood group (ABO) compatibility, identical	16 875	13 507 (90.9)	1829 (90.7)	.74
Level of HLA mismatch	13 757			<.001
0-2	16 613	547 (4.5)	42 (2.6)	<.001
3-4		4920 (40.5)	591 (36.9)	
5-6		6686 (55.0)	971 (60.5)	
Donor CMV seropositive		8346 (57.1)	1261 (63.6)	
Socioeconomic status				
College education or higher	11950	5362 (51.3)	777 (51.6)	.83
US citizenship	16 839	14 740 (99.4)	1916 (95.2)	<.001
Private insurance	14 522	8051 (63.4)	1037 (57.0)	<.001
Median household income by zip code, mean (SD), $	15 929	46 938 (17 204)	41 578 (16 293)	<.001

Abbreviations: CMV, cytomegalovirus; COPD, chronic obstructive pulmonary disease; HLA, human leukocyte antigen; ICU, intensive care unit.
[a] Values are given as number (percent) unless otherwise noted. Body mass index is calculated as weight in kilograms divided by height in meters squared.
[b] *P* values are from *t* test or χ^2 test, as appropriate.

waiting list; 16 875 patients (88.0% white and 12.0% nonwhite) underwent primary lung transplantation. There were notable differences in characteristics between the cohorts (**Table 1**). Nonwhites were younger (49 [12] vs 50 [13] years) and more commonly female (54.5% vs 46.6%) than were whites; nonwhites also had a higher average body mass index (calculated as weight in kilograms divided by height in meters squared) (25.4 [7.3] vs 24.0 [7.7]). At time of transplant, there were no significant differences between groups in rates of hospitalization, intensive care unit admission, need for mechanical ventilation, or creatinine level. However, nonwhites were more frequently taking corticosteroid therapy (58.8% vs 48.2%); they also had higher rates of comorbid conditions, including diabetes (14.5% vs 10.9%) and hypertension (24.6% vs 15.5%).

Nonwhites and whites differed in causes of lung disease requiring transplant; these were most pronounced in diagnosis groups A (eg, chronic obstructive pulmonary disease: 52.4% vs 36.6% for whites vs nonwhites) and D (eg, idiopathic pulmonary fibrosis: 26.2% vs 51.3%). Nonwhites were more likely to undergo double/bilateral lung transplantation (55.9% vs 48.6%), receive allografts from cytomegalovirus-positive donors (63.6% vs 57.1%), and have 5 to 6 human leukocyte antigen mismatches (60.5% vs 55.0%). While the cohorts did not differ significantly in educational level, nonwhites had lower rates of citizenship (95.2% vs 99.4%) and private insurance (57.0% vs 63.4%) and were from neighborhoods with lower median household income levels ($41 578 [$16 293] vs $46 938 [$17 204]).

The percentage of nonwhite patients on the lung transplant waiting list increased from 10.4% before 1996 to 17.7% between 2005 and 2009. A similar increase was seen in the percentage of nonwhite lung transplant recipients, from 8.8% to 15.0%, during the same eras. In most OPTN regions, the number of nonwhite transplant recipients also increased between eras. Organ Procurement and Transplantation Network regions 4 and 5 had the highest

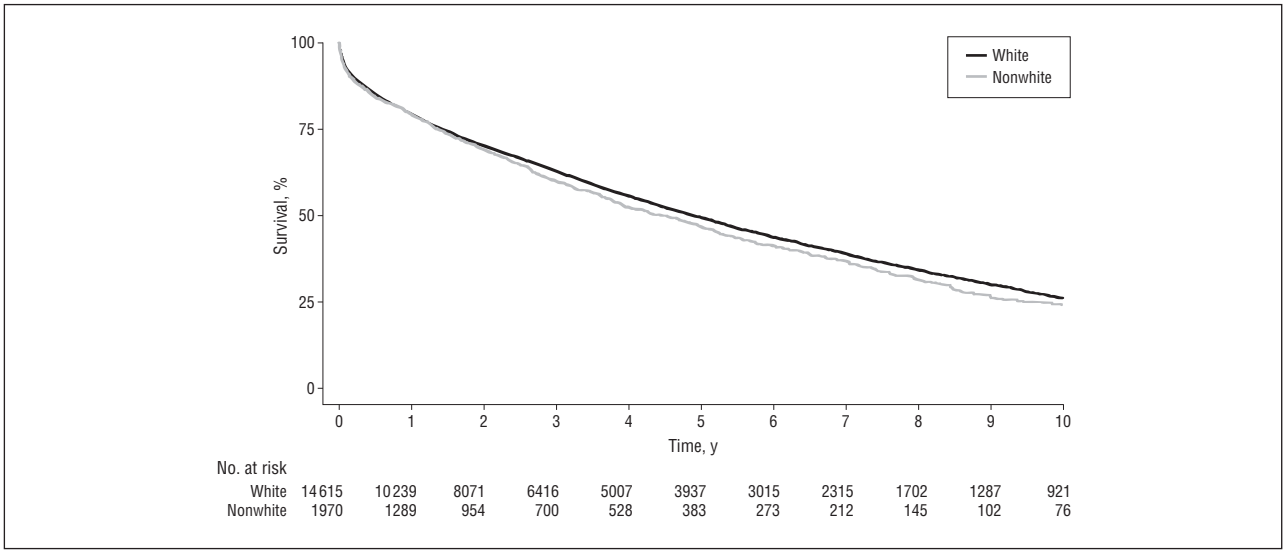

Figure 1. Unadjusted Kaplan-Meier survival curve for white and nonwhite recipients of lung transplantation. *P*=.049 by log-rank test.

percentage of nonwhite recipients (18.1% and 18.7%, respectively); regions 1 and 8 had the lowest percentage of nonwhite recipients (5.7% and 6.6%, respectively).

During the study period, there were 8654 posttransplant deaths. Nonwhites had significantly lower unadjusted survival (**Figure 1**) (*P*=.049) compared with whites. Five-year survival was 49.7% (95% confidence interval [CI], 48.7-50.6) and 46.9% (95% CI, 44.0-49.6) for whites and nonwhites, respectively. Nonwhites had an increased risk of death compared with whites (unadjusted HR, 1.07; 95% CI, 1.00-1.15; *P*=.05). However, in the final adjusted model, the finding was not statistically significant (HR, 1.06; 95% CI, 0.98-1.15; *P*=.17).

When stratified by transplant era, nonwhites had significantly lower survival than whites in the historical era (*P*=.003) but not in the modern era (*P*=.80) (**Figure 2**). Five-year survival in the historical era was 46.9% (95% CI, 45.7-48.1) and 40.9% (95% CI, 37.1-44.6) for white and nonwhites, respectively. The risk of death was higher for nonwhite compared with white recipients of transplants in the historical era, even after multivariate adjustment (**Table 2**) (overall, nonwhite; model 1 [1987-1995]: HR, 1.15; 95% CI, 1.00-1.31; *P*=.047; and model 2 [1996-2000]: HR, 1.13; CI, 1.00-1.28; *P*=.05). Nonwhite transplant recipients in the modern era had no increased risk of posttransplant death compared with whites (Table 2) (model 2 [2001-2004]: HR, 0.98; 95% CI, 0.84-1.13; *P*=.74; and model 2 [2005-2009]: HR, 0.97; 95% CI, 0.82-1.15; *P*=.73). In the modern era, 5-year survival was 52.5% (95% CI, 50.9%-54.0%) and 51.6% (95% CI 47.4%-55.7%) for whites and nonwhites. The HR estimates did not change significantly when adjusting the primary event to include patients with allograft failure who required retransplantation or when evaluating eras of equal patient cohorts.

In subgroup multivariate regression analysis, blacks who received transplants between 1996 and 2000 had an increased risk of death compared with whites (Table 2) (HR, 1.25; 95% CI, 1.07-1.45; *P*=.005). Five-year survival was 46.9% (95% CI, 45.7%-48.1%) and 39.0% (95% CI, 34.1%-43.9%) for whites and blacks in the historical era, respectively. Minority women, especially black, transplant recipients in the historical era had a higher risk of death compared with white women (model 2 [1996-2000]: nonwhite female HR, 1.22; 95% CI, 1.02 -1.46; *P*=.02). Five-year survival was 48.9% (95% CI, 47.2%-50.7%) and 36.9% (95% CI, 30.9%-42.9%) for white and black women in the historical era, respectively. In the modern era, there was no increased risk of posttransplant death among any racial subgroup compared with whites.

The change in risk of death between whites and nonwhites across transplant eras was not explained by worsened survival among whites: 1-year, 5-year, and median survival improved for all patients between the historical and modern eras.

Differences in baseline characteristics between cohorts in the historical era largely persisted into the modern era (**Table 3**). For example, nonwhites in both eras had higher rates of long-term corticosteroid use, history of hypertension, and 5 to 6 human leukocyte antigen mismatches than whites. They also had lower rates of citizenship, private insurance, and neighborhood-level median income. Cohorts in both eras did not differ significantly in cause of death (Table 3); graft failure and infection were the most common causes of death in all groups.

COMMENT

We found that nonwhite primary lung transplant recipients in the historical era (1987-2000), especially blacks and black women, were at an increased risk of death compared with white recipients. While nonwhite and white recipients differed in many baseline characteristics, the racial disparity in survival was independent of age, sex, health status, socioeconomic status, diagnosis, OPTN region, donor or allograft characteristics, and operative factors. In the modern era (2001-2009), survival improved for all transplant recipients. A greater improvement among

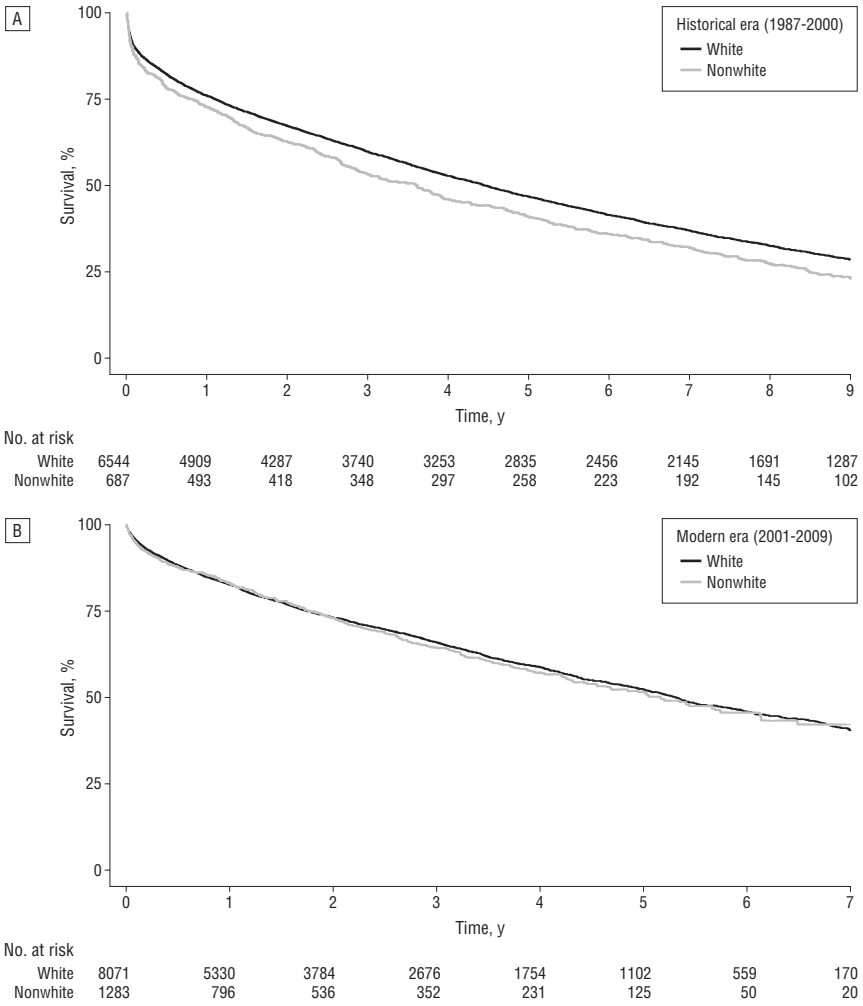

Figure 2. Unadjusted Kaplan-Meier survival curves for white and nonwhite recipients of lung transplantation by transplant era. *P*=.003 (historical era) and *P*=.80 (modern era) by log-rank test.

Table 2. Risk of Death for Nonwhites Compared With Whites by Transplant Era, Racial Group, and Sex

	Hazard Ratio (95% Confidence Interval)			
	Historical Era		Modern Era	
Variable	1987-1995	1996-2000	2001-2004	2005-2009
Overall, nonwhite				
Age-adjusted	1.22 (1.07-1.40)	1.20 (1.06-1.35)	1.06 (0.92-1.22)	1.02 (0.86-1.20)
Model 1[a]	1.15 (1.00-1.31)	1.13 (1.00-1.28)	1.00 (0.87-1.16)	1.00 (0.84-1.19)
Model 2[b]	. . .	1.15 (1.01-1.30)	0.98 (0.84-1.13)	0.97 (0.82-1.15)
By racial group[b]				
Black	. . .	1.25 (1.07-1.45)	0.97 (0.85-1.12)	
Hispanic	. . .	0.86 (0.68-1.09)	1.06 (0.88-1.28)	
Other	. . .	1.30 (0.90-1.89)	1.00 (0.74-1.37)	
By sex, nonwhite				
Male				
Age-adjusted	1.13 (0.91-1.40)	1.16 (0.96-1.40)	1.09 (0.88-1.34)	1.01 (0.81-1.26)
Model 2[b]	. . .	1.06 (0.87-1.30)	0.99 (0.79-1.23)	1.00 (0.79-1.27)
Female				
Age-adjusted	1.31 (1.09-1.56)	1.23 (1.05-1.45)	1.04 (0.86-1.25)	1.04 (0.82-1.31)
Model 2[b]	. . .	1.22 (1.02-1.46)	0.96 (0.79-1.17)	0.92 (0.71-1.20)

[a] Adjusted for age, sex, transplant era, diagnosis group, Organ Procurement and Transplant Network region, medical condition, mechanical ventilator, and body mass index.

[b] Model 1 plus community median income, insurance type, citizenship, level of education, procedure type, long-term corticosteroid use, diabetes mellitus, hypertension, creatinine level, mechanical ventilation, ABO compatibility, level of human leukocyte antigen mismatch, graft ischemic time, donor cytomegalovirus status, and donor age.

Table 3. Characteristics of Non-White and White Lung Transplant Recipients Compared by Historical (1987-2000) and Modern (2001-2009) Eras[a]

Variable	Historical Era (1987-2000)				Modern Era (2001-2009)			
	No.	Whites	Nonwhites	*P* Value	No.	Whites	Nonwhites	*P* Value
Demographic	...	6624 (90.4)	700 (9.6)	...	...	8234 (86.2)	1317 (13.8)	...
Age, mean (SD), y	7324	48 (12)	45 (11)	[c]	9551	53 (13)	51 (12)	[c]
Female sex	7324	3923 (49.7)	409 (58.4)	[c]	9551	3623 (44.0)	690 (52.4)	[c]
Body mass index, mean (SD)	7274	23.2 (5.6)	24.7 (7.5)	[c]	9544	24.7 (9.0)	25.8 (7.2)	[c]
Health status								
Medical condition	7277			NS[d]				
Not hospitalized		5954 (90.5)	635 (91.2)		9415	7279 (89.6)	1135 (87.6)	
Hospitalized, non-ICU		400 (6.1)	37 (5.3)			442 (5.4)	88 (6.8)	NS[d]
Hospitalized, ICU		227 (3.5)	24 (3.5)			399 (4.9)	72 (5.6)	
Receiving mechanical ventilation		151 (2.3)	19 (2.7)	NS[d]	9551	267 (3.2)	43 (3.3)	NS[d]
Creatinine level, mean (SD), mg/dL	5446	1.0 (1.5)	0.9 (0.5)	NS[d]	9307	0.9 (0.6)	0.9 (0.4)	NS[d]
Long-term corticosteroid use	5155	2249 (48.6)	286 (54.6)	[e]	8887	3679 (48.1)	745 (60.6)	[c]
History of diabetes mellitus	4799	281 (6.5)	32 (6.5)	NS[d]	9438	1077 (13.2)	229 (17.5)	[c]
Hypertension treated by medication	4750	470 (11.0)	76 (15.4)	[e]	7120	1151 (18.6)	273 (29.5)	[c]
Transplant factors								
Procedure type, bilateral	7316	2579 (38.9)	294 (42.0)	NS[d]	9551	4640 (56.4)	833 (63.3)	[c]
Donor age, mean (SD), y	7324	30 (13)	30 (13)	NS[d]	9551	33 (14)	33 (14)	NS[d]
Graft ischemic time, mean (SD), h	6589	4.4 (1.8)	4.4 (1.7)	NS[d]	8267	4.9 (1.7)	4.8 (1.6)	NS[d]
Identical blood group	7324	6005 (90.1)	632 (90.3)	NS[d]	9551	7502 (91.1)	1197 (90.9)	NS[d]
Level of HLA mismatch	5971							
0-2		265 (4.9)	14 (2.4)		7786	282 (4.2)	28 (2.7)	
3-4		2257 (41.8)	235 (40.7)	[f]		2663 (39.4)	356 (34.7)	[c]
5-6		2872 (53.2)	328 (56.9)			3814 (56.4)	643 (62.6)	
Donor CMV seropositive	7149	3475 (53.7)	388 (57.1)	NS[d]	9464	4871 (59.7)	873 (67.0)	[c]
Socioeconomic status								
College education or higher	3843	1721 (50.0)	189 (47.4)	NS[d]	8107	3641 (52.0)	588 (53.2)	NS[d]
US citizenship	7304	6571 (0.5)	663 (95.1)	[c]	9535	8169 (99.4)	1253 (95.3)	[c]
Private insurance	5108	3062 (66.8)	301 (57.4)	[c]	9414	4989 (61.5)	736 (56.9)	[e]
Median household income, mean (SD), $	6724	46 616 [16 851]	39 634 [14 493]	[c]	9203	47 185 (17 466)	42 564 (17 055)	[c]
Recipient cause of death	4851							
Graft failure		1307 (29.9)	151 (31.8)		2804	595 (24.4)	88 (24.0)	
Infection		1157 (26.4)	117 (24.6)			637 (26.1)	94 (25.7)	
Cardiovascular or cerebrovascular disease		369 (8.4)	47 (9.9)	NS[d]		274 (11.2)	36 (9.8)	NS[d]
Pulmonary or renal disease		755 (17.3)	78 (16.2)			479 (19.7)	83 (22.7)	
Malignant neoplasm		335 (7.7)	30 (6.3)			177 (7.3)	21 (5.7)	
Other		453 (10.4)	52 (11.0)			276 (11.3)	44 (12.0)	

Abbreviations: CMV, cytomegalovirus; COPD, chronic obstructive pulmonary disease; HLA, human leukocyte antigen; ICU, intensive care unit; NS, nonsignificant.

SI conversion factor: To convert creatinine to micromoles per liter, multiply by 88.4.

[a] Values are given as number (percent) unless otherwise noted. Body mass index is calculated as weight in kilograms divided by height in meters squared.

[b] *P* values for comparison between white and nonwhite lung transplant recipients within each era, determined using *t* test or χ^2 test, as appropriate.

[c] $P < .001$.

[d] $P > .05$.

[e] $P < .01$.

[f] $P < .05$.

nonwhites has eliminated the racial disparity in post-transplant survival.

Our findings contrast with those of previous reports of racial disparities in survival observed in many areas of health care,[1] as well as among other solid organ transplant recipients, including kidney, liver, and heart.[10-13] Racial disparities in outcomes are noted even among patients with end-stage lung disease who are on the lung transplant waiting list—blacks with chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis have worse survival compared with whites.[16,17,30] Prior studies[17,19,30,31] evaluating racial disparities after lung transplant have found equivalent survival between white and black patients. However, these studies were limited either by small sample size—especially among nonwhite recipients in disease-specific cohorts—or by patient groups drawn from both the historical and modern eras without differentiation. This sampling likely obscured racial disparities in survival that have changed.

The survival gains for nonwhite lung transplant recipients between eras likely result from multiple factors. First, they may reflect increasing awareness among the transplant community of the effect that racial disparities have on access to care and survival.[9] Our results demonstrate that both the percentage of nonwhite patients on the waiting list and undergoing transplant has

increased throughout 2 decades. This suggests that among nonwhites, access to lung transplantation—a medically complex and severely limited procedure—is improving. Despite these improvements, however, nonwhite patients remain proportionally underrepresented both in waiting list registration and transplantation compared with national estimates of racial composition.[28]

Receiving an organ transplant is a complex procedure with many potential barriers to access, including initial diagnosis, timely referral to a transplant center, pretransplant evaluation, registration to the waiting list, the transplant operation, and extensive posttransplant care. We have demonstrated that racial disparities in survival have been eliminated for patients who ultimately undergo lung transplantation; however, our results do not imply that racial disparities are no longer present in the steps leading to the operation. In fact, previous work[16,17,30] suggests that disparate outcomes persist for black patients with end-stage lung disease registered to the transplant waiting list. Among patients with end-stage kidney disease, disparities negatively affect the likelihood of transplantation for black, female, and low-income patients.[32] Other recent work,[14] however, demonstrates that changes in organ allocation policy among patients with liver failure can improve racial disparities.

While our results suggest that barriers to care may be decreasing for nonwhites overall, we did find significant regional variability in the proportion of nonwhite transplant recipients. There was more than a 3-fold difference in percentage of nonwhite recipients, from 5.7% to 18.7%, between regions 1 and 5. This finding may reflect differences in regional racial composition. For example, region 1 (northeast) represents a less racially diverse population than region 5 (California and southwest).[28] However, it may also reflect broader geographic disparities in access to care and patient outcomes that have been described in other health care fields.[33,34] In organ transplantation, regional variations in care and outcomes have not been well characterized and deserve further study.[20]

The survival gains among nonwhites in the modern era also likely resulted from broad improvements in posttransplant quality of care. Although nonwhite transplant recipients had an unfavorable baseline risk profile in both the historical and modern eras, they experienced a comparatively greater improvement as survival improved for all recipients. Improvements in nonwhite patients' outcomes might also have resulted from changes in posttransplant care that exerted differential effects across racial groups. For example, tacrolimus, a calcineurin inhibitor associated with improved outcomes among blacks,[35,36] surpassed cyclosporine as the primary immunosuppressant at the transition between the historical and modern transplant eras.[37-40] Before 1999, more than 75% of lung transplant recipients were receiving cyclosporine 1 year after transplant[37]; current registry data[18] reveal that nearly 70% of patients are now receiving tacrolimus after 1 year. This single example of a marked change in practice within a 10-year span likely reflects other broad improvements in quality of care as the field of lung transplantation has advanced.

Our study has several limitations. First, it is based on information submitted to UNOS from multiple transplant centers for more than 2 decades. As a result, discrepancies in data entry, collection, and classification may exist between centers and across time. We were limited by nonrandom missing data for some variables among recipients of lung transplants performed before 1996. However, we believe that our analysis demonstrates consistency in the overall findings. Second, because the racial disparity in risk of death was relatively modest, it is possible that residual confounding may explain some of the effect. The included variables may, for example, reflect additional unobserved differences in access to timely and high-quality medical care known to exist among nonwhite patients with pulmonary disease.[41,42] However, we aimed to select a comprehensive set of covariates known to affect posttransplant survival. Third, this study was not designed to address the specific changes in transplant care that have eliminated the racial disparities across transplant eras.

In summary, we have demonstrated that in the historical era of lung transplantation, nonwhites had an increased risk of death compared with whites. In the modern era, this racial disparity has been eliminated likely due, in part, to improved access to and quality of care.

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REFERENCES

1. Fiscella K, Franks P, Gold MR, Clancy CM. Inequality in quality: addressing socioeconomic, racial, and ethnic disparities in health care. *JAMA.* 2000;283 (19):2579-2584.

2. National Healthcare Disparities Report, 2006: full report. http://www.ahrq.gov/qual/nhdr06/report/. Accessed June 12, 2009.
3. Kuehn B. AHRQ: US quality of care falls short: patient safety declining, disparities persist. *JAMA*. 2009;301(23):2427-2428.
4. *Healthy People 2010: Understanding and Improving Health*. 2nd ed. Washington, DC: US Government Printing Office; 2000.
5. Satcher D, Fryer GE Jr, McCann J, Troutman A, Woolf SH, Rust G. What if we were equal?: a comparison of the black-white mortality gap in 1960 and 2000. *Health Aff (Millwood)*. 2005;24(2):459-464.
6. Woolf SH, Johnson RE, Fryer GE Jr, Rust G, Satcher D. The health impact of resolving racial disparities: an analysis of US mortality data. *Am J Public Health*. 2004;94(12):2078-2081.
7. Jha AK, Fisher ES, Li Z, Orav EJ, Epstein AM. Racial trends in the use of major procedures among the elderly. *N Engl J Med*. 2005;353(7):683-691.
8. Vaccarino V, Rathore SS, Wenger NK, et al; National Registry of Myocardial Infarction Investigators. Sex and racial differences in the management of acute myocardial infarction, 1994 through 2002. *N Engl J Med*. 2005;353(7):671-682.
9. Higgins RS, Fishman JA. Disparities in solid organ transplantation for ethnic minorities: facts and solutions. *Am J Transplant*. 2006;6(11):2556-2562.
10. Young CJ, Kew C. Health disparities in transplantation: focus on the complexity and challenge of renal transplantation in African Americans. *Med Clin North Am*. 2005;89(5):1003-1031, ix.
11. Nair S, Eustace J, Thuluvath PJ. Effect of race on outcome of orthotopic liver transplantation: a cohort study. *Lancet*. 2002;359(9303):287-293.
12. Kirklin JK, Naftel DC, Bourge RC, et al. Evolving trends in risk profiles and causes of death after heart transplantation: a ten-year multi-institutional study. *J Thorac Cardiovasc Surg*. 2003;125(4):881-890.
13. Isaacs RB, Nock SL, Spencer CE, et al. Racial disparities in renal transplant outcomes. *Am J Kidney Dis*. 1999;34(4):706-712.
14. Moylan CA, Brady CW, Johnson JL, Smith AD, Tuttle-Newhall JE, Muir AJ. Disparities in liver transplantation before and after introduction of the MELD score. *JAMA*. 2008;300(20):2371-2378.
15. Hardy D, Xia R, Liu CC, Cormier JN, Nurgalieva Z, Du XL. Racial disparities and survival for nonsmall-cell lung cancer in a large cohort of black and white elderly patients. *Cancer*. 2009;115(20):4807-4818.
16. Lederer DJ, Caplan-Shaw CE, O'Shea MK, et al. Racial and ethnic disparities in survival in lung transplant candidates with idiopathic pulmonary fibrosis. *Am J Transplant*. 2006;6(2):398-403.
17. Lederer DJ, Benn EK, Barr RG, et al. Racial differences in waiting list outcomes in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2008;177(4):450-454.
18. Christie JD, Edwards LB, Aurora P, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-fifth official adult lung and heart/lung transplantation report—2008. *J Heart Lung Transplant*. 2008;27(9):957-969.
19. Lingaraju R, Pochettino A, Blumenthal NP, et al. Lung transplant outcomes in white and African American recipients: special focus on acute and chronic rejection. *J Heart Lung Transplant*. 2009;28(1):8-13.
20. Chakkera HA, Chertow GM, O'Hare AM, Amend WJ Jr, Gonwa TA. Regional variation in kidney transplant outcomes: trends over time. *Clin J Am Soc Nephrol*. 2009;4(1):152-159.
21. Eckhoff DE, Young CJ, Gaston RS, et al. Racial disparities in renal allograft survival: a public health issue? *J Am Coll Surg*. 2007;204(5):894-903.
22. Adult Lung Transplant Candidate Registration Worksheet. http://www.unos.org/docs/Lung-Adult_Transplant_Candidate_Registration.pdf. Accessed June 12, 2009.
23. UNOS Adult Thoracic-Lung Transplant Recipient Registration Worksheet. http://www.unos.org/docs/Thoracic-Lung-Adult_Transplant_Recipient_Registration.pdf. Accessed June 12, 2009.
24. Adult Thoracic Transplant Recipient Follow-Up Worksheet. http://www.unos.org/docs/Thoracic-Lung-Adult_Transplant_Recipient_Follow-Up.pdf. Accessed June 12, 2009.
25. Revisions to the standards for the classification of federal data on race and ethnicity. *Fed Regist*. 1997;62:36873-36946.
26. Kawut SM, Lederer DJ, Keshavjee S, et al. Outcomes after lung retransplantation in the modern era. *Am J Respir Crit Care Med*. 2008;177(1):114-120.
27. Egan TM, Murray S, Bustami RT, et al. Development of the new lung allocation system in the United States. *Am J Transplant*. 2006;6(5 pt 2):1212-1227.
28. U.S. Bureau of the Census. Census of population and housing, 2000: summary file 3, national. 2002.
29. Royston P. Multiple imputation of missing values. *Stata Journal*. 2004;4(3):227-241.
30. Lederer DJ, Arcasoy SM, Barr RG, et al. Racial and ethnic disparities in idiopathic pulmonary fibrosis: a UNOS/OPTN database analysis. *Am J Transplant*. 2006;6(10):2436-2442.
31. Shorr AF, Helman DL, Davies DB, Nathan SD. Sarcoidosis, race, and short-term outcomes following lung transplantation. *Chest*. 2004;125(3):990-996.
32. Alexander GC, Sehgal AR. Barriers to cadaveric renal transplantation among blacks, women, and the poor. *JAMA*. 1998;280(13):1148-1152.
33. Fisher ES, Wennberg DE, Stukel TA, Gottlieb DJ, Lucas FL, Pinder EL. The implications of regional variations in Medicare spending: part 2: health outcomes and satisfaction with care. *Ann Intern Med*. 2003;138(4):288-298.
34. Fisher ES, Wennberg DE, Stukel TA, Gottlieb DJ, Lucas FL, Pinder EL. The implications of regional variations in Medicare spending: part 1: the content, quality, and accessibility of care. *Ann Intern Med*. 2003;138(4):273-287.
35. Mehra MR, Uber PA, Scott RL, Park MH. Ethnic disparity in clinical outcome after heart transplantation is abrogated using tacrolimus and mycophenolate mofetil-based immunosuppression. *Transplantation*. 2002;74(11):1568-1573.
36. Neylan JF. Racial differences in renal transplantation after immunosuppression with tacrolimus versus cyclosporine. *Transplantation*. 1998;65(4):515-523.
37. Hosenpud JD, Bennett LE, Keck BM, Fiol B, Boucek MM, Novick RJ. The Registry of the International Society for Heart and Lung Transplantation: sixteenth official report—1999. *J Heart Lung Transplant*. 1999;18(7):611-626.
38. Hosenpud JD, Bennett LE, Keck BM, Boucek MM, Novick RJ. The Registry of the International Society for Heart and Lung Transplantation: seventeenth official report—2000. *J Heart Lung Transplant*. 2000;19(10):909-931.
39. Hosenpud JD, Bennett LE, Keck BM, Boucek MM, Novick RJ. The Registry of the International Society for Heart and Lung Transplantation: eighteenth official report—2001. *J Heart Lung Transplant*. 2001;20(8):805-815.
40. Trulock EP, Edwards LB, Taylor DO, et al. The Registry of the International Society for Heart and Lung Transplantation: twentieth official adult lung and heart–lung transplant report—2003. *J Heart Lung Transplant*. 2003;22(6):625-635.
41. Bach PB, Cramer LD, Warren JL, Begg CB. Racial differences in the treatment of early-stage lung cancer. *N Engl J Med*. 1999;341(16):1198-1205.
42. Grant EN, Lyttle CS, Weiss KB. The relation of socioeconomic factors and racial/ethnic differences in US asthma mortality. *Am J Public Health*. 2000;90(12):1923-1925.

INVITED CRITIQUE

Is Time on the Side of Diversity in Lung Transplantation?

Despite the fact that the first successful lung transplant was performed only 27 years ago, a multitude of changes involving surgical technique, organ preservation, and patient care validates Liu and colleagues' analysis of the UNOS lung transplant database. Noting the limitations of the database, Liu and colleagues found a survival benefit for all patients regardless of race, which was based on the implementation of the Lung Allocation Score. More important, the survival gap that existed between white and other ethnic groups has been eliminated in the past 10 years.

Although the incidence of negative prognostic factors—idiopathic pulmonary fibrosis, pulmonary hypertension, and human leukocyte antigen mismatch[1-3]—has increased, nonwhite lung transplant recipients had survival rates comparable with those of