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Spatially Weighted Coronary Artery Calcium Score and Coronary Heart Disease Events in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Abstract

Background.—A limitation of the Agatston coronary artery calcium (CAC) score is that it does not use all of the calcium density information in the CT scan such that many individuals have a score of zero. We examined the predictive validity for incident coronary heart disease events of the spatially weighted coronary calcium score (SWCS), an alternative scoring method for CAC that assigns scores to individuals with Agatston CAC = 0.

Methods.—The Multi-Ethnic Study of Atherosclerosis (MESA) is a longitudinal study that conducted a baseline exam in 2000–2002 in 6,814 participants including CT scanning for CAC.

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Subsequent exams and systematic follow-up of the cohort for outcomes were performed. Statistical models were adjusted using the MESA risk score based on age, sex, race/ethnicity, systolic blood pressure, use of hypertension medications, diabetes, total and high-density lipoprotein (HDL) cholesterol, use of lipid lowering medications, smoking status, and family history of heart attack.

Results.—In the 3,286 participants with Agatston CAC = 0 at baseline and for whom SWCS was computed, 98 incident CHD events defined as definite or probably myocardial infarction or definite CHD death occurred during a median follow-up of 15.1 years. In this group SWCS predicted incident CHD events after multivariable adjustment (hazard ratio = 1.30 per standard deviation of ln(SWCS), 95% CI, 1.04–1.60; p=0.005); and progression from Agatston CAC = 0 at baseline to CAC > 0 at subsequent exams (multivariable adjusted incidence rate difference per standard deviation of ln(SWCS) per 100 person-years 1.68, 95% CI, 1.03–2.33; p<0.0001).

Conclusions.—SWCS predicts incident CHD events in individuals with Agatston CAC score=0 as well as conversion at repeat CT scanning at later exams to Agatston CAC > 0. SWCS has predictive validity as a subclinical phenotype and marker of CHD risk in individuals with Agatston CAC = 0.

Keywords

Atherosclerosis; coronary artery calcium score

INTRODUCTION

Atherosclerosis is an inflammatory process leading to plaque formation that results from intra-cellular accumulation of low density lipoprotein (LDL) cholesterol in macrophages in the arterial wall.[1–5] Calcification is a response to inflammation in the plaque,[6] thereby providing a biological rationale for the measurement of coronary artery calcium (CAC) as a risk factor for coronary heart disease (CHD). Scoring systems have been developed to quantitate CAC reproducibly from computerized tomography (CT) images. Of these, the most widely used is the Agatston CAC score.[7] Agatston CAC score has been shown to be highly predictive for CHD[8] and cardiovascular disease (CVD) events[9] and is widely used in risk stratification, particularly in individuals who are at intermediate risk for CVD based on traditional risk factors.[10,11]

A limitation of the Agatston CAC score is that it does not use all of the calcium density information in the CT scan. Approximately half of the MESA cohort had Agatston coronary artery calcium (CAC) score = 0 at the baseline exam,[12] with Agatston CAC = 0 being more common in younger individuals. An alternative scoring system, termed spatially weighted coronary calcium score (SWCS) and described in a previous MESA publication,[12] has been used to assign scores to individuals with Agatston CAC = 0. The SWCS aligns closely with the Agatston score for those with Agatston CAC > 0[12] and, like the Agatston score, predicts CHD events in the cohort as a whole, that is, among individuals with CAC =0 and CAC > 0 at baseline considered together.[12] In this previous study, among individuals with Agatston CAC = 0, there was a statistically non-significant association of SWCS and CHD risk, but data were available for only six years of follow-up, in which only 22 incident CHD events

occurred in this group. Thus, the predictive ability of SWCS for CHD events in this group was underpowered. We therefore examined the predictive ability of SWCS for incident CHD events using follow-up data through 2016, with a median of approximately 15 years of follow-up, among those with Agatston CAC score = 0 at baseline in the MESA cohort. Additionally, we examined the predictive ability of SWCS for incidence of Agatston CAC > 0 in follow-up CT scans at MESA exams 2 and 3. Exam 2 took place from September 2002 through February 2004. Exam 3 took place from March 2004 through September 2005.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Participants and Baseline Measures

The Multi-Ethnic Study of Atherosclerosis (MESA) is a population-based study of 6,814 men and women aged 45–85 years, without known clinical cardiovascular disease at time of entry, recruited from six U.S. communities (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; northern Manhattan, NY; and St. Paul, MN). Sampling and recruitment procedures have been reported.[13] Questionnaires were used to assess age, gender, race/ethnicity, educational and income levels, occupational information, smoking status, and medication use for diabetes mellitus, lipid lowering, and hypertension. Classification of race/ethnicity was based on self-identification using questions based on the U.S. 2000 census questionnaire. Height and weight were measured, and body mass index (BMI) was computed as kg/m^2. Blood pressure was measured in the seated position three times at one minute intervals using an appropriately sized cuff and following a standardized protocol.[14] The average of the last two measurements was used for analysis. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or self-reported high blood pressure and on treatment with medication for hypertension.[15] Diabetes was defined as being on treatment with insulin or oral medication for diabetes or fasting glucose ≥126 mg/dl.[16] Fasting blood specimens were analyzed for serum glucose, total cholesterol, high density lipoprotein (HDL) cholesterol, and triglyceride levels. The baseline exam was conducted between 8/1/2000 and 7/30/2002. Centrally trained and certified study staff performed all participant measurements. Institutional Review Board approval was obtained at all MESA sites. Consent was obtained from all participants.

CT Scanning and CAC Measurement

Coronary artery calcium (CAC) was assessed at the six MESA field centers using either an electron-beam CT scanner (at the Chicago, Los Angeles, and New York centers) or a multidetector CT system (at the Baltimore, Forsyth County, and St. Paul centers).[17] Certified technologists scanned all participants twice over phantoms of known physical calcium concentration. A radiologist or cardiologist read all CT scans at a single center (Los Angeles Biomedical Research Institute at Harbor–University of California Los Angeles Medical Center, Torrance) using an interactive scoring system. The reader–work station interface calibrated each tomographic image according to the estimated attenuation of the calcium phantom and then identified and quantified the coronary calcium in each image. The

Agatston CAC score[7] was calculated for each scan, and the mean of the two scans was used in all analyses. Intra-observer and inter-observer agreement were excellent (kappa statistics, 0.93 and 0.90, respectively). The SWCS were calculated from the CT scans at the baseline exam and the randomly selected 50% of participants who had repeat CT scanning at exam 2 and the remaining 50% who had repeat scanning at exam 3.

Spatially Weighted Calcium Score

The procedure for calculating SWCS has been described in detail in a previous publication and appendix.[12] As in reading the CT scans for the Agatston score, a set of voxels was identified by the reader as representing the coronary arteries. A weight was assigned to each voxel using a weighting function with parameters derived from the scan's phantom, so that scores across images were comparable. Each voxel was then assigned a score based on the weight assigned to it and its neighbors. This procedure used surrounding information to increase accuracy by upweighting voxels with neighboring voxels that had high attenuation levels and down-weighting those whose neighbors had low attenuation levels.

Coronary Heart Disease Events

Incident CHD was defined as definite or probably myocardial infarction (MI) or definite CHD death.[8] Participants included in the analysis were followed for incident CHD events from the baseline exam until the end of 2016, for a median of 15.1 and maximum of 16.5 years of follow-up. In addition to five follow-up MESA examinations, a telephone interviewer contacted each participant every 9 to 12 months to inquire about interim hospital admissions, cardiovascular outpatient diagnoses, and deaths. To verify self-reported diagnoses, copies were requested of all death certificates and medical records for all hospitalizations and outpatient cardiovascular diagnoses. Next of kin interviews for out of hospital cardiovascular deaths were obtained. Medical records were obtained for approximately 99% of reported hospitalized cardiovascular events and information on 97% of reported outpatient cardiovascular diagnostic encounters. Follow-up telephone interviews were completed in 90% of living participants. Trained personnel abstracted medical records suggesting possible cardiovascular events. Two physicians independently reviewed all abstracted medical records for endpoint classification and assignment of incidence dates, using pre-specified criteria. Descriptions of MESA events definitions and follow-up procedures have been previously published.[8] MESA CHD event ascertainment was supplemented by including events missed by MESA with MI events found from Medicare claims data and CHD deaths found in the National Death Index.

Statistical Analysis

Cox regression for the participants with baseline SWCS measured and Agatston CAC = 0 was used to estimate the relationship (hazard ratio) of the natural logarithm (ln) of baseline SWCS as a continuous variable per standard deviation (SD) of ln(SWCS) and in quartiles with the risk of CHD. In sensitivity analyses we also tested whether a cubic spline function improved the fit compared to a linear function for ln(SWCS) with no evidence of improvement (data not shown). We estimated hazard ratios for CHD before and after adjustment for traditional CHD risk factors. For the adjusted Cox models, we used the MESA risk score[18] to adjust for potential confounding factors. The risk score incorporates

information for age, sex, race/ethnicity, MESA site, systolic blood pressure, use of hypertension medications, diabetes, HDL cholesterol, use of lipid lowering medications, smoking status, and family history of heart attack. This was done because the number of events was too small to allow for interpretable coefficients with all covariates included individually in the final model. To evaluate potential differences in the association between ln(SWCS) and incident CHD by age groups, gender, and race/ethnic groups, we also added interaction terms to the model, with no evidence of effect modification by those participant characteristics (data not shown).

We modeled the incidence rate (per 100 person years) of Agatston CAC > 0 at Exams 2 or 3 as a function of the ln(SWCS) using weighted least squares for linear regression with weights equal to the time between baseline and Exams 2 or 3.[19] Based on this approach, the model coefficient estimates the incidence rate difference of CAC > 0 for a SD increment of the ln(SWCS) reported per 100-person years. A robust variance estimator[20] was used in models that were unadjusted and adjusted for the variables listed in Table 1. All analyses were carried out using STATA 16.0.

RESULTS

In the MESA sample of 6,814 participants at baseline, 29 participants with no follow-up were excluded from the analyses. Of the remaining 6,785 participants, 6,541 had SWCS computed (Figure 1). As previously reported, individuals with CAC > 0 at the baseline exam were older, more likely to be male, white or Caucasian, and more likely to have CHD risk factors compared to individuals with CAC = 0 (Table 1). Among the 3,286 participants with CAC = 0 at baseline and for whom SWCS was computed, 15 were missing data for one or more covariates included in the multivariable models and were excluded, so that 3,271 individuals were included in these models. In this group, there were 98 incident CHD events during the follow-up period.

In the Cox model for incident CHD, the unadjusted hazard ratio per SD of ln(SWCS) was 1.40 (95% CI, 1.14–1.80; p=0.0023). The hazard ratio adjusted for covariates using the MESA risk score was 1.30 (95% CI, 1.04–1.60). As shown in Table 2, the cumulative CHD event rates were progressively greater in each quartile of SWCS at baseline among those with Agatston CAC = 0 at the baseline line exam. This was also the case after multivariable adjustment (Table 3). As shown in Figure 2, very few events occurred during the first five years after the baseline CT scan with Agaston CAC = 0. Also as shown in Figure 2, the quartiles became more separate with longer time of follow-up.

The rate of transition from Agatston CAC = 0 to CAC > 0 was 7 per 100 person-years for both the transition from baseline to Exam 2 and from baseline to Exam 3. This indicates a constant rate for this transition. For risk of progression from Agatston CAC = 0 at baseline to Agatston CAC > 0 at either Exam 2 or Exam 3, we observed an unadjusted rate difference of 1.95 CAC transition events per 100 person years per SD increase of ln(SWCS) (p<0.0001). After multivariable adjustment, a one SD increase in ln(SWCS) was associated with 1.68 (95% CI, 1.03–2.33; p<0.0001) more CAC transition events per 100 person-years

(Table 4). Also as shown in Table 4, other established risk factors for CHD were associated with the transition from CAC = 0 to CAC > 0.

DISCUSSION

Many individuals have coronary artery calcium scores of zero based on the Agatston scoring method. In the MESA cohort, which was aged 45–84 years at the baseline exam, slightly more than half of the cohort had Agatston CAC = 0. Individuals with Agatston CAC = 0 are at low risk for incident CHD and CVD events, compared to individuals with Agatston CAC > 0.[8] However, it is known that this risk is not absent and that some individuals with Agatston CAC = 0 develop CHD over time.[21,22] We report here that a clinically underused scoring method, Spatially Weighted Calcium Score, is predictive of incident CHD events over 15 years among individuals with Agatston CAC = 0 at baseline in the MESA cohort. We also found that among these individuals, higher SWCS at baseline predicted Agatston CAC score > 0 at repeat CT scanning at either Exam 2 or Exam 3 beyond traditional CVD risk factors.

Progression of Agatston CAC score over time has previously been shown to predict incident CHD, over and above the baseline CAC score.[23,24] The 10-year CHD events rates among individuals with Agatston CAC = 0 are low and have been previously reported from the MESA cohort.[22] Data from other studies with different lengths of follow-up confirm this finding.[25–27] However, these reports as well as the data reported here show individuals with Agatston CAC = 0 have residual risk.[28] Several mechanisms for residual risk have been hypothesized, including levels of triglyceride-rich lipoproteins and their remnants, lipoprotein(a), HDL-mediated cholesterol efflux,[29] and inflammation.[28]

Our data indicate that SWCS is a measure of residual risk for CHD over long-term follow-up. The SWCS adds to the prediction information of Agatston CAC = 0 by leveraging calcium density information in neighboring voxels. The SWCS is thus able to provide additional information on patient level CHD risk. Because of the high correlation of SWCS to Agatston CAC score among individuals with Agatston CAC > 0,[12] traditional risk CVD risk factors that predict Agatston CAC score[30,31] will predict SWCS as well. The relationship of traditional risk factors, other than cholesterol level, to Agatston CAC score appears to be weaker in younger individuals.[32] The degree to which newer, residual CVD risk factors are associated with SWCS remains to be investigated.

Identifying individuals with CAC = 0 who remain at risk of developing CHD could contribute to refinement of cardiovascular disease guidelines and clinical practice. A recent analysis showed that the average time period to CAC > 0 among MESA participants with mean age 58 years and CAC = 0 at baseline ranged from 3 to 7 years of age.[33] The authors concluded that a 3 to 5-year time frame seemed reasonable to recommend repeating CT scanning among individuals of similar age to MESA and with CAC = 0. Repeating a CT scan, however, involves cost and radiation exposure. Maximizing the information already available in the baseline exam among those with CAC = 0 to predict who will convert to CAC > 0 may help to delay the need to repeat a CT scan.

An important question is whether the risk throughout SWCS levels among those with CAC = 0 is linear or if there is a threshold (a level below which there is no residual risk for CHD). In the quartile analysis, while the unadjusted model showed similar risk for quartiles 1 and 2, the adjusted models showed a progressive increased risk, suggesting no threshold. Additional research with longer follow-up, in different populations, and with larger sample sizes would be needed to further evaluate the shape of the dose-response relationship between SWCS and CHD.

Validated measures of subclinical CVD and CHD in younger individuals are lacking. Agatston CAC score is the best validated measure of subclinical CHD, but presence of Agatston CAC is strongly related to age and Agatston CAC score is commonly zero in younger individuals. Carotid intima-medial thickening has been extensively investigated as a subclinical measure but is at best weakly predictive for CHD events specifically as well as for CVD events more generally, in most studies.[9,34,35] Thus, SWCS may have a useful role as a subclinical measure of CHD, particularly in younger individuals in whom longer term risk is of interest. For instance, in young adults, SWCS could be useful to investigate novel and established risk factors for CHD risk as well as the potential effects of prevention interventions in altering atherosclerosis progression.

By leveraging calcium density information available in neighboring voxels, the SWCS is able to assign quantitative scores to individuals with Agatston CAC = 0, thus supporting risk prediction in this group. An additional advantage of SWCS compared to the Agatston score is that it is continuous through the origin and normally distributed on the logarithmic scale. The SWCS thus avoids the statistical challenges in modeling the Agatston score, which is sometimes referred to as a zero-inflated variable and requires two-part models.[36] These models can be complex, especially in describing associations between covariates and CAC progression or development.[36]

Other strengths include the rigorous follow-up and adjudication of incident CHD events in the MESA study, the well characterized set of covariates, and the length of follow-up available. The long-term follow-up is especially important in light of the very small number of CHD events that occurred in individuals with Agatston CAC = 0 during the first five years of follow-up. Of equal importance is that even in this group, a significant number of events occurred during the ensuing 10 years of observation.

Limitations include the relatively small number of incident events occurring in individuals with Agatston CAC=0, which limits power to detect possible differences by gender or race/ethnicity. Neither of these variables met criteria for inclusion in the final multivariable model. MESA participants were not all scanned at each Exam, some having a second scan at Exam 2 and others at Exam 3, and without subsequent scanning. Another limitation is that different scanner types were used at different MESA field centers. However, these scanners were phantom-calibrated[17] and previously reported findings have shown that differences in scanner type did not contribute importantly to differences in scores.[8] We also note that it is possible that use of thinner CT slices for image reconstruction might allow detection of micro-calcification in those with measured Agatston scores = 0. However, increased noise

becomes a significant concern with thinner slices, especially as the kv and ma are fixed and adjusted for 2.5–3.0 mm slice thickness.

In summary, SWCS is a novel calcium scoring method that assigns numerical values to individuals with Agatston CAC = 0. SWCS predicts incident CHD events and conversion from Agatston CAC = 0 to > 0 in fully adjusted models. SWCS may be a useful subclinical phenotype and marker of CHD risk with Agatston CAC = 0, particularly in younger individuals in whom Agatston CAC score is often zero and for whom longer term risk is of interest. The potential role of SWCS or other alternative methods for scoring coronary calcium in risk prediction merits further research.

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Abbreviations

CAC	Coronary artery calcium
CHD	Coronary heart disease
CI	Confidence interval
CT	Computerized tomographic
HDL	High density lipoprotein
ln	Natural logarithm
MESA	Multi-Ethnic Study of Atherosclerosis
MI	Myocardial infarction
SD	Standard deviation
SWCS	Spatially weighted calcium score

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CLINICAL PERSPECTIVE

Calcification in response to inflammation in coronary artery plaque can be measured quantitatively by CT scanning. The most widely used scoring system is the Agatston coronary artery calcium (CAC) score. Agatston CAC score has been shown to be highly predictive for coronary heart disease (CHD) events and is widely used in risk stratification, particularly in individuals who are at intermediate risk for CHD based on traditional risk factors. A limitation of the Agatston CAC score is that many individuals have scores of zero, especially younger individuals. The Agatston CAC score does not use all of the calcium density information in the CT scan, and an alternative scoring method, termed spatially weighted coronary calcium score (SWCS), has been used to assign quantitative scores to individuals with Agatston CAC=0. Here we report that among individuals with Agatston CAC=0, the SWCS score predicted incident CHD events over 15 years, as well as progression from Agatston CAC=0 to Agatston CAC > 0. Thus, SWCS may be a clinically useful subclinical phenotype and marker of CHD risk, particularly among younger individuals in whom Agatston CAC score is often zero and for whom longer term risk is of interest.

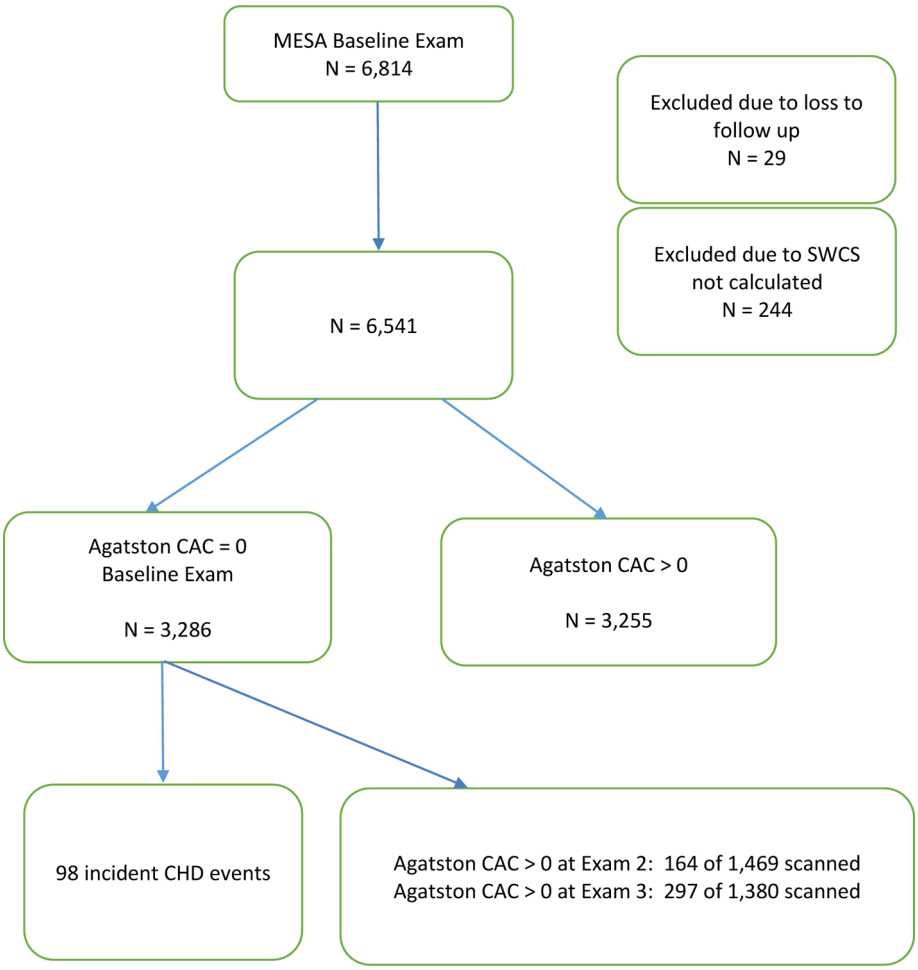

Figure 1.
Flow Chart

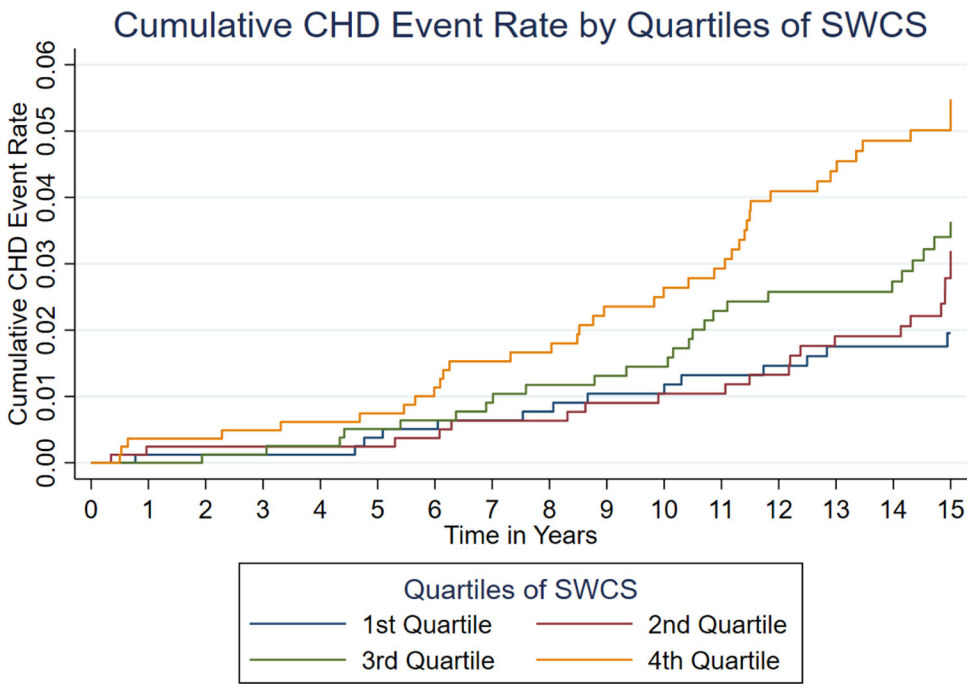

Figure 2.
Cumulative CHD event rates by quartile of SWCS

Table 1.

Descriptive statistics comparing MESA participants with Agatston coronary artery calcium (CAC) = 0 vs. CAC > 0 at the MESA baseline exam 2000–2002 included in the analysis.

	CAC = 0			CAC > 0		
Variable	**N**	**Mean**	**Std. Dev.**	**N**	**Mean**	**Std. Dev.**
Age (years) at baseline exam	3,286	57.96	9.14	3,255	66.41	9.51
Body mass index (kg/m^2)	3,286	28.29	5.64	3,255	28.36	5.32
Systolic blood pressure (mmHg)	3,285	122.40	20.47	3,253	130.86	21.69
Diastolic blood pressure (mmHg)	3,285	71.30	10.23	3,253	72.54	10.23
Total cholesterol (mg/dL)	3,272	193.72	35.02	3,246	194.53	36.27
High density lipoprotein (HDL) cholesterol (mg/dL)	3,271	52.48	15.06	3,244	49.45	14.51
Agatston Coronary Artery Calcium score (CAC)	3,286	0.00		3,255	291.01	545.60
Spatially Weighted Calcium Score (SWCS)	3,286	3.11	9.13	3,255	194.34	366.65
		N	**%**		**N**	**%**
Sex						
Female		2,082	63.36		1,380	42.4
Male		1,204	36.64		1,875	57.6
Race/Ethnicity						
White or Caucasian		1,068	32.50		1,428	43.87
Chinese-American		395	12.02		395	12.14
Black or African-American		1,031	31.38		782	24.02
Hispanic		792	24.10		650	19.97
Smoking						
Never		1,821	55.64		1,459	44.92
Former		1,010	30.86		1,370	42.18
Current		442	13.50		419	12.9
Diabetes at baseline exam						
Normal		2,581	78.86		2,211	68.14
Impaired Fasting Glucose		388	11.85		518	15.96
Untreated Diabetes		67	2.05		103	3.17
Treated Diabetes		237	7.24		413	12.73
Hypertension medication						
No		2,331	70.98		1,770	54.39
Yes		953	29.02		1,484	45.61
Statin use at baseline exam						
No		90.29	90.29		2,588	79.63
Yes		9.71	9.71		662	20.37

Table 2.

Cox model for 15-year incidence of CHD by quartile of ln (SWCS) for participants with Agatston CAC = 0; N=3,286.

Covariate	Haz. Ratio	95% Conf. Interval	P>|z|
Quartiles of ln (SWCS)			
Quartile 1 * (n = 14)	1	reference	
Quartile 2 (n = 21)	1.33	(0.68,2.61)	0.398
Quartile 3 (n = 25)	1.79	(0.95,3.38)	0.072
Quartile 4 (n = 38)	2.62	(1.44,4.78)	0.002

CHD = coronary heart disease. ln = natural logarithm.

SWCS = spatially weighted calcium score. n = number of events.

* Reference category.

Table 3.

Cox model for 15-year incidence of CHD by quartiles of ln (SWCS) for participants with Agatston CAC = 0, with adjustment for covariates using the MESA risk score[18]; N=3,271. Covariates as of baseline exam.

Covariate	Haz. Ratio	95% Conf. Interval	P>|z|
Quartiles of ln (SWCS)			
Quartile 1 *	1	reference	
Quartile 2	1.46	(0.74,2.88)	0.270
Quartile 3	1.70	(0.88,3.26)	0.114
Quartile 4	2.32	(1.24,4.32)	0.008
MESA Risk Score	1.40	1.23,1.59	<0.0001

CHD = coronary heart disease. ln = natural logarithm.

SWCS = spatially weighted calcium score.

*Reference category.

Table 4.

Regression model for the transition from baseline Agatston coronary artery calcium (CAC) score = 0 to CAC > 0 at either exam 2 or 3, adjusted for demographic variables and CHD risk factors. For continuous variables, the regression coefficients predict the rate difference for a 1 standard deviation change of the variable (in 100 person-years) of Agatston CAC going from 0 to > 0. N=2,819. Covariates as of baseline exam.

Covariate	Incidence rate difference	95% Conf. Interval	p-value
ln (SWCS) per SD (=2.221)	1.68	(1.03,2.33)	<0.0001
Age (years) per S.D. (=9.139)	2.02	(1.36,2.68)	<0.0001
Gender			
0: Female *	0	Reference	
1: Male	1.76	(0.36,3.15)	0.014
Race/Ethnicity			
1: White or Caucasian *	0	Reference	
2: Chinese-American	−1.80	(−3.72,−1.83)	0.067
3: Black or African-American	−1.95	(−3.44,−0.46)	0.010
4: Hispanic	−2.11	(−3.66,−0.56)	0.008
Body mass index (kg)/(m^2) per SD (=5.642)	0.17	(−0.54,0.87)	0.644
Cigarette smoking status			
0: Never *	0	Reference	
1: Former	1.27	(−0.01,2.55)	0.052
2: Current	1.77	(0.02,3.53)	0.048
Hypertension medication			
No *	0	Reference	
Yes	2.18	(0.79,3.57)	0.002
Systolic blood pressure (mmHg) per SD (=20.470)	0.90	(−0.02,1.81)	0.054
Diastolic blood pressure (mmHg) per SD (=10.233)	−0.19	(−1.06,0.67)	0.660
Total cholesterol (mg/dL) per S.D. (=35.024)	0.84	(0.26,1.42)	0.005
HDL cholesterol (mg/dL) per S.D. (=15.055)	−0.95	(−1.59,−0.30)	0.004
Statin use			
No *	0	Reference	
Yes	2.16	(0.21,4.10)	0.030
Diabetes			
No	0	Reference	
Yes	1.79	(−0.52,4.11	0.129
Constant	−12.75	(−20.57,−4.94)	0.001

* Reference category.

SD = standard deviation. ln = natural logarithm. CHD = coronary heart disease. SWCS = spatially weighted calcium score. HDL = high density lipoprotein.