Donor Ethnicity and Kidney Transplant Outcomes in African Americans

Kalathil K. Sureshkumar*, Khaled Nashar, and Bhavna Chopra

Division of Nephrology and Hypertension, Medicine Institute, Allegheny General Hospital, Allegheny Health Network, Pittsburgh, Pennsylvania

ABSTRACT

Background. Transplantation of African American (AA) compared to non-AA donor kidneys is generally associated with inferior outcomes. It is unclear whether enhanced genetic risk associated with AA donor kidneys would be counterbalanced by favorable immunologic matching when AA donor kidneys are transplanted into AA recipients. We aimed to compare the outcomes of AA vs non-AA deceased-donor kidneys (DDKs) stratified by kidney donor profile index (KDPI) that were transplanted into AA recipients.

Methods. Using the Organ Procurement and Transplant Network/United Network for Organ Sharing database, we identified AA DDK recipients from 2000 to 2015 who received peri-operative induction followed by calcineurin inhibitor/mycophenolate mofetil maintenance. These patients were divided into 4 KDPI groups (0%-20%, 21%-50%, 51%-85%, and 86%-100%). Adjusted long-term graft and patient outcomes were compared between AA recipients of kidneys from AA vs non-AA donors in each KDPI category using a multivariable Cox model.

Results. Among a total of 17,516 AA DDK transplant recipients, 3303 were in KDPI 0%-20% (AA donor = 239; non-AA donor = 3064), 5821 in KDPI 21%-50% (AA donor = 1414; non-AA donor = 4407), 6364 in KDPI 51%-85% (AA donor = 1619; non-AA donor = 4745), and 2028 in KDPI 86%-100% (AA donor = 932; non-AA donor = 1096) groups. Adjusted overall graft, death-censored graft, and patient survival were similar between AA recipients of AA vs non-AA donor kidneys across all KDPI groups.

Discussion. Our study showed similar outcomes for transplanting AA vs non-AA deceased-donor kidneys into AA recipients despite the generally observed inferior outcomes associated with AA donor kidney transplantation.

AFRICAN Americans (AAs) are at increased risk for developing kidney diseases. Around 32% of patients with end-stage renal disease were of AA ethnicity even though they constitute only 13% of the United States population based on a 2010 United States Renal Data System annual report [1]. Genetic predispositions such as the presence of apolipoprotein L1 gene (*APOL1*) renal risk variants and sickle cell trait could be contributing to this higher risk, in addition to cultural and socioeconomic factors [2,3]. Earlier studies have shown inferior outcomes associated with transplantation of AA donor compared to non-AA donor kidneys [4–6]. It is unclear whether enhanced genetic risk associated with AA donor kidneys would be counterbalanced by favorable immunologic matching when AA donor kidneys are transplanted into AA recipients. We aimed to compare the outcomes of AA vs non-AA deceased-donor kidneys (DDKs) stratified by kidney donor profile index (KDPI) that were transplanted into AA recipients.

The data reported here have been supplied by the United Network for Organ Sharing as the contractor for the Organ Procurement and Transplant Network. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by Organ Procurement and Transplant Network or the US Government.

*Address correspondence to Kalathil K. Sureshkumar, MD, FRCP (Glasgow), FASN, Division of Nephrology and Hypertension, Allegheny General Hospital, 320 East North Avenue, Pittsburgh, PA 15212. E-mail: kalathil.sureshkumar@ahn.org

0041-1345/20
https://doi.org/10.1016/j.transproceed.2020.06.042

Table 1. Demographic Characteristics of the Study Population by KDPI Groups

	KDPI 0%-20%		KDPI 21%-50%		KDPI 51%-85%		KDPI 85%-100%	
	AA Donor n = 239	Non-AA Donor n = 3064	AA Donor n = 1414	Non-AA Donor n = 4407	AA Donor n = 1619	Non-AA Donor n = 4745	AA Donor n = 932	Non-AA Donor n = 1096
Donor age (mean years ± SD)	19 ± 3	23 ± 6*	24 ± 8	35 ± 11*	39 ± 14	47 ± 14*	53 ± 13	62 ± 9*
Donor gender (male, %)	85	75*	75	62*	51.7	51.8	44.5	42.9
KDPI (%)	16 ± 6	10 ± 3*	34.6 ± 8	35.4 ± 9†	70 ± 10	67 ± 10†	93 ± 4	92 ± 4†
ECD (%)	0	0	0	0.03	4.9	23.9*	64	90*
DCD (%)	0.3	8.5*	4.6	15*	6.1	15.2*	5.9	9.6†
HLA mismatch	4.2 ± 1.5	4.4 ± 1.4‡	4.0 ± 1.6	4.4 ± 1.3*	4.1 ± 1.5	4.5 ± 1.3*	4.5 ± 1.3	4.7 ± 1.1†
Recipient age (mean years ± SD)	45 ± 13	46 ± 13	46 ± 13	49 ± 12*	50 ± 12	52 ± 12*	55 ± 11	59 ± 10†
Recipient diabetes (%)	36.7	37.1	32.9	33.2	33.4	35.2	41.9	48†
Dialysis duration (months ± SD)	54 ± 44	55 ± 42	57 ± 46	59 ± 43	64 ± 47	60 ± 44*	56 ± 37	50 ± 34‡
Calculated PRA	23 ± 35	19 ± 32†	24 ± 36	18 ± 32*	23 ± 35	15 ± 28*	13 ± 27	8 ± 20*
Cold ischemia time (hours)	15 ± 8	16 ± 8	16 ± 8	17 ± 9*	18 ± 9	18 ± 9	19 ± 10	19 ± 9
Kidney on pump	17.5	28*	27.2	35.5*	35.9	43.4*	53.5	56
Delayed graft function (%)	13.8	19.8‡	19.7	31.3*	29.6	36.9*	36.7	36.8
Induction type (depleting, %)	75	76	79	77	80.9	76.6*	78.5	77.5
Steroid maintenance (%)	78	77	78	77	75	77	72.8	75.7
Previous transplant (%)	16	11.4	14.2	10.3*	13	8.6*	7.2	4.2†
Transplant year	2008 ± 4	2008 ± 4	2009 ± 4	2009 ± 4	2009 ± 4	2009 ± 4	2008 ± 4	2009 ± 3

Abbreviations: AA, African American; DCD, donation after cardiac death; ECD, expanded criteria donor; KDPI, kidney donor profile index; PRA, panel-reactive antibody.
*$P < .001$.
†$P < .005$.
‡$P < .05$.

MATERIALS AND METHODS

The study protocol was approved by the Institutional Review Board. Using the Organ Procurement and Transplant Network/United Network for Organ Sharing database, we identified DDK transplant recipients from January 2000 to December 2015 who were of AA ethnicity and received peri-operative induction followed by calcineurin inhibitor/mycophenolate mofetil maintenance along with/without steroids. These patients were subsequently divided into 4 KDPI groups (0%-20%, 21%-50%, 51%-85%, and 86%-100%). KDPI was implemented in December 2014 for grading and allocation of DDKs in the United States and can be calculated retrospectively [7]. AA donor ethnicity is 1 of 10 risk variables used in calculating the KDPI score, which ranges from 0% to 100%, with lower scores reflecting better quality kidneys and improved projected long-term outcomes [8]. Patients who received no induction or different maintenance immunosuppression were excluded from our analysis.

Adjusted long-term graft and patient outcomes were compared between AA recipients of kidneys from AA vs non-AA donors in each KDPI category using a multivariable Cox model. A graft was considered failed when the patient went back on maintenance dialysis, was retransplanted, or died. Values are expressed as hazard ratios with 95% confidence intervals. Covariates included in the analysis were as follows: donor related including age, sex, expanded criteria donor kidney, donation after cardiac death kidney, and cause of donor death; recipient related including age, diabetes mellitus, dialysis duration, panel-reactive antibody titer, previous transplant, and human leukocyte antigen mismatch; transplant related including type of induction, cold ischemia time, kidney on pump, delayed graft function (defined as the need for dialysis within the first week after transplantation), and steroid maintenance. Values are expressed as either mean ± standard deviation or as percentages. A P value $<.05$ was considered statistically significant. Statistical analysis was performed using SPSS v18 (IBM, Armonk, NY, United States).

RESULTS

Median follow-up of the whole study group was 48.1 months (range, 20.7-83.7 months). Among a total of 17,516 AA kidney transplant recipients, 3303 were in the KDPI 0%-20% group (AA donor = 239; non-AA donor = 3064), 5821 were in the KDPI 21%-50% group (AA donor = 1414; non-AA donor = 4407), 6364 were in the KDPI 51%-85% group (AA donor = 1619; non-AA donor = 4745), and 2028 were in the KDPI 86%-100% group (AA donor = 932;

Table 2. Adjusted Graft and Patient Outcomes

	KDPI 0%-20% AA Donors, n = 239 Non-AA Donors, n = 3064		KDPI 21%-50% AA Donors, n = 1414 Non-AA Donors, n = 4407		KDPI 51%-85% AA Donors, n = 1619 Non-AA Donors, n = 4745		KDPI 85%-100% AA Donors, n = 932 Non-AA Donors, n = 1096	
Outcomes	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Adjusted overall graft survival	1.09 (0.95-1.26)	.24	1.01 (0.95-1.08)	.68	1.04 (0.98-1.10)	.17	1.05 (0.97-1.14)	.25
Adjusted death-censored graft survival	1.00 (0.83-1.21)	.99	1.03 (0.95-1.12)	.50	1.01 (0.94-1.09)	.75	1.08 (0.98-1.19)	.11
Adjusted patient survival	0.74 (0.52-1.04)	.08	1.00 (0.84-1.19)	1.00	0.86 (0.75-1.00)	.50	0.94 (0.76-1.16	.57

Abbreviations: AA, African American; CI, confidence interval; HR, hazard ratio; KDPI, kidney donor profile index.

non-AA donor = 1096). Demographic characteristics of the different KDPI groups are shown in Table 1. AA donors were younger and had higher average KDPI values across all KDPI groups; there were more male donors in the first 2 KDPI groups compared to non-AA donors. There were more donation after cardiac death kidneys among non-AA donors, with higher levels of HLA mismatches and more kidneys on pump, and recipients of AA kidneys included more patients with previous transplants and higher panel-reactive antibody levels. When compared to AA donor kidneys, a higher proportion of non-AA donor kidneys were expanded criteria donor in the last 2 KDPI groups. Recipients of non-AA donor kidneys in the last 3 KDPI groups were older, and there were more recipients with diabetes in the 86%-100% KDPI group compared to recipients of AA donor kidneys. Recipients of AA donor kidneys had longer dialysis vintage in the last 2 KDPI groups, and delayed graft function was higher among recipients of non-AA donor kidneys in the first 3 KDPI groups.

Adjusted overall graft, and death-censored graft, survivals were similar between AA recipients of AA vs non-AA donor kidneys across all KDPI groups, as shown in Table 2. Table 1. Similarly, adjusted patient survival for AA recipients of AA vs non-AA donor kidneys was similar among all KDPI groups (Table 2).

DISCUSSION

Our analysis showed similar adjusted graft survival following transplantation of AA vs non-AA donor kidneys into AA recipients in all KDPI categories of donor kidneys. There were also no significant differences in patient survival following transplantation of AA vs non-AA donor kidneys into AA recipients.

Previous studies have demonstrated inferior graft outcomes associated with transplantation of AA vs non-AA donor kidneys [4–6]. Though AA ethnicity is adjusted as a variable in calculating KDPI, graft outcomes were found to be inferior with AA compared to non-AA donor kidneys among KDPI 51%-85% and 86%-100% categories [5]. Other unmeasured variables such as the presence of 2 *APOL1* renal risk variants and sickle cell trait are possible explanations for these findings [2,3]. About 13% of the AA population is thought to harbor 2 *APOL1* renal risk variants. When compared to AA donors with 1 or no *APOL1* renal risk variants, kidney transplants from AA donors who possessed 2 *APOL1* renal risk variants experienced shortened graft survival [2,9]. In fact, graft survivals were similar for kidneys from AA donors with 1 or 0 *APOL1* risk variants compared to kidneys recovered from European American donors [10]. Transplant outcomes were unaffected by the presence of 2 *APOL1* risk variants in kidney transplant recipients [11]. The ongoing National Institutes of Health–initiated prospective *APOL1* Long-Term Kidney Transplantation Outcomes Network study will shed further light on the impact of the *APOL1* genotype on the outcomes of living and deceased AA donor kidney transplants in the United States (NCT 03615235) [12]. Another potential reason for inferior outcomes with AA compared to non-AA donor kidney transplantation is the higher prevalence of sickle cell trait in the AA population, which is associated with a faster decline in kidney function [3].

It is interesting to note in this context that our current study found similar graft and patient outcomes following transplantation of AA vs non-AA donor kidneys into AA recipients. Similar outcomes of AA vs non-AA donor kidney transplantation into AA recipients could likely be due to balancing of unfavorable genetic risks in AA donor kidneys with favorable ethnicity-related immunologic matching in AA donor-recipient combination. It is also possible that the adverse influence of genetic, immunologic, pharmacokinetic, and possibly socioeconomic factors in AA recipients could have masked any favorable effects of non-AA donor kidneys transplanted into AA recipients.

Our study has limitations. The retrospective design of our study can only suggest associations but cannot prove causation. We cannot exclude residual confounding despite using an adjusted model. The database lacks granularity on factors such as immunosuppressive medication doses and drug levels, which can affect transplant outcomes. However, a large number of patients nationally adds to the validity of our findings.

In conclusion, our study demonstrates similar outcomes for transplanting AA vs non-AA deceased-donor kidneys into AA recipients despite the generally observed inferior outcomes associated with AA donor kidney transplantation.

REFERENCES

[1] US Renal Data System. USRDS 2010 annual data report: atlas of chronic kidney disease and end stage renal disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2010.

[2] Freedman BI, Julian BA, Pastan SO, et al. Apolipoprotein L1 gene variants in deceased organ donors are associated with renal allograft failure. Am J Transplant 2015;15:1615–22.

[3] Olaniran KO, Allegretti AS, Zhao SH, et al. Kidney function decline among black patients with sickle cell trait and sickle cell disease: an observational study. J Am Soc Nephrol 2020;31:393–404.

[4] Swanson SJ, Hypolite IO, Agodoa LY, et al. Effect of donor factors on early graft survival in adult cadaveric renal transplantation. Am J Transplant 2002;2:68–75.

[5] Sureshkumar KK, Chopra B. Impact of donor ethnicity on long-term kidney transplant outcomes: analysis by kidney donor profile index categories. Exp Clin Transplant 2020;18:144–8.

[6] Molnar MZ, Kovesdy CP, Bunnapradist S, et al. Donor race and outcomes in kidney transplant recipients. Clin Transplant 2013;27:37–51.

[7] Organ Procurement and Transplantation Network. Policy 8: allocation of kidneys. http://optn.transplant.hrsa.gov/ContentDocuments/OPTN_Policies.pdf. accessed 01.05.20.

[8] Chopra B, Sureshkumar KK. Changing organ allocation policy for kidney transplantation in the United States. World J Transplant 2015;5:38–43.

[9] Freedman BI, Pastan SO, Israni AK, et al. APOL 1 genotype and kidney transplant outcomes from deceased African American donors. Transplantation 2016;100:191–202.

[10] Department of Health and Human Services. Organ Procurement and Transplant Network. OPTN/SRTR 2010 annual data report. Rockville, MD: OPTN/SRTR; 2011.

[11] Lee BT, Kumar V, Williams TA, et al. The *APOL1* genotype of African American kidney transplant recipients does not impact 5-year allograft survival. Am J Transplant 2012;12:1924–8.

[12] *APOL1* Long-Term Kidney Transplantation Outcomes Network (APOLLO) clinical centers: (Collaborative U01). Bethesda, MD: National Institutes of Health; 2017. NCT 03615235.