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Outcome disparities between African Americans and Caucasians in contemporary kidney transplant recipients

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ABSTRACT

Background: Racial disparities in African-American (AA) kidney transplant have persisted for nearly 40 years, with limited data available on the scope of this issue in the contemporary era of transplantation.
Methods: Descriptive retrospective cohort study of US registry data including adult solitary kidney transplants between Jan 1, 2005 to Dec 31, 2009.
Results: 60,695 recipients were included; 41,426 Caucasians (68%) and 19,269 AAs (32%). At baseline, AAs were younger, had lower college graduation rates, were more likely to be receiving public health insurance and have diabetes. At one-year post-transplant, AAs had 62% higher risk of graft loss (RR 1.62, 95% CI 1.50–1.75) which increased to 93% at five years (RR 1.93, 95% CI 1.85–2.01). Adjusted risk of graft loss, accounting for baseline characteristics, was 60% higher in AAs (HR 1.61 [1.52–1.69]). AAs had significantly higher risk of acute rejection and delayed graft function.
Conclusion: AAs continue to experience disproportionately high rates of graft loss within the contemporary era of transplant, which are related to a convergence of an array of socioeconomic and biologic risk factors.

1. Introduction

The first kidney transplant was performed in 1954, when Dr. Joseph E. Murray transplanted a living donor kidney from one twin to another at Brigham Hospital in Boston, MA. Since that time, kidney transplantation has grown from an experimental procedure to the treatment option of choice in eligible patients with end-stage renal disease (ESRD). It has been clearly demonstrated that this procedure dramatically extends both the length of quality of a person's life, as compared to remaining on dialysis.[1,2]

Persistent racial disparities in kidney transplant graft survival have been well documented over this same period; first reported in 1977 and extended through contemporary eras.[3] Although graft survival rates have dramatically improved over the past 40 years, based on the most recent data, racial disparities in graft outcomes have remained.[4] There have been numerous studies focused on trying to understand the prevailing risk factors that disproportionately impact African-American (AA) kidney transplant recipients. Previous research has demonstrated that AAs have a number of significant disadvantages that likely contribute to this disparity, including gene variants, socioeconomics, reduced access to pre-emptive transplants and living donors, and a higher burden of comorbidities.[5–13]

Since the 1990s, there have been substantial changes to how organs are allocated, improvements in HLA antibody measurement and matching techniques, and significant advancements in immunosuppressant medications.[14] Since this time, there is paucity in published studies determining if these changes have impacted the magnitude of racial disparities in kidney transplant outcomes.[7] Over this same timeframe, many changes have occurred to the transplant registry with regards to the type and completeness of baseline demographics and transplant variables. With a lack of published studies assessing disparities in AA recipients since these changes, it is currently unclear if they have impacted these inequalities. Thus, the objective of this study was to utilize U.S. national registry data from a more contemporary timeframe of 2005–2009 and describe racial disparities in AA kidney transplantation, allowing for an updated assessment to guide future interventions.[15,16]

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2. Material and methods

2.1. Study design and patients

This was a retrospective analysis of the UNOS registry database, which was linked to the Social Security Death Master File (SSDMF) to obtain accurate patient death dates. The UNOS registry contains data regarding every organ donation and transplant event occurring in the U.S. since October 1, 1987.[17] After local IRB approval and signing a data use agreement (DUA), we obtained Standard Transplant Analysis and Research (STAR) de-identified datasets in SAS format, which were pre-linked to the SSDMF data. The time period for this study focused on transplant events occurring between Jan 1, 2005 and Dec 31, 2009, with follow up through December 31, 2014. Patients were included if they were adult recipients (≥18 years of age at the time of transplant) of kidney transplants which occurred within the U.S. during the pre-specified timeframe. Pediatrics, recipients of non-renal organs and those that were not either AA or Caucasian were excluded.

2.2. Outcome measurements

The primary outcome measure for this study was death-censored graft loss at one, three and five years post-transplant, which is defined as either a return to chronic dialysis or retransplantation. Patients that died with a functioning allograft were not included as graft loss events, but were censored at the date of death. We also analyzed mortality rates at one, three and five years post-transplant. Overall graft loss, a composite of either graft loss or death, was analyzed at the same time periods. Additional outcomes that were assessed included delayed graft function (defined as the need for dialysis within 7 days of transplant), acute rejection (defined as either biopsy proven or empirically treated) at any time after transplant, and graft function (defined as the serum creatinine [mg/dL] at last follow up).

2.3. Exposure variables

The primary variable of interest for this analysis was race, which was self-identified as detailed in the UNOS registry. For ease of presentation of the data, we restricted this study to only include non-Hispanic Whites (Caucasians) and non-Hispanic Blacks (AAs). Baseline recipient sociodemographics (age, gender, body mass index [BMI], functional status, education and insurance), comorbidities (reason for ESRD, cardiovascular disease [CVD] comorbid conditions and time on dialysis and waitlist), donor characteristics (age, gender, race, and donor type), transplant characteristics/immunologic risks (HLA mismatches, PRA, cold ischemic time, previous kidney transplant) and immunosuppression (induction and maintenance therapy) were compared between groups. Expanded criteria donor (ECD) was defined as age ≥60 years or age ≥50 years with at least two of the following: history of hypertension, death due to CVA or terminal serum creatinine of ≥1.5 mg/dL. Panel reactive antibody (PRA), which is a measure of recipient sensitization to HLA antigens (pre-existing HLA antibodies) was assessed as 0–100%, reporting both the peak and most current values.

2.4. Statistical analysis

Standard descriptive statistics were used to compare categorical and continuous variables stratified by recipient race. For continuous variables, results are reported as means ± standard deviations (SD); for continuous variables that are not normally distributed, such as time on dialysis, HLA mismatches and PRA, results are reported as medians with interquartile ranges (IQR). Categorical variables are presented as percentages. Statistical comparisons between groups were conducted using the Student's T-test for two independent samples for continuous variables, the Mann Whitney *U* test for continuous variables that were not normally distributed and the Chi square test for categorical data. Survival curves were estimated using Cox regression analyses, with both unadjusted (race only) and fully adjusted modeling (all baseline variables listed in the exposure section above). As a sensitivity analysis, to determine the impact of missing data, we conducted multiple imputation and estimated the effect of race on outcomes with this dataset, comparing it with the estimates from the complete case dataset (see Supplemental Tables 1 and 2) Statistical significance was based on a two-sided p-value of less than 0.05. Statistical analyses were performed using SPSS (version 23.0, IBM Corp, Armonk, NY) and SAS version 9.4 (SAS Institute, Cary, NC).

3. Results

3.1. Study population

The complete UNOS STAR file contained 394,359 kidney transplant events that occurred between Oct 1, 1987 and Sept 1, 2014. Of these, 19,313 were excluded for being <18 years of age, 37,810 were excluded for receiving non-renal transplants and 62,813 were excluded for being non-Caucasian or non-AA recipients. Finally, 213,728 recipients were excluded for receiving transplants outside the specified time period (2005–2009), leaving 60,695 transplant recipients in the final study cohort; of which, 41,426 (68%) were Caucasian and 19,269 (32%) were AA (See Supplemental Fig. 1). The mean follow up was 5.1 ± 2.4 years.

3.2. Baseline recipient sociodemographics

AAs had significantly different baseline characteristics, when compared to Caucasians (Table 1). AAs were, on average, younger (mean age: AA 49.0 ± 12.9 vs. 51.5 ± 13.8 years; $p < 0.001$), more likely to be female (40.5% vs. 37.9%; $p < 0.001$) and had a higher BMI (28.4 ± 5.6 vs. 27.6 ± 5.4 kg/m^2; $p < 0.001$). AAs were also more likely to be socioeconomically disadvantaged, including a lower college graduation rate (18.4% vs. 29.0%; $p < 0.001$) and more likely to be receiving public health insurance (72.7% vs. 50.2%; $p < 0.001$). AAs were more likely to have hypertension (92.5% vs. 86.0%; $p < 0.001$) and diabetes (33.3% vs. 29.1%; $p < 0.001$), but less likely to have a history of PVD (3.1% vs. 4.7%; $p < 0.001$) or angina (7.7% vs. 10.3%; $p < 0.001$). Finally, AAs were more likely to be receiving dialysis at the time of transplant (81.3% vs. 56.8%; $p < 0.001$), to be on dialysis for a longer period of time (median years: 4.0 [2.4–6.0] vs. 2.4 [1.3–4.0] years; $p < 0.001$) and to be on the wait list nearly twice as long (median years: 2.1 [0.9–3.8] vs. 1.1 [0.4–2.3]; $p < 0.001$).

AA recipients received organs from younger donors (mean donor age: 38.9 ± 15.4 vs. 40.9 ± 14.5; $p < 0.001$) that were less likely to be female (44.1% vs. 49.8%; $p < 0.001$), more likely to be AA (34.5% vs. 5.2%; $p < 0.001$) and less likely to be living donors (22.0% vs. 47.3%; $p < 0.001$). AAs were also more likely to receive organs from expanded criteria donors (14.8% vs. 12.7%; $p < 0.001$) and cardiac death donors (9.2% vs. 6.0%; $p < 0.001$). AA recipients had greater numbers of HLA mismatches (median: 5 [3–5] vs. 4 [2–5]; $p < 0.001$), a higher peak PRA (median: 2% [0–27] vs. 0% [0–13]; $p < 0.001$) and longer cold ischemic times (15.4 [8.0–22.4] vs. 10.0 [1.3–19.2]; $p < 0.001$).

In terms of immunosuppression, AA were more likely to receive cytolytic induction therapy (60.2% vs. 55.1%; $p < 0.001$) and be discharged on maintenance regimens consisting of tacrolimus