Published in final edited form as:

Atherosclerosis. 2011 October ; 218(2): 344–349. doi:10.1016/j.atherosclerosis.2011.05.033.

Associations of cardiovascular risk factors, carotid intima-media thickness and left ventricular mass with inter-adventitial diameters of the common carotid artery: the Multi-Ethnic Study of Atherosclerosis (MESA)

Joseph F. Polak, MD, MPH¹, Quenna Wong, BS², W. Craig Johnson, MS², David A. Bluemke, MD, PHD³, Anita Harrington, BS, RVT¹, Daniel H. O'Leary, MD¹, and N. David Yanez, PhD²

¹Department of Radiology, Tufts Medical Center, 800 Washington Street, Boston MA 02111

²Collaborative Health Studies Coordinating Center University of Washington Collaborative Health Studies Coordinating Center, Building 29, Suite 310 6200 NE 74th Street Seattle, WA 98115

³Radiology and Imaging Sciences, National Institutes of Health, 10 Center Drive, Rm 1C355 Bethesda MD 20892

Abstract

Background—Common carotid artery inter-adventitial diameter (IAD) and intima-media thickness (IMT) are measurable by ultrasound. IAD may be associated with left ventricular mass (LV mass) while IMT is a marker of subclinical atherosclerosis. It is not clear if IAD is associated with LV mass after accounting for IMT and traditional cardiovascular risk factors.

Methods—IAD and IMT were measured on participants of the Multi-Ethnic Study of Atherosclerosis (MESA) IMT progression study. A total of 5641 of the originally enrolled 6814 MESA participants were studied. LV mass was measured by magnetic resonance imaging. Multivariable linear regression was used with IAD as the outcome and adjustment for risk factors, as well as IMT and LV mass.

Results—Traditional cardiovascular risk factors, height, weight and ethnicity were significantly associated with IAD. After adjustment for risk factors, a one mm difference in IMT was associated with a 1.802 mm (95% CI: 1.553, 2.051) higher mean IAD. A one gm difference in LV mass was associated with a 0.006 mm (95% CI: 0.005, 0.007) higher mean IAD. LV mass was independently associated with IAD after adjusting for cardiovascular risk factors and IMT. These associations were slightly different for men and women.

Conclusions—Inter-adventitial diameters are associated with left ventricular mass after adjusting for cardiovascular risk factors and IMT. IAD might serve as a surrogate for left ventricular mass and have predictive value for cardiovascular outcomes.

© 2011 Elsevier Ireland Ltd. All rights reserved.

Corresponding author: Joseph F. Polak MD, MPH, Department of Radiology, Tufts Medical Center, 800 Washington Street, Box 299, Boston MA, 02111, Tel: (001) 617-636-0036; Fax (001) 617-636-0067.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Keywords

carotid arteries; ultrasonics; hypertrophy; magnetic resonance imaging; remodeling; risk factors; left ventricle

Introduction

The increase in diameter of the coronary and carotid arteries that occurs in response to the deposition of atherosclerotic plaque is referred to as the Glagov phenomenon¹. This adaptive response is therefore directly linked to the atherosclerotic process

Arterial diameters also increase as blood pressure increases²⁻⁵. Increases in left ventricular mass (LV mass) are associated with chronic blood pressure elevation⁶ and with larger common carotid artery lumen diameters as well as external (adventitia to adventitia) diameters^{7, 8}.

Inter-adventitial diameter (IAD) of the carotid artery is non-invasively measured with ultrasound. IAD is known to be associated with carotid artery intima-media thickness (IMT) and blood pressure^{2-4, 9, 10} while there are no data confirming an association with LV mass. If present, the association between IAD and LV mass might be weakened by taking into consideration traditional cardiovascular risk factors, height, weight and the presence of subclinical disease measured as carotid artery IMT.

We hypothesize that IAD is independently associated with LV mass and that IAD might be a marker of elevated LV mass after accounting for IMT and traditional risk factors. We study these possibilities in participants of a multi-ethnic cohort: the Multi-Ethnic Study of Atherosclerosis (MESA).

Materials and Methods

Population

MESA recruited and examined a multiethnic population of 6814 men and women aged 45-84 with no history of clinical cardiovascular disease¹¹. The MESA cohort is composed of white, African-American, Hispanic-American, and Chinese participants. Participants were excluded if they had physician diagnosis of heart attack, stroke, transient ischemic attack, heart failure, angina, atrial fibrillation or history of any cardiovascular procedure, weight above 300 lbs, pregnancy, or any medical conditions that would prevent long-term participation. MESA protocols and all studies described herein have been approved by the Institutional Review Boards of all collaborating institutions and are HIPAA compliant.

Risk factors and anthropomorphic variables

Weight was measured after an overnight fast in pounds (lbs) and height measurements in centimeters (cm). Age, gender, race/ethnicity, and medical history were self-reported. Use of lipid-lowering and anti-hypertensive medications was also recorded.

Current smoking was defined as self-report of one or more cigarettes in the last 30 days. Resting systolic and diastolic blood pressures (BP) were measured three times in the seated position using a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, Florida). The average of the last two measurements was used in the analyses. Hypertension was defined as a systolic blood pressure ≥ 140 mm Hg, a diastolic blood pressure ≥ 90 mm Hg, or currently taking anti-hypertensive medications.

Glucose and lipids were measured after a twelve-hour fast. Diabetes mellitus was determined using the 2003 ADA fasting criteria algorithm¹². Total cholesterol was measured using a cholesterol oxidase method (Roche Diagnostics), as was HDL after precipitation of non-HDL cholesterol with magnesium/dextran, triglycerides using Triglyceride GB reagent (Roche Diagnostics).

Carotid artery measures

Participants were examined supine with the head rotated 45° towards the left side. Imaging was done parallel to the right common carotid artery with the jugular vein above (or at 45 degrees from the vertical if the internal jugular vein was not present). The image was centered on a 10 mm segment of the right common carotid artery at least 5 mm below (caudad to) the right common carotid artery bulb. A matrix array probe (M12L, General Electric, Milwaukee, WI) was used, with the frequency set at 13 MHz. Images acquired for 20 seconds at 32 frames-per-second were digitized and automated inter-adventitial diameter measurements (near wall inter-adventitial interface to far wall inter-adventitial interface) made. The end-diastolic diameter was obtained from the smallest diameter of the inter-adventitial diameter-versus-time curve.

The reproducibility of the measurements was assessed by replicate readings of the same series of images on 139 participants giving an overall intra-class correlation coefficient (ICC) of 0.990 (95% CI: 0.987, 0.993). The intra-reader ICC was 0.997 (95% CI 0.991, 0.999) while the inter-reader ICC was 0.989 (95% CI 0.985, 0.993).

Images selected at end-diastole were used for measurements of the mean far wall common carotid IMT¹³.

Left ventricular mass

The six MESA field centers used 1.5-Tesla magnets for their evaluation of LV mass according to a standard protocol¹⁴.

All images were acquired during a 12 to 15 second breath hold at resting lung volume. Short-axis cine images were acquired from the end-diastolic image and image data were analyzed using MASS software (version 4.2; Medis, The Netherlands). The papillary muscles were excluded from the LV mass measurement. LV mass was determined by the sum of the myocardial area (the difference between endocardial and epicardial contours) times slice thickness plus image gap multiplied by the specific gravity of myocardium (1.05 g/mL).

Statistical Analysis

Descriptive and summary statistics are reported as mean and standard deviation for continuous variables and count and percent for categorical variables.

We used linear regression with robust standard errors to investigate associations between IAD and traditional cardiovascular risk factors. We considered unadjusted models and fully adjusted models (including age, gender, race, height, weight, HDL and total cholesterol with lipid-lowering medications, diabetes status, blood pressures and anti-hypertensive medication use, and cigarette smoking status with pack-years of cigarette smoking). Height and weight were included to adjust for confounding due to body size.

To investigate associations between IAD and subclinical disease measures, we considered the same set of models as described for the risk factors. Specifically, we looked at left ventricular end-diastolic mass and far wall mean carotid IMT at diastole. Models including

IMT were corrected for measurement error by regression calibration¹⁵ using the STATA function *rcal*. Replicate reads of single ultrasound scans^{15, 16} were used to estimate the variance of the measurement error.

All analyses were performed using Intercooled STATA 10.0 (StataCorp, College Station, Texas).

Results

Baseline demographics are summarized in Table 1. Of the 5641 subjects studied, 52% were female, while African-Americans formed 26% of the group, Chinese 12%, Hispanic 22% and the rest were Caucasian (40%).

Key associations between IAD and cardiovascular risk factors are shown in Table 2. For unadjusted analyses, positive associations with IAD were seen for age, male gender, height and weight, lipid-lowering medication use, all diabetes categories (treated diabetes, untreated diabetes, impaired fasting glucose compared to normal), systolic blood pressure and anti-hypertensive medication use, former cigarette smoking and pack-years smoked and for Chinese as well as African-Americans as compared to Caucasians. Negative associations were seen for HDL-cholesterol and for total cholesterol.

The associations of total cholesterol, IFG and untreated diabetes, and former cigarette smoking status with IAD seen in unadjusted analyses were not significant after full adjustment. IAD was associated with all other cardiovascular risk factors.

Both common carotid IMT and LV mass were associated with IAD in all unadjusted and fully adjusted analyses (Figures 1 and 2). After adjustment for all risk factors, a one mm difference in IMT was associated with a 1.802 mm (95% CI: 1.553, 2.051) higher mean IAD and a ten gm difference in LV mass was associated with a 0.06 mm (95% CI: 0.05, 0.07) higher mean IAD. When IMT and LV mass were both included in the model, a one mm difference in IMT was associated with a 1.623 mm (95% CI: 1.372, 1.874) higher mean IAD and a ten gm difference in LV mass was associated with a 0.05 mm (95% CI: 0.04, 0.06) higher mean IAD.

We further investigated possible gender specific differences in the strength of these associations. IAD was associated with IMT and left ventricular mass remained significant for each gender. A one mm difference in IMT was associated with a 1.580 mm [95% CI: 1.248, 1.911] higher mean IAD for women and a 1.982 mm [1.620, 2.344] higher mean IAD for men. The effect of including both IMT and LV mass in the models slightly attenuated the respective beta-coefficients (Table 3).

Discussion

We have found significant associations between inter-adventitial diameters of the common carotid artery and LV mass after adjustment for traditional cardiovascular risk factors, height, weight and IMT. These associations are slightly different in separate analyses performed for men and women.

Our findings cast some insight into the associations between subclinical atherosclerosis and carotid artery diameters and extend the findings to a multi-ethnic cohort. We show a positive association between IAD and IMT with an approximately 1.81 mm higher mean IAD for a difference 1 mm in mean IMT. This is consistent with the Glagov hypothesis of arterial remodeling¹ and our results support findings from the Bruneck Study¹⁰ and CHS (Cardiovascular Health Study)⁸.

The association between inter-adventitial diameters and left ventricular mass is consistent with a coupling between blood pressure, ventricular mass and arterial diameter. Blood pressure elevation increases the diameter of arteries^{5, 17, 18} and promotes the development of left ventricular hypertrophy⁶. Our observations show an association between carotid diameter and LV mass similar to those reported in the CHS study⁸ albeit CHS did not measure carotid artery inter-adventitial diameter but rather the lumen (intima-lumen interface to lumen-intima interface) diameter and the outer (adventitia-to-adventitia) diameter. We are, in fact, the first large study reporting an association between IAD and LV mass.

We observe a positive association of IAD with systolic pressure but a negative one with diastolic pressure. This suggests that increases in pulse pressure might be an important biological mechanism responsible for increases in IAD. While we cannot confirm causation in our cross-sectional analyses, this possibility appears quite plausible.

We show that ethnicity is associated with inter-adventitial diameters. Prior studies have shown an association between IMT and IAD in a Northern European population^{10, 19}. The Atherosclerosis Risk in Communities (ARIC) study, composed of whites and African-Americans, did not mention if ethnicity was associated with inter-adventitial diameters⁹ whereas we observe such a difference (Table 2). Given that we adjusted for height and weight, differences in body morphology are unlikely to account for the association with ethnicity. The association of IAD with height and weight suggests that both variables might need to be accounted for when IAD enters as an independent predictor variable in cross-sectional or outcome studies.

We, as others^{9, 10}, note an inverse association between IAD and cholesterol. We cannot offer an explanation for this observation.

Our study is limited by its cross-sectional nature. We cannot address whether IAD is predictive of cardiovascular outcomes. Others studies indicate either the absence²⁰ or presence²¹ of a significant association between IAD and cardiovascular outcomes. This issue needs additional outcome studies.

Conclusions

We have shown that the inter-adventitial diameter of the common carotid artery is associated with left ventricular mass after taking into consideration cardiovascular risk factors and IMT. This observation suggests that the inter-adventitial diameter of the common carotid artery might have predictive value for certain cardiovascular events by acting as a marker of increased left ventricular mass.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of human atherosclerotic coronary arteries. *New England Journal of Medicine*. 1987; 316:1371–1375. [PubMed: 3574413]
2. Eigenbrodt ML, Bursac Z, Rose KM, Couper DJ, Tracy RE, Evans GW, Brancati FL, Mehta JL. Common carotid arterial interadventitial distance (diameter) as an indicator of the damaging effects of age and atherosclerosis, a cross-sectional study of the Atherosclerosis Risk in Community Cohort

- Limited Access Data (ARICLAD), 1987-89. Cardiovascular Ultrasound. 2006; 4:1. [PubMed: 16390545]
3. Jensen-Urstad K, Jensen-Urstad M, Johansson J. Carotid artery diameter correlates with risk factors for cardiovascular disease in a population of 55-year-old subjects. *Stroke*. 1999; 30:1572-1576. [PubMed: 10436103]
 4. Mannami T, Baba S, Ogata J. Potential of carotid enlargement as a useful indicator affected by high blood pressure in a large general population of a Japanese city: the Suita study. *Stroke*. 2000; 31:2958-2965. [PubMed: 11108756]
 5. Virmani R, Avolio AP, Mergner WJ, Robinowitz M, Herderick EE, Cornhill JF, Guo SY, Liu TH, Ou DY, O'Rourke M. Effect of aging on aortic morphology in populations with high and low prevalence of hypertension and atherosclerosis. Comparison between occidental and Chinese communities. *American Journal of Pathology*. 1991; 139:1119-1129. [PubMed: 1951629]
 6. Lauer MS, Anderson KM, Levy D. Influence of contemporary versus 30-year blood pressure levels on left ventricular mass and geometry: the Framingham Heart Study. *Journal of the American College of Cardiology*. 1991; 18:1287-1294. see comment. [PubMed: 1833430]
 7. Kronmal RA, Smith VE, O'Leary DH, Polak JF, Gardin JM, Manolio TA. Carotid artery measures are strongly associated with left ventricular mass in older adults (a report from the Cardiovascular Health Study). *American Journal of Cardiology*. 1996; 77:628-633. [PubMed: 8610615]
 8. Polak JF, Kronmal RA, Tell GS, O'Leary DH, Savage PJ, Gardin JM, Rutan GH, Borhani NO. Compensatory increase in common carotid artery diameter. Relation to blood pressure and artery intima-media thickness in older adults. Cardiovascular Health Study. *Stroke*. 1996; 27:2012-2015. [PubMed: 8898807]
 9. Crouse JR, Goldbourt U, Evans G, Pinsky J, Sharrett AR, Sorlie P, Riley W, Heiss G. Risk factors and segment-specific carotid arterial enlargement in the Atherosclerosis Risk in Communities (ARIC) cohort. *Stroke*. 1996; 27:69-75. [PubMed: 8553406]
 10. Kiechl S, Willeit J. The natural course of atherosclerosis. Part II: vascular remodeling Bruneck Study Group. *Arteriosclerosis, Thrombosis & Vascular Biology*. 1999; 19:1491-1498.
 11. Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Greenland P, Jacob DR Jr, Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M, Tracy RP. Multi-ethnic study of atherosclerosis: objectives and design. *American Journal of Epidemiology*. 2002; 156:871-881. [PubMed: 12397006]
 12. Genuth S, Alberti KGMM, Bennett P, Buse J, Defronzo R, Kahn R, Kitzmiller J, Knowler WC, Lebovitz H, Lernmark A, Nathan D, Palmer J, Rizza R, Saudek C, Shaw J, Steffes M, Stern M, Tuomilehto J, Zimmet P. Expert Committee on the D. and Classification of Diabetes, M. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care*. 2003; 26:3160-3167. see comment. [PubMed: 14578255]
 13. O'Leary DH, Polak JF, Kronmal RA, Kittner SJ, Bond MG, Wolfson SK Jr, Bommer W, Price TR, Gardin JM, Savage PJ. Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. The CHS Collaborative Research Group. *Stroke*. 1992; 23:1752-1760. [PubMed: 1448826]
 14. Natori S, Lai S, Finn JP, Gomes AS, Hundley WG, Jerosch-Herold M, Pearson G, Sinha S, Arai A, Lima JAC, Bluemke DA. Cardiovascular function in multi-ethnic study of atherosclerosis: normal values by age, sex, and ethnicity. *AJR*. 2006; 186:S357-365. [PubMed: 16714609]
 15. Carroll, RJ.; Ruppert, D.; Stefanski, LA.; Crainiceanu, CM. *Measurement Error in Nonlinear Models: A Modern Perspective*. 2nd. Chapman Hall/CRC; Boca Raton, FL: 2006.
 16. Hardin JW, Schmiediche H, Carroll RJ. The regression-calibration method for fitting generalized linear models with additive measurement error. *The Stata Journal*. 2003; 3:361-372.
 17. Young W, Gofman JW, Tandy R, Malamud N, Waters ES. The quantitation of atherosclerosis. II Quantitative aspects of the relationship of blood pressure and atherosclerosis. *American Journal of Cardiology*. 1960; 6:294-299. [PubMed: 13846654]
 18. Young W, Gofman JW, Tandy R, Malamud N, Waters ES. The quantitation of atherosclerosis. I. Relationship to artery size. *American Journal of Cardiology*. 1960; 6:288-293.

19. Bonithon-Kopp C, Touboul PJ, Berr C, Magne C, Ducimetiere P. Factors of carotid arterial enlargement in a population aged 59 to 71 years: the EVA study. *Stroke*. 1996; 27:654–660. [PubMed: 8614925]
20. Bots ML, Grobbee DE, Hofman A, Witteman JCM. Common carotid intima-media thickness and risk of acute myocardial infarction: the role of lumen diameter. *Stroke*. 2005; 36:762–767. [PubMed: 15746451]
21. Eigenbrodt ML, Sukhija R, Rose KM, Tracy RE, Couper DJ, Evans GW, Bursac Z, Mehta JL. Common carotid artery wall thickness and external diameter as predictors of prevalent and incident cardiac events in a large population study. *Cardiovascular Ultrasound*. 2007; 5:11. [PubMed: 17349039]

Figure 1.

Scatter plot of Inter-Adventitial diameters as a function of mean far wall common carotid artery with an explained variability of 17.1% in a linear regression model. The size of the hexagonal points on the graph represents groupings of individual points with similar values according to the figure legend on the right.

Figure 2.

Scatter plot of Inter-Adventitial diameters as a function of left ventricular mass (LV mass) with an explained variability of 16.9% in a linear regression model. The size of the hexagonal points on the graph represents groupings of individual points with similar values according to the figure legend on the right.

Table 1
Means (SD) or count (%) of baseline measures of demographics, risk factors, and subclinical disease measures

Baseline demographics, risk factors, and subclinical disease measures		N=5641
Age		61.92 +/- 10.14
Gender (male/female)		2706 (48%) / 2935 (52%)
Ethnicity (Caucasian, Chinese, African-American, Hispanic)		2230 (40%) / 690 (12%) / 1493 (26%) / 1228 (22%)
HDL Cholesterol (mg/dl)		50.99 +/- 14.69
Total Cholesterol (mg/dl)		194.13 +/-35.27
Lipid-lowering medications		916 (16%)
Height (cm)		166.61 +/- 10.01
Weight (lbs)		173.10 +/-37.55
Diabetes mellitus by 2003 ADA fasting criteria algorithm		
Normal		4186 (74%)
IFG (Impaired Fasting Glucose)		766 (14%)
Untreated diabetes		146 (3%)
Treated Diabetes		527 (9%)
Systolic Pressure (mmHg)		125.89 +/- 21.16
Diastolic Pressure (mmHg)		71.81 +/- 10.25
Hypertension by JNC VI (1997) criteria		2460 (44%)
Anti-hypertensive medication use		2046 (36%)
Cigarette smoking status	Never	2847 (50%)
	Former	2073 (37%)
	Current	708 (13%)
Pack-years of cigarette smoking		11.11 +/-22.22
Far wall mean IMT, at Diastole		0.68 +/-0.19
LV end-diastolic mass (g)		145.12 +/-39.30
Inter-adventitial diameter at Diastole		7.55 +/- 0.90

Table 2
Coefficient estimates [95% confidence intervals] for risk factors or subclinical disease measures in unadjusted, minimally adjusted, and fully adjusted models¹ with inter-adventitial diameter (IAD) as the outcome

	Unadjusted model	Fully adjusted model ²
Age	0.032 [0.030, 0.034] [‡]	0.025 [0.023, 0.028] [‡]
Gender Male	0.601 [0.557, 0.646] [‡]	0.407 [0.344, 0.469] [‡]
Race (reference Caucasian)		
Chinese	0.080 [0.004, 0.155] *	0.301 [0.233, 0.369] [‡]
African-American	0.198 [0.136, 0.259] [‡]	0.083 [0.029, 0.137] [‡]
Hispanic	0.018 [-0.041, 0.078]	0.084 [0.029, 0.138] [‡]
Height (cm)	0.013 [0.010, 0.016] [‡]	0.008 [0.004, 0.011] [‡]
Weight (lbs)	0.004 [0.003, 0.005] [‡]	0.004 [0.003, 0.004] [‡]
HDL Cholesterol (mg/dl)	-0.011 [-0.013, -0.010] [‡]	-0.003 [-0.004, -0.001] [‡]
Total Cholesterol (mg/dl)	-0.001 [-0.002, -0.001] [‡]	0.000 [-0.001, 0.000]
Lipid-lowering medication use	0.115 [0.051, 0.179] [‡]	-0.061 [-0.118, -0.004] *
Diabetes mellitus by 2003 ADA fasting criteria algorithm (reference Normal)		
Impaired fasting Glucose	0.318 [0.245, 0.392] [‡]	0.014 [-0.052, 0.080]
Untreated Diabetes	0.308 [0.172, 0.443] [‡]	0.017 [-0.104, 0.137]
Treated Diabetes	0.466 [0.385, 0.547] [‡]	0.112 [0.036, 0.189] [‡]
Systolic blood pressure (mmHg)	0.014 [0.013, 0.015] [‡]	0.013 [0.011, 0.014] [‡]
Diastolic blood pressure (mmHg)	0.000 [-0.003, 0.003]	-0.007 [-0.011, -0.004] [‡]
Anti-hypertensive medication use	0.231 [0.181, 0.281] [‡]	0.095 [0.048, 0.141] [‡]
Cigarette smoking status (reference Never)		
Former	0.067 [0.003, 0.132] *	-0.032 [-0.079, 0.016]
Current	-0.009 [-0.098, 0.079]	0.126 [0.056, 0.196] [‡]
Pack-years of cigarette smoking	0.005 [0.003, 0.007] [‡]	0.002 [0.001, 0.003] [‡]
LV end-diastolic mass (g)	0.009 [0.009, 0.010] [‡]	0.006 [0.005, 0.007] [‡]
Far wall mean IMT, at Diastole³	2.822 [2.566, 3.078] [‡]	1.802 [1.553, 2.051] [‡]
LV end-diastolic mass (g)	0.008 [0.007, 0.008] [‡]	0.005 [0.004, 0.006] [‡]
Far wall mean IMT, at Diastole⁴	2.473 [2.238, 2.708] [‡]	1.623 [1.372, 1.874] [‡]

* denotes p-value ≤0.05;

[†] denotes p-value ≤ 0.01 ;

[‡] denotes p-value ≤ 0.001 .

¹ Each cell in this table represents a different regression model. Therefore actual estimates of covariates are not reported for every model.

² Models are fully adjusted for age, gender, race, height, weight, HDL, Total cholesterol, lipid-lowering medications, diabetes status, hypertension status, systolic and diastolic pressures, cigarette smoking status, and pack-years of cigarette smoking.

³ Regression calibration using far wall mean IMT from original baseline replicate reads was applied to obtain bias corrected coefficient estimates and robust standard errors.

Table 3
Coefficient estimates [95% confidence intervals] for risk factors or subclinical disease measures in unadjusted, minimally adjusted, and fully adjusted models with inter-adventitial diameter (IAD) as the outcome keeping each gender separate

	Fully adjusted ⁴ model (Females only)	Fully adjusted ⁴ model (Males only)
Age	0.029 [0.026, 0.032] [‡]	0.021 [0.017, 0.025] [‡]
Race (reference Caucasian)		
Chinese	0.362 [0.272, 0.451] [‡]	0.255 [0.152, 0.358] [‡]
African-American	0.075 [0.007, 0.142] [*]	0.105 [0.018, 0.193] [*]
Hispanic	0.115 [0.046, 0.184] [‡]	0.052 [-0.033, 0.138]
Height (cm)	0.008 [0.004, 0.012] [‡]	0.005 [-0.001, 0.011]
Weight (lbs)	0.002 [0.002, 0.003] [‡]	0.006 [0.004, 0.007] [‡]
HDL Cholesterol (mg/dl)	-0.005 [-0.006, -0.003] [‡]	0.001 [-0.002, 0.004]
Total Cholesterol (mg/dl)	0.000 [-0.001, 0.000]	0.000 [-0.001, 0.001]
Lipid-lowering medication use	-0.102 [-0.172, -0.031] [‡]	-0.037 [-0.126, 0.053]
Diabetes mellitus by 2003 ADA fasting criteria algorithm (reference Normal)		
Impaired fasting Glucose	-0.011 [-0.098, 0.077]	0.025 [-0.069, 0.119]
Untreated diabetes	0.100 [-0.097, 0.297]	-0.042 [-0.190, 0.106]
Treated Diabetes	0.140 [0.040, 0.240] [‡]	0.071 [-0.043, 0.186]
Systolic blood pressure (mmHg)	0.010 [0.008, 0.012] [‡]	0.016 [0.013, 0.019] [‡]
Diastolic blood pressure (mmHg)	-0.003 [-0.007, 0.000]	-0.014 [-0.020, -0.009] [‡]
Anti-hypertensive medication use	0.083 [0.024, 0.142] [‡]	0.120 [0.047, 0.194] [‡]
Cigarette smoking status (reference Never)		
Former	-0.032 [-0.096, 0.032]	-0.002 [-0.073, 0.069]
Current	0.129 [0.038, 0.221] [‡]	0.153 [0.047, 0.259] [‡]
Pack-years of cigarette smoking	0.001 [-0.001, 0.003]	0.002 [0.000, 0.003] [‡]
LV end-diastolic mass (g)	0.007 [0.006, 0.009] [‡]	0.005 [0.004, 0.006] [‡]
Far wall mean IMT, at Diastole ⁵	1.580 [1.248, 1.911] [‡]	1.982 [1.620, 2.344] [‡]
LV end-diastolic mass (g)	0.006 [0.005, 0.008] [‡]	0.004 [0.003, 0.005] [‡]
Far wall mean IMT, at Diastole ⁵	1.544 [1.195, 1.894] [‡]	1.669 [1.311, 2.026] [‡]

* denotes p-value ≤0.05;

[‡] denotes p-value ≤0.01;

[‡] denotes p-value ≤0.001.

⁴ Models are fully adjusted for age, race, height, weight, HDL, Total cholesterol, lipid-lowering medications, diabetes status, hypertension status, systolic and diastolic pressures, cigarette smoking status, and pack-years of cigarette smoking.

⁵ Regression calibration using far wall mean IMT from original baseline replicate reads was applied to obtain bias corrected coefficient estimates and robust standard errors.