Published in final edited form as:
*Arterioscler Thromb Vasc Biol*. 2010 November ; 30(11): 2289–2296. doi:10.1161/ATVBAHA.110.208181.

# Risk Factor Differences for Aortic vs. Coronary Calcified Atherosclerosis: the Multi-Ethnic Study of Atherosclerosis

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## Abstract

**Objective—**To compare and contrast coronary artery calcium (CAC) with abdominal aortic calcium (AAC) in terms of their associations with traditional and novel cardiovascular disease (CVD) risk factors.

**Methods and Results—**We measured both AAC and CAC using computed tomography (CT) scans in 1974 men and women aged 45–84 years from a multi-ethnic cohort. Traditional and novel CVD risk factors were examined separately in relation to AAC and CAC, employing logistic regression for qualitative categorical comparisons and multiple linear regression for quantitative continuous comparisons. AAC was significantly associated with cigarette smoking and dyslipidemia, and showed no gender difference. In contrast, CAC showed much weaker associations with smoking and dyslipidemia, and a strong male predominance. Age and hypertension were associated similarly and significantly with AAC and CAC. Novel risk factors generally showed no independent association with either calcium measure, although in subset analyses phosphorous, but not calcium, was related to CAC. The ROC curves for the qualitative results and the r-squared values for the quantitative analyses were both much higher for AAC than for CAC.

**Conclusions—**AAC showed stronger correlations with most CVD risk factors than did CAC. The predictive value of AAC compared to CAC for incident CVD events remains to be evaluated.

### Keywords

aorta; calcium; coronary disease; imaging; risk factors

## Introduction

In the Multi-Ethnic Study of Atherosclerosis (MESA), cardiovascular disease (CVD) risk factors are modestly associated with coronary artery calcium (CAC) assessed by computed tomography (CT) in both cross-sectional [1] and longitudinal progression analyses [2]. These

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There are no conflicts of interest.

results are concordant with other studies [3, 4]. Less attention has been paid to risk factors for abdominal aortic calcification (AAC), another important measure of subclinical CVD. It is unclear as to the degree that CAC and AAC are similar pathophysiologic processes. A study of 650 patients with full body scans suggested somewhat stronger correlations for hypercholesterolemia, cigarette smoking, and diabetes with AAC than CAC [5]. Two smaller studies limited to women showed only minor difference in the associations between standard CVD risk factors and CAC vs. AAC[6, 7]. A recent study in MESA compared AAC and thoracic aortic calcium, but CAC was not included [8]. However, no data have been published comparing CT quantitative assessment of AAC and CAC with both standard and newer risk factors. In an ancillary study to the MESA, we quantified both AAC and CAC by CT scans, and we compared and contrasted standard and novel CVD risk factor associations for AAC and CAC in a cross-sectional analysis.

## Methods

### Study Participants

MESA is a prospective cohort study investigating subclinical atherosclerosis in 6814 individuals aged 45–84 years without known clinical CVD at baseline. Women made up 53% of the cohort and four ethnic groups were represented; 38% Caucasian, 28% African American, 22% Hispanic, and 12% Chinese. The cohort was recruited and initially examined from 2000–2002 at six field centers: Baltimore, MD; Chicago, IL; Los Angeles, CA; New York, NY; St Paul, MN; and Winston-Salem, NC. Individuals were excluded if they had clinical CVD, including physician-diagnosed myocardial infarction, angina, stroke, transient ischemic attack, or heart failure, use of nitroglycerin, current atrial fibrillation, or had undergone a procedure related to CVD. A detailed description of the study design, recruitment methods, examination components, and data collection has been published[9].

After the MESA study began an ancillary study measured AAC and CAC at the same examination in a random sample of MESA participants, recruited during follow-up visits between August 2002 and September 2005 from five of the six MESA field centers: those above with the exception of Baltimore, MD. Of 2202 MESA participants recruited, 2172 agreed to participate, and 1990 satisfied eligibility criteria. 1974 participants had complete CT scanning of their abdominal aorta. Further details about the MESA study design have been published elsewhere and are available on at www.mesa-nhlbi.org.

### Risk Factor Assessment

Standardized questionnaires at the baseline examination were used to obtain information about participant demographics, medical history, and medication usage including current blood pressure and cholesterol-lowering medications. Height, weight, and blood pressure were measured at the baseline examination. Body mass index (BMI) was calculated as weight (kg)/height ($m^2$). Resting blood pressure (BP) was measured three times in the seated position using a Dinamap automated sphygmomanometer, and the average of the 2nd and 3rd readings was used for this analysis. Blood samples were obtained after a 12-hour fast to measure glucose, total cholesterol, HDL cholesterol (HDL-C), triglycerides, and creatinine. Estimated glomerular filtration rate (eGFR) was calculated using the 4 variable Modification of Diet in Renal Disease equation. LDL cholesterol (LDL-C) was calculated using the Friedewald equation.

Diabetes was classified as having a fasting blood glucose >125 mg/dl and/or the self-reported use of hypoglycemic medications. Impaired fasting glucose (IFG) status was defined as fasting glucose 101–125 mg/dl. Participants were classified by never, former, or current use of cigarettes, and pack-years of cigarette smoking in ever smokers was calculated.

The following novel risk factors were also measured: C-reactive protein (CRP), interleukin-6 (IL-6), fibrinogen, homocysteine, D-dimer, factor VIII, plasmin anti-plasmin complex (PAP), insulin, and Chlamydia pneumoniae titer. CRP and fibrinogen were measured by immunonephelometry using the BNII instrument ((N High Sensitivity CRP, N Antiserum to Human Fibrinogen; Dade Behring Inc., Deerfield, IL). IL-6 was measured by ultra-sensitive ELISA (Quantikine HS Human IL-6 Immunoassay; R&D Systems, Minneapolis, MN). Homocysteine was measured by fluorescence polarization immunoassay (IMx Homocysteine Assay, Axis Biochemicals ASA, Oslo, Norway) using the IMx Analyzer (Abbott Diagnostics, 100 Abbott Park Rd, Abbott Park, Illinois). Factor VIII coagulant activity and D-dimer were determined utilizing the STA-R automated analyzer (STA-Deficient VIII, Liatest D-DI, Diagnostica Stago, Parsippany, NJ). PAP was measured using a two-site ELISA that detects only plasmin in complex with $\alpha_2$-antiplasmin, and not free plasmin or $\alpha_2$-antiplasmin, so it is a marker of plasmin generation[10]. Insulin was determined using the Linco Human Insulin Specific RIA Kit (Linco Research, Inc., St. Charles, MO 63304). IgG antibodies to *C. pneumoniae* were detected using a microimmunofluorescent antibody assay employing a two stage sandwich procedure for the qualitative and semi-quantitation detection (Focus Technologies, Cypress, CA).

In addition, data on serum calcium and phosphorous were available from a separate ancillary study on 1125 of the 1974 participants in Table 1 (57.0%)

## Subclinical Vascular Disease Assessment

To measure AAC, electron-beam computed tomography (EBCT) scanners were used at Northwestern and UCLA (Imatron C-150). These were set as follows: scan collimation of 3mm; slice thickness of 6mm; reconstruction using 25 6mm slices with 35 cm field of view and normal kernel. Multi-detector computed tomography mode scanners were used at the remaining three field centers (Columbia, Wake Forest, and U. of MN field centers; Sensation 64, GE Lightspeed, Siemens S4+ Volume Zoom and Siemens Sensation 16). Images were reconstructed in a 35 cm field of view with 5mm slice thickness. All scan scores were brightness adjusted with a standard phantom.

Non-contrast CT images were analyzed centrally using a standard protocolby the MESA CT Reading Center. Calcium in the wall of the distal abdominal aorta in the 8 cm segment proximal to the aortic bifurcation was measured. Calcification was identified as a plaque of $\geq 1 mm^2$ with a density of >130 Hounsfield units and quantified using the previously described Agatston scoring method [11].

At the same scanning examination, CAC was measured using either electron-beam tomography (EBT) (3 sites) or multi-detector CT (2 sites). Participants were scanned twice consecutively and each scan was read by a single trained physician-reader independently at a centralized reading center (Harbor-UCLA Medical Center/Los Angeles Biomedical Research Institute, Torrance, CA). The methodology for acquisition and interpretation of the scans, as well as reproducibility of the readings, has been reported previously[12]. The results from the two scans were averaged to provide a more accurate point estimate of the amount of calcium present. The Agatston score was calculated as previously described [11] and scores were adjusted using a standard calcium phantom that was scanned along with the participant[13]. The phantom contained 4 bars of known calcium density, and calibrates the X-ray attenuation level between measurements conducted on different machines. This was important as scanners were changed between baseline and follow-up at 3 of the 6 sites. Any detectable calcium was defined as a CAC score greater than 0; a minimum focus of calcification was based on at least 4 contiguous voxels, which resulted in identification of calcium of 1.15 $mm^3$ for the MDCT scanners and 1.38 $mm^3$ for the EBT scanners [12]. The nominal section thickness was 3.0 mmfor EBT scanners

and 2.5 mm for MDCT. The distribution of CAC in MESA at baseline by age, gender and ethnicity has been published previously [14].

### Statistical methods

For potential risk factors, we tabulated the mean value and distribution of continuous variables across first those with zero vs. non-zero AAC, and then zero vs. non-zero CAC. Two sets of multivariate models were employed. The first set of models was logistic regression and separately compared the zero vs. non-zero AAC and zero vs. non-zero CAC groups. In logistic regression models, each potential risk factor was first adjusted for age, gender, and ethnicity. Risk factors that were significant ($p<0.05$) for either AAC or CAC were included in a second multivariate model that included adjustment for each of the other risk factors. Receiver operating characteristic (ROC) curves were calculated alternately for prediction of the presence of AAC, and for the presence of CAC, first using only age, sex, and ethnicity, and then all the significant risk factors. Additional analyses included gender-specific models.

In the second set of models multiple linear regression was employed with either lnAAC+1 or lnCAC+1 as the dependent variable, and r-squared values were calculated. Since the natural logarithm of the calcium scores was used, 1 was added to each score in order to include the zero scores. Using the risk factors selected in the final logistic model above, the linear model predicted lnAAC +1 and the second model lnCAC +1. Analyses were performed using Stata 10.0 (College Station, TX). All p values were two-tailed (alpha=0.05).

## Results

Figure 1 shows the distribution of AAC and CAC in the study population, with percentages in parentheses. 21.1% had neither AAC nor CAC, 21.1 % had AAC-only, 7.3% had CAC-only, and 50.5% had both AAC and CAC. Thus, 1413 (997+416) (71.6%) had non-zero AAC and 1141 (997+144) (57.8%) had non-zero CAC. Among those with both AAC and CAC, the Spearman correlation for the amount of AAC and CAC was $r = 0.38$, $p < .0001$.

Table 1 shows the $10^{th}$, $50^{th}$ and $90^{th}$ percentile Agatston scores and distribution of potential risk factors stratified by absence or presence of AAC and CAC. The Agatston scores for AAC were much higher than those for CAC, such that the $50^{th}$ percentile for AAC and $90^{th}$ percentile for CAC were similar. In these unadjusted analyses, with the exception of C. pneumoniae titer (and calcium and phosphorous in the subset), analysis of variance showed that each of these variables differed significantly for either the AAC or the CAC comparisons.

After adjustment of each of these variables for age, sex, and ethnicity, the variables which showed no significant association in these logistic models in either the AAC or CAC analysis were education, eGFR, homocysteine, D-dimer, PAP, and C. pneumoniae titer, so these variables were not further considered. Among the five blood pressure variables, SBP and hypertension treatment were arbitrarily selected for a second model to avoid co-linearity. This second model added each of the remaining variables from Table 1, each adjusted for each other. Variables lacking significant relationships in the second model were income, BMI, triglycerides, CRP, IL-6, fibrinogen, insulin, and Factor VIII. Sex-specific analyses showed similar results so both sexes were combined to maximize power in these analyses.

Variables included in the final logistic models are shown in Table 2. Differences in numbers between tables reflect missing data for one or more variables. Note that odds ratios (ORs) presented are not good approximations of the relative risk since the prevalence of both AAC and CAC was relatively high. Of interest is that none of the novel risk factors met the selection criteria for Table 2, and neither calcium nor phosphorous were significant in the subset. For AAC, there was a positive risk factor association for age and inverse associations for Black

and Hispanic ethnicity. There were strong associations for the smoking variables; OR 1.72 for past smoking, 3.32 for current smoking, and an independent additional OR of 1.88 per 20 pack years. HDL-C showed a strong inverse association, OR 0.77 per standard deviation (SD), LDL-C a strong positive association, OR 1.52 per SD, and lipid medication use was additionally and independently significant, OR=2.43. SBP and hypertensive medication use showed independent positive associations.

Associations for CAC were similar to AAC for age, ethnicity, and SBP, and though significant the hypertensive medication association was less strong. CAC showed a strong male predominance, OR = 2.83, in sharp contrast to AAC, which was not associated with gender. Current smoking was much weaker for CAC, and the pack-yrs association was null. HDL-C was not significantly associated with CAC, and the associations for LDL-C and lipid meds were weaker than for AAC.

Figure 2a shows ROC curves for the prediction of AAC, and Figure 2b for the prediction of CAC, with the blue lines utilizing only age, gender, and ethnicity, and the red lines utilizing all the risk factors in table 2. The C-statistics were higher for AAC, and the difference between the minimally and fully adjusted curves were more than twice as large for AAC (+ 0.065) than for CAC (+0.024), indicating that a greater proportion of the variance in AAC vs. CAC was explained by risk factors beyond age, gender and ethnicity.

Table 3 shows the results of the multiple linear regression analyses separately for lnAAC+1 and lnCAC+1. In these models, risk variables are predicting the extent of calcified plaque in participants, rather than the presence or absence as in Table 2. Table 3 shows risk estimates per SD change for continuous variables and percent change for categorical variables. The results of these models were quite consistent with the results in Table 2. For the full cohort, age, gender, and ethnic associations were similar to the results in Table 2. The smoking variables were much stronger for AAC. The lipid variables were again much strong predictors of lnAAC+1 than lnCAC+1. The r-squared for the lnAAC+1 model was larger (0.439) than for the lnCAC+1 model (0.314). In the subset with calcium and phosphorous measurements, there was no association between calcium and either lnAAC+1 or lnCAC +1. However, there was a strong positive association between phosphorous and lnCAC+1 (coefficient = 0.21, $p < .01$), but not lnAAC+1 (coefficient= 0.04, p=.59).

In sensitivity analyses, we compared the logistic models for AAC with and without adjustment for CAC, and the CAC models with and without adjustment for AAC. Results were similar, although as expected risk factor differences were sharpened by adjustment for the other (correlated) calcium score. In addition, mutinomial logistic regression was used to evaluate risk factor differences across the four mutually exclusive groups in Figure 1: neither AAC nor CAC, AAC only, CAC only, and both AAC and CAC. Results again were similar to the results in Table 2 for the CAC only and AAC only phenotypes, and the results for the AAC and CAC phenotype were similar to those for AAC only. However, the smaller numbers per group made the results less stable.

## Discussion

Two previous small studies have suggested little difference in the association of standard CVD risk factors for atherosclerotic calcification of the coronary arteries compared to the distal aorta [6, 7]. One study did suggest possibly stronger risk factor correlations for AAC than CAC [5]. Estrogen alone, but not combination HRT, has been correlated with less CAC progression in women [15]. One study reported no independent association in men or women of AAC with any of several sex hormones measured[16]. Earlier studies did not evaluate novel risk factors such as inflammatory and thrombotic factors.

AAC and CAC were both common in this cohort free of clinical CVD at baseline. The major finding was a stronger association of most standard CVD risk factors with AAC compared to CAC. Both measures were positively correlated to a similar degree with age and hypertension. In contrast, the results for gender and ethnicity were markedly different. CAC was much more common in men (OR=2.83), while AAC was not (OR=0.91). The inverse association between AAC and African-American ethnicity was stronger than for CAC.

Two major cardiovascular risk factors - cigarette smoking and dyslipidemia, also showed clear differences. AAC was strongly and significantly associated with all smoking measures, while CAC showed much weaker associations. For example, for AAC, the OR for current smoking was 3.32, while for CAC the OR was 1.51. For the dyslipidemia measures, the associations were again stronger for AAC. HDL-C was strongly protective for AAC; OR per SD = 0.77, but null for CAC, OR = 0.91. LDL-C showed a stronger positive association for AAC (OR = 1.52), than for CAC (OR = 1.22). Lipid-lowering medication was more strongly associated with AAC (OR = 2.43) than with CAC (OR = 1.62).

Models exploring risk factor relationships with the continuous distribution of AAC and CAC (Table 3) were quite consistent with the categorical models above, and actually accentuated the AAC vs. CAC differences somewhat. The subset models in Table 3 adjusting also for calcium and phosphorous were consistent with recent studies showing that higher serum phosphorus levels are associated with CAC in community living populations[17, 18]. The lack of association of phosphorous with AAC requires future study.

Recent in vitro and autopsy studies have provided new insights to mechanisms contributing to deposition of calcium within atherosclerotic lesions and within the arterial media [19, 20]. These studies demonstrate that higher extracellular phosphorus may activate the calcific process through a sodium phosphate transporter on the cell surface, Pit-1, which appears both necessary and sufficient for calcification to ensue [19]. It is possible that the process begins in the necrotic core of atherosclerotic lesions and later transforms vascular smooth muscle cells to an osteoblast-like phenotype, involving deeper layers of the arterial wall including the arterial media [20]. The positive association of phosphorous with CAC in our data is consistent with these concepts. Others have argued that intimal (atherosclerotic) and medial calcification are distinct vasculopathies [21, 22]. To our knowledge, the relative distribution of calcium (intimal vs. medial) in the coronary arteries vs. aorta in community-living humans is unknown. Whether these factors may help explain the relatively dramatic differences in association with traditional CVD risk factors between these two anatomic sites observed in this study is speculative at present, and is an important area for future study.

Sensitivity analyses adjusting the AAC models for CAC and vice-versa showed even greater differences in risk factor associations. However, the interpretation of such models is unclear, since one outcome (e.g. AAC) is being adjusted for another correlated outcome (e.g., CAC) rather than for a risk factor.

Multiple novel risk markers were studied, and in univariate analysis all but one differed significantly for either AAC or CAC (Table 2). Such markers have shown strong correlations with CVD events in some studies [23]. However, in these data none remained significantly associated with AAC or CAC after adjusting for standard cardiovascular risk factors.

It is unclear why AAC would show much stronger associations with cigarette smoking and dyslipidemia than would CAC. Much evidence suggests cigarette smoking is a somewhat stronger risk factor for peripheral vs. central atherosclerosis [24], and in a separate analysis in this cohort smoking was the strongest risk factor for aortic diameter and aortic diameter was also correlated with AAC [25]. A recent review highlights the potential link between cigarette smoking, matrix metalloproteinases, and vascular disease[26]. However, the weak smoking

association for CAC was a surprise. Similarly, some evidence suggests lower HDL-C and higher triglycerides are somewhat better correlated with peripheral than central atherosclerosis, but the opposite appears to be true for LDL-C [24], and in contrast we found a weaker association of LDL-C with CAC than with AAC. In these data overall, AAC showed stronger correlations with CVD risk factors than did CAC, with the notable exception of gender.

Comparison of the results here with differences between AAC and TAC in MESA indicate that risk factors in general are somewhat stronger for AAC than TAC, but that risk factors for TAC are stronger than for CAC. Interestingly, compared to women, men are significantly more likely to have CAC but significantly less likely to have TAC, with no gender difference for AAC [8].

Our study has potential limitations. Parathormone was not measured, and calcium and phosphorous were available only on a subset. Although participants in the aortic calcium study were a random sample of those participating in the baseline examination, the baseline cohort was not a random sample of the multi-ethnic US population but rather selected with varying field site-specific criteria [9]. Thus, while these results are representative of the five participating MESA sites, they cannot necessarily be extrapolated to the general adult population. In addition, the risk factor measures were collected at the baseline examination between 2000 and 2002, while the AAC and CAC scans for this report were collected between 2002 and 2005. Thus, there was a lag between risk factor and scan data. This could have influenced the strength of associations, with some non-differential attenuation likely, but would not reasonably have affected the markedly differential associations of risk factors with AAC vs. CAC presented here.

Strengths of our study include structured, validated protocols with phantom calibration for AAC and CAC measures, as well as a standardized assessment of risk variables, with central reading centers for all variables from the five participating field centers.

In conclusion, AAC was strongly associated with age, hypertension, smoking, and dysplidemia, and varied sharply with ethnicity. In contrast, CAC showed a strong male predominance, and although associated with age and hypertension, showed weaker associations with smoking and dyslipidemia, unexpected findings for an atherosclerotic measure. CAC, especially higher levels, has proved strongly predictive of future CVD events, [27, 28] as has the presence of AAC measured by standard lumbar radiographs [29, 30]. CAC has also been shown in the MESA to significantly improve risk prediction beyond standard risk factors [31]. Future analyses in this cohort will explore the quantitative association by CT of AAC with future CVD events, taking into account the CAC, to determine if AAC predicts events independent of the CAC burden.

## Acknowledgments

This research was supported by NIH grants HL72403 and HL091217, and by contracts N01-HC-95159 through N01-HC-95169 with the National Heart, Lung, and Blood Institute.

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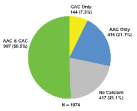

**Figure 1.**
Prevalence of Abdominal Aortic Calcium (AAC) and Coronary Artery Calcium (CAC).

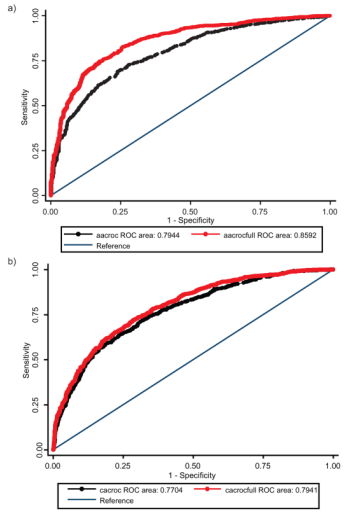


**Figure 2.**

Receiver Operating Characteristic (ROC) Curves for risk factor prediction of the presence of a) AAC and b) CAC. Black line - age, gender, and ethnicity. Red line – all risk factors in Table 2.

*Arterioscler Thromb Vasc Biol*. Author manuscript; available in PMC 2011 November 1.

**Table 1**

Cardiovascular Risk Factors by the Absence or Presence of AAC and CAC

| | AAC=0 | AAC>0 | p Value | CAC=0 | CAC>0 | p Value |
|---|---|---|---|---|---|---|
| N | 561 | 1413 | | 833 | 1141 | |
| Agatston Score | | | | | | |
| 10th percentile | -- | **42** | -- | -- | **5** | |
| 50th percentile | -- | **722** | -- | -- | **103** | |
| 90th percentile | -- | **4673** | -- | -- | **843** | |
| Age at baseline | **55.4** (7.8) | **64.8** (9.2) | <0.001 | **57.7** (8.6) | **65.3** (9.4) | <0.001 |
| Gender | | | | | | |
| Men | **47.4%** | **51.7%** | | **38.0%** | **59.5%** | <0.001 |
| Women | **52.6%** | **48.3%** | 0.089 | **62.0%** | **40.5%** | |
| Ethnic group | | | | | | |
| Caucasian | **29.2%** | **44.3%** | | **33.7%** | **44.7%** | |
| Chinese | **12.3%** | **13.5%** | | **14.1%** | **12.4%** | |
| African-American | **27.6%** | **18.1%** | | **25.1%** | **17.7%** | |
| Hispanic | **30.8%** | **24.1%** | <0.001 | **27.2%** | **25.2%** | <0.001 |
| Smoking status | | | | | | |
| Never | **60.5%** | **40.4%** | | **54.2%** | **40.1%** | |
| Former | **31.4%** | **47.1%** | | **33.0%** | **49.7%** | |
| Current | **8.1%** | **12.5%** | <0.001 | **12.8%** | **10.2%** | <0.001 |
| Pack-years | **4.1** (10.2) | **14.9** (28.7) | <0.001 | **8.4** (26.8) | **14.3** (24.0) | <0.001 |
| Education† | | | | | | |
| <high school | **16.9%** | **18.9%** | | **17.8%** | **18.7%** | |
| high school+ | **41.7%** | **47.6%** | | **46.0%** | **45.8%** | |
| college+ | **41.4%** | **33.6%** | 0.005 | **36.2%** | **35.5%** | 0.872 |
| Income† | | | | | | |
| <$50,000 | **53.1%** | **63.2%** | | **59.6%** | **60.8%** | |
| $50,000 – $99,000 | **29.0%** | **22.6%** | | **24.9%** | **24.0%** | |
| >$99,000 | **17.9%** | **14.3%** | <0.001 | **15.5%** | **15.2%** | 0.858 |
| BMI | **28.0** (5.4) | **28.2** (5.2) | 0.511 | **27.8** (5.4) | **28.4** (5.1) | 0.024 |
| Systolic BP, mmHg | **117.8** (19.8) | **126.5** (20.7) | <0.001 | **119.9** (20.3) | **127.0** (20.7) | <0.001 |

| | AAC=0 | AAC>0 | p Value | CAC=0 | CAC>0 | p Value |
|---|---|---|---|---|---|---|
| Diastolic BP, mmHg | **70.2** (9.9) | **70.0** (9.8) | 0.739 | **69.4** (10.0) | **70.6** (9.8) | 0.006 |
| Pulse pressure, mmHg | **47.6** (14.9) | **56.4** (17.2) | <0.001 | **50.5** (16.3) | **56.4** (17.2) | <0.001 |
| HTN medications | | | | | | |
| no | **73.4%** | **49.4%** | | **68.9%** | **31.1%** | |
| yes | **26.6%** | **50.7%** | <0.001 | **46.9%** | **53.1%** | <0.001 |
| HTN | | | | | | |
| No | **69.4%** | **46.0%** | | **64.7%** | **43.8%** | |
| Yes | **30.7%** | **54.0%** | <0.001 | **35.4%** | **56.2%** | <0.001 |
| Glycemic status | | | | | | |
| Normoglycemic | **80.2%** | **67.1%** | | **77.0%** | **66.4%** | |
| IFG | **10.5%** | **16.4%** | | **12.2%** | **16.6%** | |
| Diabetes | **9.3%** | **16.4%** | <0.001 | **10.8%** | **17.0%** | <0.001 |
| LDL, mg/dl | **113.2 (29.3)** | **111.4 (32.1)** | 0.274 | **114.2 (30.9)** | **110.3 (31.5)** | 0.006 |
| HDL, mg/dl | **53.6 (16.2)** | **50.7 (14.6)** | <0.001 | **53.2 (15.6)** | **50.3 (14.7)** | <0.001 |
| Triglycerides, mg/dl* | **107 [71,151]** | **118 [81.8,170]** | <0.001 | **110 [76,160]** | **117 [79,166]** | 0.170 |
| Lipid lowering meds | | | | | | |
| No | **87.8%** | **69.8%** | | **83.5%** | **68.6%** | |
| Yes | **12.2%** | **30.2%** | <0.001 | **16.5%** | **31.4%** | <0.001 |
| eGFR, ml/min/1.73 m2 | | | | | | |
| <60 | **5.7%** | **12.2%** | | **6.3%** | **13.3%** | |
| ≥60 | **94.3%** | **87.8%** | <0.001 | **93.7%** | **86.7%** | <0.001 |
| CRP, mg/L* | **1.64 [0.77,4.01]** | **1.93 [0.87,4.28]** | 0.034 | **1.8 [0.82,4.1]** | **1.9 [0.86,4.2]** | 0.606 |
| IL-6, pg/ml* | **0.97 [0.65,1.53]** | **1.23 [0.80,1.89]** | <0.001 | **1.04 [0.67,1.63]** | **1.25 [0.82,1.93]** | <0.001 |
| Homocysteine, umol/L* | **8.3 [6.9,9.9]** | **9 [7.5,10.8]** | <0.001 | **8.2 [7,9.9]** | **9.1 [7.7,11]** | <0.001 |
| Fibrinogen, mg/dl | **332 (65.4)** | **349 (72.0)** | <0.001 | **338.5 (68.7)** | **348.1 (71.7)** | 0.003 |
| Insulin, mU/L* | **5.1 [3.5,7.8]** | **5.7 [3.8,9.1]** | 0.002 | **5.1 [3.6,7.9]** | **5.9 [3.9,9.2]** | <0.001 |
| D-dimer, ng/ml* | **.18 [.10,.32]** | **.23 [.15,.39]** | <0.001 | **.18 [.10,.32]** | **.23 [.15,.42]** | <0.001 |
| Plasmin anti-plasmin, ng/ml | **4.52 (1.88)** | **4.75 (2.32)** | 0.037 | **4.57 (1.81)** | **4.77 (2.46)** | 0.056 |
| Chlamydia pneumoniae positive | **74.7%** | **76.9%** | 0.569 | **75.2%** | **77.1%** | 0.600 |
| FVIII, % | **93.2 (34.7)** | **97.8 (36.0)** | 0.009 | **93.1 (34.5)** | **98.9 (36.3)** | <0.001 |
| Calcium, mg/dl ** | **9.02 (0.48)** | **9.05 (0.52)** | 0.320 | **9.01 (0.49)** | **9.06 (0.52)** | 0.094 |

| | AAC=0 | AAC>0 | p Value | CAC=0 | CAC>0 | p Value |
|---|---|---|---|---|---|---|
| Phosphorus, mg/dl ** | **3.45 (0.50)** | **3.42 (0.53)** | 0.360 | **3.46 (0.52)** | **3.41 (0.53)** | 0.098 |

† Self-reported at baseline.

Data are means (± standard deviations) or proportions unless otherwise indicated.

p Value represents difference in means, medians or proportions.

* Data are medians (25th percentile, 75th percentile).

** Subset, N= 1125, with calcium and phosphorous measurements

## Table 2

Multivariable Logistic Model Analyses for the Presence of AAC and CAC

| | OR (95% CI)[a] | |
|---|---|---|
| | Multivariable adjusted models | |
| | **AAC (0 vs. non-zero)** | **CAC (0 vs. non-zero)** |
| N | 552 vs. 1371 | 813 vs. 1110 |
| Area Under ROC Curve/C-statistic | | |
| age-, gender-, race-adjusted model | 0.794 | 0.770 |
| fully adjusted model | 0.859 | 0.794 |
| Age at baseline (per 10 years) | **3.41** (2.89–4.02) | **2.43** (2.14–2.77) |
| Male gender (vs. female) | **0.91** (0.69–1.20) | **2.83** (2.23–3.60) |
| Ethnic group (vs. Caucasian) | | |
| Chinese | **1.19** (0.79–1.80) | **0.79** (0.55–1.11) |
| African-American | **0.29** (0.21–0.41) | **0.43** (0.32–0.58) |
| Hispanic | **0.49** (0.36–0.68) | **0.71** (0.54–0.94) |
| Smoking status (vs. never) | | |
| Former | **1.72** (1.24–2.40) | **1.79** (1.38–2.31) |
| Current | **3.32** (2.04–5.41) | **1.51** (1.05–2.17) |
| Pack-years (per 20 pack-years) | **1.88** (1.44–2.45) | **1.02** (0.93–1.12) |
| Systolic BP (per SD, 20.8 mmHg) | **1.21** (1.05–1.39) | **1.23** (1.09–1.38) |
| Any antihypertensive meds. (vs. no) | **2.09** (1.54–2.83) | **1.69** (1.33–2.16) |
| Glycemic status (vs. normoglycemia) | | |
| Impaired fasting glucose | **1.28** (0.96–1.72) | **1.01** (0.79–1.30) |
| Diabetes | **1.37** (0.89–2.10) | **1.42** (0.99–2.03) |
| HDL-cholesterol (per SD, 15.2 mg/dL) | **0.77** (0.67–0.88) | **0.91** (0.81–1.03) |
| LDL-cholesterol (per SD, 31.3 mg/dL) | **1.52** (1.34–1.74) | **1.22** (1.09–1.36) |
| Any lipid-lowering meds (vs. no) | **2.43** (1.59–3.72) | **1.62** (1.18–2.23) |
| Calcium (per SD, 0.51 mg/dl)** | **1.09** (0.90–1.31) | **1.10** (0.94–1.29) |
| Phosphorus (per SD, 0.52 mg/dl)** | **0.96** (0.79–1.17) | **1.11** (0.95–1.31) |

[a] Estimated from multivariable logistic regression models. All variables shown in the table were entered in the models simultaneously

* $p<0.05$

** Subset, N= 1098, with calcium and phosphorous measurements

## Table 3

Multiple Linear Regression Models for Correlates of lnAAC+1 and lnCAC+1

| | **lnAAC+1** | **lnCAC+1** |
|---|---|---|
| N | 1923 | 1923 |
| R-squared | 0.439 | 0.314 |
| | Coeff (p value) | Coeff (p value) |
| Age at baseline (per 10 years) | **1.53** (<.01) | **0.97** (<.01) |
| Male gender (vs. female) | −**0.06** (0.66) | **1.13** (<.01) |
| Ethnic group (vs. Caucasian) | | |
| Chinese | −**0.23** (0.21) | −**0.39** (0.02) |
| African-American | −**1.52** (<.01) | −**0.99** (<.01) |
| Hispanic | −**0.79** (<.01) | −**0.42** (<.01) |
| Smoking status (vs. never) | | |
| Former | **0.94** (<.01) | **0.58** (<.01) |
| Current | **1.78** (<.01) | **0.35** (0.04) |
| Pack-years (per 20 pack-years) | **0.31** (<.01) | **0.08** (0.06) |
| Systolic BP (per SD, 20.8 mmHg) | **0.25** (<.01) | **0.22** (<.01) |
| Any antihypertensive meds (vs. no) | **0.72** (<.01) | **0.53** (<.01) |
| Glycemic status (vs. normoglycemia) | | |
| Impaired fasting glucose | **0.22** (0.10) | −**0.06** (0.63) |
| Diabetes | **0.30 (**.10) | **0.46** (<0.01) |
| HDL-cholesterol (per SD, 15.2 mg/dL) | −**0.28** (<.01) | −**0.02** (0.78) |
| LDL-cholesterol (per SD, 31.3 mg/dL) | **0.52** (<.01) | **0.19** (<.01) |
| Any lipid-lowering meds (vs. no) | **1.11** (<.01) | **0.51** (<.01) |
| Calcium (per SD, 0.51 mg/dl)** | **0.09** (0.26) | **0.07** (0.31) |
| Phosphorus (per SD, 0.52 mg/dl)** | **0.04** (0.59) | **0.21** (<.01) |

** Subset, N= 1098, with calcium and phosphorous measurements