Supplementary Data

Derivation of Alternate Expressions for Distensibility Coefficient of the Vessel

Calculation of the distensibility coefficient (DC) and equivalent expressions using calculus are shown in Supplementary Table S1. The alternate continuous measures and linear approximations are derived using standard differential calculus. The alternate linear approximation of DC is two times the slope for the logarithmic transformation of the diameter. DC can thus be evaluated as the beta coefficient in linear regression models. In the usual linear approximation, the choice of D_{dia} or D_{sys} or some mean value of diameter is forced. However, such a choice is made moot in the alternate linear approximation.

Growth Curve Model

The growth curve mixed effects regression model formulation is an obvious way to yield a coefficient that represents the slope $\Delta(g(D))/\Delta P$, where $g(D)$ is two times the logarithmic transform of D. For a binary covariate (e.g., F = 0 if male, 1 if female) the model would be specified as:

$$[g(D)]_{ij} = \beta_0 + \beta_1 \overline{P}_j + \beta_2(\overline{P}_j - P_{ij}) + \beta_3 F \overline{P}_j + \beta_4 F(\overline{P}_j - P_{ij}) + \gamma_j + \eta(\overline{P}_j - P_{ij}) + \varepsilon_{ij}$$

for the ith condition (diastole or systole) of the jth individual. Random effects are estimated for the average diameters and the diameter-g(D) slope for every individual (γ and η, respectively), and the coefficients β_3 and β_4 can be interpreted as the fixed-effect association of the binary covariate with the mean diameter and the fixed-effect difference in slopes (i.e., the DC) associated with the covariate. This specification can be generalized to any categorical covariate. The associations of age with slopes were approximately linear; therefore, a continuous variable for age effect was included in the current analysis.

Supplementary Figure S1 shows the modeling for a random sample of 5 women (closed symbols, solid lines) and 5 men (open symbols, dotted lines) from the dataset. The symbols represent the diastolic and systolic diameters plotted against the diastolic and systolic pressures. These plots are centered on the average of the systolic and diastolic pressures of the individual. For 1 individual, this is demonstrated: the diastolic pressure of 63 mm Hg and systolic pressure of 120 mm Hg are plotted on either side of the their average, that is, 91.5 mm Hg. The diameters on the vertical axis are plotted on the logarithmic scale. The average blood pressure (BP) is a covariate in the mixed model (mm). In every individual, the following random effects are estimated: a mean diameter (where the plotted line for the individual crosses the vertical axis) and a slope (the slope of the line joining individual diastolic and systolic measures). There is also an overall intercept and slope for groups (shown as thicker lines) that can be compared as a fixed effect. The fixed effect for the intercept (difference between the intercepts of the thick dotted and thick solid lines) is the average difference in the diameters (on the log scale) between men and women. The difference in DCs between men and women can be derived from the difference in the slopes of the thick lines.

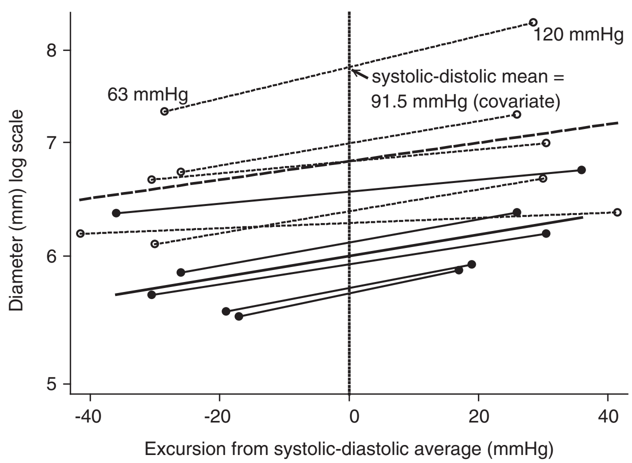
Comparison of MM Results for DC with Traditionally Calculated DC

Supplementary Table S2 and S3 show various models assessing the association of carotid diameters and pressures with age, sex, and race. Model 0, a linear regression model for log(systolic diameter) as the dependent variable assumes that if diastolic diameter and systolic and diastolic pressures (all log-transformed) are held constant as covariates, any association of the other covariates must reflect associations with arterial distensibility. However, model 0 imposes a linear combination of log-transformed diastolic diameter and systolic and diastolic pressures. In model 0, age, sex, race, and the age-sex interaction had significant associations in the regression analysis. In model 1, DC is calculated for every person, and age, sex, race, and the age-sex interaction had significant associations in the regression analysis. After adjusting model 1 for systolic and diastolic pressures and diastolic diameter, however, there were large changes in all coefficients of association, and the age-sex interaction was no longer significant. Model 2, the mixed model, simultaneously assesses the association of covariables with mean arterial diameter and the DC. All associations with DC were approximately as strong as model 1. In addition, the arterial diameter (intercept) is greater with greater age, but this association is significantly greater in women than men. Ethnic differences in diameter are also seen, with Chinese having the smallest diameter and Hispanics having the largest diameter. These associations have no counterpart in model 0 and model 1.

Supplementary Table S1. Traditional Calculations and Alternate Mathematically Equivalent Calculations for Distensibility and Compliance Coefficients

	Continuous measure	*Alternate continuous measure*	*Linear approximation*	*Alternate linear approximation*
Distensibility coefficient	$\frac{2}{\overline{D}} \times \frac{dD}{dP}$	$\frac{2 \times d(\log_e(D))}{dP}$	$\frac{2}{\overline{D}} \times \frac{\Delta D}{\Delta P}$	$\frac{2 \times \Delta(\log_e(D))}{\Delta P}$

D, diameter of the artery; *P*, blood pressure within the artery; Δ, the difference between systolic and diastolic measurements; $\overline{D}$, the appropriate mean value of the diameter. In practice, $\overline{D}$ may be approximated to the systolic or diastolic diameter.[5]



SUPPLEMENTARY FIG. S1. Pictorial explanation of mixed model analysis of log(diameter) vs. blood pressure to obtain associations of distensibility coefficient.

Supplementary Table S2. Association of Age, Sex, and Race with Carotid Artery Distensibility Coefficient and Diameter, Adjusted for Traditional Risk Factors

	*Difference in DC (2*slope) mm Hg^{-1}*	*% Larger carotid diameter (intercept)*
Covariate	*Beta coefficients* (p *values)*	
Sex (male vs. female) at 65 years of age	1.00×10^{-4} (0.012)	4.32% (8.8×10^{-22})
Age (difference per year among females)	-4.98×10^{-5} (3.5×10^{-176})	0.25% (9.6×10^{-36})
Difference of age-associated slope between men vs. women	7.78×10^{-6} (0.003)	−0.10% (1.2×10^{-4})
Height (difference per cm of height)	2.74×10^{-6} (0.19)	0.19% (2.3×10^{-17})
White	Reference	Reference
Chinese vs. White	-1.72×10^{-4} (2.8×10^{-4})	−3.67% (6.0×10^{-13})
African American vs. White	-3.05×10^{-4} (2.0×10^{-20})	−0.42% (0.26)
Hispanic vs. White	-2.63×10^{-4} (5.6×10^{-12})	0.76% (0.07)
Overall test for race/ethnicity	$p = 3.2 \times 10^{-21}$	$p = 9.6 \times 10^{-14}$
Type 2 diabetes vs. not	-1.23×10^{-4} (0.001)	1.79% (1.2×10^{-5})
Current smoker vs. not	0.020 (3.3×10^{-6})	2.03% (3.3×10^{-6})
HDL-C 40–59 (vs. HDL-C 60+)	-3.50×10^{-5} (0.28)	1.85% (5.2×10^{-7})
HDL-C < 40 (vs. HDL-C 60+)	-7.18×10^{-5} (0.089)	1.75% (1.8×10^{-4})
Overall test for HDL-C	0.24	2.4×10^{-6}
Total cholesterol 200-239 (vs. < 200)	3.10×10^{-5} (0.29)	−1.0% (0.002)
Total cholesterol 240 + (vs. < 200)	-3.10×10^{-5} (0.50)	−0.58% (0.25)
Overall test for total cholesterol	0.36	0.006

Intercept, mixed model intercept coefficient corresponding to group difference between geometric means in percent; slope, mixed model slope coefficient corresponding to distensibility coefficient (DC) difference by group; 2*slope, difference in DC; to allow for judging of magnitude of coefficients, the standard deviation of DC = 1.1×10^{-3}; for example, the beta coefficient for age in women is -4.98×10^{-5}/mm Hg; this means that, on average, keeping other covariates constant, if 2 women differ 1 year in age, the older would have DC lower by -4.98×10^{-5}/mm Hg, which corresponds to 0.044 SD units. The SI unit for distensibility, kPa^{-1} = 7.5 mm Hg^{-1}.

HDL-C, high-density lipoprotein cholesterol.

Supplementary Table S3. Association of Age, Sex, and Race with Carotid Artery Distension, Diameter, and Distensibility-Related Parameters Using Different Models of Association

Covariate	*Model 0*[a]	*Model 1*	*Model 1 adjusted*	*Model 2 slope*	*Model 2 intercept*
	Beta coefficients and $\|t\|$, $\|z\|$ *or chi*^{2} *statistics*[b]				
Sex (male vs. female) at 65 years of age	0.46% $\|t\|=4.27$	7.74e-5, $\|t\|=2.05$	1.21e-4, $\|t\|=3.37$	4.12e-5, $\|z\|=2.12$	4.83%, $\|z\|=11.23$
Age (difference per year among females)	−0.07% $\|t\|=14.2$	−5.27e-5, $\|t\|=30.55$	−2.71e-5, $\|t\|=15.77$	−2.52e-5, $\|z\|=28.91$	0.24%, $\|z\|=11.81$
Difference in age-associated slope between men vs. women	0.02% $\|t\|=2.42$	9.22e-6, $\|t\|=3.74$	2.62e-6, $\|t\|=1.19$	3.57e-6, $\|z\|=2.77$	−0.10%, $\|z\|=3.42$
Height (difference per cm of height)	0.02% $\|t\|=3.70$	2.19e-6; $\|t\|=1.10$	5.24e-06; $\|t\|=2.91$	1.54e-06, $\|z\|=1.49$	0.19%, $\|z\|=8.53$
White	Ref				
Chinese vs. White	−0.41% $\|t\|=3.39$	−1.80e-4, $\|t\|=4.06$	−1.25e-4, $\|t\|=3.14$	−9.44e-5, $\|z\|=4.00$	−3.77%, $\|z\|=7.51$
African American vs. White	−0.34% $\|t\|=3.84$	−3.15e-4, $\|t\|=9.92$	−1.38e-4, $\|t\|=4.75$	−1.53e-4, $\|z\|=9.44$	−0.09%, $\|z\|=0.25$
Hispanic vs. White	−0.46% $\|t\|=4.65$	−2.83e-4, $\|t\|=7.71$	−1.63e-4, $\|t\|=4.93$	−1.41e-4, $\|z\|=7.43$	1.15%, $\|z\|=2.75$
Race omnibus	$chi^2_3=9.54=9.54$ $p<0.001$	$chi^2_3=39.22=39.22$ $p<0.001$	$chi^2_3=11.62=11.62$ $p<0.001$	$chi^2_3=106.08=106.08$ $p<0.001$	$chi^2_3=63.5=63.5$ $p=0.0025$

[a]Model 0, log(systolic diameter) adjusted for systolic, diastolic pressures log(diastolic diameter), and height; Model 1, DC difference by group; Model 1 adj, Model 1 adjusted for systolic and diastolic pressures and diastolic diameter; Model 2 slope, mixed model slope coefficient corresponding to DC difference by group; Model 2 intercept, mixed model intercept coefficient corresponding to group difference between geometric means in percent.

[b]$|t|$, $|z|$ or chi^2 statistics of the coefficients have been shown because many have significance levels <0.001. Model comparisons in terms of strength of association can be carried out using the test statistics; the t distribution is approximately equal to the z distribution for this sample size.