



## Donor Family History of ESKD and Long-term Outcomes Among African American Living Kidney Donors: A Retrospective Cohort Study

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**Rationale & Objective:** Live kidney donation is associated with a small increased risk for kidney disease and hypertension in African American donors. We investigated a possible association between donor family history of end-stage kidney disease (ESKD) and their postdonation kidney function and the development of hypertension. We tested whether this association was modified by kidney donation.

**Study Design:** Retrospective cohort.

**Setting & Participants:** Former African American live kidney donors between 1993 and 2010. Healthy nondonors were selected from the Coronary Artery Disease in Young Adults (CARDIA) Study.

**Exposure:** Family history of ESKD in a first-degree relative.

**Outcomes:** Kidney function and blood pressure  $\geq$  140/90 mm Hg or use of antihypertensive medications at follow-up.

**Analytical Approach:** Donors were grouped based on family history of ESKD. Outcomes were first compared between donor groups and then between donors and healthy nondonors matched for demographics, follow-up time, and family history. A mixed-effect model was used to compare outcomes.

**Results:** Of 179 donors, 139 (78%) had a first degree relative with ESKD. Predonation characteristics were similar between the 2 groups. At a median follow-up of 11 years postdonation, there was no difference in postdonation estimated glomerular filtration rates ( $68 \pm 19$  vs  $69 \pm 13$  mL/min/1.73 m<sup>2</sup>;  $P = 0.71$ ) and the presence of albuminuria ( $P = 0.16$ ). There was a trend toward a higher incidence of hypertension (51% vs 35%;  $P = 0.08$ ) among donors with a family history of ESKD than for those without. Although there was no difference in annual change in estimated glomerular filtration rate ( $P = 0.17$ ), the risk for hypertension was higher in donors than nondonors (relative risk, 2.44 [95% CI, 1.56–3.84]), but there was no interaction by family history ( $P = 0.11$ ).

**Limitations:** Retrospective small study. Lack of data across donor-recipient specific biological relationship.

**Conclusions:** Family history of ESKD is not associated with postdonation kidney function among African American kidney donors. Live kidney donation is associated with an increased risk for hypertension among African Americans, independent of donor family history of ESKD.

### Visual Abstract included

Complete author and article information provided before references.

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Transplantation offers patients with end-stage kidney disease (ESKD) a longer life with renewed freedom, productivity, and quality of life.<sup>1-3</sup> The number of people in need of a transplant continues to increase and there are too few deceased donors to meet the demand.<sup>4</sup> The alternative, a transplanted kidney from a living donor, offers advantages of superior rates of kidney allograft and patient survival.<sup>5,6</sup> As we encourage live kidney donation, it is essential that we continue to improve our current knowledge on long-term risks associated with donor nephrectomy across all races.

Recent studies suggest that there are racial differences in long-term outcomes.<sup>7,8</sup> We reported a higher risk for postdonation hypertension in African American donors compared with nondonors with similar indicators of baseline health.<sup>9</sup> Muzaale et al<sup>8</sup> reported a 15-year higher cumulative incidence of ESKD in African American donors (0.75%) than non-African American donors (0.25%) and was also noted to be higher in donors biologically related to their recipients (0.34%) when compared with unrelated donors (0.15%). A recent retrospective national study from a large database reported a higher risk for ESKD among

biologically related donors, and the magnitude of this increased risk varied by racial groups and type of biological relationship between donor and recipient.<sup>10,11</sup> These findings suggest that the poor kidney outcomes observed in a small proportion of donors could be explained by the effects of donation and their familial predisposition.

Genetic variants in apolipoprotein L1 (APOL1) are thought to explain part of this increased risk for nondiabetic kidney disease among African Americans.<sup>12</sup> It is possible that the increased risk for ESKD in donors may be partially explained by APOL1 variants that are shared between the donor and their related recipient. Our current knowledge of the impact of APOL1 variants on postdonation kidney function is limited<sup>13</sup> and therefore APOL1 testing is not routinely used for donor selection. The National Institutes of Health–initiated prospective study encompassing all live African American kidney donors in United States, APOL1 Long-term Kidney Transplantation Outcomes Network (APOLLO), is designed to address some of these issues.<sup>14</sup> Until results of such studies are available, family history remains an important tool in donor selection.

**PLAIN-LANGUAGE SUMMARY**

African American live kidney donors are at higher risk for developing kidney disease than nondonors, particularly if related to their recipient. We compared the kidney function of 179 former African American live kidney donors based on their family history of kidney disease and compared it with healthy nondonor controls. We report no difference in kidney function at 11 years postdonation and a trend of higher risk for hypertension in donors with a family history of kidney disease (51% vs 35%;  $P = 0.08$ ). Two donors developed end-stage kidney disease; both were related to their recipient. Compared with nondonors, we found no difference in annual change in kidney function but a higher risk for hypertension in donors regardless of family history. Our study shows no impact of donor family history on postdonation kidney function in African Americans.

We assembled a cohort of former African American living donors to determine whether live kidney donation amplifies the risk for kidney disease and hypertension associated with a family history of ESKD in a first-degree relative.

**METHODS****Design and Setting**

We conducted a retrospective cohort study of African American live kidney donors who donated between 1993 and 2010 at 2 transplantation centers in Detroit, MI (Harper University Hospital and Henry Ford Hospital). The study protocol was approved by the institutional review board at both recruitment sites (approval numbers 015907MP4F and 5901, respectively). All donors provided written informed consent. The reporting of this study follows guidelines set out for observational studies.<sup>15</sup>

**Patients****Live Kidney Donors**

We identified 249 African American live kidney donors with blood pressure < 140/90 mm Hg (average of 3 readings), not using antihypertensive medications, not diabetic, estimated glomerular filtration rate (eGFR)  $\geq 80$  mL/min/1.73 m<sup>2</sup> using predonation serum creatinine values, and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) study equation or 24-hour urine for creatinine clearance  $\geq 80$  mL/min.<sup>16,17</sup> Five donors died during follow-up and were excluded.

Race determination was based on self-declaration. First-degree donor-recipient relationship was defined as a biological parent, child, or full sibling, as reported by the

donor. If the donor was unrelated to the recipient, the medical chart was reviewed to determine if they had a first-degree relative receiving dialysis or with a kidney transplant, and if they did, they were considered to have a family history of ESKD.

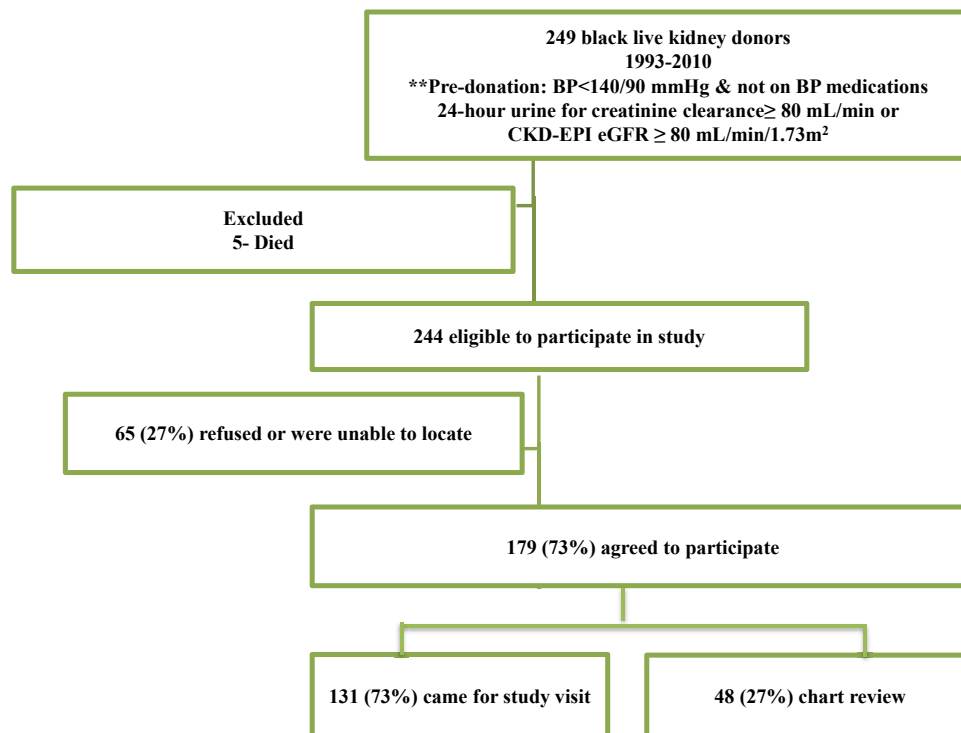
Of the 244 donors, 179 (73%) agreed to participate. Of the 65 (27%) who did not participate, 4 refused, 48 could not be contacted, and 13 could not come for an in-person interview and had no recent medical follow-up or records. Of the 179 donors who agreed to participate, 131 donors came to the study site for an interview and the remaining 48 donors gave permission to review their recent medical records (Fig 1).

At follow-up, participants were asked to complete a health questionnaire and provide blood and urine samples. Blood pressure was measured in accordance with the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines, and the average of 3 readings was recorded.<sup>18</sup> For the 48 donors who were not able to come for a study visit, we obtained recent records from their primary care physician's office. Medical records of all participants were reviewed to obtain serum creatinine values from 12 months postdonation (allowing for kidney compensation) until last follow-up time, and eGFR was calculated for each of those time points using the CKD-EPI formula. All donors were queried to determine whether they received dialysis/transplant, and when this situation occurred, follow-up time was truncated at time of ESKD onset. Their last serum creatinine value before starting dialysis was used to compute eGFR. The United Network for Organ Sharing (UNOS) was contacted by each participating center to determine whether any of their donors who had donated during the study period were on a transplant list or received a kidney transplant.

**Nondonor Controls**

A comparable group of African Americans were selected from the Coronary Artery Risk Development in Young Adults (CARDIA) cohort study.<sup>19</sup> In brief, the study, initiated in 1985, enrolled 2,637 African Americans aged 18 to 30 years to examine the cause and natural history of cardiovascular disease. At their most recent interview in 2010, participants were queried regarding family history of ESKD (dialysis/transplant) in a biological parent, child, or full sibling. After reviewing records of 2,637 participants, only 958 (36%) CARDIA participants fulfilled the restriction criteria to be considered suitable for live kidney donation.

The second step consisted of finding nondonors who matched donors with regard to age, sex, blood pressure, duration of follow-up, and first-degree relative with ESKD. A total of 60 nondonors from the 1985 CARDIA examination cohort were initially matched to 60 living kidney donors. This process was repeated with the 1995, 2000, and 2005 examination cohorts to find suitable controls.



**Figure 1.** Flow chart of participants. Abbreviations: BP, blood pressure; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate.

Some controls were selected more than once from different examination years and had different baseline examination and follow-up times. None of the controls were used twice from the same cohort. In total, 161 nondonors were successfully matched to the 161 donors (Fig S1). Fifty-one (32%) controls were used more than once but from different examination years and therefore, for any given CARDIA examination year, there were no duplicate controls. Of the 18 donors excluded from the main analyses, 11 donors could not be matched to nondonors for follow-up time.

Serum creatinine values from subsequent CARDIA examination years were used to calculate eGFR at various time points using the CKD-EPI formula. Serum creatinine was measured using an enzymatic assay. Information on the need for dialysis/transplant among CARDIA participants was also ascertained from their most recent follow-up interviews.

### Groups by Family History of ESKD

Both donors and nondonors were grouped based on family history of ESKD in a first-degree relative.

### Outcomes

The primary outcome was kidney function and hypertension at follow-up. Kidney function was measured as eGFR using the CKD-EPI formula. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or the use of antihypertensive medications. Secondary outcomes were: (1) rate of decline

in kidney function assessed by average annual change in eGFR from 1 year postdonation until last follow-up, and (2) albuminuria assessed using urinary albumin-creatinine ratio (UACR) and defined as random UACR ≥ 30 mg/g.<sup>20</sup>

Donors and nondonors were assessed for these outcomes at follow-up. We considered the predonation or baseline assessment (which depended on the year of selection) as time zero (ie, start of follow-up) for donors and nondonors, respectively.

### Statistical Analysis

Data are presented as mean ± standard deviation for normally distributed data and median with interquartile range (IQR) for nonparametric data. We assessed differences in baseline characteristics between groups using independent-sample t tests, Mann-Whitney U test, Fisher exact tests before matching, paired t tests, Wilcoxon signed rank test, McNemar test, or Mantel-Haenszel test, as appropriate after matching. We used the “greedy nearest neighbor” matching algorithm<sup>21</sup> to match nondonors to donors at a 1:1 ratio by the following characteristics: age (5-year intervals), sex, duration of follow-up (5-year intervals), systolic blood pressure (15-mm Hg interval), and family history of ESKD in a first-degree relative (no vs yes). The number of available eligible nondonors determined the donor sample size. The paired t tests or Wilcoxon signed rank test were used, as appropriate, to compare blood pressure, eGFR, and UACR at follow-up. A mixed-effect model with repeated measures was used to compare the

eGFR decline rate between donors with and without a family history of ESKD in which baseline eGFR was included and follow-up time was treated as a continuous variable. A modified Poisson model was also used to calculate the relative risk for hypertension with nondonors as reference. Analyses were adjusted for differences in health insurance, income, and education between the 2 groups. We tested for interaction in the matched donor/nondonor outcomes to see whether the effects were modified by the presence of a family history of ESKD in a first-degree relative. All tests of statistical significance were 2-tailed tests, and we interpreted  $\alpha < 0.05$  as statistically significant. We used SAS, version 9.4 (SAS Institute) to perform the analyses.

## RESULTS

A total of 179 donors were studied at a median of 11 (25th, 75th percentile, 8.3, 12.7) years after donation. Mean age at donation was  $37 \pm 9$  years, 114 (64%) were women, and 139 (78%) had a family history of ESKD in a first-degree relative. At follow-up, 64 (36%) had eGFRs  $< 60$  mL/min/1.73 m<sup>2</sup>, 84 (47%) donors had hypertension, 18 (10%) had albuminuria, and 2 (1.12%) had developed ESKD. The proportion of donors who had hypertension and eGFRs  $< 60$  mL/min/1.73 m<sup>2</sup> did not differ by type of follow-up, whether it was a study visit or a chart review ( $P = 0.68$  and  $P = 0.19$ , respectively).

### Impact of Donor Family History of ESKD in a First-Degree Relative on Outcomes

Baseline characteristics between donors with and without a family history of ESKD in a first-degree relative were similar except that donors with a positive family history of ESKD also were more likely to have a family history of hypertension (Table 1).

At follow-up (Table 2), there was no difference in eGFRs ( $68 \pm 19$  vs  $69 \pm 13$  mL/min/1.73 m<sup>2</sup>;  $P = 0.71$ ) and the proportion of donors with eGFRs  $< 60$  mL/min/1.73 m<sup>2</sup> (39% vs 28%;  $P = 0.18$ ) between donors with and without a family history of ESKD in a first-degree relative. The rate of decline in postdonation eGFRs did not differ between the 2 groups of donors (family history of ESKD positive vs negative, 0.7 [95% CI, 0.3-1.1] vs 0.1 [95% CI, 0.06-0.8] mL/min/1.73 m<sup>2</sup> per year;  $P = 0.17$ ). Of the 2 donors who developed ESKD, 1 donated to her mother, developed hypertension and proteinuria postdonation, and presented with ESKD 12 years after donation; the other had donated to his full brother and developed ESKD due to focal segmental glomerulosclerosis 18 years after donation. Both have received a kidney transplant. Per UNOS, of our study cohort of 249 donors, 5 donors had died and 2 donors reached ESKD and received a kidney transplant. None of the donors died of kidney causes. Both these donors with ESKD who received a kidney transplant participated in our study.

**Table 1.** Predonation Characteristics of Living Kidney Donors Stratified by Family History of ESKD in a First-Degree Relative

	Family History of ESKD in a First-Degree Relative		P
	Yes (N = 139)	No (N = 40)	
Age, y	37 ± 9	38 ± 9	0.64
Women	87 (63%)	26 (65%)	0.82
Weight, kg	83 ± 18	86 ± 17	0.44
Body mass index, kg/m <sup>2</sup>	29 ± 6	30 ± 5	0.53
Systolic blood pressure, mm Hg	120 ± 10	119 ± 10	0.51
Diastolic blood pressure, mm Hg	73 ± 8	74 ± 7	0.74
Serum creatinine, mg/dL	0.9 ± 0.2	0.9 ± 0.2	0.74
eGFR, mL/min/1.73 m <sup>2</sup>	108 ± 21	107 ± 16	0.85
Fasting blood glucose, mg/dL	81 ± 12	80 ± 12	0.65
Medical insurance, yes	91 (66%)	29 (73%)	0.45
Highest education			0.17
0-8th grade	5 (4%)	0 (0%)	
9-11th grade	28 (20%)	9 (22%)	
High school	54 (39%)	10 (25%)	
Some college	40 (29%)	14 (35%)	
Bachelors degree	7 (5%)	6 (15%)	
Postgraduate	4 (3%)	1 (3%)	
Individual income			0.80
<\$12,000	22 (16%)	5 (13%)	
\$12,000-\$25,000	40 (29%)	13 (32%)	
>\$25,000	76 (55%)	22 (55%)	
Employed, full- or part-time, yes	110 (79%)	36 (90%)	0.10
Family history of hypertension, yes	111 (80%)	19 (48%)	0.001

Note: Data are presented as mean ± standard deviation or number (percent). Family history of hypertension refers to a first-degree relative with hypertension. Conversion factors for units: serum creatinine in mg/dL to  $\mu$ mol/L,  $\times 88.4$ . Abbreviations: eGFR, estimated glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration equation; ESKD, end-stage kidney disease.

Although there was no statistical difference, there was a trend in higher systolic blood pressures ( $131 \pm 17$  vs  $125 \pm 16$  mm Hg;  $P = 0.06$ ), change in systolic and diastolic blood pressures since donation, and prevalence of hypertension (50% vs 35%;  $P = 0.08$ ) and albuminuria (12% vs 3%;  $P = 0.06$ ) among donors with a positive family history of ESKD in a first-degree relative.

### Comparison of Outcomes Between Donors and Nondonors Matched for Family History of ESKD

Of the 179 living kidney donors, 161 had a suitable matched nondonor control and were included in further analysis. Baseline characteristics of the 161 donors and 161 matched nondonors are summarized in Table 3. The groups were well matched on all characteristics except socioeconomic variables. The nondonors were more likely to have health insurance, a higher level of education, and a higher income than the donors. Donors and nondonors were assessed at a median of 10.4 (IQR, 7.9-12.3) and 9.9

**Table 2.** Postdonation Outcomes of Living Kidney Donors Stratified by Family History of ESKD in a First-Degree Relative

	Family History of ESKD in a First-Degree Relative		P
	Yes (N = 139)	No (N = 40)	
Time since donation, y	10.9 [8.5 to 13.1]	10.1 [7.5 to 12.1]	0.09
Postdonation weight, kg	89 ± 19	86 ± 18	0.43
Change in weight since donation, kg	+5 [0 to 13]	+2 [-5 to 5]	0.01
Serum creatinine, mg/dL	1.3 ± 0.5	1.2 ± 0.2	0.31
eGFR, mL/min/1.73 m <sup>2</sup>	68 ± 19	69 ± 13	0.71
eGFR < 60 mL/min/1.73 m <sup>2</sup>	54 (39%)	11 (28%)	0.18
eGFR < 45 mL/min/1.73 m <sup>2</sup>	14 (10%)	1 (2.5%)	0.19
eGFR < 30 mL/min/1.73 m <sup>2</sup>	4 (2.8%)	1 (2.5%)	1.00
ESKD	2 (1.4%)	0 (0%)	0.44
UACR, mg/g	4.6 [0.4 to 11.6]	3.6 [0 to 0.16]	0.16
Albuminuria	17 (12%)	1 (3%)	0.06
Systolic blood pressure, mm Hg	131 ± 17	125 ± 16	0.06
Change in systolic blood pressure since donation, mm Hg	+11 ± 17	+6 ± 16	0.06
Diastolic blood pressure, mm Hg	84 ± 25	79 ± 12	0.26
Change in diastolic blood pressure since donation, mm Hg	+8 ± 13	+5 ± 13	0.06
Hypertension	70 (50%)	14 (35%)	0.08

Note: Data are presented as mean ± standard deviation, median [25th-75th percentile], or number (percent). Conversion factors for units: serum creatinine in mg/dL to μmol/L, ×88.4. Hypertension is defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or the use of antihypertensive medications. Albuminuria defined as UACR ≥ 30 mg/g. Abbreviations and Definitions: eGFR, estimated glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration equation; ESKD, end-stage kidney disease defined as receipt of dialysis or transplant; UACR, spot urine albumin-creatinine ratio.

(IQR, 5.4-14) years after donation or cohort entry, respectively.

As anticipated, at follow-up, eGFRs were lower in donors than nondonors (69 ± 18 vs 108 ± 16 mL/min/1.73 m<sup>2</sup>; P < 0.01) due to unilateral nephrectomy. As shown in Fig 2, the rate of decline in eGFR was similar between donors and nondonors, grouped by family history of ESKD in a first-degree relative. After adjusting for socioeconomic differences, there was no difference in the rate of change in eGFR in the 2 groups (donors vs nondonors, 0.4 [95% CI, 0.1-0.7] vs 0.6 [95% CI, 0.3-0.8] mL/min/1.73 m<sup>2</sup> per year; =0.25). Median UACR was similar in donors and nondonors (3.8 [IQR, 0.2-10.5] vs 4.9 [IQR, 3.7-7.7] mg/g; P = 0.08). The incidence of albuminuria was higher but the difference was not statistically significant (15 [10.7%] vs 6 [4.2%]; P = 0.06). Two donors developed

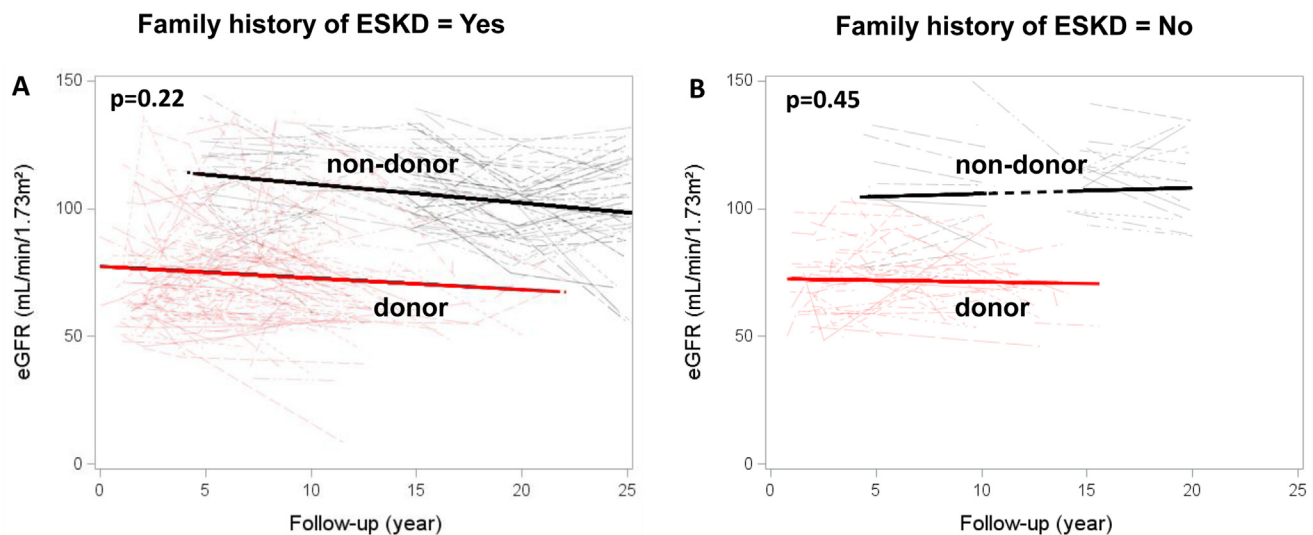
**Table 3.** Comparison of Baseline Characteristics of Donors and Nondonors Matched by Family History of ESKD in a First-Degree Relative

	Donors (N = 161)	Nondonors (N = 161)
Age, y	36 ± 8	35 ± 8
Women	65%	65%
Weight, kg	83 ± 18	82 ± 18
Body mass index, kg/m <sup>2</sup>	29 ± 6	29 ± 6
Systolic blood pressure, mm Hg	119 ± 10	117 ± 9
Diastolic blood pressure, mm Hg	73 ± 8	74 ± 9
Serum creatinine, mg/dL	0.89 ± 0.18	0.87 ± 0.15
CKD-EPI eGFR, mL/min/1.73 m <sup>2</sup>	109 ± 19	113 ± 14
Medical insurance, yes	111 (69%)	134 (83%)
Highest education		
0-8th grade	5 (3%)	0 (0%)
9-11th grade	32 (20%)	5 (3%)
High school	58 (36%)	64 (40%)
Some college	50 (31%)	58 (36%)
Bachelor degree	13 (8%)	26 (16%)
Postgraduate	3 (2%)	8 (5%)
Individual income		
<\$12,000	26 (16%)	13 (8%)
\$12,000-\$25,000	45 (28%)	19 (12%)
>\$25,000	90 (56%)	137 (85%)
Employed, full- or part-time, yes	142 (88%)	147 (91%)
First-degree relative with ESKD, yes	122 (76%)	122 (76%)
Family history of hypertension, yes	119 (74%)	116 (72%)
Duration of follow-up, y	10.4 [7.9-12.3]	9.9 [5.4-14]

Note: Data are presented as mean ± standard deviation, median [25th-75th percentile], or number (percent). Donors and nondonors were matched on the following characteristics: age (5-year interval), sex, duration of follow-up (5-year interval), systolic blood pressure (15-mm Hg interval), and family history of ESKD in a first-degree relative (no vs yes). Conversion factors for units: serum creatinine in mg/dL to μmol/L, ×88.4. Abbreviations and Definitions: CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate using the CKD-EPI equation; ESKD, end-stage kidney disease.

ESKD and both were first-degree relatives of the recipient. None of the controls developed ESKD.

Disregarding antihypertensive medication use, follow-up systolic and diastolic blood pressure levels were higher in donors compared with nondonors (systolic, 128 ± 15 vs 121 ± 16 mm Hg; P < 0.001; diastolic, 82 ± 24 vs 77 ± 11 mm Hg; P = 0.01). The incidence of hypertension was higher in donors compared with nondonors (67/161 [42%] vs 31/161 [19%]; P < 0.001). As shown in Table 4, the relative risk for hypertension in donors compared with nondonors (2.16 [95% CI, 1.50-3.10]) was not meaningfully altered after adjusting for baseline differences in health insurance, income, and education between the 2 groups (2.15 [95% CI, 1.48-3.12]). Among those with a first-degree relative with ESKD, the relative risk for



**Figure 2.** Comparison of rate of decline in estimated glomerular filtration rate (eGFR) between donors and nondonors, grouped by family history of end-stage kidney disease (ESKD) in a first-degree relative: (A) family history of ESKD is “yes” and (B) family history of ESKD is “no.” eGFR was calculated for donors and nondonors using the Chronic Kidney Disease Epidemiology Collaboration equation from serum creatinine values spanning the period from 12 months postdonation (to allow for kidney compensation in the donors) and at subsequent examination years (every 5 years for nondonors) until last follow-up. There was no difference in change in eGFR between donors and nondonors stratified by family history of ESKD in a first-degree relative.

hypertension was higher in donors than nondonors in both nonadjusted and adjusted analyses (2.50 [95% CI, 1.63–3.83] and 2.44 [95% CI, 1.56–3.84], respectively). However, in the absence of such a family history, the risk for hypertension was similar in donors and nondonors in both nonadjusted and adjusted analyses (1.33 [95% CI, 0.70–2.54] and 1.50 [95% CI, 0.73–3.02]). There was no statistical interaction by family history of ESKD ( $P = 0.11$ ), that is, the presence of a family history of ESKD in a first-degree relative (vs absence) did not modify the associations between donation (vs nondonation) and hypertension.

Of the 67 donors with hypertension, 28 (41%) were without treatment, while another 20 (29%) donors who were receiving medications had inadequately controlled blood pressure. Of the 31 nondonors with hypertension, 12 (39%) were without treatment while another 5 (16%) had inadequately controlled blood pressure while receiving medication.

## DISCUSSION

We report that 78% of African American donors have a family history of ESKD in a first-degree relative. We found no association between family history of ESKD in a first-degree relative and postdonation kidney function, but there was a trend in increased prevalence of hypertension in donors with a family history of ESKD. There was a tendency, though not statistically significant, toward a higher rate of albuminuria among donors with or without a family history of kidney disease, 12% versus 3%, likely due to low sample size. However, it should be taken with caution because albuminuria is considered an early

harbinger of kidney disease. Two donors developed ESKD and both had a family history of ESKD in a first-degree relative. Although we did not observe any difference in annual change in kidney function or eGFR, we report up to a 2-fold increase in hypertension that could be attributable to donation when donors were compared with nondonor participants (who were suitable to donate) even after accounting for a family history of ESKD.

Our findings are in line with that reported by Lentine et al<sup>22</sup>; that is, a high fraction (78%) of African American live kidney donors have a family history of ESKD and there is a lack of association between family history of ESKD in a first-degree relative and postdonation kidney function. However, our findings are not consistent with a recent study by Muzaale et al,<sup>11</sup> who reported an increased risk for ESKD in African American donors with a family history of ESKD, which varied based on relationship, that is, highest in identical twins, followed by full siblings, offsprings, and then parents. Although the median follow-up time was similar between the 2 studies, the IQR was much wider with Muzaale et al<sup>11</sup> than ours (6–18 vs 8–13 years) and therefore it is possible that our findings differ due to a lack of sufficient follow-up. There was a trend in a higher systolic blood pressure and incidence of hypertension among donors with a positive family history of ESKD; however, the difference did not reach statistical significance due to a small sample size.

The present study shows that live kidney donation did not affect the trajectory of postdonation kidney function when compared with carefully selected nondonors who were otherwise suitable to donate a kidney. The incidence of hypertension was increased by 2-fold in African

**Table 4.** Relative Risk for Hypertension in Living Kidney Donors as Compared With Matched Nondonors Stratified by the Presence of a Family History of ESKD

		No. With Hypertension	Unadjusted RR (95% CI)	Adjusted RR <sup>a</sup> (95% CI)
Overall	Nondonors (N = 161)	31 (19%)	1.0 (reference)	1.0 (reference)
	Donors (N = 161)	67 (42%)	2.16 (1.50-3.10)	2.15 (1.48-3.12)
Family history: yes	Nondonors (N = 123)	22 (18%)	1.0 (reference)	1.0 (reference)
	Donors (N = 123)	55 (45%)	2.50 (1.63-3.83)	2.44 (1.56-3.84)
Family history: no	Nondonors (N = 38)	9 (24%)	1.0 (reference)	1.0 (reference)
	Donors (N = 38)	12 (32%)	1.33 (0.70-2.54)	1.48 (0.73-3.02)

Note: Donors and nondonors were matched on the following characteristics: age (5-year interval), sex, duration of follow-up (5-year interval), systolic blood pressure (15-mm Hg interval), and family history of ESKD in a first-degree relative (no vs yes).

Abbreviations: ESKD, end-stage kidney disease; RR, relative risk.

<sup>a</sup>Hypertension risk was adjusted for health insurance, education, and income.

American live kidney donors compared with nondonor controls after accounting for a family history of ESKD in a first-degree relative. Hypertension risk was greater among donors with a family history of ESKD than those without. We had to exclude 18 donors in matched analyses predominantly due to the inability to find suitable nondonors with similar follow-up times. Both donors who developed ESKD were included in this analysis; thus, we do not believe that the results on kidney function were affected by the omission of these 18 donors. However, of these 18 donors, 15 had hypertension (88%) and therefore the relative risk for hypertension may be underestimated in this study. It is concerning that 70% of the donors who developed hypertension after donation were receiving inadequate or no treatment. Similar treatment patterns were seen among African American participants in the CARDIA cohort. This calls for a need for long-term follow-up of donors, particularly those without health insurance.

Strengths of our study include careful selection of donors and nondonor controls. More than two-thirds of CARDIA participants were excluded, illustrating the potential bias with the use of population-based estimates, which may underestimate risk among donors. A family history of ESKD was ascertained among donors who did not donate to first-degree relatives and among nondonors through a personal interview.

The major limitations of this study are the retrospective study design and modest ascertainment rate. All living donor follow-up studies have been plagued by less than desirable participation rates; our 73% participation rate is higher than that seen in other studies.<sup>2,3</sup> Reassuringly, data from UNOS suggest that none of the nonparticipating donors developed ESKD. In addition, most of the predonation characteristics of participant and nonparticipant donors were similar except for socioeconomic variables (Table S1). A third of the donors did not come for an in-person interview and their data were obtained through review of medical records. It is possible that we did not observe a statistically significant difference in the rate of decline in postdonation eGFRs based on a donor's family history due to a small sample size. Our cohort of young donors lacks sufficient follow-up time, which may limit our ability to determine ESKD rates in this population. The

outcomes did not differ among participants by follow-up type. The donors who came for an in-person interview had 3 blood pressure measurements, per JNC 7 recommendations, and one-third of the donors who had follow-up through chart review had blood pressure measurements at family physicians' offices. The prevalence of hypertension did not differ among participants by follow-up type and therefore we do not believe that the variation in obtaining blood pressure readings affected the study results. We were unable to find a suitable nondonor control for each participating donor due to the limited number of nondonors with long follow-up times. As a result, we had to use some controls multiple times (from different examination years) and therefore had a unique baseline and follow-up examination. The nondonors differed from donors on socioeconomic variables, which could have potentially affected our results. Last, our study lacks data on the specifics of the donor-recipient relationship because recent reports found differences in risk for ESKD, whereby a twin or full sibling had a higher risk for ESKD relative to an offspring or parent.

Our study did not find an association between a family history of ESKD in a first-degree relative and postdonation kidney function. The annual change in kidney function after donation was similar to that of nondonors matched for a family history of ESKD. We demonstrate that live kidney donation is associated with a 2-fold increase in risk for hypertension in African American donors compared with nondonors. A large fraction of donors are not receiving any treatment or inadequate treatment for their hypertension, which in turn could affect their long-term kidney function. Donors with a family history of ESKD and/or hypertension should be counseled to follow up with their primary care physician regularly to monitor and get prompt and adequate treatment for hypertension. The results of our study suggest that a family history of ESKD in a first-degree relative should not be used to exclude African American live kidney donors. This crude metric of risk can be refined by a specific relationship between the donor and recipient, which better captures the possibility of sharing genetic risks such as APOL1 genotype (highest when the family member with ESKD is an identical twin, followed by full-sibling, offspring, parent, half-sibling, etc).

## SUPPLEMENTARY MATERIAL

## Supplementary File (PDF)

**Figure S1:** Selection of healthy nondonors from CARDIA matched for family history of ESKD

**Table S1:** Comparison of baseline characteristics between donors who did and did not participate

## ARTICLE INFORMATION

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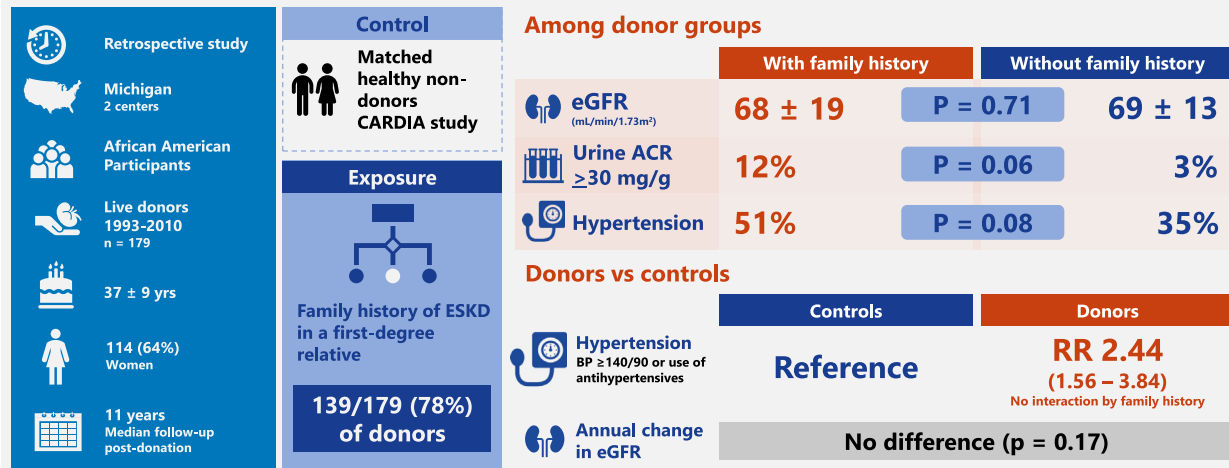
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# Does a family history of end-stage kidney disease (ESKD) affect outcomes in African American live kidney donors?



**Conclusion:** Family history of ESKD is not associated with post-donation kidney function among African American (AA) kidney donors. Live kidney donation is associated with an increased risk of hypertension among AAs, independent of donor family history of ESKD.

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