Published in final edited form as:

Eur J Prev Cardiol. 2014 May ; 21(5): 601–607. doi:10.1177/2047487312462801.

Associations Between a Parental History of Premature Cardiovascular Disease and Coronary Calcium and Carotid Intima-Media Thickness: The Coronary Artery Risk Development In Young Adults (CARDIA) Study

John T. Wilkins, MD, MS^a, Samuel Gidding, MD^b, Kiang Liu, PhD^a, Hongyan Ning, MD, MS^a, Joseph F. Polak, MD, MPH^c, and Donald M. Lloyd-Jones, MD, ScM^a

^aDepartment of Preventive Medicine Northwestern University Feinberg School of Medicine, Chicago, IL

^bThe Department of Pediatrics Nemours Cardiac Center, Wilmington, DE

^cThe Department of Radiology Tufts University, Boston, MA

Abstract

Background—It is unclear if associations between a parental history of premature CVD (pCVD) and subclinical atherosclerosis are attenuated by adjustment for long-term risk factors levels through middle adulthood.

Design—Prospective community-based cohort study

Methods—CARDIA participants who attended the year 20 exam (N=2283, mean age 45 years) were grouped by pCVD status: maternal only, paternal only, any parental, and no parental history (referent). We used separate logistic regression models, adjusted for average risk factor levels over 20 years' follow-up to assess associations of parental pCVD and subclinical atherosclerosis in offspring.

Results—White participants with any parental history of pCVD had a higher odds of CAC>0 than participants with no parental history (OR 1.55; 95% CI, 1.01-2.37). This was largely driven by the association of a paternal history of pCVD with CAC>0 (OR 2.15; 95% CI, 1.42-3.23), which was minimally attenuated by multivariable adjustment (OR 2.09; 95% CI, 1.31-3.32). Similarly, adjusted associations between parental pCVD and IMT > 90%tile were observed in white participants with a paternal history of pCVD (OR=1.93; 95% CI, 1.10-3.39) and any parental history pCVD (OR 1.67; 95% CI, 1.02-2.74). No significant associations between a parental history of pCVD and the odds of subclinical atherosclerosis were observed in black participants.

Conclusions—Parental pCVD is independently associated with early development of subclinical atherosclerosis; these associations may be race-specific for participants in their 5th decade of life.

Keywords

Family History of Premature Cardiovascular Disease; Coronary Artery Calcium; Carotid Intima-Media Thickness

Introduction

A parental history of premature cardiovascular disease (pCVD) confers an increased risk for clinical CVD development in offspring, independent of heritable traditional risk factors.(1) However, it is unclear if cumulative exposure to risk factors over young adulthood attenuates the observed association between a parental history of pCVD and risk for CVD events in offspring. Furthermore, it is unclear if these associations are manifest in younger adulthood in terms of sub-clinical atherosclerosis. Interestingly, risks for subclinical atherosclerosis associated with a parental history of pCVD may vary by race.(2, 3) Likewise, differential risks for CVD in offspring associated with maternal or paternal pCVD history may exist.(4)

The young patient with a family history of pCVD can present a clinical dilemma for the clinician. Due to the well documented associations of coronary artery calcium (CAC) and carotid artery intima-media thickness (IMT) with future CVD events, the assessment of subclinical atherosclerosis, in conjunction with a thorough assessment of traditional CVD risk factors, may be helpful in terms of patient risk stratification for future CVD events.(5, 6)

The biracial CARDIA cohort provides a unique opportunity to examine the association of a parental history of pCVD with subclinical atherosclerosis in the context of *longitudinal* risk factor levels over 20 years in white and black participants in their third and fourth decade of life, when atherosclerosis often begins. In this study we sought to: 1) investigate associations between any parental history of pCVD and CAC and carotid IMT; 2) assess the effect of race on the direction and magnitude of this association; 3) determine associations with CAC and carotid IMT between participants with a maternal or paternal history of CVD; and 4) determine whether adjustment for average risk factors over 20 years of follow up attenuates the association of parental history with CAC and carotid IMT by race.

Methods

Study sample, inclusion and exclusion criteria

CARDIA is a longitudinal, community-based cohort of 5115 black and white men and women who were enrolled at 18-30 years of age in 1985-1986. Participating field centers include: Kaiser Permanente, Oakland, CA; Northwestern University, Chicago, IL; University of Alabama in Birmingham, AL and The University of Minnesota, Minneapolis, MN. The CARDIA study was approved by the institutional review boards of all participating centers.

Thus far, the cohort has been followed through and beyond a year 20 exam. At baseline, the sample was population based and approximately equally divided by sex, race, and educational status. At year 20, CAC scanning and IMT measurements were performed. All participants with parental history survey data at Year 0, 5, and 10, and CAC score data at Year 20, or IMT at Year 20 were included. Participants were excluded if they did not report parental history data, if parental history of CVD became negative on repeat assessment, if they were missing covariate data, or if they were missing IMT or CAC data.

A total of 3548 participants attended the Year 0 and Year 20 examinations; 722 patients were excluded for either missing parental history data, or parental history data that became negative on repeat measurement. Of the participants excluded for missing parental history data, 59% were black and 41% were white. An additional 543 participants were excluded due to missing covariates, or missing CAC or IMT values at year 20.

Parental History Ascertainment and Risk Factor Measurement

Participants were administered family history questionnaires at examination Years 0, 5, and 10. At the Year 0 examination participants were asked if there was a history of “heart attack” or “stroke” in their mother or father. If they answered “yes” to either question they were asked at what age it occurred. Participants were also asked if the parent was living; if not, separate fields inquired if “heart attack” or “stroke” were the cause of death.

Age, sex, race, and smoking status were obtained from self-report. Body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. Blood pressure was measured 3 times by random zero sphygmomanometer, and the mean of the second and third measurements was used. Total cholesterol (TC) and HDL cholesterol (HDL) were measured from serum from a fasting blood draw that was separated and plasma frozen to -70°C prior to analysis in a central laboratory. LDL cholesterol (LDL) was estimated by using the Friedwald equation.⁽⁷⁾ Glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease Study formula.⁽⁸⁾ Diabetes mellitus (DM) was determined by self-report or the presence of diabetes medications. Medication history was determined by self-report, medications lists were reviewed and medications were coded as anti-hypertensive and lipid lowering medications. Income and educational status were determined by self-report.

Measurement of CAC

Participants underwent CT scanning with electron beam CT (Imatron C-150) or multidetector CT (GE Lightspeed or Siemens VZ) during their year 20 exam. All participants had 2 sets of images obtained. Forty-five to 55 (depending on heart size) sequential 3mm transverse images from the aortic root to the cardiac apex were acquired. All images were captured during ventricular diastole (80% of the R-R interval). A coronary calcium focus was defined as a region of 4 or more adjacent pixels with a CT number greater than 130 Hounsfield units. A total CAC score was computed by summing the Agatston score for each coronary artery and across all coronary arteries.⁽⁹⁾ The mean of the scores from each scan was the final CAC score. CAC was defined as present if the score was

greater than zero. Scans from participants with at least one non-zero score were reviewed by an expert investigator blinded to the scan scores.

Measurement of IMT

Ultrasound studies were acquired according to a standard protocol using a GE-Logiq-700 (Issaquah Ill). A high-resolution M12L transducer operating at a frequency of 13MHz was used to image the common carotid artery. An operating frequency of 9MHz was used to image the internal carotid artery and the carotid bulb. Image acquisition was made at end diastole.(10) Measurements of the composite IMT were used in the analysis. The composite IMT measurement is an average of all available values from the common, internal carotid and the carotid bulb IMT.

Endpoints of interest

Our primary endpoints of interest were the prevalence of CAC score > 0 at year 20, prevalence of IMT > 90thtile at year 20, and continuous IMT measurements in CARDIA participants.

Statistical Analyses

We focused on parental history of premature (< 65 years old in the mother or < 55 years old in the father) CVD and stratified participants into the following groups: maternal history of pCVD, paternal history of pCVD, or any parental history of pCVD. Any parental history included participants with either maternal or paternal history or both. All analyses used a common referent group consisting of those with no history of either maternal or paternal pCVD. The associations between a parental history of pCVD and categorical subclinical atherosclerosis (CAC > 0 & IMT>90th %tile) were examined using logistic regression modeling. We assessed for first order interactions between parental history of pCVD, race and subclinical atherosclerosis using multiplicative interactions terms. Significant interaction terms were observed, therefore our analysis was stratified by race. The prevalence of CAC >0 and carotid IMT >90th %ile were compared across strata using chi-square tests. Logistic regression models were fitted unadjusted, and adjusted in 3 separate models. Model 1 was run unadjusted, model 2 was adjusted for age and sex; model 3 was adjusted for sex, age, BMI, blood pressure; total cholesterol (TC), high density lipoprotein (HDL) cholesterol, income, GFR, use of lipid therapy, use of antihypertensive medication, educational status, income, presence of DM, and tobacco use status. For continuous variables we used the average of all available measurements from exam years 0 to 20 provided a participant had information from year 0, year 20 and at least one interim exam. The categorical variables, use of lipid therapy, use of antihypertensive medication, educational status, income, presence of DM, and tobacco use status were assigned at year 20 data. We also utilized adjusted linear regression modeling using IMT as continuous variables. All analyses were performed using SAS version 9.1 (SAS institute, Cary, NC). A *p* value of <0.05 was considered statistically significant.

Results

Baseline Characteristics

We included 2283 participants in the final analysis; there were 109 participants with maternal (only), 197 with paternal (only) and 18 with biparental history of pCVD, yielding a total of 324 with any parental history of pCVD. Compared to participants with no parental history of pCVD ($n=1959$), those with any parental history of pCVD were older, had higher blood pressure, BMI, total cholesterol, and prevalence of DM and anti-hypertension medication use. There was a higher proportion of women and a lower proportion of white participants in the any parental history of pCVD group. Longitudinal average risk factor characteristics for subclinical atherosclerosis covariates are presented in Table 1.

Measures of subclinical atherosclerosis in participants with a maternal, paternal, and any parental history of premature CVD

Unadjusted comparisons of the prevalence of $CAC > 0$, $IMT > 90\%$ tile, and IMT values (mm) between different pCVD parental history groups are presented in Table 2. Among participants with paternal and any parental pCVD the proportion with $CAC > 0$ was significantly higher compared with those who had no parental history of pCVD; there was no significant difference found between the maternal pCVD group and the referent. Composite IMT was significantly greater in the maternal and any parental group. However, the proportion of participants with $IMT > 90\%$ tile was greater in the paternal and any parental pCVD groups.

Measures of Subclinical Atherosclerosis in participants with a maternal, paternal and any parental history of pCVD when stratified by race

There was evidence for a significant interaction between any parental and paternal history of pCVD and race in association with $CAC > 0$ ($p = 0.03$ and 0.01 respectively), and composite $IMT > 90\%$ tile ($p = 0.047$ for any parental pCVD group). Thus, data are presented stratified by race. White participants with a paternal and any parental history of pCVD had significantly increased odds of $CAC > 0$ and composite $IMT > 90\%$ tile in unadjusted and fully adjusted models (Table 3). Conversely, there were no significant associations observed between a parental history of pCVD with $CAC > 0$ or $IMT > 90\%$ tile in black participants. Among whites, these associations were demonstrated in participants with any parental history of premature CVD, however the odds ratio was lower and largely driven by the paternal contribution, and the strength of the association was partially attenuated in fully adjusted models.

Discussion

Among a biracial cohort of younger adults, we observed that white participants with paternal and any parental history of pCVD had a higher odds of having $CAC > 0$ in middle age. This association was largely driven by the association of $CAC > 0$ with a reported paternal history of pCVD, and the strength of the association was only partially attenuated by adjustment for long-term average risk factor levels from young adulthood to middle age. Logistic regression models did not demonstrate an association between a parental history of pCVD

and CAC or Carotid IMT >90% tile in black participants. These data support the previous findings that a parental history of pCVD has an independent effect that increases the probability of developing subclinical atherosclerosis in offspring; however, this may not be true of black participants in their 5th decade.

Associations between a history of parental pCHD and CAC in offspring have been observed in multiple cohorts.(11-15) For example, in the significantly older MESA cohort, white, black, Hispanic, and Chinese American participants with a parental history of premature CHD had a significantly increased odds of CAC >0.(16) However, as stated above, we did not find an association between parental history of pCVD and CAC in black participants in our study. This may be an artifact of misclassification of parental history due to the younger age of our cohort, or it may imply race-specific pathophysiologic differences in the development of atherosclerosis in the young which have been previously described in the Pathological Determinants of Atherosclerosis in Youth Cohort.(17) In an analysis of year 15 data from CARDIA, Fornage demonstrated an association between a parental history of myocardial infarction and stroke and CAC. The associations were race-specific, as black participants had a significant adjusted association between a paternal history of stroke and white participants had a significant adjusted association between a paternal history of myocardial infarction and CAC. Similar to our data, the associations were largely driven by the paternal history of CVD. Our study and the Fornage study differ in several important ways. First, we used a composite exposure of parental history of *pCVD*, whereas Fornage examined myocardial infarction and stroke as different exposures. Second, the analysis by Fornage did not include carotid IMT as a measure of subclinical atherosclerosis. Third, we included FH data from year 10, thus the average age of parents having CVD events as likely greater than the average age of parents having events analyzed in the Fornage analysis. The older ages of parents having events may dilute some of the associations with coronary subclinical atherosclerosis, as younger individuals having events may portend greater inherited risk to offspring. Fourth, an adjustment for *average* risk factors over 20 years of follow up was not performed in the year 15 analysis.(3)

Our results are similar to several other studies which demonstrated an association between parental CVD and increased carotid IMT. In the older, predominantly white Framingham Offspring Cohort, Wang et al. demonstrated an association between a parental history of pCVD and carotid IMT. Notably, there was no difference in internal carotid IMT between maternal and paternal history of pCVD groups.(18) A race-specific association was detected by Benson, et al. in the Atherosclerosis at Risk in Communities Studies, as whites with an elevated Family Risk Score had a higher odds of increased carotid IMT. However, similar to our results, no significant association was detected in black participants.(2)

Given the association of parental history of pCVD with offspring CVD *events* in both whites and blacks, individuals with a parental history of pCVD likely have increased predilection for the development of early subclinical atherosclerosis and increased overall burden of atherosclerosis.(19) As such, it is surprising that the increased likelihood of CAC and carotid IMT was not observed in black participants or participants with a maternal history of premature CVD. In the present study this race-specific association may be partially explained by the lower prevalence of CAC in blacks when compared to whites, which has

been observed in other cohorts.(20) Furthermore, the lack of an association may be due to decreased power to detect associations given the smaller sample size of the respective race subgroups or due to misclassification of self-reported parental history in either group. It is also possible that CAC and carotid IMT do not associate with parental history in these groups due to differences in the rate and/or timing of the development of subclinical atherosclerosis in blacks and whites. For example, it may be that CAC and increased carotid IMT do not become prevalent until the 6th decade or later in blacks. Specifically in regards to CAC, perhaps differences in CAC prevalence between blacks and whites may not be due to differences in the total burden of atherosclerosis per se, but may be partially explained by differences in the degree of *calcification of atherosclerosis*.(21) Alternatively, it may be that the burden of atherosclerosis may in fact be less, but differences in plaque stability, platelet function, thrombosis, inflammation may differ and explain some of the risk for CVD events in blacks with a parental history of pCVD. Clinically, these data suggest that the use of subclinical atherosclerosis to improve risk assessment in black patients in their 5th decade with family histories of pCVD may be limited. If the overall prevalence of positive CAC is low in black patients then the number needed to screen may be unacceptably high which would severely limit the utility of CAC testing in this population.

Our study benefited from a well phenotyped cohort with repeated risk factor measurements over 20 years, which allowed for more complete adjustment, particularly for risk factor burden over time. Average blood pressure values from repeated measures have been shown to be more heritable than single measurements; therefore repeated measures may more completely account for confounding from otherwise unmeasured inherited factors and yield a more accurate estimate of the association between CAC and a history of parental premature CVD.(22)

There are several limitations to our current study. First, parental history was obtained from self-report, which has been shown to have a positive predictive value of only 70% when compared with physician adjudication.(23) Regardless, most community-based observation cohorts and clinicians determine family history from self-report. Thus, these data help describe the utility of family history information obtained during a clinical interview for predicting the likelihood of subclinical atherosclerosis. Second, some pCVD events may not have been captured at year 10, since all parents of year 10 examinees may not have been old enough to have pCVD events by that time. We expect this would have led to an underestimation of parental pCVD which would bias our findings towards the null. Therefore, this may explain the lack of a significant association between a maternal history of pCVD and subclinical atherosclerosis observed in this study. Third, CAC may not capture early, non-calcified forms of atherosclerosis which could result in an under-estimate of the association between FH of pCVD and premature subclinical atherosclerosis.

In conclusion, CARDIA participants in their 5th decade with a parental history of pCVD had an increased odds for the presence of CAC and composite carotid IMT >90thtile in whites; this association was likely driven mostly by the contribution from paternal history. The risks attributable to a parental history are partially attenuated by adjustment for long-term risk factor levels measured over 20 years from young adulthood to middle age. Furthermore,

there appear to be race-specific associations between a parental history of pCVD, CAC and composite carotid IMT>90%tile in CARDIA participants.

Acknowledgments

Work on this manuscript was supported (or partially supported) by contracts: University of Alabama at Birmingham, Coordinating Center, N01-HC-95095; University of Alabama at Birmingham, Field Center, N01-HC-48047; University of Minnesota, Field Center and Diet Reading Center (Year 20 Exam), N01-HC-48048; Northwestern University, Field Center, N01-HC-48049; Kaiser Foundation Research Institute, N01-HC-48050; University of California, Irvine, Echocardiography Reading Center (Year 5 & 10), N01-HC-45134; Harbor-UCLA Research Education Institute, Computed Tomography Reading Center (Year 15 Exam), N01-HC-05187; Wake Forest University (Year 20 Exam), N01-HC-45205; New England Medical Center (Year 20 Exam), N01-HC-45204 from the National Heart, Lung and Blood Institute.

References

1. Lloyd-Jones DM, Nam BH, D'Agostino RB Sr, Levy D, Murabito JM, Wang TJ, et al. Parental Cardiovascular Disease as a Risk Factor for Cardiovascular Disease in Middle-aged Adults: A Prospective Study of Parents and Offspring. *JAMA*. 2004; 291(18):2204–11. [PubMed: 15138242]
2. Bensen JT, Li R, Hutchinson RG, Province MA, Tyroler HA. Family history of coronary heart disease and pre-clinical carotid artery atherosclerosis in African Americans and whites: The ARIC study. *Genetic Epidemiology*. 1999; 16(2):165–78. [PubMed: 10030399]
3. Fornage M, Lopez DS, Roseman JM, Siscovick DS, Wong ND, Boerwinkle E. Parental History of stroke and myocardial infarction predicts coronary artery calcification: The Coronary Artery Risk Development in Young Adults (CARDIA) study. *Euro J Cardiovasc Prev Rehabil*. 2004; 11(5):421–6.
4. Sesso HD, Lee IM, Gaziano JM, Rexrode KM, Glynn RJ, Buring JE. Maternal and Paternal History of Myocardial Infarction and Risk of Cardiovascular Disease in Men and Women. *Circulation*. 2001; 104:393–8.
5. Polonsky TS, McClelland RL, Jorgensen NW, Bild DE, Burke GL, Guerci AD, et al. Coronary Artery Calcium Score and Risk Classification for Coronary Heart Disease Prediction. *JAMA*. 2010; 303(16):1610–6. [PubMed: 20424251]
6. Greenland P, Bonow RO, Brundage BH, Budoff MJ, Eisenberg MJ, Grundy SM, et al. ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring By Computed Tomography in Global Cardiovascular Risk Assessment and in Evaluation of Patients With Chest Pain: A Report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) Developed in Collaboration With the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. *J Am Coll Cardiol*. 2007; 49(3):378–402. [PubMed: 17239724]
7. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, Without Use of the Preparative Ultracentrifuge. *Clin Chem*. 1972; 18(6):499–502. [PubMed: 4337382]
8. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D, et al. A More Accurate Method To Estimate Glomerular Filtration Rate from Serum Creatinine: A New Prediction Equation. *Annals of Internal Medicine*. 1999; 130(6):461–70. [PubMed: 10075613]
9. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol*. 1990; 15:827–32. [PubMed: 2407762]
10. O'Leary DH, Polak JF, Kronmal RA, Savage PJ, Borhani NO, Kittner SJ, et al. Thickening of the Carotid Wall: A Marker for Atherosclerosis in the Elderly? *Stroke*. 1996; 27(2):224–31. [PubMed: 8571414]
11. Barrett-Connor E, Khaw K. Family history of heart attack as an independent predictor of death due to cardiovascular disease. *Circulation*. 1984; 69(6):1065–9. [PubMed: 6713610]

12. Colditz GA, Stampfer MJ, Willett WC, Rosner, Speizer FE, Hennekens CH. A Prospective Study Of Parental History Of Myocardial Infarction and Coronary Heart Disease in Women. *Am J Epidemiol.* 1986; 123(1):48–58. [PubMed: 3940442]
13. Li R, Bensen JT, Hutchinson RG, Province MA, Hertz-Picciotto I, Sprafka JM, et al. Family risk score of coronary heart disease (CHD) as a predictor of CHD: the atherosclerosis risk in communities (ARIC) study and The NHLBI Family Heart Study. *Genetic Epidemiology.* 2000; 18(3):236–50. [PubMed: 10723108]
14. Myers RH, Kiely DK, Cupples LA, Kannel WB. Parental history is an independent risk factor for coronary artery disease: The Framingham Study. *Am Heart J.* 1990; 120(4):963–9. [PubMed: 2220549]
15. Myers, ea. Parental history is an independent risk factor for coronary artery disease: the Framingham Study. *Am Heart J.* 1990; 120:963–9. [PubMed: 2220549]
16. Nasir K, Budoff MJ, Wong ND, Scheuner M, Herrington D, Arnett DK, et al. Family History of Premature Coronary Heart Disease and Coronary Artery Calcification: Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation.* 2007; 116:619–26. [PubMed: 17646582]
17. McGill HC Jr, McMahan CA, Zieske AW, Sloop GD, Walcott JV, Troxclair DA, et al. Associations of Coronary Heart Disease Risk Factors With the Intermediate Lesion of Atherosclerosis in Youth. *Arterioscler Thromb Vasc Biol.* 2000; 20(8):1998–2004. [PubMed: 10938023]
18. Wang TJ, Nam BH, D'Agostino RB, Wolf PA, Lloyd-Jones DM, MacRae CA, et al. Carotid Intima-Media Thickness Is Associated With Premature Parental Coronary Heart Disease: The Framingham Heart Study. *Circulation.* 2003; 108:572–6. [PubMed: 12874190]
19. ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring by Computed Tomography in Global Cardiovascular Risk Assessment and in Evaluation of Patients With Chest Pain. *Circulation.* 2007; 115(3):402–26. [PubMed: 17220398]
20. Bild DE, Detrano R, Peterson D, Guerci A, Liu K, Shahar E, et al. Ethnic Differences in Coronary Calcification: The Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation.* 2005; 111(10): 1313–20. [PubMed: 15769774]
21. Doherty TM, Tang W, Dascalos S, Watson KE, Demer LL, Shavelle RM, et al. Ethnic Origin and Serum Levels of 1alpha,25-Dihydroxyvitamin D3 Are Independent Predictors of Coronary Calcium Mass Measured by Electron-Beam Computed Tomography. *Circulation.* 1997; 96(5): 1477–81. [PubMed: 9315534]
22. Levy D, DeStefano AL, Larson MG, O'Donnell CJ, Lifton RP, Gavvas H, et al. Evidence for a Gene Influencing Blood Pressure on Chromosome 17: Genome Scan Linkage Results for Longitudinal Blood Pressure Phenotypes in Subjects From the Framingham Heart Study. *Hypertension.* 2000; 36(4):477–83. [PubMed: 11040222]
23. Murabito JM, Byung-Ho N, D'Agostino RB Sr, Lloyd-Jones DM, O'Donnell CJ, Wilson PWF. Accuracy of Offspring Reports of Parental Cardiovascular Disease History: The Framingham Offspring Study. *Annals of Internal Medicine.* 2004; 140:434–40. [PubMed: 15023709]

Table 1
20-Year Average Risk Factor Levels for CARDIA Participants by Parental History of pCVD Groups

	No Parental History of Premature CVD (Referent) (N=1959)		Maternal Only Premature CVD Yes (N=109)		Paternal Only Premature CVD Yes (N=197)		Any Parental Premature CVD Yes (N=324)		P value
				P value		P value		P value	
Age (yrs)	34.6 (3.5)		35.7 (3.3)	< .01	35.0 (3.7)	0.15	35.3 (3.5)	< .01	
Female (%)	56.0		71.6	< .01	59.4	0.35	63.0	0.02	
White (%)	60.3		38.5	< .01	59.9	0.90	51.2	< .01	
Systolic Blood Pressure, mmHg	109 (9)		112 (10)	<0.01	110 (9)	0.27	111 (9)	<0.01	
Diastolic Blood Pressure, mmHg	69 (7)		72 (8)	< .01	71 (7)	0.03	71 (8)	< 0.01	
Body Mass Index, kg/m ²	26.3 (5.0)		27.9 (6.4)	< .01	26.8 (5.5)	0.18	27.2 (5.9)	< .01	
Total Cholesterol, mg/dL	180.1 (28.5)		184.2 (28.2)	0.14	185.7 (27.8)	< 0.01	185.4 (28.0)	< .01	
HDL-C, (mg/dL)	53.2 (12.4)		51.7 (12.1)	0.23	52.1 (12.6)	0.24	52.0 (12.3)	0.10	
GFR (mL/min/1.73 m ²)	90.8 (14.8)		92.7 (14.7)	0.2	90.1 (13.3)	0.52	90.9 (13.8)	0.88	
Diabetes, %	7.7		11.9	0.11	12.2	0.03	12.3	<0.01	
Current Smoking, %	16.0		20.2	0.25	15.2	0.78	17.3	0.55	
Hypertension medication, %	14.5		32.1	< .01	20.3	0.03	25.0	< 0.01	
Education (%)									
High School	19.5		37.6		23.4		28.4		
College	54.1		47.7	<0.01	52.3	0.41	51.2	<0.01	
Graduate School	26.4		14.7		24.3		20.4		
Income (%)									
<\$25,000	11.7		28.0		12.8		18.1		
\$25,000-\$50,000	18.5		22.4	<0.01	14.8	0.42	18.4	<0.01	
>\$50,000	69.8		49.6		72.5		63.5		

* Data are presented as mean (SD) unless otherwise indicated

Table 2
Unadjusted Comparisons of CAC and IMT Between Parental pCVD Groups

	No Parental History of pCVD (Referent)	Maternal Only pCVD history	Paternal Only pCVD history	Any Parental (Mother and/or Father) pCVD history	P value
	No (N=1959)	Yes (N=109)	Yes (N=197)	Yes (N=324)	P value
CAC > 0, %	16.6	20.2	26.4	23.8	< .01
Composite Carotid IMT, mm (SD)	0.88 (.17)	0.93 (.22)	0.90 (0.18)	0.91 (0.19)	< .01
Composite Carotid-IMT > 90th Percentile, %	9.3	12.8	15.2	13.9	0.01

Table 3
Associations Between Maternal, Paternal, and Maternal and Paternal History of pCVD and CAC > 0 and IMT > 90%tile Stratified by Race

OR and 95% CI of logistic regression models for the association of parental pCVD and CAC>0 (403/2283) No Parental History of pCVD as Referent	White			Black		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Maternal history of CVD	0.87 (0.38, 1.98)	0.95 (0.39, 2.26)	0.53 (0.20, 1.41)	1.85 (1.00, 3.40)	1.74 (0.90, 3.33)	1.36 (0.67, 2.75)
Paternal history of CVD	2.15 (1.42, 3.23)	2.28 (1.46, 3.55)	2.09 (1.31, 3.32)	1.26 (0.67, 2.36)	1.33 (0.69, 2.56)	1.21 (0.59, 2.50)
Any Parental history of CVD	1.72 (1.18, 2.48)	1.82 (1.22, 2.71)	1.55 (1.01, 2.37)	1.50 (0.96, 2.35)	1.45 (0.91, 2.32)	1.19 (0.71, 1.99)
OR and 95% CI of logistic regression models for the association of parental pCVD and IMT>90% (228/2283) No Parental History of pCVD as Referent						
	White			Black		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Maternal history of CVD	2.41 (1.09, 5.35)	2.10 (0.93, 4.71)	1.45 (0.59, 3.59)	0.89 (0.37, 2.14)	0.80 (0.33, 1.93)	0.70 (0.28, 1.74)
Paternal history of CVD	2.22 (1.33, 3.70)	2.01 (1.19, 3.38)	1.93 (1.10, 3.39)	1.17 (0.56, 2.43)	1.20 (0.57, 2.52)	1.10 (0.51, 2.41)
Any Parental history of CVD	2.17 (1.39, 3.40)	1.93 (1.23, 3.05)	1.67 (1.02, 2.74)	1.02 (0.58, 1.81)	0.97 (0.55, 1.73)	0.86 (0.47, 1.57)

Model 1: Unadjusted

Model 2: Age and sex adjusted

Model 3: Age, sex, BMI, blood pressure; TC, HDL-C, GFR, use of antihypertensive medication, educational status, income, presence of DM, and tobacco use status adjusted. Note: mean values for continuous variables and year 20 status for categorical variables were included in the multivariable adjusted model.