Associations of Noninvasive Measures of Arterial Compliance and Ankle-Brachial Index: The Multi-Ethnic Study of Atherosclerosis (MESA)

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BACKGROUND
The association between measures of arterial compliance and peripheral arterial disease (PAD) is unclear. Early changes in arterial wall compliance could be a useful marker of patients at high risk for developing lower extremity atherosclerosis.

METHODS
We used linear and logistic regression models on baseline data from 2,803 female and 2,558 male participants in the Multi-Ethnic Study of Atherosclerosis (MESA) to study associations between tonometry-derived baseline measures of arterial compliance (large artery compliance (C1) and small artery compliance (C2)) and the baseline ankle-brachial index (ABI), as well as change in the ABI over ~3 years of follow-up.

RESULTS
In cross-sectional analyses, lower C1 and C2 values, indicating poorer arterial compliance, were associated with lower ABI. There were significant linear trends across strata of ABI, especially in C2 which ranged from 3.7 ml/mm Hg × 100 (95% confidence interval (CI) 3.3–4.2) in women with an ABI < 0.90 to 4.2 ml/mm Hg × 100 (95% CI 4.1–4.3 $P < 0.001$) in women with ABI 1.10–<1.40. Similar significant trends ($P < 0.001$) were seen in men. In prospective analyses, those with the lowest tertile of C2 values at baseline had a greater multivariable-adjusted odds for decline in ABI of ≥ 0.15 over 3 years compared to those with the highest C2 values at baseline (odds ratio (OR) 1.80, 95% CI 1.23–2.64).

CONCLUSIONS
We observed that less compliant arteries were significantly associated with low ABI in cross-sectional analysis and with greater decline in odds of ABI over time.

Keywords: *ankle-brachial index; arterial compliance; blood pressure; hypertension; peripheral arterial disease*

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The ankle-brachial index (ABI) is a simple and noninvasive method for diagnosing and assessing severity of lower extremity peripheral arterial disease (PAD). Persons without lower extremity atherosclerosis typically have an ABI > 1.00, because of increasing blood pressures in distal vasculature related to increased arterial taper.[1] An ABI < 0.90 has good sensitivity and excellent specificity for a lower extremity arterial stenosis >50% on digital subtraction angiography.[2] However, ABI < 0.90 is a relatively late manifestation of atherosclerosis. Prior to the development of an occlusive atheroma, other functional changes in arterial wall function and structure may occur.[3,4] Identifying early changes in arterial wall function and structure could be a useful indicator of subclinical vascular disease in patients at high risk for developing lower extremity atherosclerosis. Early identification of patients with lower extremity atherosclerosis is important as people with PAD are at increased risk for cardiovascular events and functional decline, and they represent a potential target population for early preventive intervention.[5–7]

Peripheral arterial pulse wave analysis, derived from radial artery applanation tonometry, is a noninvasive technique for measuring arterial compliance. Systemic measures of large vessel compliance, C1, and small vessel compliance, C2, can be derived from this method.[8–10] Lower C2 values, indicating poorer small vessel compliance, have been observed in subjects with older age, type II diabetes mellitus, hypertension, tobacco use, and in post menopausal women with coronary heart disease. Recently, prospective data demonstrate independent associations between lower C2 and incident hypertension, coronary heart disease events, and stroke.[11,12] No such associations have been observed for C1.[13–16] As atherosclerosis is a systemic disease, alterations in radial artery pulse wave

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characteristics may be seen in patients with low ABI. Though limited, current data suggest there may be some relationship between tonometry-derived measures of arterial compliance and the existence of PAD.[17] Weak cross-sectional associations have been observed between C2 and ABI in diabetic patients, but data from large community-based samples are lacking.[13,17] To our knowledge, no prior studies have investigated longitudinal relationships between baseline arterial compliance measures and change in ABI.

We studied associations between C1 and C2 with presence and severity of PAD among participants in the Multi-Ethnic Study of Atherosclerosis (MESA) cohort. We also assessed associations of these compliance measures at baseline with changes in the ABI over time. If lower arterial compliance is associated with lower ABI values and greater declines in the ABI over time, applanation tonometry–derived arterial compliance measures could be a noninvasive technique to identify early subclinical atherosclerosis in the lower extremities. Such associations could provide mechanistic insight into factors mediating the development and progression of PAD. We hypothesized that lower C1 and C2 values, indicating lower arterial compliance, are associated with lower ABI values at baseline. We further hypothesized that lower C1 and C2 values at baseline would be associated with greater decline in the ABI at 3-year follow-up.

METHODS

Participants. The MESA cohort has been described previously.[18] In brief, between July 2000 and August 2002, 6,814 men and women who identified themselves as white, African American, Hispanic, or Chinese, were 45–84 years old, and were free of clinically apparent cardiovascular disease were recruited and participated in the baseline examination. Individuals with a history of physician-diagnosed heart attack, angina, heart failure, stroke, or transient ischemic attack, or who had undergone an invasive procedure for cardiovascular disease were excluded from participation. Participants who underwent lower extremity revascularization during follow-up and individuals with ABI > 1.40 at baseline were excluded from this analysis. The participants enrolled at baseline were eligible to participate in three subsequent study examinations occurring approximately every 18–24 months and referred to as clinic visits 2, 3, and 4.

Participants were recruited from the following six communities: Baltimore City and Baltimore County, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; Northern Manhattan and the Bronx, NY; and St. Paul, MN. The institutional review boards at all participating centers approved the study, and all participants gave informed written consent.

Data collection. At the baseline examination, standardized questionnaires were used to obtain demographic information and medication usage for high blood pressure, high cholesterol, or diabetes. Cigarette smoking was calculated in pack-years and also defined as current, former, or never. Height and weight were measured with participants wearing light clothing and no shoes. Body mass index was calculated as weight in kilograms divided by the square of height in meters. Resting blood pressure was measured three times in seated participants with a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, FL). The average of the last two measurements was used in the analysis. Hypertension was defined as the systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or current use of an antihypertensive medication.

Laboratory. At the baseline examination and at visit 3, blood was collected after a 12-h fast and stored at −70 °C. Total and high-density lipoprotein cholesterol, triglycerides, glucose, and creatinine were measured and as previously reported, low-density lipoprotein cholesterol was calculated by the Friedwald equation.[19] Diabetes was defined as fasting glucose ≥ 126 mg/dl or use of glucose-lowering medication.[20] The estimated glomerular filtration rate (eGFR) was calculated using the Modified Diet in Renal Disease (MDRD) study formula.[21]

ABI protocol. At the baseline examination and Exam 3, systolic blood pressure measurements for calculation of the ABI were obtained using a hand-held Doppler instrument with a 5-mHz probe (Nicolet Vascular, Golden, CO). In brief, systolic blood pressures were measured in the bilateral brachial, dorsalis pedis, and posterior tibial arteries. Brachial artery pressures were averaged to obtain the ABI denominator. When the two brachial artery pressures differed by 10 mm Hg or more, the higher brachial artery pressure was used as the denominator. For each lower extremity, the ABI numerator used was the highest pressure (dorsalis pedis or posterior tibial) from that leg. The lower of the right and left ABI values was used as the index ABI for that subject unless one leg yielded an ABI > 1.40 in which case the higher ABI was used, and the participant was excluded from these analyses. In the longitudinal analyses, the ABIs from the same leg were compared from baseline to Exam 3. We defined decline in ABI as a decrease in ABI > 0.15; increase in ABI was defined as an increase in ABI > 0.15, and stable ABI was defined as change ≤0.15. We chose the cut-point of 0.15 because this magnitude of change in ABI has been used to define significant progression of PAD in previous studies. Furthermore, independent associations with increased PAD symptoms and all-cause mortality and ABI decline >0.15 have been demonstrated as well.[22–24]

Determination of C1 and C2. At the baseline examination, noninvasive measures of arterial stiffness for calculating C1 and C2 were obtained with the Hypertension Diagnostics Pulse Wave CR-2000 device (Eagan, MN). The Pulse Wave CR-2000 obtains blood pressure measurements and arterial pulse waveforms with an oscillometric blood pressure module, and an arterial pulse pressure sensor. The blood pressure measurements are taken from the upper left arm, and the pulse pressure sensor is positioned on the right wrist. Participants were supine, and their right wrist was placed in the wrist stabilizer. The tonometry sensor was placed over the area of maximum

radial artery pulsation. The HDI Pulse Wave CR-2000 device makes automatic adjustments to ensure a stable waveform. A modified Windkessel model, which is analogous to an electrical circuit, is used to generate systemic arterial compliance measures. The model calculates a capacitive compliance measure, C1, to represent large arterial vessel compliance and an oscillatory or reflective element, C2, to represent small arterial vessel compliance. Several coefficients for the Windkessel formula were derived from the diastolic portion of the pressure wave form. The technique for coefficient derivation is proprietary and was unavailable to the research team. These coefficients are then multiplied by an estimated systemic vascular resistance to obtain the capacitive compliance of the proximal aorta (C1) and oscillatory compliance of small distal arteries (C2) values which represent large and small vessel compliance, respectively.[25] Systemic vascular resistance is estimated by dividing the mean arterial pressure by an estimated cardiac output. Cardiac output was estimated from ejection time, body surface area, and heart rate.[12]

Statistical analyses. Of the 5,496 MESA participants, 135 were excluded from the cross-sectional analysis, due to missing data for either baseline ABI, C1, C2, clinical covariates, or follow-up ABI measurements. A total of 5,361 had ABI measurements at both baseline and Exam 3, baseline pulse wave measures, and all covariates included in our final model.

ABI was stratified according to previously published definitions: ABI < 0.90 (definite PAD); 0.90 < ABI < 1.00 (borderline ABI); 1.00 < ABI < 1.10 (low-normal ABI); 1.10 < ABI < 1.40 (normal ABI).[26] Arterial compliance measures were analyzed as continuous variables and also were categorized into low, middle, and high according to tertiles of C1 and C2 distribution within the entire cohort. All analyses by baseline ABI groups were performed separately for women and men. Baseline characteristics of study participants were presented as mean (±s.d.) for continuous variables, or percentage for categorical variables, and linear trends across the four ABI groups were tested with ABI as a continuous variable using linear regression (for continuous variables) or Cochran-Armitage trend test (for categorical variables). In the cross-sectional analyses, general linear models were used to compute ABI group mean compliance measures, adjusted for baseline age, race, cigarette smoking, diabetes, hypertension, eGFR, and total/high-density lipoprotein cholesterol ratio. Pairwise comparison was made between the normal ABI group (referent) and the PAD, borderline, or low-normal ABI groups, and testing for linear trend was performed with continuous ABI using the general linear model.

For the longitudinal analysis, change in ABI over 3-year follow-up was categorized into three groups: ABI decline ≥ 0.15; stable ABI (change ≤ ±0.15), and ABI increase > 0.15.[27] C1 and C2 values were examined continuously and as tertiles (low, middle, and high). Separate linear and logistic regression models were used to examine the OR and 95% confidence intervals (CI) of ABI progression (ABI decrease or increase ≥ 0.15), compared to people maintaining a stable ABI (ABI change < 0.15). In the multivariate models, we first adjusted for age, gender, race, cigarette smoking, hypertension, diabetes, eGFR, total/high-density lipoprotein cholesterol ratio, heart rate, and baseline ABI. We further adjusted for height and weight. We then stratified by baseline ABI to ensure there was no residual confounding because of this variable. With stratification there was no significant change in our results, thus we pooled all baseline ABI groups and adjusted for baseline ABI in our multivariable models. Multivariable-adjusted logistic regression was used to test differences between the arterial compliance high tertile (referent) and the low or middle arterial compliance tertile. Linear trend across the arterial compliance tertiles was tested by entering natural log-transformed C1 or C2 variables in logistic regression. All analyses were performed using SAS statistical software version 9.2 (SAS Institute, Cary, NC). A P value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics

Baseline characteristics for female and male participants are shown in **Table 1**. As expected, participants with PAD had a higher mean age and higher prevalence of systolic hypertension, tobacco use, and diabetes compared to participants with a normal ABI.

Cross-sectional comparisons of C1 and C2 between different ABI categories at baseline

For both men and women, significant linear trends were observed at baseline across all ABI strata for C1 and C2. In fully adjusted analyses, C1 and C2 values, indicating poorer large and small vessel compliance, respectively, were lower in participants with lower ABI. Among women, C1 and C2 were significantly lower in the borderline ABI category as compared to the normal ABI category (**Table 2**).

Among men, C1 was not significantly lower across all low ABI strata in pairwise comparisons. C2, however, was significantly lower across all lower ABI strata when compared to the normal ABI referent.

Prospective associations between baseline measures of arterial compliance and change in ABI

Among 5,361 participants with 3-year follow-up data, 256 had a decline in ABI > 0.15. Because relatively few women had this magnitude of ABI decline, we pooled all participants and adjusted for sex. Baseline characteristics of participants in different groups of ABI change are presented in **Table 3**. When compared with the stable ABI group, participants with a decline in ABI > 0.15 were older, had a higher baseline ABI, and included a higher prevalence of cigarette smokers. Baseline characteristics associated with tertiles of C2 are shown in the **Supplementary Table S1** online. In fully adjusted models, (see **Table 4**), the lowest C2 tertile at baseline was associated with an increased risk for decline in ABI > 0.15, compared to the stable ABI group (OR 1.80, 95% CI 1.23–2.64). No significant associations between baseline C1 tertiles and ABI decline were identified.

Five hundred and sixty-eight participants had an increase in ABI > 0.15. As compared to those with no significant

Table 1 | Baseline characteristics of women and men according to ankle-brachial index, MESA (2000–2002)

	Women (*N* = 2,803)					Men (*N* = 2,558)				
	Definite PAD (<0.90)	Borderline ABI (0.90–<1.00)	Low-normal ABI (1.00–<1.10)	Normal ABI (1.10–<1.40)	*P* trend	Definite PAD (<0.90)	Borderline ABI (0.90–<1.00)	Low-normal ABI (1.00–<1.10)	Normal ABI (1.10–<1.40)	*P* trend
N	81	270	1,047	1,405		73	105	552	1,828	
Age (years)	70.2 (9.9)	64.2 (10.2)	62.2 (10.0)	59.6 (9.6)	<0.001	69.5 (9.1)	66.2 (10.1)	62.6 (10.2)	60.7 (9.8)	<0.001
Body mass index (kg/m^2)	28.4 (5.7)	28.3 (5.9)	28.1 (5.8)	29.0 (6.3)	<0.001	27.2 (3.9)	28.1 (4.8)	27.2 (4.3)	28.0 (4.3)	<0.001
Smoking (%)										
Current	14.8	16.7	10.4	10.2	0.011	27.4	19.0	18.1	11.3	<0.001
Never	51.8	53.3	60.1	61.7	0.006	20.5	26.7	36.6	44.6	<0.001
Blood pressure (mm Hg)										
Systolic	141.5 (28.7)	133.2 (23.0)	128.8 (23.3)	120.7 (20.2)	<0.001	136.6 (23.2)	132.5 (19.7)	127.0 (19.4)	124.1 (18.0)	<0.001
Diastolic	70.5 (12.1)	70.3 (11.1)	69.6 (10.3)	68.0 (9.6)	<0.001	74.2 (10.3)	75.4 (9.1)	75.4 (9.5)	75.1 (9.1)	0.199
Medication use (%)										
Blood pressure	54.3	45.2	39.2	31.2	<0.001	58.9	45.7	36.6	32.5	<0.001
Statin	30.9	19.3	14.5	12.7	<0.001	20.5	20.9	14.3	13.8	0.030
Diabetes (%)	30.9	8.1	9.9	9.7	0.005	19.2	14.3	12.3	11.9	0.106
Cholesterol (mg/dl)										
Total	203.0 (32.8)	197.3 (35.5)	200.1 (34.2)	199.1 (34.5)	0.274	187.6 (35.4)	191.1 (35.0)	189.2 (38.0)	187.6 (33.4)	0.082
HDL	53.0 (14.1)	56.5 (15.2)	57.0 (15.9)	56.4 (14.7)	0.747	44.4 (10.9)	46.3 (12.8)	45.3 (12.0)	44.9 (11.4)	0.605
Total/HDL ratio	4.1 (1.3)	3.7 (1.1)	3.7 (1.1)	3.7 (1.1)	0.120	4.4 (1.2)	4.4 (1.2)	4.4 (1.5)	4.4 (1.2)	0.265
GFR	73.0 (20.6)	79.1 (17.0)	79.9 (17.0)	81.0 (17.1)	0.001	82.3 (18.6)	81.4 (19.7)	83.7 (18.1)	82.0 (16.4)	0.876

ABI, ankle-brachial index; GFR, glomerular filtration rate; HDL, high-density lipoprotein; PAD, peripheral arterial disease.

Table 2 | Baseline measures of arterial compliance by ABI category

	Women (*N* = 2,803)					Men (*N* = 2,558)				
	Definite PAD (<0.90)	Borderline ABI (0.90–<1.00)	Low-normal ABI (1.00–<1.10)	Normal ABI (1.10–<1.40)	*P* trend	Definite PAD (<0.90)	Borderline ABI (0.90–<1.00)	Low-normal ABI (1.00–<1.10)	Normal ABI (1.10–<1.40)	*P* trend
N	81	270	1,047	1,405		73	105	552	1,828	
Large artery compliance (C1) (ml/mm Hg × 10)	11.8 (10.8, 12.8)	11.2 ** (10.6, 11.7)	11.9 (11.6, 12.1)	12.1 (11.8, 12.3)	0.008	14.7 (13.5, 15.9)	15.1 (14.1, 16.1)	14.8** (14.4, 15.2)	15.5 (15.3, 15.7)	0.001
Small artery compliance (C2) (ml/mm Hg × 100)	3.7 (3.3, 4.2)	3.4* (3.2, 3.6)	3.6* (3.4, 3.7)	4.2 (4.1, 4.3)	<0.001	4.3* (3.7, 4.9)	4.6* (4.1, 5.1)	4.9* (4.6, 5.1)	5.6 (5.5, 5.7)	<0.001

Data are expressed as mean (95% CI) unless otherwise indicated. Analyses adjusted for age, race, cigarette smoking, diabetes, hypertension, GFR, and total/ HDL cholesterol ratio.
ABI, ankle-brachial index; CI, confidence interval; GFR, glomerular filtration rate; HDL, high-density lipoprotein; PAD, peripheral arterial disease.
*P < 0.001, **P < 0.01, comparing to the reference group (ABI 1.10–<1.40).

change in ABI, those who had an increase in ABI > 0.15 were less likely to be Hispanic, and more likely to have lower baseline ABI or to be a smoker (Table 3). There were no significant associations observed between baseline C1 or C2 measures and increase in ABI > 0.15.

When examined as a log-transformed linear variable, both C1 and C2 had significant, modest β coefficients for decline in ABI ≥ 0.15 (β (s.e.): 0.08 (0.04) P < 0.05; and 0.11 (0.03) P < 0.001, respectively) and increase in ABI ≥ 0.15 (β (s.e.): 0.13 (0.04) P < 0.01; and 0.09 (0.03) P < 0.001, respectively).

DISCUSSION

Findings reported here demonstrate that in cross-sectional analyses, lower ABI values are associated with significantly lower small artery compliance (C2) among men and women participants in MESA. Large artery compliance, C1, was less strongly associated with ABI in both men and women, and pairwise comparisons revealed only modest differences in C1 in the lower ABI strata. However, in pairwise comparisons, small artery compliance, C2, was significantly lower across most low ABI strata compared with the reference ABI category

Table 3 | Associations of baseline characteristics with 3-year ABI change

	ABI change at follow-up exam relative to baseline		
	Decline ≥0.15	Change <0.15 (Referent)	Increase ≥ 0.15
N	256	4,537	568
Age (years)	63.3 (10.4)**	61.5 (10.0)	60.7 (10.1)
Male, *N* (%)	125 (48.8)	2,167 (47.8)	266 (46.8)
Ankle-brachial index	1.17 (0.12)*	1.12 (0.10)	1.05 (0.12)*
Race, *N* (%)			
White	99 (38.7)	1780 (39.2)	239 (42.)
Chinese	23 (9.0)	571 (12.6)	65 (11.4)
African American	77 (30.1)	1173 (25.8)	167 (29.4)
Hispanic	57 (22.3)	1013 (22.3)	97 (17.1)**
Body mass index (kg/m^2)	28.7 (6.2)	28.1 (5.2)	29.1 (5.8)*
Smoking, *N* (%)			
Current	47 (18.4)**	551 (12.1)	58 (10.2)
Never	116 (45.3)	2321 (51.2)	306 (53.9)
Blood pressure (mm Hg)			
Systolic	126.4 (22.8)	125.2 (20.6)	126.8 (21.3)
Diastolic	71.0 (10.3)	71.9 (10.1)	72.4 (11.1)
Blood pressure medication use, *N* (%)	102 (39.8)	1,590 (35.0)	211 (37.1)
Hypertension, *N* (%)	118 (46.1)	1,925 (42.4)	255 (44.9)
Diabetes, *N* (%)	38 (14.8)	504 (11.1)	62 (10.9)
Total/HDL cholesterol ratio	4.1 (1.3)	4.1 (1.2)	4.0 (1.2)
Glomerular filtration rate	79.7 (18.6)	81.2 (17.1)	81.8 (16.7)
Large vessel compliance (C1) (ml/mm Hg × 10)	13.1 (5.9)	13.5 (5.5)	13.7 (5.9)
Small vessel compliance (C2) (ml/mm Hg × 100)	4.2 (2.6)***	4.6 (2.8)	4.7 (3.1)

Data are expressed as mean (s.d.) unless otherwise indicated.
ABI, ankle-brachial index; HDL, high-density lipoprotein.
*$P < 0.001$, **$P < 0.01$, ***$P < 0.05$.

(ABI 1.00–<1.40). In men, C2 was significantly lower across all low ABI strata. In prospective analyses, lower values of C2 at baseline were positively associated with a higher incidence of ABI decline > 0.15 at 3 years of follow-up.

PAD, at least as determined by ABI, is primarily a disease of the large, muscular arteries that supply the lower extremities. It may therefore be somewhat surprising that C2 appears to have a stronger cross-sectional and longitudinal association with ABI than does C1. However, decreases in arterial compliance may occur in the distal arterial bed with the development of atherosclerotic disease; this may be easier to measure or may exhibit more exaggerated differences than changes in the mechanical properties of large arteries supplying the lower extremity. In addition, some researchers have theorized that low C2 may be tightly linked to endothelial dysfunction, a well-validated marker of atherosclerosis.[28]

To our knowledge, there are no previous reports of an independent prospective association between C2 and a decline in ABI. As postulated above, it may be that C2 is detecting decreased arterial compliance because of endothelial dysfunction in the small vessels which may portend an increased probability of advancing lower extremity atherosclerosis. This suggests that, although the geographic distribution of atherosclerosis may vary, some systemic functional and structural changes may occur. We suspect the significant linear trend and β coefficients for an association of lower C2 with both an increase *and* a decrease in ABI is because of increased arterial stiffness occurring in atherosclerotic and calcified forms of PAD progression. Alternatively, the significant β coefficients of small magnitude observed may be due to the large sample size studied or residual confounding despite multivariable adjustment.

Associations between arterial compliance and ABI have been investigated in two other small cross-sectional studies. Duprez *et al.* found a significant correlation between ABI and C2 ($r = 0.36$, $P < 0.02$) in 43 patients with advanced PAD.[17] C2 values have been shown to associate with higher prevalence of hypertension, older age, smoking, diabetes, and with higher Framingham Risk Scores as well.[9,13–16] Thus, it was not surprising that unadjusted positive associations between ABI and C2 were observed in the MESA cohort, but the associations we observed remained significant even after multivariate adjustment.

Our study benefited from data collected in a large, well-phenotyped community-based sample of asymptomatic individuals. One limitation of our current study, as mentioned above, may be the geographic nature of atherosclerotic disease. PAD is primarily a disease of the large, muscular arteries of the lower extremity. However, these compliance measures were derived from pulse contour analysis of wave forms taken from the radial artery. Structural and functional changes may occur systemically in muscular arteries, suggesting that compliance derived from arterial pulse wave contour analysis from the radial artery may reflect compliance in the lower extremity arteries. However, there is some doubt that radial artery–derived compliance measures truly represent systemic vascular compliance.[29] It would be useful to derive C1 and C2 measured in the lower extremity in patients with PAD to control for this confounder and to further elucidate potential mechanisms for the observed associations between C2 and ABI.

The method for calculating C1 and C2 from radial artery pulse wave analysis is partially proprietary and unavailable to the research team. As such, if some of our covariates are included in the mathematical transformation function that is applied to the radial artery diastolic pressure decay curve, variable redundancy in the adjusted models may have occurred which could have decreased their accuracy.

In conclusion, lower arterial compliance is associated with lower ABI values in the MESA cohort. However, the strength of this association is modest. Low baseline C2 values, indicating lower small arterial compliance, are associated with a higher incidence of significant decline in ABI at 3 years of follow-up,

Table 4 | Odds ratios for ABI decline ≥ 0.15 over 3 years according to tertiles of baseline arterial compliance among all participants

Tertile of compliance	Large vessel compliance		Small vessel compliance	
	N/total	OR (95% CI)	*N*/total	OR (95% CI)
Unadjusted				
Low	100/1,608	1.34 (0.99–1.83)	106/1,598	1.46 (1.08–1.99)**
Middle	81/1,589	1.09 (0.79–1.50)	76/1,597	1.03 (0.74–1.43)
High (referent)	75/1,596	1.00	74/1,598	1.00
P for trend		0.107		0.015
Model 1				
Low		1.32 (0.91–1.92)		1.84 (1.26–2.67)*
Middle		1.07 (0.77–1.51)		1.15 (0.81–1.64)
High (referent)		1.00		1.00
P for trend		0.233		0.001
Model 2				
Low		1.17 (0.79–1.73)		1.80 (1.23–2.64)**
Middle		1.01 (0.72–1.43)		1.15 (0.81–1.64)
High (referent)		1.00		1.00
P for trend		0.779		0.002

The tertile cut-points for each compliance measure were as follows: large vessel compliance: low, <10.7; middle, 10.7–<15.0; high (reference), >15.0; small vessel compliance: low, <2.8; middle, 2.8–<5.1; high (reference), >5.1. Model 1: adjusted for age, gender, race, cigarette smoking, hypertension, diabetes, GFR, ratio of total to HDL cholesterol, and baseline ABI. Model 2: model 1 plus additionally adjusted for height, weight, and heart rate. *P* value for linear trend across the arterial compliance tertiles was tested by entering log-transformed C1 or C2 variable in logistic regression.
ABI, ankle-brachial index; CI, confidence interval; GFR, glomerular filtration rate; HDL, high-density lipoprotein; OR, odds ratio.
*$P < 0.001$, **$P < 0.01$, comparing to the reference group (highest tertile of arterial compliance or normal ABI).

even after adjustment for risk factors for PAD. Thus, radial artery tonometry–derived C2 may provide additional information about the extent and potential for progression of PAD. Further study may be warranted on the strength, mechanisms of association, and possible clinical utility of these measures.

Supplementary material is linked to the online version of the paper at http://www.nature.com/ajh

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