***Title*: Associations of cardiovascular disease risk factors with density and volume components of coronary artery calcium (CAC): the Multi-Ethnic Study of Atherosclerosis**

***Short Title:*** Thomas, Risk factors for CAC density and volume

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**Abstract**

*Background:* Coronary artery calcium (CAC) predicts incident cardiovascular disease (CVD) beyond traditional risk factors. While higher CAC volume is associated with higher CVD risk, higher CAC density is associated with lower CVD risk. Whether risk factors for CAC volume and CAC density are similar or distinct is unknown. We sought to evaluate the independent associations of CVD risk factors with CAC volume and CAC density.

*Methods:* Baseline measurements from 6,814 participants free of clinical CVD were collected for the Multi-Ethnic Study of Atherosclerosis between 2000 and 2002. Participants with no CAC (n=3,416) and missing data were excluded, for a final analytic sample of 3,375 participants. Multivariable linear regression models were used to evaluate independent predictors of CAC density and CAC volume.

*Conclusions:* Whereas most CVD risk factors were associated with higher CAC volume, the same risk factors were associated with lower CAC density. For example, diabetes was associated with higher natural logarithm (*ln*) transformed CAC volume (standardized β= 0.44 ln-units, $p<0.01$) but lower CAC density (β= -0.07 Hounsfield unit (Hu) category unit, $p<0.01$). Relative to Non-Hispanic White, Chinese, African-American, and Hispanic race/ethnicities were associated with lower *ln* CAC volume (β= -0.62, -0.52, and -0.40 ln-units, respectively, $p<0.01$ for each), and higher CAC density (β= 0.41, 0.18, and 0.21 Hu category units, respectively, $p<0.01$ for each). CAC density and CAC volume were also differentially associated with race/ethnicity.

## Introduction

As a marker of underlying coronary artery atherosclerosis, coronary artery calcium (CAC) has been observed to be associated with in increased risk of coronary events.[1] The predominant metric used to quantify CAC is the Agatston score, which is comprised of the two-dimensional area of CAC and a four-point multiplicative factor based on the maximum plaque density within each plaque [2]. Thus, a higher density of CAC will increase the Agatston score. However, at any level of CAC, a higher CAC density has been observed to be associated with *lower* cardiovascular disease (CVD) risk.[3] This observation is consistent with studies that have found sparsely calcified atherosclerotic plaques to more frequently result in coronary events compared to heavily calcified plaques.[4-6] Taken together, these findings suggest that a higher density of CAC may be associated with lower, rather than higher, CVD risk.[3]

These findings also highlight the need to evaluate the associations of CVD risk factors with CAC separated into its components of volume and density. Risk factors such as race/ethnicity, family history of CVD, alcohol consumption, and adiposity have previously been linked to CVD risk,[7-10] yet the independent associations of each with CAC volume and CAC density are unknown. Therefore, within a multi-ethnic population, we aimed to elucidate the associations of participant characteristics and CVD risk factors with CAC volume and CAC density.

## Methods

### *MESA Study Design*

The Multi-Ethnic Study of Atherosclerosis (MESA) started in July 2000 to evaluate the progression of subclinical CVD in a cohort consisting of four race/ethnicity groups. The design

of this prospective cohort study has been previously described in detail.[11] Briefly, community-dwelling individuals aged 45-84 years were recruited from six study sites: Baltimore, MD; Chicago, IL; Winston-Salem, NC; Los Angeles, CA; New York, NY; and St. Paul, MN. The study population had an approximate ethnic composition of 38% Non-Hispanic White (NHW), 28% African-American, 23% Hispanic, and 11% Asian (predominantly Chinese). Participants with any history of clinically apparent CVD or major obstacles to follow-up were excluded from the study. Measurements at the first examination between July 2000 and July 2002 included a participant questionnaire, collection of fasting blood samples, and cardiac CT imaging. The institutional review boards of the six study centers have each approved the study protocol. Written informed consent was obtained from all participants.

*Computed Tomography*

Cardiac CT scans were performed using either a cardiac-gated electron-beam CT scanner at the Chicago, Los Angeles, and New York sites (Imatron C-150; Imatron, South San Francisco, CA) or an electrocardiogram-triggered multidetector CT system at the Baltimore, Winston-Salem, and St. Paul sites. (Lightspeed, General Electric Medical Systems, Waukesha, WI or Volume Zoom, Siemens, Erlanger, Germany). All scans included a phantom of known calcium concentration for calibration. Scans were performed in duplicate for each participant by trained technologists and read centrally at the Harbor-UCLA Research and Education Institute.

*Coronary Artery Calcium Scoring*

The CAC scoring protocol has been described in detail previously.[12] Briefly, proprietary software was employed to detect and quantify regions of calcification within the coronary

arteries. A trained image analyst delineated the course of the coronary arteries, in which the imaging software detected areas of possible calcification. Attenuation between scans was standardized against a calcium phantom, and a calcified plaque was defined as any area greater than 5.5 $mm^3$ (electron beam CT) or 4.6 $mm^3$ (multidetector CT) of attenuation >130 Hounsfield Units (Hu). A total plaque volume score was obtained for each participant by multiplying the total area of calcification in scans of the coronary arteries by the slice thickness (3mm for electron beam CT or 2.5 mm for multidetector CT). Additionally, individual plaque areas were multiplied by a density factor of 1, 2, 3 or 4 corresponding to the maximum Hu attenuation within each plaque (130-199 Hu=1, 200-299 Hu=2, 300-399 Hu=3, 400+ Hu=4).[2] These plaque-specific scores were then summed for all CT slices of the heart to produce the Agatston score, which reflects CAC areas upweighted for plaque density. Results from the duplicate scans of each participant were averaged for final volume and Agatston scores.

The average CAC density score of all defined plaques for each participant was obtained by dividing the Agatston score (Agatston = Area*Density Factor) scores by the total CAC area. CAC area was derived by dividing the total CAC volume by the CT scan slice thickness.[3] As the CAC density score can only be determined in participants with identified CAC volume, participants with CAC volume equal to zero were excluded.

*Questionnaire*

Participants completed self-report questionnaires on pertinent health history including: tobacco usage, alcohol consumption, medical diagnoses, family history of CVD, medication use, and typical walking pace, annual income, and level of educations. Tobacco usage and alcohol consumption were classified as: never, former, or current.

*Measurements and Laboratory Tests*

Height and weight were measured after participants removed shoes and heavy clothing. Body mass index (BMI) was computed as weight (kg)/squared height ($m^2$). Hip and waist circumference were also measured and used to determine the waist-hip ratio (WHR). Resting systolic and diastolic blood pressure (SBP, DBP) measurements were taken in triplicate after 5 minutes of rest from the right arm of participants in the seated position with a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, FL). The average of the latter two measurements was used in analyses.

Venous blood samples were collected from participants after a 12-hour overnight fast. Blood sample measurements included high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides, total cholesterol, and glucose levels. Diabetes was defined as either fasting glucose levels >125 mg/dL or use of hypoglycemic medications or insulin. Gender, age, total cholesterol, HDL, SBP, antihypertensive use, and tobacco usage were used to calculate the Global Framingham Risk Score (GFRS). Serum C-reactive protein and fibrinogen concentrations were measured using the BN II nephelometer (Dade Behring Inc., Deerfield, IL). Serum interleukin-6 (IL-6) concentration was measured using ultrasensitive ELISA (Quantikine HS Human interleukin-6 Immunoassay, R& D Systems, Minneapolis, MN).

*Statistical Analyses*

The exposure variables considered were age, gender, race/ethnicity, total cholesterol, HDL-C, SBP, DBP, antihypertensive medication use, smoking status, diabetes, statin use, BMI, waist circumference, hip circumference, WHR, GFRS, family history of myocardial infarction (MI),

family history of stroke, typical walking pace, alcohol consumption status (never, former, current), amount of alcohol consumed, IL-6, fibrinogen, and CRP concentrations. The outcome variables were CAC density and CAC volume, each analyzed separately.

The participants were divided into quartiles of CAC density and volume. Quartile means and percentages were computed for continuous and categorical exposure variables, respectively. Analyses of covariance (ANCOVA) were performed to determine associations of exposure variables across quartiles of CAC density and volume, adjusted for age, gender, and CAC density (for models evaluating CAC volume) or CAC volume (for models evaluating CAC density). These covariates were standardized to their mean values of 66.4 years, 57% male, and 2.69 units of CAC density or 257.9 $mm^3$ of CAC volume.

Multivariable linear regressions analyses were performed to evaluate the associations of the exposure variables with CAC density and volume, respectively. For regression analyses, continuous variables were all scaled to standard deviation units. Because CAC volume has a highly skewed distribution, CAC volume scores were log transformed (i.e. natural logarithm *[ln]* volume score) to reduce skewness. Associations between individual exposure variables and CAC density and volume were adjusted for age, gender, and CAC density or volume, henceforth referred to as "minimally adjusted" regression models. Next, we created an intermediate multivariable model incorporating all exposure variables. Then, exposure variables found in the 2013 ACC/AHA ASCVD Pooled Cohort Equations,[13] statin use, and any exposure variables with $p<0.10$ in the intermediate models were forced into the fully-adjusted final multivariable models. The exposure variables included in both CAC volume and CAC density final fully-adjusted models were age, gender, race/ethnicity, annual income, total cholesterol, HDL, SBP, smoking status, diabetes status, antihypertensive use, statin use, BMI, walking pace, and IL-6. Level of

education, family history of MI, alcohol consumption amount, and CRP were also included in the final CAC volume model. Variables excluded from both final models were smoking amount, hip circumference, waist circumference, WHR, alcohol consumption status, and fibrinogen.

All statistical analyses were performed in SPSS version 22 (IBM Corporation, Armonk, NY). Statistical significance was defined as a two-tailed p-value of less than 0.05.

## Results

Of the 6,814 MESA participants, 3,398 had CAC volume scores >0 and were retained in the analysis. Two individuals were missing values for SBP, two for DBP, 11 for HDL-C, and 9 for total cholesterol. These participants were also excluded from the analyses to give a final analytic sample size of 3,375 individuals.

Table 1 displays the cohort characteristics stratified by quartiles of ascending CAC volume. Variables that showed a significant monotonic increase with increasing quartiles of CAC volume included SBP, former and current smoking status, diabetes, antihypertensive medication use, statin use, BMI, waist circumference, hip circumference, WHR, GFRS, family history of MI, and IL-6. The proportions of Chinese and Hispanics relative to NHW had a significant monotonic decrease across ascending volume quartiles.

Table 2 displays the cohort characteristics stratified by quartiles of ascending CAC density. Across ascending quartiles, the proportion of Chinese increased monotonically, whereas NHW decreased monotonically. In African Americans and Hispanics, there were no clear trends across quartiles. Among the other risk factors, none increased monotonically across density quartiles. HDL concentration was significantly higher in the highest density quartile compared to

the lowest. Family history of MI, BMI, waist circumference, the GFRS, CRP, and IL-6 decreased monotonically across increasing quartiles of density.

Table 3 displays the associations of CVD risk factors with *ln* CAC volume in minimally-adjusted and fully-adjusted multivariable regression models, which included adjustment for CAC density. Beta coefficients for continuous variables are per standard deviation change in the predictor. CAC density was positively associated with *ln* CAC volume (β=0.88 ln-units and 0.94 ln-units in minimally-adjusted and fully-adjusted models, respectively). Compared to NHW, the other three races/ethnicities were each significantly associated with lower *ln* CAC volume. The race/ethnicity variables were among the strongest inverse associations with *ln* CAC volume in the fully-adjusted model (β= -0.62, -0.52, and -0.40 ln-units for Chinese, African-American, and Hispanic, respectively). Age, male gender, college or greater level of education, total cholesterol, diabetes, antihypertensive medication use, BMI, family history of MI, and amount of alcohol consumption were all positively associated with *ln* CAC volume in the fully-adjusted model. Annual income greater than $100,00, average and brisk walking paces, and CRP were inversely associated with *ln* CAC volume. Systolic BP, current smoking status, and IL-6 had borderline positive associations with *ln* CAC volume in the fully-adjusted model that were not statistically significant.

Table 4 shows associations of risk factors with CAC density in minimally-adjusted and fully-adjusted multivariable models. *Ln* CAC volume was positively associated with CAC density (β=0.44 Hu category units). With NHW as the reference, race/ethnicity variables were among the strongest positive correlates of CAC density in the fully-adjusted model (β= 0.41, 0.18, 0.21 Hu category units for Chinese, African American, and Hispanic, respectively). Age, annual income greater than $100,000, HDL-C, and brisk walking pace were positively associated

with CAC density, while male gender, diabetes, and BMI were inversely associated with CAC density. Compared to no walking, stroll, average pace, and stride had borderline positive associations with CAC density in the fully-adjusted model that were not statistically significant. Total cholesterol and systolic BP had borderline inverse associations with CAC density in the fully-adjusted model that were not statistically significant.

Figure 1 graphically summarizes the magnitude and direction of the associations between CVD risk factors and CAC volume and CAC density. β-coefficients from the fully-adjusted multivariable linear regression models are plotted. For risk factors retained in the multivariable models, the associations for density and volume tended to be in opposite directions. The associations for race/ethnicity were as strong or stronger than most of the traditional risk factor associations.

## Discussion

In a large, multi-ethnic cohort of community-living individuals with quantifiable CAC who are free of clinical CVD, we found that many CVD risk factors were generally associated with CAC volume and CAC density in opposite directions. For instance, diabetes and BMI were associated with higher CAC volume but lower CAC density. Moreover, HDL-C, a risk factor known to be inversely associated with CHD risk,[14] and faster walking paces were associated with higher CAC density. These observations are consistent with previous findings from this cohort demonstrating that a higher CAC density is associated with a lower risk of CHD and CVD events at any level of CAC volume.[3]

Our findings also support the observation that the standard Agatston scoring method of up-weighting CAC scores to account for increased CAC density may be suboptimal. Several

studies have demonstrated the associations of CVD risk factors with a higher CAC Agatston score,[15-17] but to our knowledge no previous study has differentiated CVD risk factor associations with CAC volume and CAC density independently. We demonstrated that many CVD risk factors were associated with a lower CAC density, despite the fact that lower CAC density results in a lower Agatston score. As both higher CAC volume and CAC density result in higher Agatston scores, these findings suggest that CVD risk factors may have complex associations with the Agatston score, as they may simultaneously serve to increase the volume score and lower the density score.

The MESA has allowed for the elucidation of differences in the relationship of risk factors with CAC volume versus CAC density among different race/ethnicity groups, which has not been studied previously. We found a striking difference in associations of CVD risk factors with CAC volume and CAC density between race/ethnicity groups. Specifically, results for NHW participants showed lower CAC density and higher CAC volume compared to the other race/ethnicity groups even after multivariable adjustment.

Annual income was found to have a positive association with CAC density and an inverse association with CAC volume. These observations, along with the association of a college education with higher CAC volume, suggest that there may be additional factors not captured in the models that influence CAC density and volume. For instance, in one study, living in a city center was independently associated with the presence of CAC, potentially mediated by exposure to air pollution.[15] That components of CAC may have different associations among those of different income and education levels may be explained by unmeasured variables.

In clinical trials, statins have been strongly associated with improved cardiovascular outcomes,[18, 19] yet the findings of our study suggest statin use to have a non-statistically

significant association with increased CAC volume and decreased CAC density, an association that runs contrary than what would be expected given the associations of other CVD risk factors that we demonstrated in this cohort. Although there is evidence to suggest that statin therapies may be associated with progression of CAC,[20, 21] these studies uniformly used the Agatston score, so it is possible CAC may actually have been decreasing. The findings of our study likely represent confounding by indication, with participants treated with statins being more likely to have a risk factor prolife associated with a greater burden of CVD.

Among the strengths of this study are its large sample size, uniform availability of CAC measurements, a broad range of CVD risk factors, and the multi-ethnic nature of the study population. The study also has important limitations. First, we did not measure the density of individual plaques, but rather an average of all calcified plaques identified in the coronary tree. Adults with clinical CVD at baseline were excluded from participating in the MESA. Participants without detectable CAC were excluded by necessity as it is not possible to measure CAC density in such individuals. As such, the study sample here was middle aged, multi-ethnic, and had detectable CAC but no clinically apparent CVD. Whether results will generalize to other populations is presently uncertain.

In conclusion, we demonstrated the differential association of demographic factors and CVD risk factors with CAC density and volume. CVD risk factors were generally associated with higher CAC volume but lower CAC density. NHW race was strongly associated with higher CAC volume but lower CAC density. These findings suggest a complex association between CVD risk factors and CAC volume and density components, and highlight a limitation of the Agatston method of CAC scoring. Given the apparently protective associations between high CAC density and CHD and CVD events observed previously in this cohort, future studies should

address whether modification of CVD risk factors might have a dual effect of reducing CAC volume and increasing CAC density.

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## References


1. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, Liu K, Shea S, Szklo M, Bluemke DA, O'Leary DH, Tracy R, Watson K, Wong ND and Kronmal RA. Coronary Calcium as a Predictor of Coronary Events in Four Racial or Ethnic Groups. *New England Journal of Medicine*. 2008;358:1336-1345.
2. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Jr. and Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *Journal of the American College of Cardiology*. 1990;15:827-32.
3. Criqui MH, Denenberg JO, Ix JH, McClelland RL, Wassel CL, Rifkin DE, Carr JJ, Budoff MJ and Allison MA. Calcium density of coronary artery plaque and risk of incident cardiovascular events. *Jama*. 2014;311:271-8.
4. Ehara S, Kobayashi Y, Yoshiyama M, Shimada K, Shimada Y, Fukuda D, Nakamura Y, Yamashita H, Yamagishi H, Takeuchi K, Naruko T, Haze K, Becker AE, Yoshikawa J and Ueda M. Spotty calcification typifies the culprit plaque in patients with acute myocardial infarction: an intravascular ultrasound study. *Circulation*. 2004;110:3424-9.
5. Shemesh J, Apter S, Itzchak Y and Motro M. Coronary calcification compared in patients with acute versus in those with chronic coronary events by using dual-sector spiral CT. *Radiology*. 2003;226:483-8.
6. Leber AW, Knez A, White CW, Becker A, von Ziegler F, Muehling O, Becker C, Reiser M, Steinbeck G and Boekstegers P. Composition of coronary atherosclerotic plaques in patients with acute myocardial infarction and stable angina pectoris determined by contrast-enhanced multislice computed tomography. *The American journal of cardiology*. 2003;91:714-8.
7. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD and Bauman A. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Medicine and science in sports and exercise*. 2007;39:1423-34.
8. Despres JP. Body fat distribution and risk of cardiovascular disease: an update. *Circulation*. 2012;126:1301-13.
9. Pearson TA. Alcohol and heart disease. *Circulation*. 1996;94:3023-5.
10. Rigotti NA and Clair C. Managing tobacco use: the neglected cardiovascular disease risk factor. *European heart journal*. 2013;34:3259-67.
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 and Tracy RP. Multi-Ethnic Study of Atherosclerosis: objectives and design. *American journal of epidemiology*. 2002;156:871-81.
12. Carr JJ, Nelson JC, Wong ND, McNitt-Gray M, Arad Y, Jacobs DR, Jr., Sidney S, Bild DE, Williams OD and Detrano RC. Calcified coronary artery plaque measurement with cardiac CT in population-based studies: standardized protocol of Multi-Ethnic Study of Atherosclerosis (MESA) and Coronary Artery Risk Development in Young Adults (CARDIA) study. *Radiology*. 2005;234:35-43.
13. Goff DC, Jr., Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, Greenland P, Lackland DT, Levy D, O'Donnell CJ, Robinson JG, Schwartz JS, Shero ST, Smith SC, Jr., Sorlie P, Stone NJ, Wilson PW, Jordan HS, Nevo L, Wnek J, Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH, DeMets D, Hochman JS, Kovacs RJ, Ohman EM,

Pressler SJ, Sellke FW, Shen WK, Smith SC, Jr. and Tomaselli GF. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:S49-73.
14. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs DR, Jr., Bangdiwala S and Tyroler HA. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation*. 1989;79:8-15.
15. Lambrechtsen J, Gerke O, Egstrup K, Sand NP, Norgaard BL, Petersen H, Mickley H and Diederichsen AC. The relation between coronary artery calcification in asymptomatic subjects and both traditional risk factors and living in the city centre: a DanRisk substudy. *Journal of internal medicine*. 2012;271:444-50.
16. Kronmal RA, McClelland RL, Detrano R, Shea S, Lima JA, Cushman M, Bild DE and Burke GL. Risk factors for the progression of coronary artery calcification in asymptomatic subjects: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation*. 2007;115:2722-30.
17. Oei HH, Vliegenthart R, Hofman A, Oudkerk M and Witteman JC. Risk factors for coronary calcification in older subjects. The Rotterdam Coronary Calcification Study. *European heart journal*. 2004;25:48-55.
18. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM, Jr., Kastelein JJ, Koenig W, Libby P, Lorenzatti AJ, MacFadyen JG, Nordestgaard BG, Shepherd J, Willerson JT and Glynn RJ. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. *The New England journal of medicine*. 2008;359:2195-207.
19. Taylor F, Huffman MD, Macedo AF, Moore TH, Burke M, Davey Smith G, Ward K and Ebrahim S. Statins for the primary prevention of cardiovascular disease. *The Cochrane database of systematic reviews*. 2013:Cd004816.
20. Saremi A, Bahn G and Reaven PD. Progression of vascular calcification is increased with statin use in the Veterans Affairs Diabetes Trial (VADT). *Diabetes care*. 2012;35:2390-2.
21. Schmermund A, Achenbach S, Budde T, Buziashvili Y, Forster A, Friedrich G, Henein M, Kerkhoff G, Knollmann F, Kukharchuk V, Lahiri A, Leischik R, Moshage W, Schartl M, Siffert W, Steinhagen-Thiessen E, Sinitsyn V, Vogt A, Wiedeking B and Erbel R. Effect of intensive versus standard lipid-lowering treatment with atorvastatin on the progression of calcified coronary atherosclerosis over 12 months: a multicenter, randomized, double-blind trial. *Circulation*. 2006;113:427-37.

**Figure Title:** Independant associations of CVD risk factors with CAC volume and density.

**Figure Legend:** Standardized β coefficients from multivariable regression models. Variables on the vertical axis are the predictor variables. The outcome variable is either (a) *ln* CAC volume ($mm^3$) or (b) CAC density (Hu category unit). Single asterisk indicates $p<0.05$ and double asterisk indicates $p<0.01$. Coefficients between *ln* CAC volume and CAC density cannot be quantitatively compared due to inherent unit differences between measurements of CAC volume and CAC density.

Table 1: Cohort characteristics by quartiles of CAC volume in the Multi-Ethnic Study of Atherosclerosis

| | Total Cohort | Quartile 1 | Quartile 2 | Quartile 3 | Quartile 4 | p value* |
|---|---|---|---|---|---|---|
| CAC volume range (mm^3) | 2-4992 | 2.34-24.54 | 24.55-85.19 | 85.20-273.53 | 273.5-4991.9 | |
| N | 3398 | 852 | 847 | 850 | 849 | |
| Density (Hu category unit) | 2.69 | **2.07** | **2.70** | **2.91** | **3.09** | **<0.01** |
| Age (years) | 66.35 | **62.95** | **65.17** | **67.25** | **70.05** | **<0.01** |
| Male | 58% | **46%** | **53%** | **61%** | **72%** | **<0.01** |
| Ethnicity | | | | | | |
| Caucasian | 44% | **32%** | **38%** | **49%** | **58%** | **<0.01** |
| Chinese | 12% | **19%** | **15%** | **10%** | **4%** | **<0.01** |
| African American | 24% | 26% | 26% | 22% | 23% | 0.17 |
| Hispanic | 20% | **23%** | **22%** | **19%** | **16%** | **0.01** |
| Education | | | | | | |
| <High school | 19% | 21% | 20% | 18% | 16% | 0.07 |
| High school+ | 35% | **31%** | **34%** | **37%** | **39%** | **0.02** |
| College+ | 46% | 48% | 46% | 45% | 45% | 0.61 |
| Annual Income | | | | | | |
| <$50,000 | 63% | 64% | 66% | 63% | 61% | 0.33 |
| $50,000-$99,999 | 24% | 22% | 23% | 26% | 26% | 0.20 |
| $100,000+ | 13% | 14% | 12% | 12% | 13% | 0.52 |
| Total cholesterol (mg/dL) | 194.62 | 193.59 | 192.43 | 195.78 | 196.68 | 0.10 |
| HDL (mg/dL) | 49.41 | 50.43 | 49.49 | 48.94 | 48.79 | 0.18 |
| Systolic BP (mmHg) | 130.81 | **127.53** | **131** | **131.48** | **133.23** | **<0.01** |
| Diastolic BP (mmHg) | 72.57 | **71.42** | **72.96** | **72.53** | **73.36** | **<0.01** |
| Smoking status | | | | | | |
| Never | 45% | **52%** | **46%** | **42%** | **38%** | **<0.01** |
| Former | 42% | **37%** | **42%** | **44%** | **46%** | **0.01** |
| Current | 13% | **11%** | **12%** | **13%** | **16%** | **0.04** |
| Smoking amount (Pack-years) | 14.70 | **12.11** | **12.29** | **14.88** | **19.52** | **<0.01** |
| Diabetes | 18% | **12%** | **15%** | **19%** | **25%** | **<0.01** |
| Hypertension meds | 46% | **37%** | **43%** | **48%** | **55%** | **<0.01** |
| Statins | 20% | **15%** | **19%** | **21%** | **25%** | **<0.01** |
| BMI (kg/m^2) | 28.36 | **27.07** | **28.07** | **28.79** | **29.52** | **<0.01** |
| Waist circumference (cm) | 99.69 | **99.33** | **99.03** | **100.89** | **102.5** | **<0.01** |
| Hip circumference (cm) | 105.32 | **102.6** | **105.09** | **106.21** | **107.42** | **<0.01** |
| WHR | 0.95 | **0.94** | **0.94** | **0.95** | **0.95** | **<0.01** |
| GFRS | 18.34 | **16.63** | **18.06** | **18.71** | **19.97** | **<0.01** |
| Family history of MI | 45% | **38%** | **45%** | **50%** | **60%** | **<0.01** |
| Typical walking pace | | | | | | |
| No walking | 5% | **2%** | **7%** | **5%** | **7%** | **<0.01** |
| Stroll | 26% | 22% | 27% | 26% | 27% | 0.09 |
| Normal | 49% | **56%** | **45%** | **48%** | **48%** | **<0.01** |
| Brisk | 18% | 18% | 18% | 19% | 17% | 0.75 |
| Stride | 2% | 2% | 2% | 1% | 1% | 0.10 |
| Alcohol consumption status | | | | | | |
| Never | 19% | **24%** | **22%** | **17%** | **15%** | **<0.01** |
| Former | 25% | **22%** | **29%** | **25%** | **25%** | **0.03** |
| Current | 55% | **54%** | **49%** | **57%** | **60%** | **<0.01** |
| Alcohol consumption (drinks/week) | 5.62 | **5.25** | **5.17** | **5.38** | **6.62** | **0.02** |
| IL-6 (mg/dL) | 1.67 | **1.58** | **1.59** | **1.72** | **1.81** | **0.01** |
| Fibrinogen (mg/dL) | 353.80 | 348.43 | 353.07 | 354.00 | 359.73 | 0.09 |
| CRP (mg/dL) | 3.79 | 3.48 | 3.44 | 4.10 | 4.15 | 0.06 |

Participants stratified by quartiles of ascending CAC volume. Analysis includes only participants with CAC volume >0. Means and frequencies were adjusted for age, gender, and CAC density by ANCOVA. The covariates of age, gender (proportion of males), and CAC density were normalized to their mean values of 66.35 years, 57% male, and 2.69 Hu category units, respectively. Abbreviations: Hu=Hounsfield Units, BMI=Body Mass Index, WHR=waist-hip ratio, GFRS=Global Framingham Risk Score, MI=myocardial infarction, IL-6= interleukin-6, CRP=C-reactive protein, *for trend across quartiles

Table 2: Cohort characteristics by quartiles of CAC density in the Multi-Ethnic Study of Atherosclerosis

| | Total Cohort | Quartile 1 | Quartile 2 | Quartile 3 | Quartile 4 | p value* |
|---|---|---|---|---|---|---|
| Density range (Hu category units) | 1.00-4.00 | 0.80-2.23 | 2.23-2.79 | 2.70-3.17 | 3.18-4.00 | |
| N | 3398 | 850 | 849 | 850 | 849 | |
| CAC volume (mm^3) | 2.69 | **70.49** | **178.38** | **411.68** | **370.93** | **<0.01** |
| Age (years) | 66.35 | **65.79** | **66.68** | **66.23** | **66.71** | **<0.01** |
| Male | 58% | **61%** | **58%** | **56%** | **56%** | **<0.01** |
| Ethnicity | | | | | | |
| Caucasian | 44% | **52%** | **48%** | **48%** | **29%** | **<0.01** |
| Chinese | 12% | **6%** | **7%** | **11%** | **25%** | **<0.01** |
| African American | 24% | **22%** | **27%** | **25%** | **23%** | **0.03** |
| Hispanic | 20% | **21%** | **19%** | **17%** | **23%** | **0.01** |
| Education | | | | | | |
| < High school | 19% | **20%** | **17%** | **17%** | **21%** | **0.04** |
| High school+ | 35% | **39%** | **36%** | **37%** | **29%** | **<0.01** |
| College+ | 46% | 42% | 47% | 46% | 50% | 0.05 |
| Annual Income | | | | | | |
| <$50,000 | 63% | 64% | 62% | 65% | 64% | 0.53 |
| $50,000-$99,999 | 24% | **26%** | **27%** | **24%** | **21%** | **0.04** |
| $100,000+ | 13% | **11%** | **12%** | **12%** | **16%** | **0.03** |
| Total cholesterol (mg/dL) | 194.62 | 193.74 | 195.96 | 194.61 | 194.15 | 0.62 |
| HDL (mg/dL) | 49.41 | **48.35** | **49.15** | **49.09** | **51.06** | **<0.01** |
| Systolic BP (mmHg) | 130.81 | 131.37 | 131.12 | 131.46 | 129.29 | 0.12 |
| Diastolic BP (mmHg) | 72.57 | 72.73 | 72.82 | 72.34 | 72.37 | 0.73 |
| Smoking status | | | | | | |
| Never | 45% | 43% | 44% | 43% | 48% | 0.14 |
| Former | 42% | 43% | 44% | 43% | 41% | 0.62 |
| Current | 13% | 14% | 13% | 14% | 11% | 0.42 |
| Smoking amount (Pack-years) | 14.70 | **16.35** | **14.95** | **15.38** | **12.13** | **0.01** |
| Diabetes | 18% | **22%** | **19%** | **15%** | **16%** | **0.01** |
| Hypertension meds | 46% | 50% | 46% | 45% | 42% | 0.08 |
| Statins | 20% | **24%** | **17%** | **20%** | **19%** | **0.01** |
| BMI (kg/m^2) | 28.36 | **29.25** | **28.96** | **28.14** | **27.09** | **<0.01** |
| Waist circumference (cm) | 99.69 | **102.10** | **101.21** | **98.64** | **96.79** | **<0.01** |
| Hip circumference (cm) | 105.32 | **106.86** | **106.90** | **105.13** | **102.40** | **<0.01** |
| WHR | 0.95 | **0.95** | **0.95** | **0.94** | **0.94** | **<0.01** |
| GFRS | 18.34 | **18.99** | **18.51** | **18.42** | **17.44** | **<0.01** |
| Family history of MI | 0.451 | **0.52** | **0.50** | **0.49** | **0.43** | **<0.01** |
| Typical walking pace | | | | | | |
| No walking | 5% | **6%** | **8%** | **6%** | **2%** | **<0.01** |
| Stroll | 26% | 27% | 26% | 25% | 25% | 0.83 |
| Normal | 49% | 49% | 48% | 50% | 51% | 0.72 |
| Brisk | 18% | 18% | 16% | 18% | 20% | 0.24 |
| Stride | 2% | 1% | 1% | 2% | 2% | 0.20 |
| Alcohol consumption status | | | | | | |
| Never | 19% | **15%** | **17%** | **21%** | **24%** | **<0.01** |
| Former | 25% | **26%** | **27%** | **27%** | **21%** | **0.01** |
| Current | 55% | 58% | 55% | 51% | 55% | 0.06 |
| Alcohol consumption (drinks/week) | 5.62 | 6.46 | 5.17 | 5.38 | 5.47 | 0.11 |
| IL-6 (mg/dL) | 1.67 | **1.77** | **1.76** | **1.64** | **1.53** | **<0.01** |
| Fibrinogen (mg/dL) | 353.80 | 359.20 | 354.72 | 349.19 | 352.07 | 0.14 |
| CRP (mg/dL) | 3.79 | **4.07** | **4.20** | **3.45** | **3.45** | **0.04** |

Participants stratified by quartiles of ascending CAC density. Analysis includes only participants with CAC volume >0. Means and frequencies were adjusted for age, gender, and CAC volume by ANCOVA. The covariates of age, gender (proportion of males), and CAC volume were normalized to their mean values of 66.35 years, 57% male, and 257.86 mm3, respectively. Abbreviations: Hu=Hounsfield Units, BMI=Body Mass Index, WHR=waist-hip ratio, GFRS=Global Framingham Risk Score, MI=myocardial infarction, IL-6= interleukin-6, CRP=C-reactive protein, *for trend across quartiles

Table 3. Associations of cardiovascular disease risk factors with ln CAC volume in the Multi-Ethnic Study of Atherosclerosis

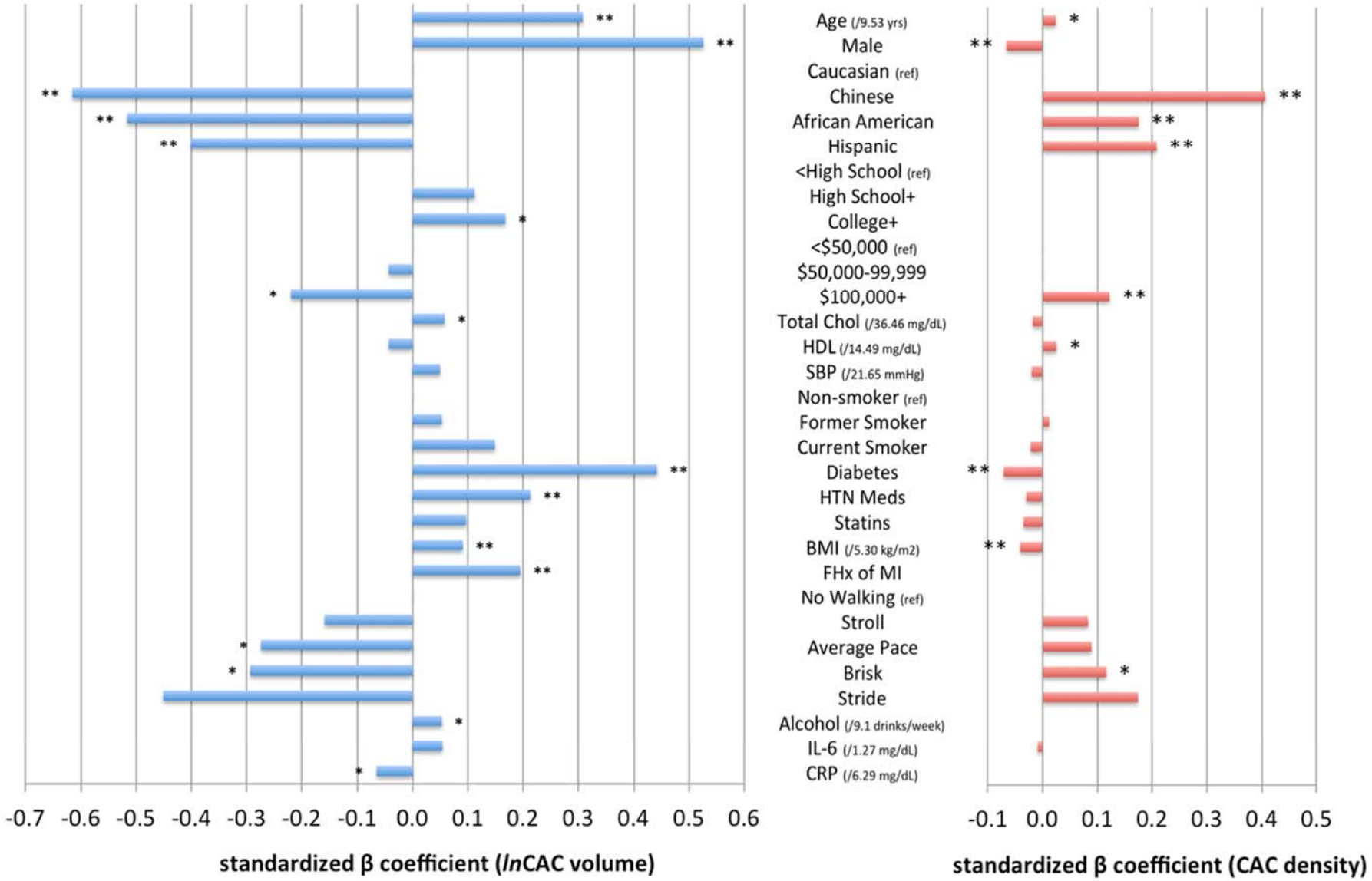
| | Minimally-adjusted | | | | Fully-adjusted | | | |
|---|---|---|---|---|---|---|---|---|
| | β | 95% CI | | p value | β | 95% CI | | p value |
| CAC Density score (/0.695 Hu category unit) | **0.88** | **0.84** | **0.93** | **<0.01** | **0.94** | **0.89** | **0.99** | **<0.01** |
| Age (/9.53 yrs) | **0.34** | **0.30** | **0.38** | **<0.01** | **0.31** | **0.25** | **0.37** | **<0.01** |
| Male | **0.50** | **0.41** | **0.58** | **<0.01** | **0.53** | **0.41** | **0.65** | **<0.01** |
| Ethnicity | | | | | | | | |
| Caucasian (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| Chinese | **-0.77** | **-0.91** | **-0.63** | **<0.01** | **-0.62** | **-0.83** | **-0.41** | **<0.01** |
| African-American | **-0.29** | **-0.40** | **-0.19** | **<0.01** | **-0.52** | **-0.64** | **-0.39** | **<0.01** |
| Hispanic | **-0.34** | **-0.45** | **-0.23** | **<0.01** | **-0.40** | **-0.55** | **-0.26** | **<0.01** |
| Level of education | | | | | | | | |
| < High school (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| High school+ | **0.18** | **0.06** | **0.30** | **<0.01** | 0.11 | -0.05 | 0.27 | 0.16 |
| College+ | 0.09 | -0.03 | 0.21 | 0.13 | **0.17** | **0.00** | **0.33** | **0.04** |
| Annual income | | | | | | | | |
| <$50,000 (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| $50,000-$99,999 | 0.09 | -0.02 | 0.20 | 0.09 | -0.04 | -0.17 | 0.08 | 0.49 |
| $100,000+ | -0.05 | -0.18 | 0.09 | 0.50 | **-0.22** | **-0.38** | **-0.06** | **0.01** |
| Total cholesterol (/36.46 mg/dL) | 0.03 | -0.02 | 0.07 | 0.25 | **0.06** | **0.01** | **0.11** | **0.03** |
| HDL (/14.49 mg/dL) | **-0.06** | **-0.11** | **-0.02** | **0.01** | -0.04 | -0.10 | 0.01 | 0.13 |
| Systolic BP(/21.65 mmHg) | **0.09** | **0.05** | **0.14** | **<0.01** | 0.05 | 0.00 | 0.10 | 0.07 |
| Diastolic BP (/10.22 mmHg) | **0.06** | **0.02** | **0.11** | **0.01** | | | | |
| Smoking status | | | | | | | | |
| Never (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| Former | **0.19** | **0.10** | **0.28** | **<0.01** | 0.05 | -0.05 | 0.16 | 0.33 |
| Current | **0.27** | **0.13** | **0.40** | **<0.01** | 0.15 | -0.01 | 0.31 | 0.06 |
| Smoking amount (/24 pack-years) | **0.13** | **0.09** | **0.17** | **<0.01** | | | | |
| Diabetes | **0.36** | **0.26** | **0.47** | **<0.01** | **0.44** | **0.31** | **0.58** | **<0.01** |
| Hypertension meds | **0.30** | **0.21** | **0.38** | **<0.01** | **0.21** | **0.11** | **0.32** | **<0.01** |
| Statins | **0.25** | **0.14** | **0.35** | **<0.01** | 0.10 | -0.03 | 0.22 | 0.13 |
| BMI (/5.30 kg/m^2) | **0.19** | **0.15** | **0.23** | **<0.01** | **0.09** | **0.03** | **0.15** | **<0.01** |
| Waist circumference (/13.87 cm) | **0.18** | **0.14** | **0.23** | **<0.01** | | | | |
| Hip circumference (/11.21 cm) | **0.18** | **0.13** | **0.22** | **<0.01** | | | | |
| WHR (/0.077) | **0.11** | **0.06** | **0.15** | **<0.01** | | | | |
| Family history of MI | **0.34** | **0.25** | **0.42** | **<0.01** | **0.20** | **0.10** | **0.29** | **<0.01** |
| Typical walking pace | | | | | | | | |
| No walking (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| Stroll | -0.09 | -0.29 | 0.11 | 0.36 | -0.16 | -0.40 | 0.08 | 0.20 |
| Average pace | **-0.25** | **-0.43** | **-0.06** | **0.01** | **-0.27** | **-0.51** | **-0.04** | **0.02** |
| Brisk | **-0.24** | **-0.44** | **-0.03** | **0.02** | **-0.29** | **-0.55** | **-0.04** | **0.02** |
| Stride | **-0.52** | **-0.91** | **-0.13** | **0.01** | -0.45 | -0.91 | 0.00 | 0.05 |
| Alcohol consumption status | | | | | | | | |
| Never (reference) | -- | -- | -- | -- | | | | |
| Former | -0.07 | 0.08 | 0.34 | 0.32 | | | | |
| Current | **0.17** | **0.11** | **0.33** | **0.04** | | | | |
| Alcohol consumption (/9.1 drinks/week) | **0.01** | **0.00** | **0.01** | **<0.01** | **0.05** | **0.00** | **0.10** | **0.03** |
| IL-6 (/1.27 mg/dL) | **0.09** | **0.05** | **0.13** | **<0.01** | 0.05 | 0.00 | 0.11 | 0.06 |
| Fibrinogen (/75.93 mg/dL) | **0.06** | **0.01** | **0.10** | **0.01** | | | | |
| CRP (/6.29 mg/dL) | 0.04 | 0.00 | 0.08 | 0.06 | **-0.07** | **-0.13** | **-0.01** | **0.04** |

Beta coefficients for continous variables are per one standard deviation change in predictor. Analysis includes only participants with CAC volume >0. The left column shows minimally-adjusted analyses (adjustment for age, gender, and CAC density). All listed predictor variables were then included in an intermediate multivariable model (not shown). Only those variables previously shown to be strongly tied to CVD risk (i.e. components of the pooled cohort equations and statin use) and any others that yielded p<0.10 were included in the final fully-adjusted multivariable model, shown on the right. Abbreviations: ln= natural log, Hu=Hounsfield Units, BMI=Body Mass Index, WHR=waist-hip ratio, GFRS=Global Framingham Risk Score, MI=myocardial infarction, IL-6= interleukin-6, CRP=C-reactive protein

Table 4. Associations of cardiovascular disease risk factors with CAC density in the Multi-Ethnic Study of Atherosclerosis

| | Minimally-adjusted | | | | Fully-adjusted | | | |
|---|---|---|---|---|---|---|---|---|
| | β | 95% CI | | p value | β | 95% CI | | p value |
| ln CAC volume (/1.62 ln-units) | **0.41** | **0.39** | **0.43** | **<0.01** | **0.44** | **0.42** | **0.46** | **<0.01** |
| Age (/9.53 yrs) | **0.03** | **0.01** | **0.05** | **0.02** | **0.02** | **0.00** | **0.05** | **0.05** |
| Male | -0.04 | -0.08 | 0.00 | 0.07 | **-0.07** | **-0.11** | **-0.02** | **<0.01** |
| Ethnicity | | | | | | | | |
| Caucasian (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| Chinese | **0.40** | **0.34** | **0.46** | **<0.01** | **0.41** | **0.34** | **0.47** | **<0.01** |
| African-American | **0.09** | **0.05** | **0.14** | **<0.01** | **0.18** | **0.12** | **0.23** | **<0.01** |
| Hispanic | **0.13** | **0.09** | **0.18** | **<0.01** | **0.21** | **0.15** | **0.26** | **<0.01** |
| Level of education | | | | | | | | |
| < High school (reference) | -- | -- | -- | -- | | | | |
| High school+ | **-0.07** | **-0.13** | **-0.02** | **0.01** | | | | |
| College+ | -0.01 | -0.07 | 0.04 | 0.60 | | | | |
| Annual income | | | | | | | | |
| <$50,000 (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| $50,000-$99,999 | -0.05 | -0.09 | 0.00 | 0.06 | 0.00 | -0.05 | 0.05 | 0.99 |
| $100,000+ | 0.06 | -0.01 | 0.12 | 0.07 | **0.12** | **0.06** | **0.19** | **<0.01** |
| Total cholesterol (/36.46 mg/dL) | -0.01 | -0.03 | 0.01 | 0.52 | -0.02 | -0.04 | 0.00 | 0.07 |
| HDL (/14.49 mg/dL) | **0.04** | **0.02** | **0.06** | **<0.01** | **0.03** | **0.00** | **0.05** | **0.03** |
| Systolic BP (/21.65 mmHg) | **-0.02** | **-0.04** | **0.00** | **0.04** | -0.02 | -0.04 | 0.00 | 0.06 |
| Diastolic BP (/10.22 mmHg) | -0.01 | -0.03 | 0.01 | 0.29 | | | | |
| Smoking status | | | | | | | | |
| Never (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| Former | -0.04 | -0.08 | 0.01 | 0.09 | 0.01 | -0.03 | 0.05 | 0.58 |
| Current | **-0.06** | **-0.12** | **0.00** | **0.05** | -0.02 | -0.09 | 0.04 | 0.49 |
| Smoking amount (/24 pack-years) | **-0.03** | **-0.05** | **-0.01** | **0.01** | | | | |
| Diabetes | **-0.08** | **-0.13** | **-0.03** | **<0.01** | **-0.07** | **-0.12** | **-0.02** | **<0.01** |
| Hypertension meds | **-0.06** | **-0.10** | **-0.02** | **<0.01** | -0.03 | -0.07 | 0.01 | 0.15 |
| Statins | **-0.06** | **-0.10** | **-0.01** | **0.02** | -0.04 | -0.08 | 0.02 | 0.17 |
| BMI (/5.30 kg/m^2) | **-0.08** | **-0.10** | **-0.06** | **<0.01** | **-0.04** | **-0.06** | **-0.02** | **<0.01** |
| Waist circumference (/13.87 cm) | **-0.07** | **-0.09** | **-0.05** | **<0.01** | | | | |
| Hip circumference (/11.21 cm) | **-0.08** | **-0.10** | **-0.06** | **<0.01** | | | | |
| WHR (/0.077) | **-0.02** | **-0.04** | **0.00** | **0.02** | | | | |
| Family history of MI | **-0.08** | **-0.11** | **-0.04** | **<0.01** | | | | |
| Typical walking pace | | | | | | | | |
| No walking (reference) | -- | -- | -- | -- | -- | -- | -- | -- |
| Stroll | **0.11** | **0.02** | **0.20** | **0.02** | 0.08 | -0.01 | 0.18 | 0.09 |
| Average pace | **0.14** | **0.05** | **0.22** | **<0.01** | 0.09 | -0.01 | 0.18 | 0.06 |
| Brisk | **0.14** | **0.05** | **0.23** | **<0.01** | **0.12** | **0.02** | **0.22** | **0.02** |
| Stride | **0.27** | **0.09** | **0.44** | **<0.01** | 0.17 | -0.01 | 0.35 | 0.06 |
| Alcohol consumption status | | | | | | | | |
| Never (reference) | -- | -- | -- | -- | | | | |
| Former | **-0.11** | **-0.17** | **-0.05** | **<0.01** | | | | |
| Current | **-0.11** | **-0.16** | **-0.06** | **<0.01** | | | | |
| Alcohol consumption (9.1 drinks/week) | -0.01 | -0.04 | 0.01 | 0.20 | | | | |
| IL-6 (/1.27 mg/dL) | **-0.04** | **-0.06** | **-0.02** | **<0.01** | -0.01 | -0.03 | 0.01 | 0.36 |
| Fibrinogen (/75.93 mg/dL) | -0.02 | -0.04 | 0.00 | 0.05 | | | | |
| CRP (/6.29 mg/dL) | **-0.02** | **-0.04** | **0.00** | **0.02** | | | | |

Beta coefficients for continous variables are per one standard deviation change in predictor. Analysis includes only participants with CAC volume >0. The left column shows minimally-adjusted analyses (adjustment for age, gender, and ln CAC volume). All listed predictor variables were then included in an intermediate multivariable model (not shown). Only those variables previously shown to be strongly tied to CVD risk (i.e. components of the pooled cohort equations and statin use) and any others that yielded p<0.10 were included in the final fully-adjusted multivariable model, shown on the right. Abbreviations: ln=natural log, Hu=Hounsfield Units, BMI=Body Mass Index, WHR=waist-hip ratio, GFRS=Global Framingham Risk Score, MI=myocardial infarction, IL-6= interleukin-6, CRP=C-reactive protein


Age (/9.53 yrs)
Male
Caucasian (ref)
Chinese
African American
Hispanic
<High School (ref)
High School+
College+
<$50,000 (ref)
$50,000-99,999
$100,000+
Total Chol (/36.46 mg/dL)
HDL (/14.49 mg/dL)
SBP (/21.65 mmHg)
Non-smoker (ref)
Former Smoker
Current Smoker
Diabetes
HTN Meds
Statins
BMI (/5.30 kg/m2)
FHx of MI
No Walking (ref)
Stroll
Average Pace
Brisk
Stride
Alcohol (/9.1 drinks/week)
IL-6 (/1.27 mg/dL)
CRP (/6.29 mg/dL)
-0.7 -0.6 -0.5 -0.4 -0.3 -0.2 -0.1 0.0 0.1 0.2 0.3 0.4 0.5 0.6
standardized β coefficient (lnCAC volume)
-0.1 0.0 0.1 0.2 0.3 0.4 0.5
standardized β coefficient (CAC density)

Figure