Apolipoprotein L1 gene (*APOL1)* genotype and kidney outcomes after living kidney donation: Living Donor Extended Time Outcomes (LETO) study results

Chi-yuan Hsu, M.D., M.Sc.[1], Ying Gao, M.Sc.[1], Barry I. Freedman, M.D.[2], Mitchell R. Lunn, M.D., M.A.S.[3], Anthony N. Muiru, M.D., M.P.H[1], Mark A. Schnitzler, Ph.D.[5], Jasmin Divers, Ph.D.[4], Roslyn B. Mannon, M.D.,[6] Nicholette D. Palmer, Ph.D.[2], Amy B. Karger, M.D., Ph.D.[7], Krista L. Lentine, M.D., Ph.D.[5 *], Meyeon Park, M.D., M.A.S.[1] *

* co-senior authors

for the *APOL1* Long-Term Kidney Transplantation Outcomes Network (APOLLO) Consortium

1. University of California, San Francisco, San Francisco, CA, USA
2. Wake Forest University, Winston-Salem, NC, USA
3. Stanford University, Palo Alto, CA, USA
4. New York University, Mineola, NY, USA
5. Saint Louis University, St Louis, MO, USA
6. University of Nebraska, Omaha, NE, USA
7. University of Minnesota, Minneapolis, MN, USA

Correspondence to:
Chi-yuan Hsu, MD, MSc
Division of Nephrology
University of California, San Francisco
500 Parnassus Avenue, MUW 418A, Box 0532
San Francisco, CA 94143-0532
USA
Email: Chi-yuan.Hsu@ucsf.edu
Tel: 415-353-2379
Fax: 415-476-3381

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KEY POINTS

Question: Do living kidney donors with apolipoprotein L1 gene (*APOL1*) high-risk genotypes have higher risk of reduced kidney function after kidney donation?

Findings: In this retrospective cohort study of 445 Black and 208 White kidney donors, nearly two decades after kidney donation, Black kidney donors with *APOL1* high-risk genotypes had more than twice the risk of reduced kidney function (estimated glomerular filtration rate <45 ml/min/1.73m^2). Black donors without *APOL1* high-risk genotypes had similar outcomes as White donors.

Meaning: Incorporating *APOL1* genotyping into the donor evaluation process will identify living kidney donation candidates at higher risk for adverse outcomes after nephrectomy.

(100 words)

ABSTRACT

Importance Accurate understanding of long-term risks after living kidney donation is critical to inform evidence-based policies for donor candidate evaluation and selection.

Objective To determine whether apolipoprotein L1 gene (*APOL1*) polymorphisms associate with worse kidney function after living kidney donation.

Design Retrospective cohort study.

Setting We obtained contact information for all living kidney donors in the U.S. who donated from 2000-2008 from the Scientific Registry of Transplant Recipients. After using online search tools to update addresses and telephone numbers, we invited Black and White U.S. living kidney donors who donated in 2000-8 to participate. Enrolled study participants had home-based research visits conducted by a subcontract agency between March 2020 and March 2024.

Participants U.S. living kidney donors from 2000-2008.

Exposures Apolipoprotein L1 gene (*APOL1*) polymorphisms, race.

Main outcomes and measures The primary outcome was serum creatinine estimated glomerular filtration rate (eGFR) <45 ml/min/1.73m² at time of home-based research visits. Additional outcomes were eGFR <60 ml/min/1.73m², albuminuria ≥30 or ≥300 mg/g, and hypertension.

Results We enrolled 445 Black kidney donors (66% female, mean [SD] age 38 [10] years) and 208 White kidney donors (67% female, mean [SD] age 44 [10] years). 68 of the Black donors (15.3%) had *APOL1* high-risk genotypes (G1/G1, G2/G2, or G1/G2). A median of 18.5 [interquartile range 16.9, 20.5] years after donation, 46 (7.0%) participants developed eGFR <45 ml/min/1.73m^2. Black kidney donors with *APOL1* high-risk genotypes had higher risk of developing eGFR <45 ml/min/1.73m² (relative risk 2.31, 95% CI: 1.16 to 4.61; p = 0.02) than those without. No significant difference in eGFR <45 ml/min/1.73m² was observed between Black donors without *APOL1* high-risk genotypes and White donors. Black kidney donors, especially those with *APOL1* high-risk genotypes, were more likely to develop eGFR <60 ml/min/1.73m², elevated albuminuria and hypertension.

Conclusions and Relevance *APOL1* genotype is an important risk factor for reduced kidney function post-donation. These results suggest that all Black living donor candidates should undergo *APOL1* genotyping and that prediction tools for risk of kidney disease after living kidney donation should consider *APOL1* genotype instead of race.

(339 out of 350 word limit for Abstract)

Living kidney donation is a unique medical procedure in which the primary beneficiary is the recipient, not the donor. To ground evidence-based policies and practices for donor candidate evaluation, selection, and informed consent, an accurate understanding of long-term post-donation risks is crucial.[1-6] However, few research studies have enrolled living kidney donors and systematically assessed kidney health using a research protocol.

While findings from past studies have generally been reassuring, these data[7-9] are limited by relatively short post-donation follow-up time and under-representation of minority populations at higher risk for kidney disease. Analyses based on linkage to administrative data reported that Black donors have two- to three-fold higher post-donation risk of receiving a diagnosis of chronic kidney disease (CKD) or end-stage kidney disease (ESKD) than White donors.[10-13]

The discovery that apolipoprotein L1 gene (*APOL1*) polymorphisms increase the risk of CKD among persons with recent African ancestry[14,15] has spurred interest in *APOL1* genotyping in the living donor candidate evaluation.[1,16,17] Doshi et al. reported a very high risk of ESKD among Black kidney donors with *APOL1* high-risk genotypes (2 out of 19 donors [11%] after a median follow-up of 12 years).[18] However, routine genotyping for *APOL1* among Black kidney donor candidates is controversial and not currently implemented at many transplant centers.[19-21]

To complement the prospective National Institute of Diabetes and Digestive and Kidney Diseases *APOL1* Long-term Kidney Transplantation Outcomes Network (APOLLO),[22] this Living Donor Extended Time Outcomes (LETO) retrospective cohort ancillary study was conducted to address critical knowledge gaps in the evidence base for *APOL1* genotyping in the evaluation of living donor candidates.

METHODS

This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients

in the U.S., submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. After obtaining APOLLO Central Institutional Review Board (IRB) approval from the Wake Forest University School of Medicine (location of the APOLLO Data Coordinating Center) and internal SRTR approval, SRTR provided the research team with names, identifiers, and contact information of all living kidney donors in the U.S. who donated from 2000-2008. Whitepages.com (Premium) and other online search tools were used to locate updated addresses and telephone numbers. Donors were contacted and invited to participate in LETO by research coordinators based at the University of California, San Francisco. Informed consent was obtained via U.S. postal mail or online for all participants before conduct of home-based research visits by a subcontract agency (ExamOne for all but one visit).

After pilot-testing and refining remote recruitment strategies from a few APOLLO main clinical centers, we reached out to a subset of randomly selected White donors who donated between January 2000 and December 2006 (n=1000 out of 30671). Given the smaller pool of Black donors, we attempted to contact all who donated between January 2000 and December 2008 (n=7375). Toward the end of enrollment, we also approached kidney donors identified as neither Black nor White but only one ultimately underwent home-based research visit and will not be further considered. Race was defined per the SRTR registry. After March 2023, a question regarding self-identified race was asked of all participants.

Home-based Research Visits

At the home-based research visits, height, weight, waist circumference, and blood pressure were measured, the last using a standardized protocol following American Heart Association guidelines.[23] All participants completed a questionnaire regarding their health status.

Blood was collected in red top (serum)(centrifuged) and EDTA (plasma) tubes and shipped (along with a random spot urine) overnight on cold packs to the Clinical Laboratory Improvement Amendments (CLIA)-certified Advanced Research and Diagnostic Laboratory at the University of Minnesota.[24] Serum creatinine was measured using an IDMS-traceable enzymatic assay and urine albumin using an immunoturbidimetric method. DNA was extracted and purified from the plasma buffy coat using a modified salt precipitation method and shipped to Wake Forest University School of Medicine.

Genotyping

At the Wake Forest APOLLO CLIA-certified lab, A*POL1* kidney risk variants G1 (rs73885319, p.S342G, and rs60910145, p.I384M) and G2 (rs71785313, p.N388_Y389del) were genotyped among Black kidney donors using custom TaqMan assays (Applied Biosystems). Non-risk *APOL1* variants were designated as G0. Participants with G1/G1, G2/G2, or G1/G2 were classified as having *APOL1* high-risk genotypes.

In exploratory analyses, risk associated with having one kidney risk variant (i.e., G1/G0 or G2/G0) were assessed).[25] The *APOL1* missense variant p.N264K (chr22:36265628 C > A; rs73885316) was genotyped in the Wake Forest research lab using a pre-designed TaqMan assay.[26]

Outcome

The *a priori* specified primary outcome was eGFR <45 ml/min/1.73m^2 at the time of the home-based research visit (using the 2021 serum creatinine-based CKD-EPI eGFR equation[27]). This threshold was selected[28] as there is consensus that this represents a clinically significant reduction in kidney function.

The secondary outcome was eGFR <60 ml/min/1.73m^2. Tertiary outcomes included urine albumin-creatinine ratio (UACR) ≥30 or ≥300 mg/g[29] and hypertension. Hypertension was

deemed present if there was i) observed systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or ii) participant-reported diagnosis of hypertension by healthcare provider and use of antihypertensive medications.[9] Kidney donors who had developed ESKD at time of LETO study visit were classified as having these outcomes, regardless of actual readings.

Assessment of Selection Bias

Because a potential source of bias is donor death between time of donation (2000-2008) and start of LETO recruitment (2020), we assessed the mortality rates through 2019 using the death date determined from Social Security Administration variable (PERS_SSA_DEATH_DT) in the SRTR living donor file. Limited cross-linkages of SRTR data with National Death Index were performed as validation.

Because selective study enrollment could be another potential source of bias, we compared the pre-donation characteristics according to SRTR for those who enrolled into LETO with the pre-donation characteristics for those did not. In addition, to assess if risk of ESKD differed among living kidney donors who enrolled into LETO vs. those who did not, we completed a cross-linkage of SRTR data with the comprehensive national chronic dialysis and kidney transplant registry United States Renal Data System (USRDS)[30] in 2024.

Statistical Analysis

Descriptive statistics were reported as means with standard deviations (SDs) or medians with interquartile ranges (IQRs) for continuous variables, and as frequencies and percentages for categorical variables. Comparison of continuous characteristics between Black and White donors, as well as between Black donors with and without *APOL1* high-risk genotypes, were performed using Student's *t* test or the Wilcoxon rank-sum test, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

Modified Poisson regression with robust error variance[31] was used to estimate the relative risks (RRs) and 95% confidence intervals (CIs) for binary outcomes. In the primary analysis, the presence or absence of eGFR <45 ml/min/1.73m^2 was compared between Black living kidney donors with or without *APOL1* high-risk genotypes. Both groups of Black donors were subsequently compared with White donors. Widths of 95% CIs have not been adjusted for multiplicity.

Since genetic variants are typically not associated with lifestyle or environmental factors that could act as confounders, we adjusted for covariates only if known risk factors for CKD prior to kidney donation were differentially distributed among Black participants with and without *APOL1* high-risk genotypes. This ended up being only kidney function at time of donation. We conducted a complete cases analysis (n = 426 out of 445) and entered pre-donation eGFR into the model as a linear term.

Statistical analyses were conducted using SAS, version 9.4 (SAS Institute).

RESULTS

LETO study visits occurred between March 2020 and March 2024. We were able to reach and obtain consent to enroll from 550 Black living kidney donors who donated from 2000-8. Among them, 450 underwent home-based research visits (along with 210 White donors). After excluding participants without serum or without DNA, the final analysis dataset included 445 Black donors and 208 White donors who donated at 163 transplant centers across the U.S.

According to SRTR data (and supported by a limited National Death Index cross-linkage), among those eligible for LETO study, the death rate between kidney donation (2000-8) and 2019, which would have prevented enrollment, was estimated to be <2% (**eTable 1a and eTable 1b**). The distributions for age, serum creatinine, blood pressure, and body mass index of LETO participants at time of donation were similar to those of the underlying national pool of eligible donors, although there was over-representation of female donors (**eTable 2**). The rates

of ESKD among Black and White LETO study participant were similar to those of the underlying national pool of eligible donors according to a cross-link with U.S. Renal Data System (**eTable 3**).

Table 1 displays characteristics of LETO participants. Among the subset of LETO participants who provided information on self-identified race, 97% of those classified as Black in SRTR self-identified as being Black (including Black and multiracial/Hispanic) and 98% of participants classified as White in SRTR self-identified as White (including White and multiracial/Hispanic).

Sixty-eight of the 445 (15.3%) Black donors enrolled into LETO had an *APOL1* high-risk genotype. At median 18.2 years post-donation (interquartile range [IQR] 16.6-20.5), three of the 445 Black donors developed ESKD (one with *APOL1* high-risk genotype), and all three had undergone kidney transplant at the time of the LETO study visits. Among Black LETO participants, 34 (7.6%) developed an eGFR <45 ml/min/1.73m^2, 10 among the 68 donors with *APOL1* high-risk genotypes (14.7%) and 24 among the 377 donors without (6.4%) (p=0.02) (**Table 2**). Compared with Black kidney donors without *APOL1* high-risk genotypes, Black donors with high-risk genotypes had more than twice the risk of developing an eGFR <45 ml/min/1.73m^2 (relative risk [RR] 2.31; 95% CI: 1.16, 4.61; p =0.02; **Table 3**). Black donors with *APOL1* high-risk genotypes had higher risk of developing an eGFR <60 ml/min/1.73m^2 than Black donors without *APOL1* high-risk genotypes (RR 1.50; 95% CI: 1.18, 1.90) (**Table 3**).

Among the 208 White donors, none developed ESKD and 12 (5.8%) had eGFR <45 ml/min/1.73m^2 at median 18.9 years (IQR 17.4-20.4) post-donation (**Table 2**). No statistically significant difference was observed between Black donors without *APOL1* high-risk genotypes and White donors in terms of risk of eGFR <45 ml/min/1.73m^2 (RR 1.10; 95% CI: 0.56, 2.16; p=0.77). Differences in risk of having eGFR <45 ml/min/1.73m^2 after kidney donation appeared confined to those with *APOL1* high-risk genotypes (RR 2.55; 95% CI: 1.15, 5.64; p=0.02)

(**Figure 1**). Similar trends were seen for the secondary outcome of eGFR <60 ml/min/1.73m^2 (**Figure 1**).

At time of kidney donation, Black kidney donors with *APOL1* high-risk genotypes had higher serum creatinine concentrations than their counterparts without (1.01 vs. 0.93 mg/dl; p = 0.007) (**Table 1**). Adjusting for eGFR at time of donation weakened the association between *APOL1* genotypes and risk of developing an eGFR <45 ml/min/1.73m^2 with a reduction in RR from 2.31 to 1.91, and the confidence interval bounds included the possibility of no effect (**eTable 4**).

Among Black living donors, *APOL1* high-risk genotypes were associated with higher risk of having UACR ≥300 mg/g after donation (RR 3.84; 95% CI: 1.11, 13.22) (**Table 3**). Differences in UACR ≥30 mg/g or presence of hypertension were less notable (**Table 3**). Elevated albuminuria level and hypertension were less common among White donors after donation (**Table 2**).

The effect of *APOL1* genotypes among Black kidney donors was stronger among those with age above median (38 years) at donation (RR 4.19 [95% CI 1.82, 9.63] vs. 0.82 [95% CI 0.19, 3.48] for eGFR <45 ml/min/1.73m^2) (**eTable 5**). Black kidney donors with one *APOL1* kidney risk variant (G1/G0 or G2/G0) did not have higher risk for study outcomes than those with zero (G0/G0) (**eTable 6**).

Among the Black LETO study participants, 14 carried the missense variant p.N264K; however, none carried a high-risk APOL1 genotype (G1/G1, G1/G2, G2/G2).

DISCUSSION

Approximately 18.5 years post-donation, Black living kidney donors with *APOL1* high-risk genotypes had a more than two-fold higher risk of developing an eGFR <45 ml/min/1.73m^2 compared with those without *APOL1* high-risk genotypes and compared with White donors.

Black donors lacking *APOL1* high-risk genotypes did not have higher risk of developing eGFR <45 ml/min/1.73m^2 than White donors.

Black donors have been underrepresented in prior investigations of long-term outcomes after kidney transplantation (**eTable 7**).[7-9,32] Compared with the most relevant prior study which was by Doshi et al.,[18] LETO was larger, had longer follow-up, included White donors for comparison, and was national in scope with representation from 163 (vs. 2) transplant centers (**eTable 7**). The prevalence of *APOL1* high-risk genotypes in LETO was comparable (15.3% vs. 14.0%) and those with high-risk genotypes had lower pre-donation eGFR. These findings are consistent with an autopsy study by Hoy et al. who reported that among Black Americans without kidney disease, *APOL1* high-risk genotypes were associated with exaggerated age-related nephron loss that could lead to accentuated susceptibility to kidney disease.[33] Similar to the findings of Doshi et al., a lower eGFR at follow-up was observed among Black donors with *APOL1* high-risk genotypes than without. However, the severity of kidney function loss in LETO appeared less pronounced. Doshi et al. reported that two of 19 Black kidney donors with *APOL1* high-risk genotypes developed ESKD after median 12 years of follow-up. In contrast, in LETO, there was one case of ESKD among 68 Black kidney donors with *APOL1* high-risk genotypes after median 18.5 years follow-up.

The higher risk of ESKD among Black compared with White donors among LETO participants is consistent with prior publications.[11,12] Lentine et al. reported in linkage studies to Medicare and private insurance billing claims, that Black kidney donors had higher risks of being diagnosed with post-donation proteinuria and nephrotic syndrome than White kidney donors.[11] We noted in LETO that Black donors generally had higher albuminuria levels than White donors post-donation and among Black donors, those with *APOL1* high-risk genotypes had higher UACR post-donation than those without. Lentine et al. also reported that, compared with White donors, Black donors had higher risk of being diagnosed with post-donation hypertension.[11] This

was also observed among LETO participants. Furthermore, Black donors with *APOL1* high-risk genotypes had higher prevalence of hypertension than those without.

Currently, the practice of *APOL1* genotyping among living donor candidates is controversial.[19,34-36] The magnitude of the effect size observed in the LETO study supports that all Black living donor candidates should undergo *APOL1* genotyping. Our results suggest that genotyping should not be limited to younger donors, because the association with eGFR <45 ml/min/1.73m^2 was stronger among older donors in *a post-hoc* subgroup analysis. We believe that our results contribute valuable information on risk stratification among donor candidates and donors. Any such universal *APOL1* genotyping should be implemented with proper education, counseling, and shared decision-making, including discussion of potential additional "second hits" (e.g., viral infections) contributing to the nephropathy associated with *APOL1* high-risk genotypes.[37,38]

The 2017 Kidney Disease: Improving Global Outcomes (KDIGO) "Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors"[1] recommended the use of a prediction tool incorporating ten predictive factors to estimate the projected 15-year and lifetime incidence of kidney failure in the evaluation of living donor candidates, one of which is race (Black or White) (http://www.transplantmodels.com/esrdrisk/).[3] Our results support that instead of considering race, the prediction tool should consider *APOL1* genotype,[39] resonating with calls to replace race in medical algorithms without sacrificing risk prediction accuracy.[40,41]

Limitations of this study include that we were unable to determine persistence of low eGFR. However, participants volunteered for a home-based research visit at a time of their choosing, so they were unlikely to be acutely ill or having acute kidney injury. Our study consisted only of research volunteers, a limitation shared by all studies enrolling living kidney donors and using pre-specified research protocols to systematically assess post-donation health status. We note that age, pre-donation serum creatinine, pre-donation blood pressure and body mass index distributions among LETO study participants were similar to that of other living

kidney donors in the country from 2000-8 who did not enroll. In addition, the rates of ESKD were similar. Further arguing against substantial selection bias, our observed magnitude of increased risk for kidney disease after donation comparing Black vs. White donors is similar to that reported in prior studies using nationally representative data.[10,11,24] It is unlikely that those who donated in 2000-8 would be aware of their *APOL1* genotype and have that influence their likelihood of LETO study participation. We believe that the inability to recruit donors due to death is not a major threat to internal validity because of the low risk of death between donation and LETO recruitment. While there are advantages to a prospective study design,[8,9,22] retention is challenging in prospective cohort studies of long duration as illustrated by the experience of Kasiske et al. who initially enrolled 205 living kidney donors but were only able to retain 136 by year nine.[8] Our study was primarily designed to examine the effect of *APOL1* genotypes among donors after nephrectomy, so data from non-donor controls are less relevant. But because LETO did not have (matched) non-donor controls, we were unable to isolate or directly quantitate the effect of donation and our estimation of risk should not be confused with a corresponding value for risk of donation vs. non-donation in a person with *APOL1* high-risk genotype.

In conclusion, using a robust, national protocol, we found a strong association between *APOL1* high-risk genotypes and reduced kidney function (eGFR <45 ml/min/1.73m^2) an average of 18.5 years after living kidney donation. These findings are relevant to guidelines and policies for living donor candidate evaluation.

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Disclaimer: The data reported here have been supplied by the Hennepin Healthcare Research Institute (HHRI) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government.

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Table 1. Characteristics of the Living Donor Extended Time Outcomes (LETO) study participants

	All donors (n=653)	**Black donors (n=445)**	**Black donors with *APOL1* high-risk genotypes (n=68)**	**Black donors without *APOL1* high-risk genotypes (n=377)**	**White donors (n=208)**	**P-value for presence vs. absence of *APOL*1 high-risk genotypes among Black donors[§]**	**P-value for Black vs. White donors[§]**
At time of donation (data from SRTR)							
Female, n (%)	436 (66.8)	295 (66.3)	42 (61.8)	253 (67.1)	141 (67.8)	0.39	0.71
Age, years, mean ± SD	40.0 ± 10.0	38.3 ± 9.5	37.1 ± 10.0	38.5 ± 9.4	43.6 ± 10.0	0.29	<0.001
Body mass index, kg/m^2, mean ± SD	27.2 ± 4.5 (n =553)	27.6 ± 4.6 (n=371)	28.0 ± 4.5 (n=61)	27.5 ± 4.6 (n=310)	26.3 ± 4.3 (n=182)	0.47	0.001
Serum creatinine, mg/dl, mean ± SD	0.92 ± 0.21 (n =623)	0.94 ± 0.21 (n=426)	1.01 ± 0.26 (n=65)	0.93 ± 0.20 (n=361)	0.88 ± 0.19 (n=197)	0.007	0.002
eGFR (ml/min/1.73m^2), mean ± SD	92.0 ± 17.5 (n =623)	91.3 ± 17.3 (n=426)	87.5 ± 20.9 (n=65)	92.0 ± 16.6 (n=361)	93.5 ± 17.9 (n=197)	0.05	0.15
eGFR (ml/min/1.73m^2), median [IQR]	91.6 [79.6, 105.7] (n=623)	91.4 [78.9, 104.8] (n=426)	85.2 [70.1, 104.1] (n=65)	91.6 [80.4, 104.8] (n=361)	93.8 [82.6, 107.4] (n=197)	0.07	0.17
Systolic blood pressure, mmHg, mean ± SD	120.4 ± 13.9 (n =493)	120.8 ± 13.4 (n=342)	118.8 ± 11.5 (n=54)	121.1 ± 13.7 (n=288)	119.6 ± 14.8 (n=151)	0.24	0.39
Diastolic blood pressure, mmHg, mean ± SD	73.2 ± 9.6 (n =493)	73.2 ± 8.8 (n=342)	73.7 ± 8.6 (n=54)	73.1 ± 8.9 (n=288)	73.1 ± 11.1 (n=151)	0.67	0.95
At LETO study visit							
Years since donation, median [IQR]	18.5 [16.9, 20.5]	18.2 [16.6, 20.5]	18.5 [16.5, 20.7]	18.2 [16.7, 20.5]	18.9 [17.4, 20.4]	0.60	0.01
Age, years, mean ± SD	58.7 ± 10.0	56.8 ± 9.4	55.8 ± 9.7	57.0 ± 9.4	62.6 ± 10.2	0.34	<0.001
Body mass index, kg/m^2, mean ± SD	29.9 ± 6.0	30.6 ± 5.7	30.9 ± 5.0	30.5 ± 5.9	28.3 ± 6.2	0.59	<0.001
Serum creatinine *(*)* (mg/dl), mean ± SD	1.14 ± 0.30	1.18 ± 0.33	1.35 ± 0.56	1.14 ± 0.26	1.08 ± 0.21	<0.001	<0.001
eGFR (ml/min/1.73m^2), mean ± SD *(*)*	64.5 ± 14.4	63.7 ± 14.9	57.7 ± 16.0	64.8 ± 14.5	66.3 ± 13.1	<0.001	0.03
eGFR (ml/min/1.73m^2), median [IQR] *(*)*	63.2 [55.0,72.7]	62.3 [53.8,71.8]	57.7 [50.0,66.3]	62.8 [54.7,72.1]	66.6 [57.4,74.5]	0.001	0.004
Urine albumin-creatinine ratio, mg/g, median [IQR] *(*)*	6.3 [3.3, 16.0] (n=646)	6.6 [3.3, 19.1] (n=439)	8.2 [4.6, 24.3] (n=65)	6.3 [3.2, 17.1] (n=374)	5.4 [3.3, 11.5] (n=207)	0.06	0.11
Systolic blood pressure, mmHg, mean ± SD *(*)*	124.6 ± 14.2	126.2 ± 14.2	126.3 ± 11.7	126.1 ± 14.6	121.1 ± 13.7	0.91	<0.001
Diastolic blood pressure, mmHg, mean ± SD *(*)*	77.6 ± 9.0	78.6 ± 9.0	79.2 ± 7.3	78.5 ± 9.3	75.3 ± 8.7	0.56	<0.001

(*) Including observed serum creatinine, eGFR, urine albumin-creatinine ratio and blood pressure readings at time of LETO study visit for the three

LETO study participants who themselves developed end-stage kidney disease and received kidney transplant.

APOL1, apolipoprotein L1 gene; eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation; SRTR, Scientific Registry of Transplant Recipients

[§] Continuous characteristics between Black and White donors, as well as between Black donors with and without *APOL1* high-risk genotypes, were compared using Student's *t* test or the Wilcoxon rank-sum test where appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

Table 2. Outcomes among the Living Donor Extended Time Outcomes (LETO) study participants

	All donors (n=653)	**Black donors (n=445)**	**Black donors with *APOL1* high-risk genotypes (n=68)**	**Black donors without *APOL1* high-risk genotypes (n=377)**	**White donors (n=208)**	**P-value for presence vs. absence of *APOL1* high-risk genotypes among Black donors[§]**	**P-value for Black vs. White donors[§]**
ESKD, n (%)	3 (0.5)	3 (0.7)	1 (1.5)	2 (0.5)	0 (0)	0.39	0.56
eGFR < 45 ml/min/1.73m^2, n (%) *(*)*	46 (7.0)	34 (7.6)	10 (14.7)	24 (6.4)	12 (5.8)	0.02	0.38
eGFR < 60 ml/min/1.73m^2, n (%) *(*)*	253 (38.7)	188 (42.2)	40 (58.8)	148 (39.3)	65 (31.3)	<0.001	0.01
Urine albumin-creatinine ratio ≥ 30 mg/g, n (%) *(*)*	100 (15.5) (n=646)	77 (17.5) (n=439)	15 (23.1) (n=65)	62 (16.6) (n=374)	23 (11.1) (n=207)	0.20	0.04
Urine albumin-creatinine ratio ≥ 300 mg/g, n (%) *(*)*	15 (2.3) (n=646)	10 (2.3) (n=439)	4 (6.2) (n=65)	6 (1.6) (n=374)	5 (2.4) (n=207)	0.05	1.00
Hypertension, n (%) *(*)*	277 (42.4)	211 (47.4)	39 (57.4)	172 (45.6)	66 (31.7)	0.07	<0.001

(*) Regardless of observed eGFR, urine albumin-creatinine ratio and blood pressure readings at time of LETO study visit, the three LETO study participants who themselves developed end-stage kidney disease and received kidney transplant were classified as eGFR <45 ml/min/1.73m^2, urine albumin-creatinine ratio ≥ 300 mg/g and having hypertension.

APOL1, apolipoprotein L1 gene; ESKD, end-stage kidney disease; eGFR, estimated glomerular filtration rate; SD, standard deviation

[§]Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

Table 3. Relative risks for decreased kidney function, increased albuminuria and hypertension among 445 Black living kidney donors with and without *APOL1* high-risk genotypes

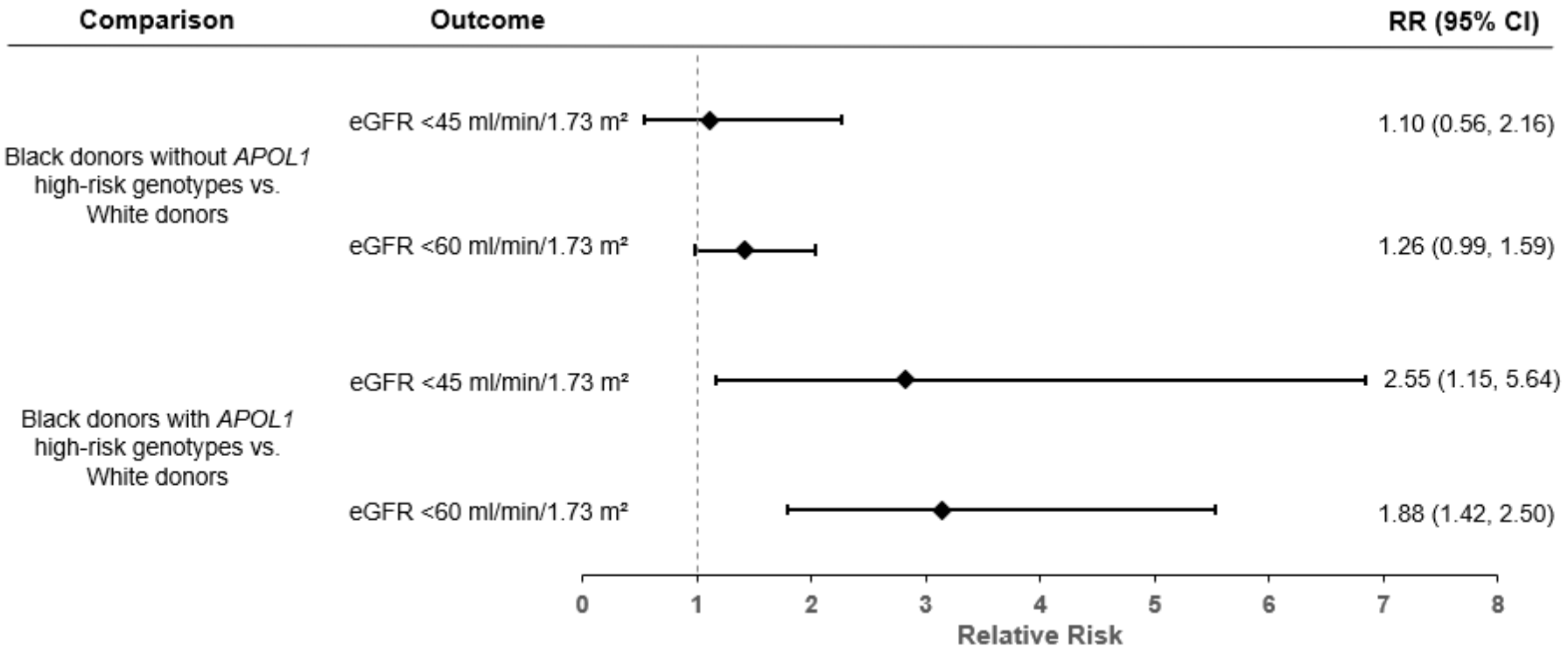
	Reduced kidney function			Increased albuminuria¶		Hypertension§
	ESKD	eGFR <45 ml/min/1.73m^2	eGFR <60 ml/min/1.73m^2	Urine albumin-creatinine ratio ≥ 300 mg/g	Urine albumin-creatinine ratio ≥ 30 mg/g	
Presence vs. absence of *APOL1* high-risk genotypes	2.77 (95% CI: 0.25, 30.15) (p=0.40)	2.31 (95% CI: 1.16, 4.61) (p=0.02)	1.50 (95% CI: 1.18, 1.90) (p<0.001)	3.84 (95% CI: 1.11, 13.22) (p=0.03)	1.39 (95% CI: 0.85, 2.29) (p=0.19)	1.26 (95% CI: 1.00, 1.59) (p=0.05)

¶ Among 439 Black donors with urine samples

§ Hypertension defined as i) observed systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or ii) participant-reported diagnosis of hypertension by healthcare provider and use of antihypertensive medications

APOL1, apolipoprotein L1 gene; eGFR, estimated glomerular filtration rate; CI, confidence interval

Figure 1. Relative risks for decreased kidney function comparing Black living kidney donors with and without *APOL1* high-risk genotype vs. White living kidney donors



APOL1, apolipoprotein L1 gene; eGFR, estimated glomerular filtration rate; CI, confidence interval; RR, relative risk