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Distribution of Coronary Artery Calcium Scores by Framingham 10-Year Risk Strata in the MESA (Multi-Ethnic Study of Atherosclerosis)

Potential Implications for Coronary Risk Assessment

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Objectives By examining the distribution of coronary artery calcium (CAC) levels across Framingham risk score (FRS) strata in a large, multiethnic, community-based sample of men and women, we sought to determine if lower-risk persons could benefit from CAC screening.

Background The 10-year FRS and CAC levels are predictors of coronary heart disease. A CAC level of 300 or more is associated with the highest risk for coronary heart disease even in low-risk persons (FRS, <10%); however, expert groups have suggested CAC screening only in intermediate-risk groups (FRS, 10% to 20%).

Methods We included 5,660 Multi-Ethnic Study of Atherosclerosis participants. The number needed to screen (number of people that need to be screened to detect 1 person with CAC level above the specified cutoff point) was used to assess the yield of screening for CAC. CAC prevalence was compared across FRS strata using chi-square tests.

Results CAC levels of more than 0, of 100 or more, and of 300 or more were present in 46.4%, 20.6%, and 10.1% of participants, respectively. The prevalence and amount of CAC increased with higher FRS. A CAC level of 300 or more was observed in 1.7% and 4.4% of those with FRS of 0% to 2.5% and of 2.6% to 5%, respectively (number needed to screen, 59.7 and 22.7, respectively). Likewise, a CAC level of 300 or more was observed in 24% and 30% of those with FRS of 15.1% to 20% and more than 20%, respectively (number needed to screen, 4.2 and 3.3, respectively). Trends were similar when stratified by age, sex, and race or ethnicity.

Conclusions Our study suggests that in very low-risk individuals (FRS ≤5%), the yield of screening and probability of identifying persons with clinically significant levels of CAC is low, but becomes greater in low- and intermediate-risk persons (FRS 5.1% to 20%). (J Am Coll Cardiol 2011;57:1838–45) © 2011 by the American College of Cardiology Foundation

In the current clinical practice of preventive cardiology, the intensity of treatment is matched to the severity of the patient's overall (global) cardiovascular risk status based on the principle that the highest-risk patients will benefit the most from drug treatments, with less absolute benefit for lower-risk patients. The Framingham risk score (FRS) is considered a useful tool in the estimation of 10-year risk of coronary heart disease (CHD), but fails to identify many people destined to have a CHD event (1). Thus, additional tests of cardiovascular risk such as coronary artery calcium (CAC) scoring have been evaluated as possible ways to improve global CHD risk assessment. CAC has been shown to provide incremental CHD risk prediction beyond traditional risk factors, and patients with advanced CAC burden (CAC scores: ≥300 or 400) have the greatest risk (2–6).

Although proposed as an adjunctive tool for risk assessment, CAC scoring has not been recommended for wide-

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spread population screening in recent consensus statements (5,7,8) and instead has been regarded as most promising in modifying risk assessment primarily in intermediate-risk patients in whom the estimated 10-year CHD risk is between 10% and 20% by FRS (5,8). Recent data from the Multi-Ethnic Study of Atherosclerosis (MESA) suggested that in low-risk women, a very high CAC score (≥300) was associated with an adjusted hazard ratio of 8 for major coronary events compared with those without detectable CAC (3). However, whether lower-risk patients might benefit from CAC testing is not yet answered.

Although a few studies have examined the relationship between FRS and CAC prevalence and amount (2,9–14), it is still not yet known whether additional CAC testing in low- to intermediate-risk patients would be a useful way to find additional high-risk patients who might merit more intensive risk factor treatments. These previous studies have been limited by small sample size, referral-based samples, homogenous racial and sex compositions, and self-report of risk factors, with sparse data on stratification by age, sex and race or ethnicity. In addition, it is unclear how many people at selected levels of risk would require screening to detect 1 person with a CAC level of 300 or more.

The aim of the present study was to ascertain the prevalence and distribution of CAC across FRS in a large, multiethnic, multicenter, community-based sample of men and women stratified by age, sex, and race or ethnicity. Based on these relationships, the yield of screening, and therefore FRS ranges where CAC scoring might be beneficial in risk assessment, may become apparent and may aid further risk stratification for the large number of asymptomatic individuals predicted to be at low or intermediate 10-year risk by traditional risk factors alone.

Methods

The MESA is a prospective cohort study examining measures of subclinical atherosclerosis, progression of subclinical atherosclerosis, and conversion to clinical events. Details of the study design, as well as inclusion and exclusion criteria and baseline characteristics, have been described previously (15). Briefly, at baseline, the cohort included 6,814 participants (3,213 men and 3,601 women) 45 to 84 years of age from 4 different racial or ethnic groups (38% white, 28% black, 22% Hispanic, and 12% Chinese) in 6 U.S. communities, including Baltimore, Maryland; Chicago, Illinois; Forsyth, North Carolina; Los Angeles, California; New York, New York; and St. Paul, Minnesota. The participants were free of clinical cardiovascular disease at first examination (July 2000 through August 2002).

For the current study, we included men and women 79 years of age or younger at baseline (n = 6,526) because FRS could not be calculated in individuals older than 79 years of age. Participants with diabetes were excluded from our analyses (n = 811) because they were considered high risk in current National Cholesterol Education Program Adult Treatment Panel III guidelines (16), and our study focused on evaluating yield of screening in individuals at lower risk. Finally, 55 additional participants were excluded because of missing FRS equation covariates (n = 7) and absence of measured CAC (n = 48). Baseline examination, laboratory data, and cardiac computed tomography methods have been described elsewhere (6,15).

Abbreviations and Acronyms

CAC = coronary artery calcium

CHD = coronary heart disease

FRS = Framingham risk score(s)

NNS = number needed to screen

Definitions. Body mass index was defined as weight in kilograms divided by height in meters squared. Presence or absence of family history of heart attack was determined at baseline and was described further in detail during the second examination. Current smoking was defined as smoking cigarettes within the past 30 days. Medication use was derived from medication lists and clinical staff entry of prescribed medications. Aspirin use was defined as 3 days or more per week at baseline.

Agatston CAC measurement and scoring have been described previously (17). There was excellent agreement between and within readers for presence and amount of calcified plaque (kappa: >0.90 and >0.99, respectively). For this study, Agatston CAC scores were obtained from the baseline MESA examination 1 (2000 through 2002). CAC scores were categorized as CAC of more than 0, 100 or more, or 300 or more. Concurrent FRS 10-year risk for CHD (16) was calculated and stratified as follows: 0% to 2.5%, 2.6% to 5%, 5.1% to 7.5%, 7.6% to 10%, 10.1% to 15%, 15.1% to 20%, and more than 20%. We chose these defined CAC cutoff points rather than mutually exclusive CAC categories because the study aimed to examine screening, rather than risk prediction thresholds.

Statistical analysis. All analyses were performed using SAS software version 9.2 (SAS Institute, Cary, North Carolina). A 2-tailed value of $p < 0.05$ was considered statistically significant. The 10-year FRS estimates for all participants at examination 1 were calculated based on age, total and high-density lipoprotein cholesterol levels, current smoking status, systolic blood pressure, and the use of antihypertensive medication using the risk prediction functions from the National Cholesterol Education Program Adult Treatment Panel III guidelines (16). Baseline characteristics were compared according to FRS 10-year risk categories and by CAC classification using general linear models for continuous variables and cross-tabulations for categorical variables. The prevalence of CAC strata across FRS 10-year strata were compared using the chi-square test. The comparison was assessed further after stratification by age, sex, and race. The yield of screening for CAC was assessed using the number needed to screen (NNS), which was calculated by dividing the total number of participants within each FRS stratum by the number of people with

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CAC of more than 0, of 100 or more, or of 300 or more within that FRS stratum. The NNS defines the number of people who need to be screened to identify 1 individual with a CAC value above the specified CAC cutoff point within each FRS category. For the purposes of our study, CAC amount is represented by median CAC scores within FRS groups.

Multivariate analyses were carried out to determine the relationship between CAC of 300 or more (advanced CAC) and FRS distributions. The associations of 10-year FRS levels with CAC of 300 or more were examined (separately) using logistic regression models, and the multivariate-adjusted odds ratios and their 95% confidence intervals were assessed. Covariates included race or ethnic background, body mass index, family history of heart attack, use of aspirin, family income, education, health insurance, marital status, beta blocker use, calcium channel blocker use, and angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use, as shown in Table 1. A model containing these covariates plus strata of 10-year FRS covariates were fitted to estimate their association. This model was chosen based on known associations of certain racial or ethnic groups with increased CAC, FRS, or both; risk factors known to be associated with CHD, but not included in the FRS model; and socioeconomic factors. We focused our multivariate analysis on CAC of 300 or more because advanced CAC (CAC score ≥300 or 400) has been associated with the highest risk for CHD events (2–4,6,18).

Table 1 Baseline Characteristics by Coronary Artery Calcium Score Categories (n = 5,660)

	Coronary Artery Calcium Score Categories								
Characteristics	0 (n = 3,034)	>0 (n = 2,626)	p Value	<100 (n = 4,497)	≥100 (n = 1,163)	p Value	<300 (n = 5,086)	≥300 (n = 574)	p Value
Mean age (yrs)	57.4 ± 8.8	65.0 ± 9.0	<0.01	59.2 ± 9.2	67.8 ± 8.1	<0.01	60.3 ± 9.4	68.9 ± 7.6	<0.01
Female	63.6	41.4	<0.01	58.2	34.4	<0.01	56.1	28.4	<0.01
Race			<0.01			<0.01			<0.01
White	35.8	47.8		37.8	55.1		39.4	59.1	
Black	29.3	22.2		12.4	9.4		26.8	19.0	
Chinese American	11.8	11.8		27.7	19.8		12.4	6.5	
Hispanic	23.1	18.2		22.2	15.7		21.4	15.5	
SBP (mm Hg)	121.4 ± 20.2	129.1 ± 20.9	<0.01	123.3 ± 20.4	131.6 ± 21.3	<0.01	124.1 ± 20.6	133.2 ± 21.5	<0.01
DBP (mm Hg)	71.2 ± 10.3	73.0 ± 10.2	<0.01	71.6 ± 10.3	73.3 ± 10.1	<0.01	71.8 ± 10.3	74 ± 10	<0.01
BMI (kg/m^2)	28.0 ± 5.5	28.1 ± 5.2	0.58	28.1 ± 5.5	28.1 ± 5.0	0.63	28.1 ± 5.4	28.1 ± 4.7	0.96
Total cholesterol (mg/dl)	194.5 ± 34.7	196 ± 35.4	0.10	195 ± 35.0	195.8 ± 35.3	0.50	195.2 ± 35.0	195.1 ± 35.1	0.95
HDL cholesterol (mg/dl)	53.0 ± 15.2	49.9 ± 14.5	<0.01	52.1 ± 15.0	49.8 ± 14.7	<0.01	51.8 ± 15.0	49.6 ± 14.5	<0.01
LDL cholesterol (mg/dl)	116.6 ± 30.3	120.1 ± 31.8	<0.01	117.8 ± 30.9	120.0 ± 31.6	0.03	118.1 ± 31.0	119.1 ± 31.5	0.46
Current smoking	13.3	13.8	0.59	13.5	13.2	0.79	13.4	13.9	0.73
HTN treatment	23.0	36.1	<0.01	25.9	41.2	<0.01	27.5	43.2	<0.01
Lipid treatment	9.6	19.6	<0.01	12.2	22.4	<0.01	13.2	23.3	<0.01
Family history	35.5	46.0	<0.01	37.9	49.9	<0.01	39.0	52.6	<0.01
Physical activity (MET min/week)	927 ± 2,714	1,055 ± 3,076	0.09	977 ± 2,937	1,022 ± 2,691	0.63	970 ± 2,893	1,135 ± 2,837	0.19
Education			0.04			0.01			0.51
Less than high school	16.1	15.8		16.5	13.9		16.1	14.5	
High school	16.3	19.1		16.9	20.3		17.4	19.2	
College	48.4	45.6		47.5	45.5		47.2	46.0	
Graduate school	19.3	19.5		19.2	20.3		19.3	20.4	
Married	61.5	62.9	0.30	62.0	62.6	0.73	62.1	62.9	0.70
Annual income			<0.01			0.02			0.32
<$25,000	26.2	31.2		27.6	32.4		28.1	31.9	
$25,000–$50,000	28.9	28.8		29.1	28.0		29.0	27.7	
$50,000–$75,000	19	16.4		18.1	16.5		17.9	17.0	
>$75,000	25.9	23.6		25.3	23.1		25.0	23.4	
Health insurance	74.2	69.0	<0.01	72.9	67.6	<0.01	72.2	67.8	0.02
Medications									
Aspirin	13.5	23.9	<0.01	15.4	29.6	<0.01	16.7	32.9	<0.01
ACEI/ARB	7.0	13.2	<0.01	8.2	16.2	<0.01	8.9	18.1	<0.01
Beta-blocker	7.0	10.8	<0.01	8.0	12.0	<0.01	8.4	12.2	<0.01
Nitrates	0.1	0.2	0.36	0.1	0.2	0.76	0.2	0.0	0.34
CCB	8.0	13.7	<0.01	9.5	15	<0.01	10.1	15.5	<0.01

Values are mean ± SD or %.

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; CCB = calcium channel blocker; DBP = diastolic blood pressure; HDL = high-density lipoprotein; HTN = hypertension; LDL = low-density lipoprotein; MET = metabolic equivalent; SBP = systolic blood pressure.

Results

Baseline characteristics. Our study sample was made up of a total of 5,660 MESA men and women (mean age: 60.9 years, 53% women) from 4 different racial or ethnic groups (41% white, 26% black, 12% Chinese, and 21% Hispanic). There were significant differences in most traditional risk factors, sociodemographic factors, and medication use between participants using all 3 CAC cutoff points (CAC >0 vs. CAC = 0, CAC ≥100 vs. CAC <100, and CAC ≥300 vs. CAC <300) (Table 1). As expected, most of the baseline characteristics, including traditional cardiovascular risk factors, were significantly different across FRS strata (data not shown).

Distribution of CAC prevalence and amount compared across FRS strata. Table 2 displays the comparison of CAC prevalence and amount using different cutoff points across FRS strata. The median CAC scores (among those with CAC >0) with interquartile ranges across FRS strata also are shown. For the entire cohort, the median CAC scores were greater with higher FRS (Spearman correlation coefficient: 0.45, $p < 0.01$). Similarly, CAC prevalence (for each CAC cutoff point) increased with greater FRS (all $p < 0.01$ for trend) (Fig. 1). Within each CAC category, the NNS to detect 1 participant with CAC of more than the selected CAC cutoff point decreased with higher FRS (Table 2). For example, among those with CAC of 300 or more, the NNS decreased from 59.7 for FRS of 0% to 2.5% to 3.3 for FRS of more than 20%. Likewise, within each FRS stratum, the NNS increased with increasing CAC severity category. The pattern of results was similar when we used CAC of 400 or more as the cutoff point for advanced CAC.

Data were stratified further by sex (Table 3), which revealed that the prevalence of CAC of more than 0, of 100 or more, and of 300 or more and median CAC scores were higher in women than in men for the lower FRS strata, equivocal between men and women in the intermediate FRS strata, and generally slightly higher in men than in women for the higher FRS strata. Stratification by age (45 to 54 years, 55 to 64 years, and 65 to 79 years) generally followed the same pattern as the overall cohort (data not shown), with median CAC scores and prevalence of CAC of more than 0, CAC of 100 or more, and CAC of 300 or more increasing across advancing age groups. When stratified by race or ethnicity, whites exhibited the highest median CAC scores and the highest prevalence of CAC of more than 0, CAC of 100 or more, and CAC of 300 or more in each FRS stratum, with higher disparity between whites and the rest of the racial or ethnic groups as CAC severity increased.

Univariate and multivariate analyses for odds of advanced CAC (CAC ≥300) across FRS strata. Compared with FRS of more than 20% as the referent group, the unadjusted odds ratios for CAC of 300 of more were significantly lower with lower FRS and increased steadily with higher FRS (Table 4). The multivariate odds ratios for CAC across FRS strata followed the same pattern, with significantly increasing odds

Table 2 CAC Prevalence, Amount, and Number Needed to Screen Compared With Framingham Risk Score Categories

CAC Score Group	Framingham Risk Score Categories (n = 5,660)						p Value
	0.0% to 2.5% (n = 1,730)	2.6% to 5.0% (n = 1,045)	5.1% to 7.5% (n = 442)	7.6% to 10.0% (n = 779)	10.1% to 15.0% (n = 617)	15.1% to 20.0% (n = 793)	>20% (n = 254)	
Median CAC score*	28.6 (7.4–91.6)	39.7 (11.9–140.6)	62.5 (15.9–211.2)	71.5 (19.3–257)	111.6 (27.7–284.1)	134.6 (33.5–427.6)	198.6 (56.5–483.7)	
CAC >0 (n = 2,626)	22.3	39.3	44.8	57.6	63.9	73.0	82.3	<0.01
NNS (CAC >0)	4.5	2.5	2.2	1.7	1.6	1.4	1.2	
CAC ≥100 (n = 1,163)	5.1	12.6	18.3	24.8	33.2	40.9	54.7	<0.01
NNS (CAC ≥100)	19.4	7.9	5.5	4.0	3.0	2.5	1.8	
CAC ≥300 (n = 574)	1.7	4.4	7.5	13.1	15.6	24.1	30.3	<0.01
NNS (CAC ≥300)	59.7	22.7	13.4	7.6	6.4	4.2	3.3	

Values are median (interquartile range) or %. *Among those with CAC >0.
CAC = coronary artery calcium; NNS = number needed to screen to identify 1 individual with CAC value above a specified CAC cutoff point, within each specified Framingham risk score stratum.

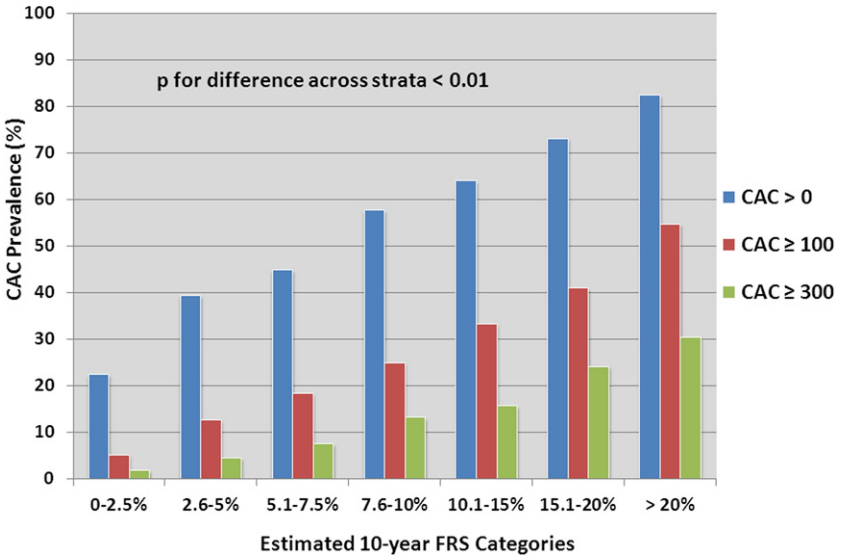

Figure 1 Coronary Calcium Prevalence by Framingham Risk Score

Bar graph showing the prevalence of categories of coronary artery calcium (CAC) scores (CAC) (>0, ≥100, and ≥300) compared across 10-year Framingham risk score (FRS) strata.

ratios for CAC of 300 or more with greater FRS, even after adjusting for race or ethnicity, socioeconomic factors, as well as other cardiovascular risk factors not included in the FRS equation.

Discussion

Major findings. We found a significant direct relationship between 10-year predicted FRS and CAC prevalence and amount such that the lower FRS risk strata had lower prevalence of CAC and lower median CAC scores. With higher FRS strata, prevalence of CAC and CAC burden increased in a stepwise fashion and demonstrated good linear correlation. For the overall cohort, among those with FRS of 0.0% to 2.5% and 2.6% to 5.0%, only 1.7% and 4.4% of our study population, respectively, had CAC scores of 300 or more. However, 24% and 30% of participants had CAC scores of 300 or more in the 15.1% to 20.0% and more than 20% FRS strata, respectively. Similar to the trend in CAC prevalence, the yield of screening for CAC decreased in a stepwise fashion across greater FRS strata: the numbers of people who needed to be screened to identify 1 person with CAC level of 300 or more (NNS for CAC: ≥300) were 59.7 and 22.7 in individuals with FRS of 0.0% to 2.5% and 2.6% to 5.0%, respectively, compared with 4.2 and 3.3 in those with FRS of 15.1% to 20.0% and more than 20%, respectively. Data remained essentially unchanged when stratified by age, sex, or race or ethnicity. Likewise, multivariate analysis showed significantly increasing odds for CAC level of 300 or more with greater FRS strata.

Potential clinical implications. CAC score is related directly to incidence of CHD events such that advanced CAC burden (CAC ≥300 or 400) poses the highest risk for CHD events (2–4,6,18). As such, we focus our discussion on the association of FRS with CAC of 300 or more, which is the definition of advanced CAC used in the current study.

According to current National Cholesterol Education Program Adult Treatment Panel III guidelines (16), individuals with an FRS of more than 20% are considered to be at high risk for CHD events and should be managed appropriately with drug therapy and lifestyle modifications. Therefore, no further risk assessment is considered necessary in these individuals. However, for the large proportion of low- to intermediate-risk populations, the intervention goals are defined less clearly and may be difficult to interpret in the absence of additional information such as that provided by a CAC score. Hence, our data address the potential for modification of risk category in the predicted low- and intermediate-risk patient populations. The high rate of CAC of 300 or more in the FRS category with predicted risk of 15.1% to 20.0% suggests a group at high risk for CHD who particularly may benefit from screening for CAC of 300 or more to aid further risk factor interventions, especially in situations where there is uncertainty regarding the use of drug therapy. However, the low rate of CAC of 300 or more in the lowest FRS risk categories (FRS 0% to 5%) suggests that this group is far less likely to yield a high CAC score on further CAC testing.

For this study, we chose the NNS as a tool to help evaluate potential thresholds or the yield of screening for CAC across FRS strata. The NNS (an extension of the concept of the number needed to treat) has been described in the literature as the number of people who need to be

Table 3 CAC Prevalence and Amount Compared With Framingham Risk Score Categories, Stratified by Sex

CAC Score Group	Framingham Risk Score Categories (n = 5,660)						p Value
	0.0% to 2.5% (n = 1,730)	2.6% to 5.0% (n = 1,045)	5.1% to 7.5% (n = 442)	7.6% to 10.0% (n = 779)	10.1% to 15.0% (n = 617)	15.1% to 20.0% (n = 793)	>20% (n = 254)	
Men (n = 2,660)								
Median CAC score*	37.1 (9.3–128.3)	19.1 (5.9–51)	32.8 (10.5–175.7)	72 (18.9–257)	111.7 (27.6–279.7)	142.4 (35.5–455.6)	207.9 (64.9–586.7)	
CAC >0 (n = 1,538)	20.0	29.5	40.0	56.7	64.7	72.8	82.1	<0.01
CAC ≥100 (n = 763)	5.7	5.5	12.8	25.0	33.6	41.1	55.1	<0.01
CAC ≥300 (n = 411)	1.4	2.2	6.4	12.7	15.2	24.5	32.4	<0.01
Women (n = 3,000)								
Median CAC score*	27.8 (7.3–91.5)	52 (18.1–158.9)	95.1 (30.1–231.4)	63 (20.1–262.7)	111.5 (28–314.7)	104.4 (15.2–364.5)	176.9 (41.1–313.7)	
CAC >0 (n = 1,088)	22.4	44.6	50.2	60.8	61.9	75.4	83.0	<0.01
CAC ≥100 (n = 400)	5.1	16.5	24.6	24.0	32.3	38.5	53.2	<0.01
CAC ≥300 (n = 163)	1.7	5.0	8.7	14.6	16.4	20.0	21.3	<0.01

Values are median (interquartile range) or %. *Among those with CAC >0.
Abbreviations as in Table 2.

Table 4 Univariate and Multivariable Odds Ratios and 95% CIs for CAC Score ≥300 by Framingham Risk Score Strata

FRS Categories	Odds Ratios (95% CI) for CAC ≥300	
	Unadjusted	Adjusted*
>20%	1.0	1.0
15% to 20%	0.73 (0.53 to 1.00)	0.68 (0.48 to 0.95)
10.1% to 15.0%	0.42 (0.30 to 0.60)	0.39 (0.27 to 0.57)
7.6% to 10.0%	0.35 (0.25 to 0.49)	0.32 (0.22 to 0.46)
5.0% to 7.5%	0.19 (0.12 to 0.29)	0.19 (0.12 to 0.31)
2.6% to 5.0%	0.11 (0.07 to 0.16)	0.10 (0.06 to 0.15)
0.0% to 2.5%	0.04 (0.03 to 0.06)	0.04 (0.02 to 0.06)

*Model adjusted for race/ethnicity, body mass index, family history of heart attack, aspirin use, education, marital status, income, and health insurance.
CI = confidence interval; FRS = Framingham risk score; other abbreviation as in Table 2.

screened to prevent 1 death or 1 adverse event (19). This initial definition has been modified in the literature (20,21), but to our knowledge has not been used in screening for subclinical CHD. For the purposes of this study, NNS was defined as the number of individuals who would have to be screened to find 1 person with CAC of more than 0, 100 or more, or 300 or more, depending on the CAC category. The NNS in this case weighs the yield of screening for CAC within each FRS category from a public health perspective. Among those with CAC of 300 or more in our study, the NNS was 59.7 and 22.7 for individuals with FRS of 0.0% to 2.5% and 2.6% to 5.0%, respectively, and 4.2 and 3.3 for those with FRS of 15.1% to 20.0% and more than 20%, respectively. This represents an 18-fold difference in NNS for CAC of 300 or more (absolute difference of 56) between the lowest-risk FRS stratum (FRS 0.0% to 2.5%) and the high-risk stratum (FRS >20%). This difference remained reasonably large—a 7-fold difference (absolute difference of 19) between the subsequent lowest FRS risk stratum (FRS 2.6% to 5.0%) and the high-risk stratum, but became much smaller beyond that. It likely suggests a substantial difference (with minimal yield of screening) in the very low-risk groups (FRS 0% to 5%) compared with the higher risk groups. To put our NNS findings in context, it should be noted that among those screened, the NNS to prevent 1 death secondary to abdominal aortic aneurysm was 20.4 in the Multicentre Aneurysm Screening Study (22). This study used abdominal ultrasound to evaluate the benefit of screening for abdominal aortic aneurysms. Future studies using mortality and cardiovascular events data in the distribution of CAC by FRS strata to evaluate the concept of the NNS for CAC screening clearly are warranted.

Taken together, our prevalence and NNS data suggest the benefit of CAC testing for further risk stratification in asymptomatic low-risk (FRS of 5.1% to 10.0%) and intermediate-risk (FRS 10.1% to 20.0%) persons. Based on empiric observations, this is in agreement with several recommendations for the use of CAC testing for further risk stratification in asymptomatic people who are found to be at intermediate risk (FRS 10% to 20%) (5,8). Our study data suggest that CAC measurement should be carried out

within the context of traditional cardiovascular risk factors, rather than in isolation, and provides support for avoidance of radiation exposure as well as time, money, and effort spent on CAC measurement and scoring for clinical guidance in very low-risk patients.

Other findings. The patterns of CAC distribution differed by sex. With lower FRS, women exhibited higher CAC prevalence and amount than men. The prevalence of CAC became similar in both sexes at intermediate FRS scores and switched at higher FRS so that men (as would be expected) showed higher CAC prevalence and amount than women. This pattern is likely because at any given age, FRS is significantly lower for women than men. Consequently, there are more women than men at lower FRS stratum, because most women remain at low calculated FRS 10-year risk until 70 years of age (23–25). Also, our analysis was truncated at age 79 years. Men have higher FRS than women regardless of age, and therefore are distributed more evenly across the spectrum of FRS strata. They therefore are much of the higher FRS strata relative to women.

As expected, CAC amount and prevalence increased across FRS strata and with increasing age, which is purported to be the best surrogate marker for accumulated exposure to CHD risk factors (13). Similar to findings in other studies (26–30), the highest prevalence and severity of CAC was observed among white persons in our study, whereas the lowest prevalence was observed among black persons.

CAC of 400 or more is suggested as a reasonable definition of advanced CAC (5). However, because we had few participants in the CAC of 400 or more category, we used CAC of 300 or more, as used in other studies (2,6), in defining advanced CAC for this study. Regardless, in our analysis, the distribution of CAC by FRS strata and the trend for yield of screening for CAC of 400 or more within FRS strata were similar to what we observed when we defined advanced CAC using CAC of 300 or more as the cutoff point.

Study limitations. Because of the small numbers of participants in each age, sex, and race or ethnicity category, we could not make meaningful assessments of the findings using simultaneous stratification by age, sex, and race or ethnicity. Furthermore, these cross-sectional observational data cannot provide definitive information about the cost benefit of CAC measurement.

Conclusions

Our study showed that in a large, multiethnic, multicenter, community-based cohort of men and women, CAC prevalence was associated closely with FRS strata after multivariate analysis regardless of age, sex, or race or ethnicity. It suggests a low probability of having a high CAC score in the very low-risk population with FRS of <5%. Consequently, the yield of screening for advanced CAC burden (CAC ≥300) is lesser in this population of very low-risk persons, but seems to be higher in low- to intermediate-risk individuals with FRS of 5.1% to 20.0%.

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Key Words: atherosclerosis ■ coronary calcium ■ coronary heart disease ■ Framingham risk score ■ low risk ■ number needed to screen ■ population ■ risk factors.