Racial differences in access to lung transplantation in the United States across geographic region

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An abstract of
a thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2016

Abstract

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Objective: Prior to the introduction of a major change in the national allocation system for lung transplantation in 2005, African-Americans were less likely to receive lung transplants than Caucasians. While prior studies have shown that racial disparities have decreased in the post-policy era, no studies have re-examined racial disparities after accounting for differences in socioeconomic status, insurance status, and distance to transplant center. Additionally, no studies have identified whether or not there are regional variations in racial differences in transplant access.

Methods: We performed a retrospective cohort study on all candidates for lung transplantation waitlisted between May 4, 2005 and September 30, 2014. After performing all exclusions, our cohort included 19,162 subjects, whom we stratified by race and OPTN region. Multivariate regression was performed in order to determine the role of race in likelihood of transplantation within three years.

Results: There were no significant differences between mean times to transplantation or likelihood of transplantation within three years when comparing African-Americans and Caucasians on both a national and regional level.

Conclusions: No racial differences in likelihood of lung transplantation exist in any of the 11 OPTN regions. The current method of lung allocation provides an effective and objective way to allocate lungs in a way that limits racial disparities, even when adjusting for demographic factors, insurance status, and distance to transplant center.

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Chapter I: Background

Epidemiology of Lung Disease

Lung disease is a broad term used to describe any pathologic process that prevents the lungs from functioning properly (21). These diseases are typically divided into three categories based on the part of the lungs that they affect. Airway diseases, including chronic obstructive pulmonary disease (COPD) affect the bronchi that carry oxygen into and out of the lungs (21). Tissue diseases, which include interstitial lung disease (ILD), affect the structure of the lung tissue through scarring and deformation, making it difficult for the lungs to expand fully (21). Finally, vascular lung diseases, such as pulmonary hypertension, affect the blood vessels within the lungs (21). All three of these disease types have the capability of progressing to end-stage lung disease.

Lung transplantation is the only existing curative therapy for end-stage lung disease (1). Between 1988 and 2016, 31,232 lung transplants have taken place in the United States, representing 21.4% of total transplants performed. In 2014, 1,925 lung transplants were performed. In order to become eligible for lung transplant, a candidate must suffer from chronic lung disease, have maximized medical therapy, and fulfill criteria that will be discussed in more detail later (2). In 2012, 1,679 patients were on the waiting list for lung transplantation at the start of the year. 2,231 patients were added during the year, and 2,294 were removed. Of the patients who were removed, 1,754 were transplanted, 303 died, and 110 were too sick to be transplanted. The number of lung transplants in the United States has been rising steadily since 2005 (1). In 2010, the two most common reasons for lung transplantation in the United States were COPD, which accounted for 23% of transplant patients, and ILD, which accounted for 39% of transplant patients (1). Lung transplantation is also used as a potential therapy in patients with pulmonary vascular disease and cystic fibrosis, but these are less common reasons for transplant (1).

COPD, as described earlier, is an obstructive pulmonary disease process that is characterized by a combination of airflow limitation and air trapping caused by destruction of bronchioles, which bring air into the lungs. COPD is largely caused by smoking, although there are some genetic conditions, including alpha-1 antitrypsin disorder, which can result in its development as well. In 2014, 24 million Americans carried a diagnosis of COPD (22). Of these, 4.7 million were new diagnoses within that year. The five-year mortality rate for COPD ranges from 40-70%, and COPD is the fourth leading cause of death worldwide (23). According to the SRTR, patients with COPD currently represent 29.4% of the lung transplant waiting list (26).

ILD, in contrast, is a restrictive process in which the space around the alveoli is affected, resulting in difficulty breathing. As of 2013, 595,000 people globally were recorded as having some form of ILD, with 471,000 deaths occurring in this population (5). Because the etiologies of ILD are vast, it is difficult to determine exact incidence and prevalence of ILD in the United States, but a 2004 study suggests that the incidence is 20.2 per 100,000 in women and 13.2 per 100,000 in men (25). Patients with ILD currently represent 49.5% of the lung transplant waiting list (26).

Lung Allocation and the Introduction of the Lung Allocation Score (LAS)

The process of becoming a candidate for lung transplant is complex. Worldwide guidelines for recipient selection have been established by the International Society for Heart and Lung Transplantation (ISHLT), with the most recent update in 2014 (24). The

ISHLT states that lung transplantation should be "considered for adults with chronic, end-stage lung disease who meet the following general criteria:

1. High (>50%) risk of death from lung disease within 2 years if transplantation is not peformed.
2. High (>80%) likelihood of surviving at least 90 days after lung transplantation.
3. High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function (24)."

In order for a patient to officially become a candidate for transplant, he or she must be referred to a transplant pulmonologist through a primary care doctor or other healthcare professional for further workup (2). Additionally, potential candidates for transplantation must have declining lung function despite having received maximum, optimal medical therapy for his or her disease (2). After these criteria have been satisfied and a potential candidate has been referred to a transplant center, a rigorous screening process takes place, including pulmonary function tests (PFTs) to test for lung volumes and functional status, cardiac studies, tissue typing and blood typing, and laboratory tests. Social factors, including the presence of a support system and ability to engage in regular follow-up care, are also weighed in the decision whether or not to transplant an individual. Lastly, critically ill patients with systemic diseases or active infections are ineligible for lung transplant (2). Furthermore, ISHLT guidelines forbid individuals with recent history of malignancy, uncorrected atherosclerotic disease, uncorrectable bleeding diathesis, evidence of active *Mycobacterium tuberculosis* infection, substance abuse or dependence, BMI > 35.0 kg/m2, non-adherance to medical therapy, or severely limited functional status from being listed for transplant (24).

Once a patient has satisfied criteria for transplant and been medically cleared, he or she is placed onto the United States Network for Organ Sharing (UNOS) waiting list for transplant. Prior to 2005, position on the waitlist was based on a first-come, first-served basis according to blood type and distance from the donor hospital (3). In 2005, the lung allocation score (LAS) was created in order to provide a more objective way of allocating available donor lungs (3). Many factors, including diagnosis, age of the patient, BMI, presence or absence of diabetes mellitus, New York Heart Association functional ability, predicted forced vital capacity, pulmonary artery pressure, pulmonary capillary wedge pressure, creatinine level, and flow rate of supplemental oxygen at rest, are used to calculate a raw allocation score (1). The raw allocation score refers to a value between 0 and 100 which represents the patient's likelihood to benefit from a lung transplant (3). Candidates with higher LAS scores are transplanted first when donor organs become available (3). In addition to attempting to improve transplantation outcomes, the LAS intended to make allocation a more objective process with the secondary benefit of eliminating geographical, gender, and racial biases (1).

End-Stage Lung Disease Risk Factors and the Role of Race, Socioeconomic Status (SES), and Geography

Because of the wide range of end-stage lung diseases, this review will focus on COPD and ILD, the two most common reasons for transplant. As described earlier, COPD is the fourth leading cause of death in the United States (21). Risk factors for COPD include smoking, exposure to air pollution, occupational exposures, and in some cases, genetics (6). In 2011, a study showed that low SES (characterized by education level and household income) was associated with an increased risk in the development of

COPD. Additionally, it has been shown that low SES is associated with childhood respiratory infections, smoking, and housing conditions, all factors which have been implicated in the development of COPD (9). While lung disease was previously believed to affect primarily white males, COPD has been shown to impact all races and genders. The rate of hospitalization for COPD is currently equal in African-Americans and Caucasians (7).

The data regarding the relationship between SES and ILD has not been studied in as much detail. Studies conducted in the United States show that ILD occurs more frequently in Caucasians than African-Americans, but it is unclear if these findings are due to under-diagnosis of this condition in minorities (8). Several professions, which employ high numbers of African-Americans, as well as autoimmune diseases, which are most common in African-American women, have been implicated in the development of ILD (4).

Geography has also been shown to affect COPD and ILD prevalence. According to data from the CDC collected in 2011, the prevalence of COPD "varies considerably by state, from <4% in Washington to >9% in Alabama and Kentucky…the states with the highest prevalence of COPD are clustered along the Ohio and Mississippi River" (21). When comparing these trends to census data, the Southeastern United States, which has a higher percentage of African-Americans than the national average, also has a higher rate of COPD. ILD is slightly more difficult to characterize from a regional perspective as well because of its many etiologies. That being said, many occupational exposures that cause ILD are from factories (asbestosis, silicosis, beryllosis), which have been shown to be located along the Ohio River (8).

Racial Disparities in Lung Transplantation

Both post-transplant and waitlist outcomes are typically used to evaluate disparities in transplantation. While a great deal of research on both of these topics has been done in the liver and kidney literature, there is not a wealth of research about lung transplantation when looking at either of these two outcomes. Historically, African-Americans, especially women, were at an increased risk of death following transplant than Caucasian recipients (10). When looking at a cohort of patients transplanted between 2001-2009, no racial disparity in outcomes existed (10). Another cohort study of all solid-organ transplant recipients between 1990 and 2002 showed that African-Americans have comparable survival within five years when compared to Caucasians when looking at heart, kidney, lung, and liver transplants (11).

Waiting list outcomes have also been looked at as a way to characterize disparities in transplantation. In 2008, Lederer et al. published a retrospective cohort study evaluating waiting list outcomes for African-Americans prior to the introduction of the LAS. African-Americans were shown to be less likely to undergo transplantation and more likely to die on the waitlist than Caucasians, even after adjusting for age, lung function, other risk factors, and insurance coverage (13). Unlike the studies looking at post-transplant outcomes, smaller studies focusing on waitlist candidates with a specific disease process supported these data. A 2004 study showed that African-Americans with IPF were significantly more likely to die on the waitlist than Caucasians (13).

In order to investigate whether or not the introduction of the LAS had decreased racial disparity in lung transplantation, Wille et al. performed a retrospective cohort study in 2013 comparing outcomes of African-Americans on the waitlist in both pre- and post-LAS time periods (14). The data from this study supported previous claims that in the pre-LAS era, African-Americans were significantly more likely to die on the waitlist. Additionally, this study showed that of the candidates who remained on the waitlist, 56.3% of African-Americans received transplants, compared with 69.2% of Caucasians ($p < 0.05$). This study, however, revealed a significant change in these differences following the introduction of the LAS (14). No significant difference was seen across either outcome in the post-LAS era (14). African-Americans were just as likely to be transplanted as their Caucasian counterparts (86.0% vs. 86.7%, p=NS), and there was no difference in the percentage of each race that died or was removed from the waitlist due to sickness (14.0% vs. 13.3%, p=NS). Overall, these data suggested that the LAS had, as of 2010, made progress towards eliminating racial disparities between African-Americans and Caucasians in terms of both transplantation and waitlist outcomes (14).

Geographic Disparities in Lung Transplantation

A few studies have also been done to examine geographical disparities in lung transplantation. As mentioned previously, the LAS also sought to mitigate geographical disparities in transplantation. Prior to its introduction, patients living in rural areas (further from transplant centers) were less likely to be transplanted than those living close to transplant centers (3). Thabut, et al. showed that even after the introduction of the LAS, the distance from a patient’s residence to the nearest transplant center was inversely associated with the hazard of receiving a transplant (15). Studies have also looked at geographic variation by region. Candidates in the northern and northwest regions (OPTN regions 1, 6, and 9) have been shown to experience longer wait times for transplant

(Afshar). No research has been conducted to examine whether or not there is a relationship between prevalence of end-stage lung disease and rate of or time to transplant in various OPTN regions.

Chapter II: Manuscript

Introduction

The issue of racial disparities in access to healthcare has been at the forefront of health policy discussions for much of the past decade. These disparities exist across all facets of healthcare, including solid organ transplantation. In lung transplantation, efforts have been made to address these racial disparities through the introduction of the lung allocation score (LAS) in 2005 (3). The LAS is “a numerical value used to prioritize waitlist candidates based on a combination of waitlist urgency and post-transplant survival” (1). This score takes into consideration variables such as disease process, age, lung volumes, and functional capabilities of the patient (3). The LAS was designed with the intent to make allocation an overall more objective process with the secondary benefit of eliminating geographical, gender, and racial biases associated with the previous system, which allocated lungs using a first-come first-serve basis incorporating distance from the donor hospital (1). The LAS also seeks to deliver lungs to those believed to have the greatest benefit from lung transplantation.

In 2008, Lederer et al. published a retrospective cohort study evaluating waiting list outcomes for African-Americans prior to the introduction of the LAS. Using a cohort of 280 African-Americans and 5,272 Caucasians with COPD listed for lung transplant between 1995 and 2004 (13), it was shown that African-Americans were “less likely to undergo transplantation and more likely to die on the waitlist” than their Caucasian counterparts even after adjusting for age, lung function, other risk factors, and insurance coverage (13). The authors suggested that unequal access to care may be the reason for this, providing support for the idea that an objective allocation system would help eliminate racial biases. Another study, conducted in 2004, bolstered Lederer's claims, showing that African-American patients with idiopathic pulmonary fibrosis were significantly more likely to die on the waitlist as well (12).

In order to investigate whether or not the introduction of the LAS had decreased racial disparity in lung transplantation, Wille et al. performed a retrospective cohort study in 2013 comparing outcomes of African-Americans on the waitlist in both pre- and post-LAS time periods. Data obtained by Wille supported Lederer's earlier claims about racial disparities in the pre-LAS era (14) During this time period, 43.8% of African-American patients were removed from the waitlist due to death or becoming too sick, compared with only 30.8% of Caucasians ($p<0.05$). Of those who remained on the waitlist, 56.3% of African-Americans received transplants, compared with 69.2% of Caucasians ($p<0.05$) (14). This study, however, revealed a significant change in these differences following the introduction of the LAS. No significant difference was seen across either outcome. African-Americans were just as likely to be transplanted as their Caucasian counterparts (86.0% vs. 86.7%, p=NS) , and there was no difference in the percentage of each race that died or was removed from the waitlist due to sickness (14.0% vs. 13.3%, p=NS) (14). Overall, these data suggested that the LAS had, as of 2010, made progress towards eliminating racial disparities between African-Americans and Caucasians in terms of both transplantation and waitlist outcomes.

While this study demonstrates that the introduction of the LAS has made some headway in decreasing racial disparities, it is worth noting that the LAS also aimed to decrease geographical disparity by removing distance from transplant center in the algorithm used to allocate lungs. A recent study by Thabut, et al. showed that the distance from a patient's residence to the nearest transplant center was inversely associated with the hazard of receiving a transplant; this disparity existed in both the pre- and post-LAS era (15). In end-stage kidney and liver disease populations, racial differences in access to transplantation vary across geographic region (16). This relationship between race and geography has not, however, been studied in the lung transplant population.. According to the OPTN Final Rule, there should be no differences in transplant access by geographic region, and organs "should be distributed over as broad a geographic area as feasible." (OPTN) The Thabut study, as well as other research that shows that waitlisted candidates in the Northern and Northwestern United States have longer wait times than those from other regions, appears to suggest that this rule is currently being violated.

Several large studies have been performed that show racial disparities in lung transplant outcomes in the post-LAS era, but the Wille study remains the only large-scale study comparing waitlist outcomes by race (14). Additionally, no research has been done to examine racial disparities while accounting for both socioeconomic status and geographical region. We aim to perform a thorough analysis of racial disparities in the post-LAS era by looking at likelihood of transplantation in African-Americans versus Caucasians. In order to do this, we will look at all African-American and Caucasian patients listed for lung transplantation from 2005-2014. We will adjust for socioeconomic and insurance status using patient-level data. In addition to analyzing our whole cohort, we will also attempt to look at the effect of geography on racial disparities by looking at individual regions and adjusting for those who live in metropolitan areas where transplant centers are located to those who do not. We hypothesize that although the LAS has made some progress in eliminating racial disparities in lung transplantation, when the aforementioned variables are adjusted for, racial disparities will continue to exist on a national scale and also when looking at individual regions.

Methods

This study was approved by the Institutional Review Board (IRB) of Emory University, Atlanta, GA (IRB 00074904) . Patient-level and zip code data was obtained with permission from the Scientific Registry of Transplant Recipients (SRTR) under SRTR Data Release Agreement 9242, dated September 9, 2014.

Study Population

We performed a retrospective cohort study of all African-American and Caucasian adults 18 years of age or older who were waitlisted for lung transplantation between May 4, 2005 and December 31, 2013. The LAS was implemented on May 4, 2005 (3). We used the SRTR to identify all patients registered on the waiting list for lung transplantation following this date. The study population included all patients greater than or equal to 18 years of age who were categorized as African-American or Caucasian. Race was self-reported at the time of registration. Patients listed for multi-organ transplantation, including heart/lung transplants, were excluded from our study.

Data Cleaning

Data cleaning and analyses were conducted using SAS version 9.4 (Cary, NC).

Data Collection

Patient-specific data on all candidates listed for thoracic organ transplantation was obtained from SRTR Standard Analysis Files (SAF) on all solid organ transplant candidates in the United States from January 1, 1989 through September 30, 2014. 47,500 lung transplant candidates were identified after excluding candidates listed for heart/lung and heart transplants. All candidates missing values for date of waitlisting (n = 251) were excluded, as were all patients listed prior to May 4, 2005. A total of 21,814 candidates listed in the post-LAS era were identified for our study. 856 patients were excluded due to age < 18. We then excluded all patients who did not self-identify as African-American or Caucasian or for whom information about race was missing (n=1,796). Our final cohort for analysis included 19,162 candidates for lung transplantation (Figure 1). Variables collected included listing date, age, sex, race, educational level (as a proxy for SES), residential zip code, waiting time accrued, and comorbid illnesses. Data on race and sex were self-reported by candidates for transplantation.

Residential zip codes obtained from the SRTR were used to divide subjects into OPTN regions as follows (as of March 1, 2016):

- Region 1: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Eastern Vermont
- Region 2: Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania, West Virginia
- Region 3: Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, Puerto Rico

- Region 4: Oklahoma, Texas
- Region 5: Arizona, California, Nevada, New Mexico, Utah
- Region 6: Alaska, Hawaii, Idaho, Montana, Oregon, Washington
- Region 7: Illinois, Minnesota, North Dakota, South Dakota, Wisconsin
- Region 8: Colorado, Iowa, Kansas, Missouri, Nebraska, Wyoming
- Region 9: New York, Western Vermont
- Region 10: Indiana, Michigan, Ohio
- Region 11: Kentucky, North Carolina, South Carolina, Tennessee, Virginia

In the liver transplant literature, several studies categorize subjects based on whether or not they live in a metropolitan area containing at least one transplant center. We utilized a similar approach using residential zip codes. By combining zip code information from the United States Postal Service with information obtained from publicly available SRTR data on location of lung transplant centers in the United States, we were able to group subjects into two groups based on proximity to transplant center:

- Group A: within metro area of at least one lung transplant center
- Group B: outside of metro area of any lung transplant center

Candidates for transplant were divided based on the primary outcome into two groups based on whether or not they had been transplanted prior to September 30, 2014. For patients receiving transplants, length of time prior to transplant was calculated by subtracting the date of listing from the transplant date.

Analysis

Univariate comparisons by outcomes of interest (lung transplantation) were performed for the following covariates: age, gender, race, diabetes, proximity to transplant center, Medicare/Medicaid status, educational status, and cardiovascular disease. Variables significant (p less than or equal to 0.05) in the univariate analysis were included in the multivariate analysis. The presence of gender, diabetes, proximity to transplant center, and Medicare/Medicaid use were deemed to be significant in univariate models and thus these were adjusted for in the multivariate analysis. Statistical tests were 2-sided, and results with p less than or equal to 0.05 were considered significant. The Mann-Whitney test was used to compare median time to transplantation across the two racial strata.

We calculated the percent of subjects in each region who were removed from the waitlist prior to transplant (due to death, decline, or improvement in condition) in order to determine whether or not these subjects would need to be censored prior to further analysis. Only 3/11 (27.3%) of regions showed a difference in percent across the two races, which we deemed to be not significant enough to account for. A multivariate analysis was performed to determine whether race was associated with the likelihood of transplantation within three years, a standard quality measure established by the SRTR (SRTR). Adjusted odds ratios were reported for the logistic regression models. Following whole cohort analysis, similar tests were conducted for each geographic OPTN region. All statistical analyses were performed using SAS 9.4 software (Cary, NC).

Results

Of the 21,814 candidates listed for transplantation in the post-LAS era, 19,162 subjects, 17,254 (90.94%) who identified as Caucasian and 1,908 (9.96%) who identified as African-American, were included in our analysis after excluding all subjects < 18 years of age at time of listing and all subjects who did not self-identify as African-

American or Caucasian (Figure 1). Subjects with no information for race or age were also excluded from analysis. Baseline characteristics of the subjects used for analysis are shown in Table 1, stratified by race. African-American subjects were more likely to be female than their Caucasian counterparts ($p < 0.05$). The mean age for African-American subjects was also significantly younger (mean age: 51.13 vs. 54.28, $p < 0.001$). African-Americans were less likely to suffer from coronary artery disease (1.88% vs. 3.09%, $p < 0.05$) and more likely to suffer from hypertension (39.42% vs. 27.39%, $p < 0.05$). African-Americans were also more likely to use Medicare/Medicaid as a form of payment (42.24% vs. 38.82%, $p < 0.05$). Using education as a proxy for socioeconomic status, no differences between races were observed. Caucasians were more likely to live outside of a metropolitan area containing a transplant center (75.98% vs. 53.83%, $p < 0.05$). Overall, African-Americans were less likely to receive transplants than Caucasians (64.99% vs. 71.76%, $p < 0.05$).

13,621 subjects (71.08%) within our cohort received single lung transplants during our study period, including 71.76% Caucasian and 64.99% African-American ($p < 0.05$). Time to transplantation information was available for 12,518 of these subjects (Table 2). The median time to transplantation for these subjects was 60.00 days (18.00, 175.00). Caucasians (n=11,372) had a similar median time to transplant of 59.00 days (18.00, 174.00) and African-Americans (n=1,146) were found to have a median time to transplant of 67.00 days. (20.00, 184.50). There was no significant difference when comparing time to transplant across the two races. Mean time to transplant was also calculated by OPTN region in order to identify any geographic variation (Table 3). No significant difference was seen when comparing mean time to transplant by race in any region with the exception of region 2, where African-Americans were found to have a significantly longer time to transplant (161.59 vs. 112.83 days, $p = 0.001$).

We examined the percentage of candidates in each region who were removed from final analysis due to dying or being removed from analysis. There was no significant difference found when comparing the percentage of candidates from the study population that died/were removed across over the 11 OPTN regions (Table 4). Significant differences in percentage African-American and Caucasian were identified in three of the eleven regions (OPTN regions 2, 3, and 10).

In unadjusted analyses, African-Americans vs. Caucasians in Regions 1, 2, 3, and 5 were significantly less likely to receive a lung transplant within the three-year period ($p < 0.05$). In multivariate models controlling for gender, diabetes, proximity to transplant center, and Medicare/Medicaid use, no racial difference was seen in likelihood of receiving a transplant within three years across any region (Table 5).

Discussion

Lung transplantation is currently the only known treatment for end-stage lung disease. While supplemental oxygen and drug therapy can be used as temporary measures in patients suffering from these conditions, they ultimately require transplantation to survive. In the 1990s, wait times for transplant began to increase due to a limited number of available cadaveric lungs, resulting in the death of many patients on the waiting list (18). At the time, allocation of donor lungs was based on accrued time on the waiting list after matching for blood type (18). This led to many disparities in lung transplantation. African-American lung transplant candidates during this time were less likely to receive lung transplants than Caucasians on the waiting list. Additionally, those who lived further from transplant centers were shown to have a similar disparity in receiving lungs.

In liver transplantation, the Model for End-Stage Liver Disease (MELD) score was introduced in the year 2002 (19). This scoring system used objective laboratory values for serum bilirubin, creatinine, and the international normalized ratio in order to provide an objective measurement of need for transplant. Since its introduction, the MELD score been shown to decrease racial disparities in terms of likelihood of liver transplantation (20). Lung transplantation, at this time, did not have an objective system, which was postulated as a reason behind the disparities discussed above. In 2005, the LAS was introduced in order to alleviate some of these issues. The main goals of the LAS were to decrease wait-list mortality, provide transplants to those in need, and to deemphasize wait time and geography as factors in allocation (3). Pulmonologists and cardiothoracic surgeons hoped that the LAS would follow in the footsteps of the MELD score and provide an effective, objective way of allocating lungs.

Cohort studies conducted using data prior to 2005 showed that both geographic and racial disparities existed before the LAS was introduced. Therefore, we attempted to examine how, in the post-LAS era, both of these factors played a role in transplantation. According to our data, after adjusting for insurance, comorbidities, and distance from transplant center, there are no differences in either the likelihood of transplant within three years between African-Americans and Caucasians. Based on our analysis, and a similar study conducted in 2008, which did not adjust for distance from transplant center or stratify by region, we can conclude that the LAS, similarly to the MELD score, appears to be helpful in mitigating racial disparities in lung transplantation on a national scale. We further analyzed our outcome of transplant within three years by OPTN region, and found no significant differences in likelihood of transplant in any of the 11 OPTN regions. Based on these data, we reject our hypothesis that after adjusting for socioeconomic status, insurance, and distance to transplant center, racial disparities would still be present.

Study Strengths and Limitations

The strengths of this study include the large number of transplant candidates, the use of a national database rather than focusing on a single institution, and access to patient-level information that could possibly influence transplant outcomes. The study does, however, have several limitations. Racial information is self-reported, and the accuracy of this information cannot be verified.

We elected to perform a multivariate logistic regression rather than Cox proportional hazards analysis because there were disparities across the two strata in candidates dying or being removed prior to transplant in only 3 of the 11 OPTN regions. This is a limitation of our study, as by making this choice, we are not taking into account potential loss to follow up. In the future, we could censor these individuals in order to create a more robust analysis that would give us a better idea of racial disparities across all regions, including the three in which we saw differences.

The United States also has a growing Hispanic population, a large percentage of whom are affected by similar socioeconomic issues as the African-American population. We did not include subjects who identified as Hispanic in our study, which is a major limitation, especially when examining states with large Hispanic populations. Future research should be done to examine whether the LAS has had any impact on transplantation in Hispanic populations and also look at Asian and Native-American ethnic groups, which have not been studied in great detail.

Conclusions

The objective of this study was to perform a thorough analysis of racial disparities in the post-LAS era by looking at likelihood of transplantation within three years in African-Americans versus Caucasians while adjusting for socioeconomic status, insurance status, and distance from a transplant center. We reject our initial hypothesis that after these adjustments, racial disparities would persist. These data show that the LAS, which has now been in place for over ten years, has proven to be an effective and objective way to allocate lungs for transplantation. The LAS should continue to be used in the objective allocation of lungs.

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Figures and Tables

Figure 1. Algorithm for Study Inclusion

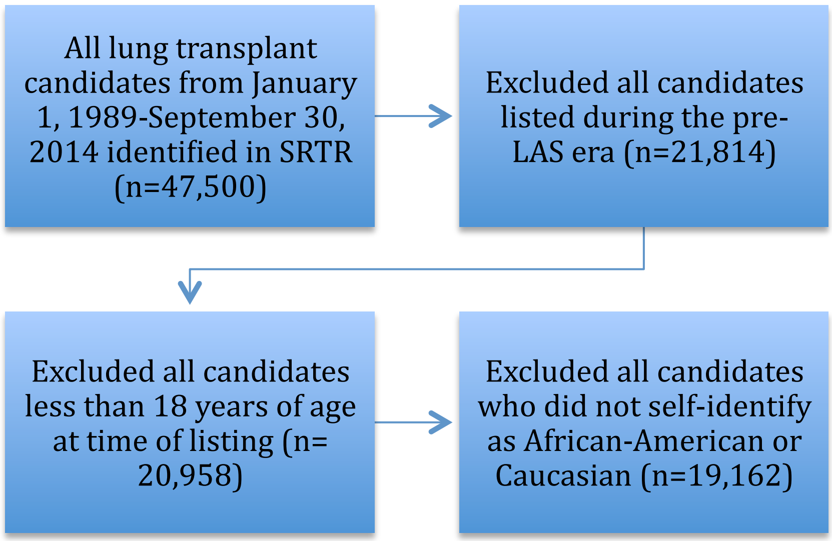

Table 1. Demographic Characteristics for Candidates Listed for Lung Transplantation from May 4, 2005-September 30, 2014, by Race

	Study Population (n=19,162)	**Caucasian (n= 17,254)**	**African-American (n=1,908)**	**p-value**
Age at Listing				p = 0.001
18-34	2,392 (12.48%)	2,228 (12.91%)	164 (8.60%)	
35-49	2,860 (14.93%)	2,270 (13.16%)	590 (30.92%)	
50-64	9,947 (51.91%)	8,947 (51.85%)	1,000 (52.41%)	
65+	3,963 (20.68%)	3,809 (22.08%)	154 (8.07%)	
Gender				p = 0.001
Male	10,598 (55.31%)	9,814 (56.88%)	784 (41.09%)	
Female	8,565 (44.69%)	7,440 (43.12%)	1,124 (58.91%)	
Comorbidities				
Coronary Artery Disease	468 (2.97%)	439 (3.09%)	29 (1.88%)	p = 0.003
Diabetes	3,626 (17.19%)	3,247 (17.10%)	379 (18.00%)	p = 0.134
Hypertension	4,564 (28.56%)	3,949 (27.39%)	615 (39.42%)	p = 0.001
Source of Payment				
Medicare/Medicaid	7,432 (39.16%)	6,634 (38.82%)	798 (42.24%)	p = 0.004
Private	10,87 (57.30%)	9,858 (57.69%)	1,016 (53.79%)	
VA	291 (1.53%)	252 (1.47%)	39 (2.06%)	
Other	381 (2.01%)	345 (2.02%)	36 (1.91%)	
Educational Level				p = 0.145
None	18 (0.09%)	16 (0.09%)	2 (0.11%)	
Grade School (0-8)	342 (1.80%)	305 (1.79%)	37 (1.96%)	
High School or GED	6,898 (36.36%)	6,238 (36.51%)	660 (34.98%)	
College/Technical School	4,669 (24.61%)	4,181 (24.47%)	488 (25.86%)	
Associate/Bachelors	3,517 (18.54%)	3,176 (18.59%)	341 (18.07%)	
Graduate Degree	1,640 (8.64%)	1,490 (8.72%)	150 (7.95%)	

Unknown	1,888 (9.95%)	1,679 (9.83%)	209 (11.08%)	
OPTN Region				
Region 1	760 (4.57%)	729 (4.89%)	31 (1.72%)	
Region 2	2,253 (12.56%)	2,018 (12.51%)	235 (13.06%)	
Region 3	2,770 (15.45%)	2,391 (14.82%)	379 (21.07%)	
Region 4	1,830 (10.21%)	1,595 (9.89%)	235 (13.06%)	
Region 5	2,312 (12.89%)	2,156 (13.36%)	156 (8.67%)	
Region 6	701 (3.91%)	680 (4.21%)	21 (1.17%)	
Region 7	1,510 (8.42%)	1,382 (8.57%)	128 (7.12%)	
Region 8	1,027 (5.73%)	980 (6.07%)	47 (2.61%)	
Region 9	285 (1.59%)	233 (1.44%)	52 (2.89%)	
Region 10	2,250 (12.55%)	2,055 (12.74%)	195 (10.84%)	
Region 11	2,174 (12.12%)	1,854 (11.49%)	320 (17.79%)	
Proximity to Transplant Center				p = 0.001
Group A (metro area)	5,025 (26.22%)	4,144 (24.02%)	881 (46.17%)	
Group B (non-metro area)	14,137 (73.77%)	13,110 (75.98%)	1,027 (53.83%)	
Transplant status (as of September 30, 2014)				p = 0.001
Transplanted	13,621 (71.08%)	12,381 (71.76%)	1,240 (64.99%)	
Not transplanted	5,541 (28.92%)	4,873 (28.24%)	668 (35.01%)	

Table 2. Mean Time from Waitlisting to Transplantation of the Study Population, Stratified by Race, Unadjusted

	Median Time to Transplant (IQR) (days)
Study Population (n=12,518)	60.00 (18.00, 175.00)
Caucasians (n=11,372)	59.00 (18.00, 174.00)
African-Americans (n=1,146)	67.00 (20.00, 184.50)

Table 3. Mean Time to Transplantation By OPTN Region, Stratified by Race, Unadjusted

	Mean Time to Transplant (days), Study Population	**Mean Time to Transplant (days), Caucasians**	**Mean Time to Transplant (days), AA**	**p-value**
Region 1 (n = 485)	170.23 +/- 210.8	170.07 +/- 211.2 (n= 472)	176.00 +/- 204.7 (n= 13)	p = 0.953
Region 2 (n= 1,536)	116.99 +/- 163.6	112.83 +/- 161.4 (n= 1,405)	161.59 +/- 180.4 (n= 131)	p = 0.001
Region 3 (n= 1,857)	135.44 +/- 185.7	132.41 +/- 182.8 (n= 1,628)	157.03 +/- 204.6 (n= 229)	p = 0.075
Region 4 (n= 1,351)	114.25 +/- 158.6	117.50 +/- 162.9 (n= 1,189)	90.42 +/- 119.8 (n= 162)	p = 0.051
Region 5 (n= 1,686)	115.20 +/- 161.6	115.73 +/- 162.3 (n= 1,585)	106.90 +/- 149.8 (n= 101)	p = 0.612
Region 6 (n= 510)	174.59 +/- 209.5	174.39 +/- 208.5 (n= 493)	180.35 +/- 244.5 (n= 17)	p = 0.961
Region 7 (n= 1,058)	171.00 +/- 201.6	168.14 +/- 208.9 (n= 978)	205.94 +/- 228.1 (n= 80)	p = 0.191
Region 8 (n= 728)	135.24 +/- 181.3	136.32 +/- 180.5 (n= 700)	108.35 +/- 201.1 (n= 28)	p = 0.466
Region 9 (n= 174)	141.16 +/- 177.47	142.09 +/- 172.2 (n= 142)	137.03 +/- 202.1 (n= 32)	p = 0.882
Region 10 (n= 1,499)	150.14 +/- 196.7	151.08 +/- 198.1 (n= 1,377)	139.52 +/- 179.4 (n= 122)	p = 0.596
Region 11 (n= 1,634)	112.41 +/- 169.5	110.51 +/- 171.4 (n= 1,403)	123.94 +/- 156.7 (n= 231)	p = 0.277

Abbreviations: AA, African-American

Table 4. Death/Removal From Waitlist Prior to Transplant By OPTN Region, Stratified by Race

	Study Population (%)	Caucasian (%)	African-American (%)	p-value
Study Population	17,372	1,303	190	
Region 1 (n = 760)	57 (7.50%)	52 (7.13%)	5 (16.13%)	p = 0.062
Region 2 (n= 2,253)	202 (8.97%)	169 (7.06%)	33 (14.04%	p = 0.003
Region 3 (n= 2,270)	220 (9.97%)	180 (7.52%)	40 (10.55%)	p = 0.044
Region 4 (n= 1,830)	180 (9.84%)	152 (9.53%)	28 (11.91%)	p = 0.250
Region 5 (n= 2,312)	187 (8.09%)	176 (8.16%)	11 (7.05%)	p = 0.624
Region 6 (n= 701)	61 (8.70%)	60 (8.82%)	1 (4.76%)	p = 0.516
Region 7 (n= 1,510)	148 (9.80%)	134 (9.69%)	14 (10.93%)	p = 0.653
Region 8 (n= 1,027)	104 (10.13%)	99 (10.10%)	5 (10.63%)	p = 0.904
Region 9 (n= 285)	21 (7.36%)	18 (7.73%)	3 (5.76%)	p = 0.624
Region 10 (n= 2,250)	165 (7.33%)	141 (6.87%)	24 (12.31%)	p = 0.005
Region 11 (n= 2,174)	148 (6.81%)	122 (6.58%)	26 (8.13%)	p = 0.313

Abbreviations: AA, African-American

Table 5. Multivariable Analyses of Likelihood of Lung Transplantation Within 3 Years of Registering on the Wait List, by Race

	N	Caucasian[a]	AA	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[b]	p-value
Study population	12,518	11,372	1,146	0.813 (0.739, 0.8962)	0.921 (0.832, 1.020)	p = 0.114
Region 1	485	472	13	0.393 (0.190, 0.816)	0.612 (0.140, 2.682)	p = 0.515
Region 2	1,536	1,405	131	0.550 (0.418, 0.723)	0.660 (0.373, 1.170)	p = 0.155
Region 3	1,857	1,628	229	0.716 (0.572, 0.894)	0.918 (0.529, 1.593)	p = 0.761
Region 4	1,351	1,189	162	0.758 (0.562, 1.024)	0.965 (0.457, 1.991)	p = 0.922
Region 5	1,686	1,585	101	0.662 (0.469, 0.931)	0.813 (0.330, 2.00)	p = 0.652
Region 6	510	493	17	1.612 (0.536, 4.853)	1.224 (0.724, 2.068)	p = 0.450
Region 7	1,058	978	80	0.6885 (0.473, 1.003)	0.978 (0.591, 1.616)	p = 0.929
Region 8	728	700	28	0.590 (0.324, 1.073)	0.739 (0.320, 1.230)	p = 0.293
Region 9	174	142	32	1.025 (0.553, 1.901)	1.325 (0.801, 2.193)	p = 0.274
Region 10	1,499	1,377	122	0.830 (0.607, 1.116)	0.910 (0.534, 1.551)	p = 0.728
Region 11	1,634	1,403	231	0.834 (0.639, 1.089)	0.924 (0.815, 1.047)	p = 0.216

Abbreviations: AA, African American; CI, confidence interval; OR, odds ratio
[a]Caucasians were the reference group for adjusted OR
[b]Adjusted for gender, diabetes, residence within a metropolitan area, and Medicare/Medicaid status