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ORIGINAL RESEARCH

Association of *APOL1* Genotypes With Measures of Microvascular and Endothelial Function, and Blood Pressure in MESA

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BACKGROUND: *APOL1* high-risk genotypes are associated with increased risk for hypertension-attributed kidney disease among Black adults in the United States. Biopsy studies show differences in kidney vasculature by *APOL1* status; less is known about the variants' associations with systemic vascular and endothelial function. Whether *APOL1* risk variants are associated with blood pressure (BP) is also uncertain.

METHODS AND RESULTS: Using linear regression, we examined cross-sectional associations of *APOL1* risk genotypes (high=2 risk alleles, low=0 or 1 risk allele) with subclinical measures of vascular function (small arterial elasticity, n=1586; large arterial elasticity, n=1586; ascending aortic distensibility, n=985) and endothelial function (flow-mediated dilation, n=777). Using linear mixed-effects models, we studied longitudinal associations of *APOL1* risk genotypes with BP (n=1619), adjusting for age, sex, and African ancestry. Among 1619 (12% *APOL1* high-risk) Black participants in MESA (Multi-Ethnic Study of Atherosclerosis), mean age was 62 years old, 58% had hypertension, and mean systolic BP was 131 mm Hg at baseline. At examination 1 (2000–2002), there was no significant difference in small arterial elasticity, large arterial elasticity, ascending aortic distensibility, or flow-mediated dilation in participants with *APOL1* high- versus low-risk genotypes ($P>0.05$ for all). Over a mean follow-up of 7.8 years, relative annual changes in systolic and diastolic BP and pulse pressure did not differ significantly by *APOL1* risk status (between-group differences of −0.20, −0.14, and −0.25, respectively; $P>0.05$ for all).

CONCLUSIONS: Among Black participants in MESA, *APOL1* high-risk genotypes were not associated with subclinical vascular and endothelial function or BP trajectories. The relationship of *APOL1* with kidney disease may be intrinsic to the kidney rather than through peripheral effects on systemic vasculature or BP.

Key Words: *APOL1* ■ apolipoprotein L1 ■ arterial stiffness ■ blood pressure ■ hypertension

Black adults are more likely to have hypertension and difficult-to-control blood pressure (BP) compared with White adults.[1–4] Although environmental factors account for some of this excess risk, genetic factors likely also contribute.[5,6] The *APOL1* high-risk genotypes, present in 12% to 14% of Black Americans, have been associated with an increased risk for various types of kidney disease, including hypertension-attributed chronic kidney disease.[7–11] Expression of APOL1 (Apolipoprotein L1) protein and mRNA has been shown in vascular endothelial and smooth muscle cells of both healthy and diseased (eg, focal segmental glomerulosclerosis and HIV-associated nephropathy) human kidneys.[12,13] Some histopathologic studies have also reported an association between the *APOL1* high-risk genotypes and arteriosclerosis, whereas others have not.[14–17] These observations have led to an interest in understanding whether the *APOL1*

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CLINICAL PERSPECTIVE

What Is New?

- *APOL1* high-risk genotypes are not associated with subclinical measures of vascular and endothelial function or blood pressure trajectories in Black adults without baseline clinical cardiovascular disease.

What Are the Clinical Implications?

- The results of the current study argue against a role of *APOL1* risk variants in the development of hypertension.

Nonstandard Abbreviations and Acronyms

AAD	ascending aortic distensibility
APOL1	apolipoprotein L1
BP	blood pressure
C1	large arterial elasticity
C2	small arterial elasticity
FMD	flow-mediated dilation
MESA	Multi-Ethnic Study of Atherosclerosis

risk variants confer an increased risk of hypertension and, if so, whether the association is mediated by kidney damage or mediates the association of *APOL1* with kidney disease.

We previously demonstrated in CARDIA (Coronary Artery Risk Development in Young Adults), a cohort of healthy young adults, that the *APOL1* risk variants were not associated with BP trajectories over the life course.[18] In contrast, others have reported a positive association using data from electronic health records.[19] Differences in study design and population may explain the discrepant findings; however, the question remains as to whether an association exists between *APOL1* and BP. Moreover, the mechanisms by which the *APOL1* risk variants relate to progressive chronic kidney disease and possibly also hypertension warrant further investigation. *APOL1* risk variants may be associated with microvascular damage. To our knowledge, no study to date has examined the association of the *APOL1* risk variants with subclinical measures of vascular function (eg, small arterial elasticity [C2], large arterial elasticity [C1], ascending aortic distensibility [AAD]) and endothelial function (eg, flow-mediated dilation [FMD]). This question is important because we previously demonstrated that decreased C2 and C1 were associated with an increased risk of incident hypertension and faster decline of estimated glomerular filtration rate.[20,21]

In a cohort of adults without baseline clinical cardiovascular disease, we aimed to determine whether the *APOL1* risk variants were associated with subclinical measures of vascular and endothelial function and BP trajectories. We hypothesized that individuals with the *APOL1* high-risk genotypes would have lower C2, C1, AAD, and FMD at baseline and greater increases in BP over time compared with individuals with low-risk genotypes.

METHODS

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Study Population

MESA (Multi-Ethnic Study of Atherosclerosis) is a prospective cohort study that began in July 2000 with the overall goal of better understanding factors related to the progression of subclinical to clinical cardiovascular disease. Details on the study design of MESA have been reported previously.[22] Briefly, 6814 men and women between the ages of 45 and 84 years old without baseline clinical cardiovascular disease were enrolled. Four racial/ethnic groups (White, Black, Hispanic, and Asian) were represented, and study participants were recruited from 6 communities in the United States (Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; New York, New York; and St. Paul, Minnesota).[22] Institutional review board approval was obtained at each study site, and all study participants provided informed consent at the initial examination.[22,23] We utilized data from the first 5 examinations: exam 1 (July 2000 to August 2002), exam 2 (September 2002 to February 2004), exam 3 (March 2004 to September 2005), exam 4 (September 2005 to May 2007), and exam 5 (April 2010 to December 2011).[24] Our study population was derived from the 1746 participants who self-identified as Black and who underwent *APOL1* genotyping, of whom 1586 had C2, 1586 had C1, 985 had AAD, and 777 had FMD measured at exam 1 and 1619 had at least 1 systolic BP measurement during follow-up (at exam 2, 3, 4, or 5; Figure S1).

Outcomes

Measurements of vascular and endothelial function were obtained at exam 1 and have been described previously.[20,21,25–31] Briefly, C2 and C1 were measured using the PulseWave CR-2000 Research CardioVascular Profiling Instrument (Hypertension Diagnostics). A tonometer was placed over the right

radial artery, which was supported by a wrist stabilizer. Measurements of the radial artery waveforms were collected for 30 seconds with accompanying systolic and diastolic BP measurements using an automated, oscillometric BP cuff in the left arm. Elasticities of the small and large arteries, or change in arterial volume per change in arterial pressure, were estimated by analysis of the diastolic pulse contour and a computer-based, third-order, 4-element Windkessel modified model.[20,21,27] In a random subset of MESA participants, 2 measurements taken on the same day were shown to have between-measure correlations of 0.84 for C2 and 0.74 for C1.[29] AAD was measured using magnetic resonance imaging (1.5-T whole-body magnetic resonance imaging systems Signa CV/I or Signa LX; General Electric Medical Systems). Images of the aorta were captured using gradient echo phase-contrast cine magnetic resonance imaging with electrocardiographic gating, and cross-sectional areas of the ascending aorta were determined using FLOW software (Medis Medical Imaging Systems). Aortic distensibility was then calculated as follows: (maximum cross-sectional area–minimum aortic cross-sectional area)/(minimum cross-sectional area×pulse pressure).[20,27,28,31]

FMD was measured using high-resolution ultrasonography of the brachial artery. After at least 6 hours of fasting and smoking, a standard BP cuff was placed on the right arm of each participant at 2 inches below the antecubital fossa. A 9-MHz linear array transducer (M12L transducer; General Electric Healthcare) was then used to image the brachial artery at 5 to 9 cm above the antecubital fossa. After images were recorded at rest, reactive hyperemia was induced by occluding the brachial artery for 5 minutes at a cuff pressure ≥50 mm Hg above the participant's systolic BP. Digitalized images were collected for 30 seconds before inflation of the cuff and for 2 minutes beginning immediately before deflation of the cuff. FMD was defined as the percentage of increase in the brachial artery with reactive hyperemia and calculated as follows: [(peak brachial artery diameter after cuff deflation–diameter at rest)/diameter at rest]×100%. Intraclass correlation coefficients were 0.90 for baseline diameter, 0.90 for maximum diameter, and 0.54 for percentage of FMD.[21,26,30]

Systolic and diastolic BPs were measured using a Dinamap BP device (Dinamap Monitor Pro 100; Critikon). At each visit, 3 resting BPs were obtained with the participant in a seated position following a 5-minute rest period. The average of the second and third BP readings was used.[22,32–34] Pulse pressure was calculated as seated systolic BP minus seated diastolic BP.[21]

Exposure

The primary exposure was *APOL1* risk status, which we defined using a recessive genetic model consistent with prior studies on *APOL1* and kidney disease.[7,8,10,35,36] DNA was extracted from buffy coat samples collected at exam 1 and genotyped for the *APOL1* risk variants (rs73885319 and rs71785313) via TaqMan assays (Applied Biosystems 7900).[22,37] The G1 risk allele (rs73885319 and rs60910145) consists of 2 missense mutations, whereas the G2 risk allele (rs71785313) consists of a 6-bp deletion.[7,8] The *APOL1* high-risk genotypes were specified by the presence of 2 risk alleles (G1/G1, G1/G2, or G2/G2), whereas the low-risk genotypes were specified by the presence of 0 or 1 risk allele (G0/G0, G1/G0, or G2/G0). As previously described, 406 ancestry-informative markers from the Affymetrix 6.0 array and 4 ancestry populations in the ADMIXMAP software were used to estimate proportion of global African ancestry.[37]

Additional Variables

Data on sociodemographic factors, personal and family medical histories, and medication use were obtained through questionnaires.[22] The MESA Typical Week Physical Activity Survey, adapted from the Cross-Cultural Activity Participation Survey, was used to quantify baseline physical activity.[22,33] Body mass index was calculated by dividing weight in kilograms by height in meters squared. Hypertension was defined by a systolic BP ≥140 mm Hg, a diastolic BP ≥90 mm Hg,[38] or use of BP-lowering medications, whereas diabetes mellitus was defined by a fasting glucose ≥126 mg/dL (measured using the Vitros analyzer; Johnson & Johnson Clinical Diagnostics) or use of glucose-lowering medications.[34,37,39] Fasting lipids were determined using the cholesterol oxidase method (for total cholesterol and high-density lipoprotein; Roche Diagnostics), the triglyceride GB reagent (for triglycerides; Roche Diagnostics), and the Friedewald equation (for low-density lipoprotein).[32,34,40] Glomerular filtration rate was estimated based on cystatin C using the Chronic Kidney Disease-Epidemiology Collaboration equation.[41] A particle-enhanced immunonephelometric assay (N Latex Cystatin C; Siemens) on a nephelometer (BNII; Siemens) and corrected for assay drift was used to measure cystatin C from serum specimens stored at –70°C.[42,43] Urine albumin was measured by nephelometry (Array 360 CE Protein Analyzer; Beckman Instruments), and creatinine was measured by the Jaffe method (Vitros 950IRC instrument; Johnson & Johnson Clinical Diagnostics) from a single morning urine sample.[43,44]

Statistical Analysis

We compared baseline characteristics, overall and by *APOL1* risk status, using count (percentage), mean

(SD), and median (interquartile range). To assess the cross-sectional associations of *APOL1* risk status with C2, C1, AAD, and FMD at exam 1, we constructed linear regression models adjusting for age, sex, and African ancestry. Utilizing linear mixed-effects models, we then examined the longitudinal associations of *APOL1* risk status with systolic BP, diastolic BP, and pulse pressure, also adjusting for age, sex, and African ancestry. To model the dependence between repeated-outcome measures, we used the autoregressive order 1 covariance structure of the residuals, which assumed that BP values measured at consecutive visits were correlated more strongly than those separated by longer time intervals. In sensitivity analyses, we further adjusted for antihypertensive medication use as a time-updated binary variable. Statistical analyses were performed using SPSS v24 (IBM Corp) and Stata release 13 (StataCorp). We considered $P<0.05$ to be statistically significant.

RESULTS

Baseline Characteristics

Based on a recessive genetic model, 12% of the study population had an *APOL1* high-risk genotype (2 risk alleles), whereas 88% had an *APOL1* low-risk genotype (0 or 1 risk allele). At baseline, mean age was 62 years old, 54% were female, 58% had hypertension, and mean systolic BP was 131±21 mm Hg. Mean estimated glomerular filtration rate (based on cystatin C) was 90±20 mL/min per 1.73 m^2, and 11% had albuminuria, which we defined by a urine albumin-to-creatinine ratio ≥30 mg/g. Although hypertension and use of anti-hypertensive medications were more common in the *APOL1* high-risk group, BP control appeared fairly similar between the 2 *APOL1* risk groups (Table 1).

Subclinical Measures of Vascular Function

Mean baseline measures of C2 and C1 did not differ significantly between the 2 *APOL1* risk groups (C2, 4.01 versus 4.20 mL/mm Hg×100; C1, 13.41 versus 13.49 mL/mm Hg×10 comparing *APOL1* high- versus low-risk, respectively). Mean baseline AAD was also comparable among *APOL1* high- versus low-risk individuals (1.55 versus 1.69 mm $Hg^{-1}\times10^3$, respectively). In unadjusted models and models adjusted for age, sex, and African ancestry, there were no significant differences in these subclinical measures of vascular function by *APOL1* risk status (Table 2).

Subclinical Measure of Endothelial Function

Mean baseline FMD was similar for the 2 *APOL1* risk groups (0.16 versus 0.15 mm comparing *APOL1* high versus low risk, respectively). In the unadjusted model and the model adjusted for age, sex, and African ancestry, FMD did not differ significantly by *APOL1* risk status (Table 2).

Blood Pressure

The mean number of BP visits was 4.5±0.85 for each *APOL1* risk group over a mean follow-up of 7.8 years. In longitudinal analyses, relative annual change in systolic BP did not differ significantly between *APOL1* high- versus low-risk individuals (between-group difference, −0.20; 95% CI, −0.48 to 0.09; $P=0.17$). Similar conclusions were obtained when considering diastolic BP or pulse pressure as the outcome of interest (Table 3; Figure).

From exam 1 to exam 5, the number of individuals receiving pharmacologic therapy for hypertension increased from 50% to 68%, with the number of individuals on ≥3 antihypertensive medications increasing from 7% to 15% (Table S1). Given this intensification in treatment over time, we further adjusted for time-updated antihypertensive medication use and still found a lack of association between *APOL1* risk status and longitudinal systolic BP, diastolic BP, or pulse pressure (between-group differences in relative annual change for *APOL1* high versus low risk of −0.18 [95% CI, −0.46 to 0.10; $P=0.22$], −0.13 [95% CI, −0.36 to 0.10; $P=0.28$], and −0.32 [95% CI, −0.69 to 0.23; $P=0.32$], respectively).

DISCUSSION

In this study, among Black individuals without baseline clinical cardiovascular disease, we found that *APOL1* risk status was not associated with subclinical measures of vascular or endothelial function. In addition, there was no association between *APOL1* risk status and change in BP levels over time. Taken together, our results provide further evidence against a role of the *APOL1* risk variants in the development of hypertension.

To our knowledge, the associations between *APOL1* and subclinical measures of vascular and/or endothelial function have not been examined previously. In MESA, we previously reported that lower C2, C1, and AAD were each associated with an increased risk of incident hypertension,[20] whereas Shimbo et al reported that lower FMD levels were associated with prevalent but not incident hypertension.[26] Given these findings, we hypothesized that if the *APOL1* risk variants were to confer an increased risk of hypertension, this might begin with subclinical changes in vascular and/or endothelial function. In the present study, however, we did not observe a significant association between *APOL1* high-risk status and baseline levels of C2, C1, AAD, or FMD. These findings warrant replication in

Table 1. Baseline Characteristics of Study Population at MESA Exam 1 by *APOL1* Risk Status

Characteristic	All (n=1619)	*APOL1* high-risk (n=190)	*APOL1* low-risk (n=1429)
Age, y	62±10	62±9	62±10
Female	876 (54)	96 (51)	780 (55)
Education			
Less than high school	180 (11)	25 (13)	155 (11)
High school graduate	312 (19)	32 (17)	280 (20)
Postsecondary	1116 (69)	132 (70)	984 (69)
Employment			
Employed	658 (41)	76 (40)	582 (41)
Unemployed/employed part-time	125 (8)	18 (10)	107 (8)
Retired/homemaker	824 (51)	95 (50)	729 (51)
Annual family income			
<$25 000	437 (29)	49 (28)	388 (29)
$25 000–$49 999	486 (33)	57 (33)	429 (32)
$50 000–$74 999	310 (21)	35 (20)	275 (21)
≥$75 000	263 (18)	32 (19)	231 (18)
Smoking status			
Never	738 (46)	84 (44)	654 (46)
Former	579 (36)	67 (35)	512 (36)
Current	291 (18)	38 (20)	253 (18)
Diabetes mellitus	274 (17)	40 (21)	234 (16)
Fasting glucose, mg/dL	100±32	102±32	100±32
Hypertension	946 (58)	119 (63)	827 (58)
Systolic BP, mm Hg	131±21	132±21	131±21
Diastolic BP, mm Hg	75±10	74±10	75±10
Pulse pressure, mm Hg	57±17	58±18	57±17
Antihypertensive medication use	802 (50)	104 (55)	698 (49)
Total cholesterol, mg/dL	190±36	190±37	190±36
Triglycerides, mg/dL	89 [66–122]	88 [65–122]	89 [66–122]
HDL, mg/dL	52±15	54±16	52±15
LDL, mg/dL	117±33	116±35	117±33
Lipid-lowering medication use	253 (16)	33 (17)	220 (15)
Body mass index, kg/m^2	30.1±5.8	30.1±6.0	30.1±5.7
Moderate-vigorous PA, MET-min/wk	4613 [2160–8588]	4455 [2135–8370]	4636 [2160–8678]
Family history of heart disease	634 (42)	63 (35)	571 (43)
$eGFR_{CysC}$, mL/min/1.73 m^2	90±20	90±19	90±20
UACR, mg/g	5.3 [3.1–12.0]	5.5 [3.3–14.5]	5.2 [3.0–11.9]
UACR ≥30	170 (11)	27 (14)	143 (10)

Values presented as mean±SD, median [interquartile range], or number (percentage). BP, blood pressure; $eGFR_{CysC}$, estimated glomerular filtration rate based on cystatin C; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MESA, Multi-Ethnic Study of Atherosclerosis; MET, metabolic equivalent; PA, physical activity; and UACR, urine albumin-to-creatinine ratio.

other cohorts of individuals with clinical cardiovascular disease or hypertension. Still, 58% of our study population already had hypertension at baseline, with 50% on antihypertensive medications.

We also reported that *APOL1* high-risk status was not associated with longitudinal change in systolic BP, diastolic BP, or pulse pressure. These findings are in line with our prior findings in CARDIA in which we also observed a lack of association between the *APOL1* risk variants and longitudinal BP change and trajectory among healthy young adults.[18] Also consistent with our findings, previous studies of admixture mapping for hypertension did not identify the chromosomal region of *APOL1*.[6,45] In contrast, utilizing data from 3 electronic medical record–linked biobanks (as part of the Electronic Medical Records and Genomics [eMERGE] Network), others have reported that the *APOL1* risk variants were associated

Table 2. Association of *APOL1* Risk Status With Subclinical Measures of Vascular and Endothelial Function at MESA Exam 1

	C2			
	n	Mean (SD) mL/mm Hg×100	Model 1 β (95% CI)	Model 2 β (95% CI)
APOL1 low-risk	1393	4.20 (2.55)	0.00 (ref)	0.00 (ref)
APOL1 high-risk	193	4.01 (2.30)	−0.15 (−0.55, 0.25)	−0.11 (−0.47, 0.24)
P value		0.33	0.47	0.54
	C1			
	n	Mean (SD) mL/mm Hg×10	Model 1 β (95% CI)	Model 2 β (95% CI)
APOL1 low-risk	1393	13.49 (5.88)	0.00 (ref)	0.00 (ref)
APOL1 high-risk	193	13.41 (2.10)	−0.06 (−0.98, 0.86)	−0.05 (−0.88, 0.78)
P value		0.85	0.90	0.91
	AAD			
	n	Mean (SD) mm Hg^{-1}×10^3	Model 1 β (95% CI)	Model 2 β (95% CI)
APOL1 low-risk	863	1.69 (1.31)	0.00 (ref)	0.00 (ref)
APOL1 high-risk	122	1.55 (0.75)	−0.22 (−0.48, 0.04)	−0.21 (−0.46, 0.03)
P value		0.09	0.10	0.09
	FMD			
	N	Mean (SD) mm	Model 1 β (95% CI)	Model 2 β (95% CI)
APOL1 low-risk	692	0.15 (0.10)	0.00 (ref)	0.00 (ref)
APOL1 high-risk	85	0.16 (0.09)	0.01 (−0.02, 0.03)	0.01 (−0.02, 0.03)
P-value		0.58	0.50	0.56

Model 1 unadjusted. Model 2 adjusted for age, sex, and African ancestry. AAD indicates ascending aortic distensibility; C1, large arterial elasticity; C2, small arterial elasticity; FMD, flow-mediated dilation; and MESA, Multi-Ethnic Study of Atherosclerosis.

with higher systolic BP within age strata of 20 to 23, 24 to 27, and 28 to 31 years old but not in older age strata.[19] Potential explanations for these incongruent findings include differences in study population, analytical approach, and sample size. In MESA and CARDIA, we utilized data that were collected prospectively and that examined *change* in BP over time but had smaller sample sizes (n=1619 for MESA

Table 3. Association of *APOL1* Risk Status With Longitudinal BP Change From MESA Exams 1 to 5

	n	Relative Annual Change % Change/Year (95% CI)	Model 1 Between-Group Difference	Model 2 Between-Group Difference
Systolic BP				
APOL1 low risk	1429	−0.10 (−0.20, −0.01)	0.00 (ref)	0.00 (ref)
APOL1 high risk	190	−0.21 (−0.46, 0.04)	−0.11 (−0.38, 0.16)	−0.20 (−0.48, 0.09)
P value			0.42	0.17
Diastolic BP				
APOL1 low risk	1429	−0.63 (−0.71, −0.55)	0.00 (ref)	0.00 (ref)
APOL1 high risk	190	−0.69 (−0.90, −0.49)	−0.06 (−0.28, 0.16)	−0.14 (−0.37, 0.09)
P value			0.57	0.24
Pulse pressure				
APOL1 low risk	1429	0.56 (0.41, 0.71)	0.00 (ref)	0.00 (ref)
APOL1 high risk	190	0.41 (0.01, 0.82)	−0.15 (−0.58, 0.28)	−0.25 (−0.71, 0.21)
P value			0.50	0.28

Model 1 unadjusted. Model 2 adjusted for age, sex, and African ancestry. BP, blood pressure; MESA, Multi-Ethnic Study of Atherosclerosis; and ref, referent.

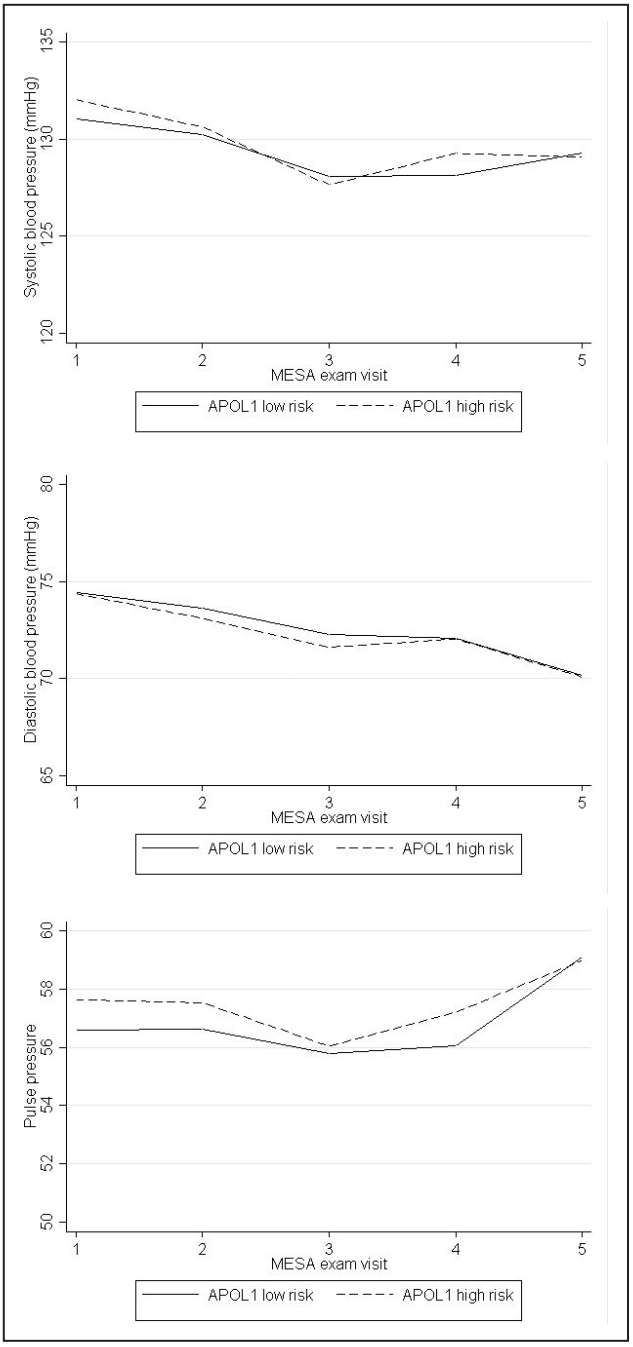

Figure. Longitudinal changes in systolic blood pressure, diastolic blood pressure, and pulse pressure by *APOL1* risk status from MESA (Multi-Ethnic Study of Atherosclerosis) exams 1 to 5.

and n=1330 for CARDIA).[18] In eMERGE, data were extracted from electronic medical records, and *differences* in BP within age strata were compared, but sample sizes were much larger (n=9203).[19] Although null, the results of the current study contribute to our understanding of the potential role of *APOL1* risk variants in extrarenal disease. In clinical practice, *APOL1* screening is already being offered to some patients. Intervention for those with high-risk genotypes may include aggressive BP monitoring and control to help prevent development or progression of chronic kidney disease. Our results provide further support for the notion that having an *APOL1* high-risk genotype without other risk factors for kidney disease may not necessarily warrant more intensive BP management beyond standard care.[36]

Interestingly, systolic BP appeared to decrease over time, particularly between MESA exams 1 and 3. On further investigation, we found that this finding was likely due to an intensification of antihypertensive treatment. In additional analyses adjusting for antihypertensive medication use, the lack of association between *APOL1* high-risk status and longitudinal systolic BP persisted, suggesting that our null findings were not due to differences in antihypertensive medication use between the 2 risk groups.

Our study has several notable strengths. First, our outcomes of interest included not only BP but also potential subclinical precursors of hypertension. Second, we leveraged prospectively collected data from a well-described cohort of individuals without baseline clinical cardiovascular disease. In particular, C2, C1, AAD, FMD, and BP were each measured in a standardized manner. Third, follow-up was relatively long at nearly 8 years, with 88% of study participants having ≥4 BP measurements over the course of 5 visits. Limitations include the cross-sectional analyses of C2, C1, AAD, and FMD at baseline; limited generalizability to other populations (eg, those with clinical cardiovascular disease, more hypertension, or moderate to severe chronic kidney disease); and potential for residual confounding. Last, the CIs around our effect suggest that there may still be an association that we were unable to detect.

In conclusion, we found that among Black individuals without baseline clinical cardiovascular disease, *APOL1* high-risk status was not associated with subclinical measures of vascular and endothelial function at baseline or changes in BP during follow-up.

ARTICLE INFORMATION

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Disclosures

Peralta is chief medical officer (CMO) for Cricket Health. The remaining authors have no disclosures to report.

Supplementary Materials

Table S1
Figure S1

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SUPPLEMENTAL MATERIAL

Table S1. Number of anti-hypertensive medications by MESA Exam visit and *APOL1* risk status.

Number of anti-hypertensive medications	All	*APOL1* high-risk	*APOL1* low-risk
Exam 1			
Mean (SD)	0.82 (1.01)	0.95 (1.09)	0.80 (0.99)
0	817 (50%)	86 (45%)	731 (51%)
1	421 (26%)	53 (28%)	368 (26%)
2	262 (16%)	31 (16%)	231 (16%)
≥3	119 (7%)	20 (11%)	99 (7%)
Exam 2			
Mean (SD)	0.91 (1.08)	1.03 (1.15)	0.90 (1.07)
0	743 (47%)	78 (42%)	665 (48%)
1	415 (26%)	52 (28%)	363 (26%)
2	267 (17%)	34 (18%)	233 (17%)
≥3	147 (9%)	20 (11%)	127 (9%)
Exam 3			
Mean (SD)	1.05 (1.10)	1.30 (1.19)	1.02 (1.09)
0	583 (40%)	57 (34%)	526 (41%)
1	428 (29%)	40 (24%)	388 (30%)
2	291 (20%)	46 (27%)	245 (19%)
≥3	161 (11%)	27 (16%)	134 (10%)
Exam 4			
Mean (SD)	1.08 (1.14)	1.16 (1.13)	1.06 (1.15)
0	586 (40%)	61 (36%)	525 (41%)
1	418 (29%)	47 (28%)	371 (29%)
2	279 (19%)	41 (24%)	238 (18%)
≥3	178 (12%)	21 (12%)	157 (12%)
Exam 5			
Mean (SD)	1.24 (1.15)	1.36 (1.16)	1.22 (1.15)
0	374 (32%)	43 (30%)	331 (33%)
1	362 (31%)	39 (27%)	323 (32%)
2	252 (22%)	36 (25%)	216 (21%)
≥3	172 (15%)	27 (19%)	145 (14%)

SD=standard deviation.

Figure S1. Flowchart of study population.