

# Quantifying the Race Stratified Impact of Socioeconomics on Graft Outcomes in Kidney Transplant Recipients

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**Background.** Socioeconomic status (SES) is a significant determinant of health outcomes and may be an important component of the causal chain surrounding racial disparities in kidney transplantation. The social adaptability index (SAI) is a validated and quantifiable measure of SES, with a lack of studies analyzing this measure longitudinally or between races. **Methods.** Longitudinal cohort study in adult kidney transplantation transplanted at a single-center between 2005 and 2012. The SAI score includes 5 domains (employment, education, marital status, substance abuse and income), each with a minimum of 0 and maximum of 3 for an aggregate of 0 to 15 (higher score → better SES). **Results.** One thousand one hundred seventy-one patients were included; 624 (53%) were African American (AA) and 547 were non-AA. African Americans had significantly lower mean baseline SAI scores (AAs 6.5 vs non-AAs 7.8;  $P < 0.001$ ). Cox regression analysis demonstrated that there was no association between baseline SAI and acute rejection in non-AAs (hazard ratio [HR], 0.92; 95% confidence interval [95% CI], 0.81-1.05), whereas it was a significant predictor of acute rejection in AAs (HR, 0.89; 95% CI, 0.80-0.99). Similarly, a 2-stage approach to joint modelling of time to graft loss and longitudinal SAI did not predict graft loss in non-AAs (HR, 1.01; 95% CI, 0.28-3.62), whereas it was a significant predictor of graft loss in AAs (HR, 0.23; 95% CI, 0.06-0.93). **Conclusions.** After controlling for confounders, SAI scores were associated with a lower risk of acute rejection and graft loss in AA kidney transplant recipients, whereas neither baseline nor follow-up SAI predicted outcomes in non-AA kidney transplant recipients.

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Although race is predominantly a social construct with some biologic differences, it has substantial real-life implications across a wide variety of health outcomes.<sup>1</sup> Within kidney transplantation (KTX), African American (AA) race is a major risk factor for reduced access to transplant and subpar graft survival.<sup>2,3</sup> This health outcomes disparity has been extensively researched over the past 4 decades, yet little has changed in its importance or magnitude.<sup>4-6</sup> Socioeconomic factors have been studied, as potential explanatory

variables that may account for a substantial amount of the risk associated between AA race and graft survival.<sup>7,8</sup> Within AA disparities, research, education,<sup>9</sup> income,<sup>7</sup> and insurance<sup>10</sup> have all been separately identified as factors that are likely to impact graft outcomes.

In the past, concurrently studying the impact of a wide array of socioeconomic status (SES) factors on health outcomes has been difficult due to a limited ability to quantify these factors. The social adaptability index (SAI) has been developed

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as a scoring mechanism that quantifies a patient's SES based on 5 domains, including education level, employment status, marital status, income level, and substance abuse.<sup>11</sup> Research has demonstrated that the SAI is a major risk determinant for health outcomes for diabetes,<sup>12</sup> chronic kidney disease,<sup>13</sup> end-stage renal disease,<sup>14</sup> and access to transplant<sup>15</sup>; more recently, 1 study demonstrated that a low baseline SAI score increased the risk of graft loss after transplantation.<sup>16</sup> However, to date, there is a lack of studies analyzing the impact of follow-up SAI score on posttransplant outcomes and assessing if these associations differ by race. Thus, the aim of this single-center longitudinal analysis was to determine the influence of baseline and follow-up SAI scores on the rates of acute rejection and graft loss in adult kidney transplant recipients, while assessing whether race impacts any of these associations.

## MATERIALS AND METHODS

### Study Design

This was a single-center longitudinal cohort study encompassing a population of racially diverse adult kidney transplant recipients with long-term follow up. Data were retrospectively collected, starting at the time of transplant and following the patients through graft loss, death, or end of follow-up, which was July 2013. The predominant exposure of interest was the SAI score, which was calculated as described below and measured at the time of transplant (baseline) and at yearly intervals thereafter (longitudinal component). Cohorts were assigned, first based on the baseline SAI, and secondly based on the slope of the patients' follow-up SAI. For the baseline SAI cohort assignment, a cut point SAI score of 6 was used, as this was the median baseline score for the entire cohort of patients. The change in follow-up SAI was calculated for each patient as the slope of the linear mixed model for follow up SAI scores available for each individual patient. Cohorts for the follow-up SAI score were assigned into 1 of 3 categories for comparison: increase in score (positive slope) no change in score (slope of zero) or decrease in score (negative slope). For both cohort comparisons (baseline SAI and follow up SAI), groups were stratified by race (AA or non-AA) to assess if this influenced any significant associations between SAI on outcomes.

### Patients

Patients were considered for inclusion in this study if they received a kidney transplant from 2005 to 2012 and were adults at the time of transplant ( $\geq 18$  years). Patients were excluded if they received a nonrenal organ transplant prior, simultaneous or subsequent to the kidney transplant or were lost to follow-up and did not have baseline data to analyze. Patients with early graft loss (defined as within 1 year of transplantation) were included in the baseline SAI analysis but excluded from the follow-up SAI analysis, because SAI slopes could not be calculated from the one baseline score.

### Outcomes

The 2 outcome measurements of interest for this study included the rates of acute rejection and graft loss, both of which were assessed in a time-dependent fashion. Time to these events was computed as the number of years starting at the time of transplant to the development of the event or end of follow-up (July 2013).

### Calculation of SAI

The SAI was calculated in a similar fashion to a previous published study in kidney transplant recipients.<sup>16</sup> It was calculated based on the 5 SES domains, including employment status, marital status, education level, substance abuse, and income. Each is scored from 0 to 3 based on the criteria below, added together in equal weighting to get the total SAI, which ranges from 0 to 15. Because income status was difficult to find in the medical record, insurance status was substituted in a similar fashion to the previous study.<sup>16</sup> Also, because education level is well documented at baseline for transplant recipients, but change in education status is not documented in the medical record, this SAI score domain was assumed to be constant in the longitudinal assessment.

- (1) Employment status: 0, unemployed or not working due to medical condition or by choice; 1, retired; 2, working part time; and 3, working full time.
- (2) Marital status: 0, never married or widowed; 1, divorced or separated; 2, married without children; and 3, married with children.
- (3) Education level: 0, below high school; 1, high school graduate; 2, college graduate; 3, postgraduate education.
- (4) Substance abuse: 0, abusing drugs, alcohol, and tobacco; 1, abusing 2 substances; 2, abusing 1 substance; 3, abusing none.
- (5) Income (primary insurance used as a surrogate): 0, no insurance; 1, Medicaid; 2, Medicare; 3, private insurance.

### Study Definitions

The following clinical definitions were used within this study: graft failure was defined as a documented return to chronic dialysis, retransplantation, or death. Acute rejection was defined as biopsy proven and at least Banff grade of 1A per the 1997 staging criteria.<sup>17</sup> Delayed graft function was defined as the need for dialysis within 7 days after transplantation.

### Immunosuppression Regimens and Follow-Up Schedule

All patients received induction therapy with either thymoglobulin 1.5 mg/kg intravenous (IV) daily for 3 to 5 doses, daclizumab 1 mg/kg IV on day 0 and day 7 after transplantation, or basiliximab 20 mg IV on day 0 and day 4 after transplantation. Choice of induction therapy was based on protocols that used thymoglobulin for high immunologic risk patients (retransplantation, cold ischemic time  $>24$  hours, or panel reactive antibody [PRA]  $>20\%$ ), and an interleukin-2 receptor antibody in all other patients. Maintenance immunosuppression consisted of tacrolimus as the first-line calcineurin inhibitor of choice, with protocols that specify dose adjustments made to maintain target trough whole blood concentrations between 8 and 12 ng/mL for weeks 1 through 6, 6 to 10 ng/mL for weeks 7 through month 12, and greater than 5 ng/mL after 1 year. In addition, our adjunct agent of choice is mycophenolate mofetil 1 g twice daily and all patients received prednisone titrated to 5 mg daily by day 60 after transplantation.

Table S1 (SDC, <http://links.lww.com/TP/B193>) displays our standard clinic and follow-up schedule for usual care of stable kidney transplant recipients. This plan is the minimum

expected follow-up and can become more intense based on acute care events, hospitalizations, rejections, or infections.

**Statistical Analysis**

Unless otherwise stated, univariate summary results are reported in mean ± SDs, with categorical data presented in percentages. Adjusted estimates from multivariable models are presented as hazard ratios (HR) with 95% confidence intervals (95% CI).

For the univariate analyses, continuous variables were compared using *t* tests (2 groups) or 1-way analysis of variance (3 groups), whereas categorical variables were compared using the Pearson  $\chi^2$  test. Kaplan-Meier curves were used to depict the survival time of the cohort with unadjusted group comparisons conducted using the Log Rank test stratified by race. For the multivariate analyses, we used a two-stage approach to jointly model the longitudinal time-varying SAI and time to graft loss. In the first stage, a longitudinal model for SAI is assumed to follow a parametric linear mixed model, where both covariate effects and subject-specific random effects are modeled parametrically (Proc MIXED, SAS 9.4). In the second stage, a Cox model (Proc PHREG, SAS 9.4) for time to graft loss is assumed. The mixed model for the longitudinal process and the Cox model for the survival process are associated through common covariates in both models and the stochastic dependence between the random-effects terms in both models. This approach is widely accepted to model longitudinal data when the predictor (SAI) and outcome (graft loss) are associated, as it leads to less bias and improved accuracy of the inferences.<sup>18-23</sup> Covariates that were included in the models include age, sex, baseline comorbidities (diabetes, hypertension, and cardiovascular disease), time on dialysis, retransplant, PRA, HLA mismatches, cold time, warm time, donor type, donor age, induction therapy, delayed graft function and acute rejection (only in the graft survival analysis). In the Cox models, robust variance was used when testing the significance of the HR estimates. Baseline and follow up missing data were minimal (<10%), and the results of the joint modeling are valid under the assumption of missing at random. Statistical significance was based on a *P* value of less than 0.05. Statistical analyses were performed using SPSS (version 22, IBM Corp, Armonk, NY) and SAS (version 9.4, SAS Institute Inc, Cary, NC).

**RESULTS**

**Patients**

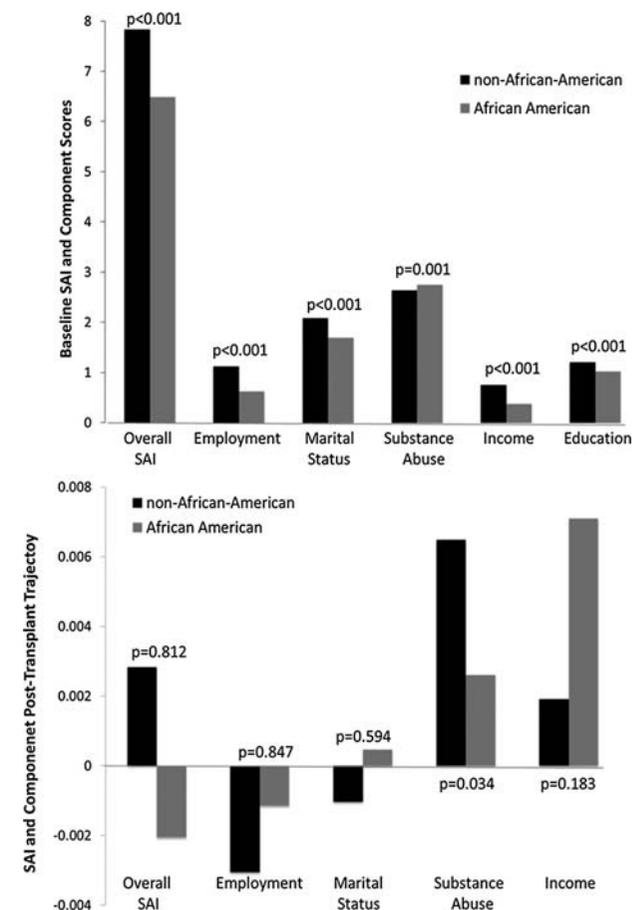
Between 2005 and 2012, a total of 1,501 kidney transplants were conducted at the study institution and screened for potential inclusion; 185 were excluded for receiving non-kidney transplants, 79 patients were excluded for being younger than 18 years, and 66 were excluded for missing data/lost to follow-up, leaving 1171 patients included in the final analysis. Mean follow-up time for the entire cohort was 5.0 ± 2.3 years; which was similar across race (non-AA 4.9 ± 2.3 vs AA 5.0 ± 2.3 years; *P* = 0.445) and baseline SAI group (SAI ≤6 5.0 ± 2.3 vs SAI >6 4.9 ± 2.3 years; *P* = 0.330).

**SAI Comparison by Race**

The top of Figure 1 displays the baseline SAI and component scores, comparing these across race. The AA patients had significantly lower mean baseline SAI scores (non-AA

7.8 vs AA 6.5; *P* < 0.001), which was driven by lower mean employment (non-AA 1.1 vs AA 0.6; *P* < 0.001), marital status (non-AA 2.1 vs AA 1.7; *P* < 0.001), income (non-AA 0.8 vs AA 0.4; *P* < 0.001), and education scores (non-AA 1.2 vs AA 1.0; *P* < 0.001); mean baseline substance abuse scores were higher in AA recipients (non-AA 2.6 vs AA 2.8; *P* = 0.001). The posttransplant follow-up SAI data are displayed in the bottom of Figure 1. The AA patients had a decrease in their posttransplant SAI slope, whereas non-AAs had an increase (AA -0.002 vs non-AA 0.003; *P* = 0.812), which was not statistically significant. Follow-up SAI component slopes were similar between AAs and non-AAs, except for substance abuse, which increased to a greater degree in non-AAs (0.006 vs 0.003; *P* = 0.034, respectively).

The baseline recipient, donor, and transplant characteristics, stratified by race and compared across baseline and follow-up SAI slopes, are displayed in Tables 1 and 2, respectively. Groups were divided by baseline SAI (≤6 vs >6) and follow-up SAI (increase, no change, or decrease in SAI slope) and compared accordingly. For both non-AAs and AAs, those with a low baseline SAI (≤6) were younger, more likely to be female, less likely to receive a preemptive transplant, and spent longer time on dialysis. Low baseline SAI was also associated with receiving a younger donor organ and having a PRA greater than 20%. Within non-AAs, low baseline SAI was associated with a lower incidence of hypertension, higher rates of retransplant, receiving a deceased donor and



**FIGURE 1.** Baseline and follow-up SAI and component scores across racial cohorts.

**TABLE 1.****Baseline characteristics compared across baseline SAI exposure cohorts and stratified by race**

Variables	African American		Non-African American	
	Baseline	Baseline	Baseline	Baseline
	SAI >6 (n = 311)	SAI ≤6 (n = 313)	SAI >6 (n = 388)	SAI ≤6 (n = 159)
Recipient characteristics				
Mean age (±SD)	53 ± 12	48 ± 14*	55 ± 13	46 ± 16*
Female sex	37%	48%*	36%	47%*
History of diabetes	42%	37%	30%	24%
History of hypertension	94%	95%	92%	85%*
History of heart disease	14%	17%	24%	17%
Preemptive	14%	7%*	38%	24%*
Mean years on dialysis (±SD)	3.2 ± 2.6	4.0 ± 3.2*	1.6 ± 2.0	2.2 ± 2.2*
Previous kidney transplant	7%	7%	11%	18%*
Donor characteristics				
Deceased donor	90%	93%	70%	80%*
Mean age (±SD)	38 ± 15	33 ± 16*	39 ± 15	34 ± 15*
AA race	29%	36%	14%	20%
Extended criteria donor	15%	9%*	18%	10%
Transplant characteristics				
Cytolytic induction	45%	46%	38%	50%*
Mean PRA (±SD)	15 ± 28	19 ± 30	14 ± 28	24 ± 35*
PRA >20%	23%	33%*	21%	31%*
PRA >80%	8%	10%	7%	16%*
Mean HLA MM (±SD)	4.6 ± 1.3	1.6 ± 1.2	3.9 ± 1.6	3.6 ± 1.7
Mean cold time (±SD), h	17.7 ± 8.9	17.7 ± 8.3	14 ± 10	16 ± 10
Mean warm time (±SD), min	37 ± 8	38 ± 8	36 ± 9	36 ± 7
Delayed graft function	17%	19%	10%	8%

\* $P < 0.05$ , as compared to the estimate in the same racial cohort.

receiving cytolytic induction therapy; this was not demonstrated in AAs.

In terms of baseline comparisons of recipient, donor, and transplant characteristics across follow-up SAI slope categories, the groups were similar for both AAs and non-AAs for the majority of variables (Table 2). Diabetes, deceased donors, cytolytic induction, mean cold ischemic time, and delayed graft function were significant different across SAI slope categories in non-AAs, whereas retransplant and deceased donor were different across SAI slope categories for AAs.

### Impact of SAI on Outcomes

There was no appreciable association between baseline SAI score and acute rejection rates for non-AAs, both when analyzed by mean score ( $7.9 \pm 2.7$  nonrejecters vs  $7.3 \pm 2.2$  rejecters;  $P = 0.207$ ) and when rejection-free survival was compared by baseline SAI score ( $\leq 6$ : 92.6% vs  $>6$ : 92.8%,  $P = 0.955$ ). Within AAs, mean baseline SAI scores were significantly lower in those that developed acute rejection ( $6.6 \pm 2.3$  nonrejecters vs  $5.8 \pm 2.3$  rejecters;  $P = 0.003$ ), and rejection-free survival was significantly lower in the low baseline SAI group ( $\leq 6$ : 81.4% vs  $>6$ : 89.7%,  $P = 0.003$ ). These data are displayed in Figure 2. There was no association in follow-up SAI scores on acute rejection for both non-AAs and AAs (data not shown).

Figure 3 displays the association between follow-up SAI slopes and graft survival rates, with the data again stratified by race. The AAs with graft loss had a downward SAI slope

(slope change per year), whereas those with graft survival had an increasing SAI slope ( $-0.09$  vs  $0.16$ ,  $P = 0.095$ ); however, this failed to reach statistical significance in univariate analysis. Non-AAs had similar trends in SAI slope based on graft status, but these were not as distinct as compared to AAs (graft loss  $-0.07$  vs graft survival  $0.06$ ,  $P = 0.427$ ). Kaplan-Meier graft survival estimates, compared across SAI slope categories and stratified by race (right side of Figure 3) demonstrated that non-AAs with an increase in SAI slope had significantly higher graft survival rates, as compared with those with no change or a decrease in SAI slope (94.4% vs. 88.8%, respectively,  $P = 0.047$ ). Within AAs, those with a decrease in SAI slope had reduced graft survival, as compared to those with no net change or with an increase (84.4% vs 91.5%, respectively;  $P = 0.368$ ); however, this failed to reach statistical significance in univariate analysis.

### Multivariable Modelling

Because of differences in a number of baseline characteristics known to influence the measured outcomes (acute rejection and graft survival) and because of the inherent association between the longitudinal SAI data and graft loss outcome, 2-stage joint models, using linear mixed model and Cox regression were used. These models were stratified by race, with the results displayed in Table 3. After adjustment, the baseline SAI failed to be associated with acute rejection in non-AAs (adjusted HR, 0.92; 95% CI, 0.81-1.05), whereas it remained a significant predictor of acute rejection in AAs (adjusted HR, 0.89; 95% CI, 0.80-0.99). Cox

**TABLE 2.**  
Baseline outcomes compared across SAI slope exposure cohorts and stratified by race

Variables	African American SAI			Non-African American SAI		
	Posttransplant slope			Posttransplant slope		
	Increase (n = 74)	No change (n = 461)	Decrease (n = 43)	Increase (n = 89)	No change (n = 362)	Decrease (n = 66)
<b>Recipient characteristics</b>						
Mean age (±SD), y	52 ± 13	51 ± 13	50 ± 12	50 ± 13	53 ± 15	50 ± 14
Female sex	32%	45%	39%	37%	41%	36%
History of diabetes*	36%	41%	35%	15%	30%	28%
History of hypertension	97%	95%	94%	90%	89%	87%
History of heart disease	16%	15%	15%	15%	24%	19%
Preemptive	14%	9%	13%	38%	35%	32%
Mean years on dialysis (±SD)	3.3 ± 2.5	3.7 ± 3.0	3.1 ± 3.0	1.4 ± 1.9	1.8 ± 2.1	1.8 ± 2.3
Previous kidney transplant**	8%	5%	15%	17%	12%	12%
<b>Donor characteristics</b>						
Deceased donor*, **	91%	93%	80%	64%	74%	82%
Mean age (±SD)	36 ± 16	35 ± 16	35 ± 13	36 ± 14	37 ± 15	36 ± 16
AA race	45%	33%	38%	30%	18%	19%
Extended criteria donor	12%	12%	8%	15%	16%	13%
<b>Transplant characteristics</b>						
Cytolytic induction*	45%	47%	41%	44%	38%	54%
Mean PRA (±SD)	15 ± 29	19 ± 30	14 ± 25	16 ± 30	17 ± 31	16 ± 30
PRA >20%**	21%	32%	20%	20%	25%	25%
PRA >80%	9%	9%	7%	9%	10%	9%
Mean HLA MM (±SD)	4.4 ± 1.5	4.6 ± 1.3	4.6 ± 1.1	3.4 ± 1.6	3.8 ± 1.7	3.8 ± 1.6
Mean Cold Time (±SD), h*	19 ± 9	18 ± 8	16 ± 11	13 ± 11	15 ± 10	17 ± 9
Mean Warm Time (±SD), min	37 ± 8	36 ± 8	36 ± 12	35 ± 10	36 ± 9	36 ± 7
Delayed graft function*	12%	18%	13%	1%	10%	10%

\*P < 0.05 for comparison within non-African Americans.

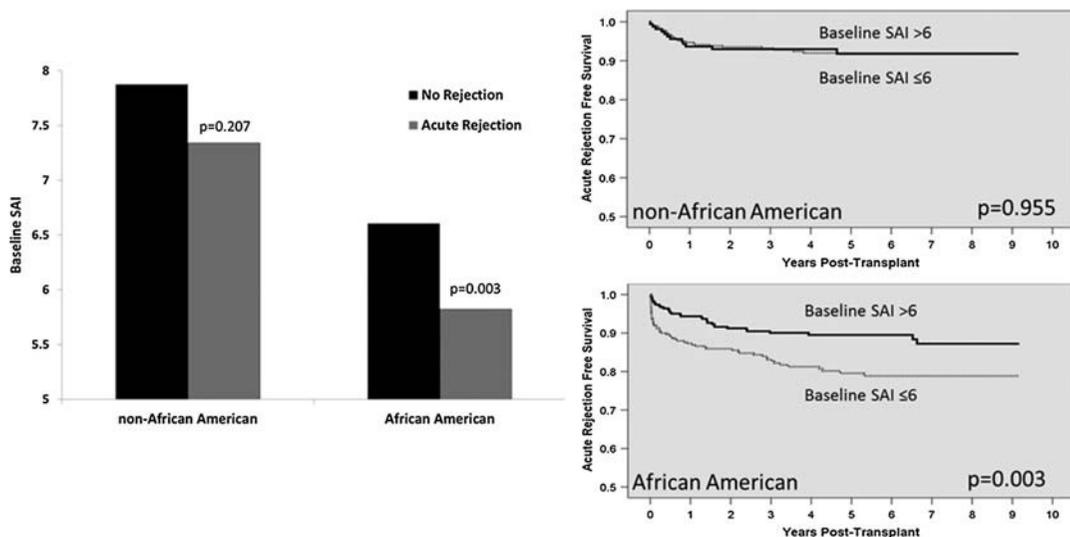
\*\*P < 0.05 for comparison within African Americans.

regression modelling using the longitudinal data demonstrated that the posttransplant SAI slope failed to predict graft loss in non-AAs (adjusted HR, 1.01; 95% CI, 0.28-3.62), whereas it was a significant predictor of graft loss in AAs (adjusted HR, 0.23; 95% CI, 0.06-0.93), such that an AA patient with a 1-point increase per year in SAI score was associated with a 77% lower risk of graft loss. For both

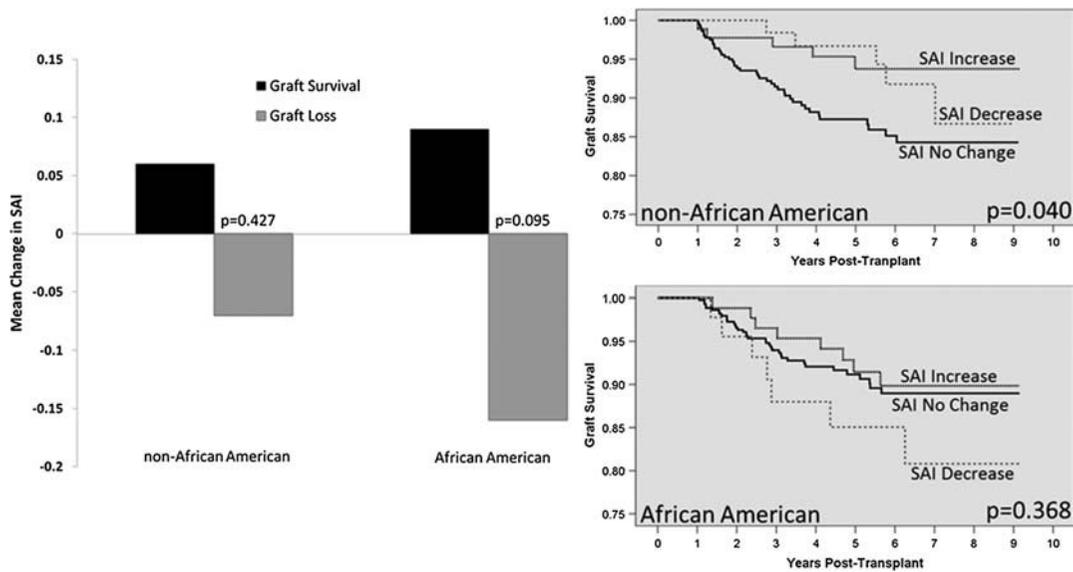
acute rejection and graft loss, an increasing SAI score was associated with reduced risk in AAs, but not in non-AAs.

**DISCUSSION**

The results of this analysis demonstrate that the impact of SES on outcomes in KTX significantly differs by race. The



**FIGURE 2.** Baseline SAI score is significantly associated with acute rejection in AAs, whereas no such association was demonstrated in non-AAs.



**FIGURE 3.** Univariate analyses assessing the association between posttransplant SAI slope and graft survival, stratified by race.

AAs with higher SES at the time of transplantation are substantially less likely to develop acute rejection, such that for a 1 point increase in the SAI, AAs have an 11% reduction in the risk of acute rejection. Concurrently, AAs that demonstrate a 1 point increase in their SAI score over 4 posttransplant years have 31% lower risk of graft loss. In non-AAs, after adjusting for confounders, the influence of SAI on clinical outcomes was not significant. These results demonstrate the substantial influence SES has on clinical outcomes within AA kidney transplant recipients and highlights the importance of focusing on interventions designed to mitigate this risk. If successful, these interventions may go a long way in reducing the racial disparity that has existed in kidney transplant since its inception.<sup>2,8,11</sup>

Previous studies have analyzed the influence of different baseline SES components on outcomes across racial cohorts, but none have done so by analyzing the change in post-transplant SES (slope change per year). Golfarb-Rumyantzev et al<sup>24</sup> used the United States Renal Data System registry to determine the influence of baseline education, citizenship, and insurance on post-transplant outcomes across race. The authors demonstrated that education and insurance were significant predictors of graft loss and patient death, with the magnitude of the association being stronger in AA recipients. This study did not analyze acute rejection rates, but did find contrary results to our study in that baseline SES factors were associated with graft loss; we found that only follow-up SAI slope was associated with graft loss. However, this comparison should be taken in context because

our analysis was conducted within single-center, whereas the Golfarb-Rumyantzev study was conducted with national data.

Butkus et al<sup>7</sup> demonstrated that graft loss due to immunologic etiologies was most prominent in young AA recipients, which was also more common in those with lower education levels and nonadherence to transplant medications. In multivariable analysis, nonadherence was the strongest risk factor for immunologic graft loss, which was associated with pre-transplant substance abuse. These results are largely similar to the findings of our study and may support biologic plausibility. It is likely that SES risk factors exert its impact on transplant outcomes through medication errors and nonadherence as intermediaries. It is interesting to note that our study found that baseline SAI was the strongest predictor of acute rejection, whereas posttransplant SAI slope predicted graft loss. We theorize that baseline SAI is a risk factor for acute rejection because it likely identifies patients that are disposed to developing medication safety events (errors and nonadherence), with these events leading to acute rejection. Posttransplant medication regimens are exceptionally complex, usually include the treatment of new or worsening comorbidities (such as diabetes or hypertension), and are often adjusted several times each week based on laboratory results.<sup>25</sup> Thus, patients with lower educational status or without strong social support networks are at substantial risk for inadvertent nonadherence.<sup>26</sup> These events are particularly troublesome in patients at higher immunologic risk, such as those that are younger, sensitized, have more HLA

**TABLE 3.** Multivariable modeling for acute rejection and graft loss, stratified by race<sup>a</sup>

Exposure	Outcome	Non-African American		African American	
		Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Baseline SAI score	Time to acute rejection	0.92 (0.81-1.05)	0.215	0.89 (0.80-0.99)	0.027
Posttransplant SAI slope (change per year)	Time to graft loss	1.01 (0.28-3.62)	0.993	0.23 (0.06-0.93)	0.039

<sup>a</sup>Multivariable models adjusted for: age, sex, baseline comorbidities (diabetes, hypertension, and cardiovascular disease), time on dialysis, retransplant, PRA, HLA mismatches, cold time, warm time, donor type, donor age, induction therapy, delayed graft function, and acute rejection (only in the graft survival analysis).

mismatches, develop delayed graft function, or receive marginal donors. As AA recipients are overrepresented in these risk groups, it is rational that these patients are at higher risk to develop deleterious clinical sequelae as a result of medication errors or inadvertent nonadherence.<sup>27-29</sup> Therefore, our finding that baseline SAI is a risk factor for acute rejection only within AA recipients is plausible in this context. Within AA recipients, immunosuppressant efficacy is more dose or concentration sensitive, thus making these patients prone to adverse events related to medication nonadherence.<sup>28,30</sup>

Posttransplant SAI slope may identify patients predisposed to nonadherence due to financial issues (cannot afford the medication or loss of insurance), loss of social support, loss of motivation or lack of understanding the importance of continued adherence to immunosuppression therapy. Thus, similar to baseline SAI, the impact of posttransplant SAI on outcomes is likely partially mediated by medication errors or nonadherence. Concordantly, AA patients are likely at higher risk for developing clinical issues secondary to nonadherence, due to having more immunologic risk factors.<sup>27</sup> It is likely that the influence of SAI on nonadherence is similar across race; yet the magnitude of nonadherence risk on adverse clinical events is more significant in AA patients.

When these results are compared to those from other countries, there are several interesting differences that are worthy of discussion. A study by Pallet et al<sup>31</sup> demonstrated a lack of racial disparities, when comparing 953 whites with 140 African Europeans at a single French transplant center. The incidence of acute rejection (31% vs 30%) and 5-year graft survival (83% in both) was similar across racial cohorts. The authors suggest that SES differences may be an important factor contributing to the racial disparities demonstrated in the United States, because SES was similar across groups in this study. Our results also support this conclusion. However, Rudge et al<sup>32</sup> demonstrated significant racial disparities within renal transplant recipients within the United Kingdom, with black patients having significantly lower 3-year graft survival. Within Canada, recent studies demonstrate similar posttransplant outcomes between whites and those of African descent,<sup>33</sup> whereas data from Australia and New Zealand demonstrate significant racial disparities comparing indigenous and nonindigenous transplant recipients.<sup>34</sup> Importantly, universal healthcare is available across all of these countries; thus, the questions as to whether components of SES influence racial disparities, at a global level, have yet to be fully answered.<sup>35</sup>

There are a number of limitations with this study that should be addressed. First, it is a retrospective analysis, and reviewing medical records for SES data is a difficult task, as this type of information is not traditionally well documented in the medical record. However, our transplant program focuses efforts to assess these socioeconomic factors during the evaluation of potential transplant recipients. Thus, baseline SAI data are easily retrievable. After transplantation, these data may be missing or not well documented. Consequently, misclassification of follow-up SAI scores is a concern. We attempted to minimize this by reviewing all available data in the medical record during the entire follow-up period, including registration information (which documents insurance, employment, and marital status at every encounter) and progress notes. The study is also a single center, and given the differences seen in these results as

compared to the Garg study,<sup>16</sup> these data may only be applicable to transplant programs with large numbers of AA patients or those with a similar distribution of socioeconomic factors. This is also the case for non-US-based transplant centers, as outcomes in patients of African descent are quite heterogeneous across different regions of the globe. Additional limitations to this retrospective study include the potential for bias and confounding. There are a large number of potential confounders that can impact acute rejection and graft loss. We attempted to account for these through the novel use of 2-stage multivariable modelling, but there are likely other variables, not in the models that influence the outcome. In particular, follow-up immunosuppression regimens, doses, and levels are likely important.

In summary, after multivariable adjustment via joint modeling, AAs with low-baseline SAI was associated with a higher risk of acute rejection, which was not demonstrated in non-AAs. The AAs with an increasing posttransplant SAI was associated with a significantly lower risk of graft loss; this was also not demonstrated in non-AAs. These data suggest that socioeconomic factors likely represent components of the causal sequence that help to explain racial disparities in KTX. Intervening to modify the impact of SES on outcomes represents a potentially promising mechanism to mitigate these disparities.

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