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Authors

Alluri, Krishna
McEvoy, John W
Dardari, Zeina A
et al.

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Original Research Article

Distribution and burden of newly detected coronary artery calcium: Results from the Multi-Ethnic Study of Atherosclerosis

Krishna Alluri MD[a,b], *John W. McEvoy MB BCh*[b], *Zeina A. Dardari MS*[b], *Steven R. Jones MD*[b], *Khurram Nasir MD, MPH*[b,c], *Ron Blankstein MD*[d], *Juan J. Rivera MD, MPH*[b,e], *Arthur A. Agatston MD*[e], *Joel D. Kaufman MD, MPH*[f,g,h], *Matthew J. Budoff MD*[i], *Roger S. Blumenthal MD*[b], *Michael J. Blaha MD, MPH*[b,*]

[a] *Department of Internal Medicine, UPMC McKeesport Hospital, McKeesport, PA, USA*
[b] *The Johns Hopkins Ciccarone Center for the Prevention of Heart Disease, Johns Hopkins Hospital, Carnegie 565A, 600 N. Wolfe Street, Baltimore, MD 21287, USA*
[c] *Center for Prevention and Wellness Research, Baptist Health Medical Group, Miami Beach, FL, USA*
[d] *Cardiovascular Division, Brigham and Women's Hospital, Boston, MA, USA*
[e] *South Beach Preventive Cardiology Center, University of Miami, Miami, FL, USA*
[f] *Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, USA*
[g] *Department of Medicine, University of Washington, Seattle, WA, USA*
[h] *Department of Epidemiology, University of Washington, Seattle, WA, USA*
[i] *Division of Cardiology, Los Angeles Biomedical Research Institute at Harbor-UCLA, Torrance, CA, USA*

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ABSTRACT

Background: The transition from no coronary artery calcium (CAC) to detectable CAC is important, as even mild CAC is associated with increased cardiovascular events. We sought to characterize the anatomic distribution and burden of newly detectable CAC over 10-year follow-up.
Methods: We evaluated 3112 participants (mean age, 58 years; 64% female) with baseline CAC = 0 from the Multi-Ethnic Study of Atherosclerosis. Participants underwent repeat CAC testing at different time intervals (between 2–10 years after baseline) per the Multi-Ethnic Study of Atherosclerosis protocol. Among participants who developed CAC on a follow-up scan, we used logistic regression and marginal probability modeling to describe the coronary distribution and burden of new CAC by age, sex, and race after adjustment for cardiovascular risk factors and time to detection.

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* Corresponding author.
E-mail address: mblaha1@jhmi.edu (M.J. Blaha).
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Right coronary artery
Left main artery
Left circumflex artery

Results: A total of 1125 participants developed detectable CAC during follow-up with a mean time to detection of 6.1 ± 3 years. New CAC was most commonly isolated to 1 vessel (72% of participants), with the left anterior descending artery (44% of total) most commonly affected followed by the right coronary (12%), left circumflex (10%), and left main (6%). These patterns were similar across age, sex, and race. In multivariate models, residual predictors of multivessel CAC (28% of total) included male sex, African American or Hispanic race, hypertension, obesity, and diabetes. At the first detection of CAC >0, burden was usually low with median Agatston CAC score of 7.1 and <5% with CAC scores >100.

Conclusion: New-onset CAC most commonly involves just 1 vessel, occurs in the left anterior descending artery, and has low CAC burden. New CAC can be detected at an early stage when aggressive preventive strategies may provide benefit.

1. Introduction

Coronary artery calcium (CAC) is an imaging marker that is nearly pathognomonic for the presence of coronary atherosclerosis[1,2] and can be detected using noncontrast cardiac CT. Indeed, CAC testing is specific for the presence of coronary atherosclerosis and highly sensitive for increasing burden of obstructive atherosclerotic coronary artery disease.[3]

CAC is also highly effective for risk stratification of selected asymptomatic patients. For example, elevated CAC >300 is associated with a nearly 10-fold increased risk of adverse coronary events after multivariate adjustment.[4] Equally important, the absence of CAC in asymptomatic adults is associated with a low mortality rate of 1% over 10 years.[5–7] Even mildly elevated CAC denotes risk, as patients with CAC scores between 1 and 10 have a 2- to 3-fold increased risk of cardiovascular adverse events and death compared with those with CAC = 0.[6,8,9]

Given these prognostic differences, a clinical finding of zero vs nonzero CAC has important implications for clinical decision making, including the decision to treat risk conditions with lifestyle vs pharmacotherapy.[10] Thus, there is a great deal of interest in studying the transition from zero to nonzero CAC. However, little is known about the characteristics of newly detected CAC, including its typical coronary distribution and burden.

To fill this gap, we used longitudinal CAC data from the Multi-Ethnic Study of Atherosclerosis (MESA) to describe the imaging characteristics related to the transition from zero to nonzero CAC. In particular, we asked the following questions: (1) At the first detection of new CAC, does CAC occur more commonly in 1 vessel vs multiple vessels? (2) Does new CAC preferentially occur in particular coronary arteries? (3) At the first detection of new CAC, what is the CAC score burden? (4) Does the coronary distribution and burden of new CAC vary by age, sex, or race?

2. Methods

2.1. The Multi-Ethnic Study of Atherosclerosis

MESA was designed to study the prevalence, risk factors, and progression of subclinical cardiovascular disease in individuals without known cardiovascular disease.[11] Between July 2000 and September 2002, MESA enrolled 6814 individuals at 6 field centers in the United States (Baltimore; Chicago; Forsyth County, North Carolina; Los Angeles; New York; and St. Paul, Minnesota) as part of a prospective cohort study that has now spanned 5 in-person visits. Participants included women and men aged 45 to 84 years who identified themselves as White, Chinese, Black, or Hispanic. The institutional review board at all participating centers approved the study, and all participants gave written informed consent.

2.2. Patient population

The study population for this analysis consisted of 3112 participants who had CAC = 0 at baseline and had at least 1 additional CT scan (scored on a per-vessel basis) during MESA follow-up.

After the initial baseline scan, participants underwent repeat CT scans during different follow-up visits as per the prespecified MESA protocol. MESA visits 2, 3, 4, and 5 included subjects who had follow-up CT scans at mean 1.7 ± 0.3, 3.2 ± 0.4, 4.9 ± 0.5, and 9.7 ± 0.6 years, respectively, after the initial baseline scan. In MESA, not all participants had follow-up scan at each of the visits. As part of the study design, approximately half (n = 1522) of the participants received repeat scan at visit 2 and the other half (n = 1425) at visit 3. Visit 4 prioritized participants without scan at visit 3 and included 677 participants with CAC = 0 on prior visits. During visit 5, a total of 1461 participants with CAC = 0 on prior visits received repeat scan and preferentially included participants with scan from visits 3 and 4 (Supplementary Fig. 1). Repeat CT scanning in MESA was unrelated to specific individual participant characteristics. All participants with CAC = 0 at baseline received at least 1 repeat scan (100%), whereas 47% had 2 total scans, 42% had 3 total scans, and 11% had 4 total scans over MESA follow-up.

2.3. Cardiac CT protocol and CAC scoring

Baseline cardiac CT was performed at 3 sites using a cardiac-gated electron-beam CT scanner and at 3 sites using 4-slice multidetector CT. Each participant was scanned twice consecutively, and the images were interpreted at the MESA CT reading center at Harbor-UCLA Medical center, Los Angeles, CA. The results of the 2 scans were averaged to

provide a more accurate point estimate of the amount of calcium present. Carr et al[12] have reported details of the methods used by MESA for CT scanning and interpretation. The amount of calcium was quantified with the Agatston scoring method.[13] When CAC was detected on CT images, its location was ascertained to left main (LM), left anterior descending (LAD), left circumflex (LCX), or right coronary arteries (RCA). Data regarding segmental distribution of CAC within individual coronary arteries were not available for our analysis. The kappa statistic for agreement on presence of any CAC was 0.92.

2.4. *Risk factor assessment*

As part of the baseline examination, study teams at each of the 6 centers collected information on cardiovascular risk factors. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglyceride, and glucose levels were measured in blood samples obtained after a 12-hour fast. The low-density lipoprotein cholesterol (LDL-C) level was determined with the Friedewald equation.[14] Hypertension (HTN) status was classified according to the Seventh Report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure.[15] Diabetes mellitus (DM) status was classified according to American Diabetes Association 2003 criteria.[16] Obesity (body mass index [BMI] $\geq$30 kg/m^2) was classified according to the World Health Organization classification. Medication use was determined by a questionnaire. Smoking status was classified as never smoker, former smoker, and current smoker. Never smoker was defined as lifetime consumption of $<$100 cigarettes and current smoker was defined as smoking within 30 days as per the National Cholesterol Education Program–Adult Treatment Panel III.[17]

3. Statistical analysis

Baseline characteristics of the overall study population (N = 3112) are presented in aggregate and by incident CAC status (follow-up CAC = 0 vs follow-up CAC $>$0). Continuous variables are presented as mean $\pm$ standard deviation, whereas categorical variables are presented as total number and the proportion of the total. Differences between 2 groups were compared using the chi-square analysis for categorical variables and using 2-sample *t* tests for normally distributed continuous variables. Kruskal-Wallis equality of population rank tests were used to compare distributions between groups of non-normally distributed continuous variables.

The remainder of the analyses focused on patients with newly detected CAC during follow-up (N = 1125). To characterize the anatomic distribution of new-onset CAC over time in MESA, we described new-onset CAC as occurring in a single vessel (LM, RCA, LAD, LCX) or in multiple vessels (2, 3, or 4 vessels). We then calculated the adjusted marginal probabilities of each CAC distribution pattern using the "margins" command in STATA version 13 (Stata Corp, College Station, TX, USA). Probabilities were postestimated following a multivariate logistic regression model adjusted for the following variables: age, race, sex, time to CAC $>$0 detection, HTN status, household income (a measure of socioeconomic status), smoking status, diabetes status, LDL-C $>$160 mg/dL, use of lipid-lowering medications, and obesity (BMI $>$30 kg/m^2). Time to CAC $>$0 detection was included in the models to account for the effect of the differential time between scans of individual participants in MESA. Marginal probabilities should not be considered the absolute prevalence of CAC by particular attribute (ie, race) but rather the residual differences in new-onset CAC that remain within that attribute after adjusting for other risk factors.

To characterize the burden of newly detected CAC over time in MESA, we assigned individuals to distinct CAC score categories (1–10, 11–100, and $>$100) as well as summarized the median Agatston score at the first detection of CAC. Using the chi-square analysis and Kruskal-Wallis testing, we assessed for differences in CAC burden by anatomic distribution (individual vessel involvement in those with single vessel CAC), as well as for differences in CAC burden between single-vessel and multivessel CAC. Statistical analysis was performed using Stata 13. A 2-sided *P* value of $<$.05 was used to indicate statistical significance.

4. Results

4.1. *Baseline characteristics*

Table 1 summarizes the characteristics of our overall study sample. A total of 3112 subjects were included in the study. Average age was 57.9 $\pm$ 9 years and approximately 64% were female. The race distribution of our sample includes 34% White, 12% Chinese American, 31% Black, and 23% Hispanic.

Approximately 1125 subjects of our study sample (36%) developed new CAC with a mean time to detection of 6.1 $\pm$ 3.4 years. The percentage of subjects who developed new CAC at visit 2, 3, 4, and 5 were 11%, 21%, 22%, and 34%, respectively. The mean time to detection of new CAC was shorter in males (5.9 $\pm$ 3.4 years) compared to females (6.3 $\pm$ 3.4 years) and did not differ among subjects from different race groups.

New CAC was more prevalent among males, and the mean age of these subjects was higher when compared to subjects who did not develop CAC on follow-up scans. There was higher prevalence of HTN, DM, and smoking among subjects with new CAC compared to those with CAC = 0. Subjects with new CAC demonstrated significantly higher systolic blood pressure, diastolic blood pressure, BMI, cholesterol, LDL-C, Framingham risk score, cardiovascular disease risk score and lower HDL-C compared to CAC = 0 group. Baseline use of lipid-lowering and antihypertensive medications was significantly higher in subjects with new CAC. Participants with new CAC also had more number of follow-up CAC scans compared to CAC = 0 group (Table 1).

4.2. *Coronary distribution of new CAC*

New CAC most commonly involved 1 vessel (unadjusted probability of 72%). Over the entire range of time from the baseline scan, 1 vessel involvement remained the most

Table 1 – Demographics and prevalence of risk factors.

Factor	Baseline CAC = 0 (N = 3112)	Follow-up CAC = 0 (N = 1987)	Follow-up CAC >0 (N = 1125)	P value
Age, y, mean ± SD	57.9 ± 9.1	56.9 ± 9.0	59.6 ± 8.9	.0001
Female, n (%)	1960 (64)	1315 (66)	645 (57)	<.0001
Race, n (%)				.022
White	1059 (34)	654 (33)	405 (36)	
Chinese	364 (12)	256 (13)	108 (10)	
Black	963 (31)	624 (31)	339 (30)	
Hispanic	726 (23)	453 (23)	273 (24)	
Smoking status, n (%)				.042
Never smoker	1740 (56)	1142 (58)	598 (53)	
Former smoker	960 (31)	584 (29)	376 (34)	
Current smoker	401 (13)	252 (13)	149 (13)	
BMI, kg/m^2, mean ± SD	28.3 ± 5.6	27.8 ± 5.6	29.1 ± 5.7	<.001
Hypertension, n (%)	1077 (35)	587 (30)	490 (44)	<.001
Diabetes, n (%)	274 (9)	138 (7)	136 (12)	<.001
Systolic blood pressure, mm Hg, mean ± SD	124.1 ± 19.8	121.7 ± 19.5	128.4 ± 19.7	.0001
Diastolic blood pressure, mm Hg, mean ± SD	72.5 ± 10	71.5 ± 10	74.3 ± 9.7	<.0001
Cholesterol, mg/dL, mean ± SD	198.1 ± 35.1	195.7 ± 34.6	202.3 ± 35.6	.0001
HDL-C, mg/dL, mean ± SD	52.6 ± 15	53.8 ± 15.4	50.4 ± 14	.0001
LDL-C, mg/dL, mean ± SD	116.3 ± 30.7	114.6 ± 30.6	119.3 ± 30.6	.0001
Antihypertensive medication, n (%)	876 (28)	478 (24)	398 (35)	<.001
Lipid-lowering medication, n (%)	330 (11)	163 (8)	167 (15)	<.001
Framingham risk score (%), mean ± SD	8 ± 6	7 ± 6	10 ± 7	.0001
CVD risk score (%), mean ± SD	7 ± 9	6 ± 8	9 ± 10	.0001
Aspirin usage, n (%)	421 (14)	221 (12)	200 (19)	<.001
Number of follow-up CAC scans, mean ± SD	1.78 ± 0.68	1.65 ± 0.69	2.01 ± 0.60	<.001

BMI, body mass index; CAC, coronary artery calcium; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; N, numbers of subjects; SD, standard deviation.

common presentation of new CAC (Fig. 1A). Among subjects with 1 vessel involvement, the LAD was the most common vessel affected, and this pattern continued over the entire range of time from baseline scans. LAD involvement was followed in order of frequency by the RCA, LCX, and LM coronary arteries (Table 2; Fig. 1B).

Multivessel involvement of new CAC was seen in 28% of subjects. With increased time from baseline scan, there was increased frequency of multivessel involvement of new CAC (15% at visit 2 vs 35% at visit 5). However, 1 vessel involvement of new CAC was the most common pattern even at visit 5, which occurred nearly 10 years after baseline scan (Table 2; Fig. 1A).

4.3. *Association between risk factors and distribution of new CAC*

Among all age, sex, and race groups, single-vessel CAC with LAD involvement was the most common phenotype. With increase in age, there was increased multivessel involvement of new CAC, which peaked in the age group of 65 to 74 years; however, single-vessel CAC with LAD involvement remained the most common presentation even in this age group (Table 3). Males compared to females and Hispanic and Black compared to White and Chinese were associated with higher residual probability of multivessel new CAC involvement after multivariate adjustment (Table 3).

The residual probability of multivessel new CAC involvement was significantly higher in subjects with HTN, DM, and obesity after adjustment for the remaining risk variables. In current smokers and in subjects with LDL-C ≥160 mg/dL and total cholesterol-to-HDL-C ratio >3, there was no increased residual probability of multivessel new CAC involvement (Table 4).

4.4. *Burden of new CAC*

Among subjects with new CAC, 52% had CAC scores of 1 to 10, 44% had CAC scores of 11 to 100, and 4% had CAC scores >100. CAC burden was higher among subjects who developed CAC in visit 4 and 5 compared to those in visit 2 and 3 (Supplementary Table 1). The burden of new-onset CAC was significantly higher in subjects with multivessel CAC compared with those with 1 vessel involvement. Of those subjects with new CAC in a single vessel, 65% had CAC scores of 1 to 10, 34% had CAC scores of 11 to 100, and 1% had CAC scores >100. Of those subjects with multivessel involvement at the time of new CAC detection, 20% had CAC scores of 1 to 10, 68% had CAC scores of 11 to 100, and 12% had CAC scores >100 (Table 5).

The median CAC score in subjects with single-vessel and multivessel involvement was 5.9 and 26.2, respectively. Among subjects with 1 vessel involvement, CAC was significantly higher in LAD and LM followed by RCA and then LCX (Table 5). There was no difference in CAC burden by age, sex, and race groups. Subjects with new-onset advanced CAC (CAC >100) were equally distributed among all age, sex, and race groups (Supplementary Table 2).

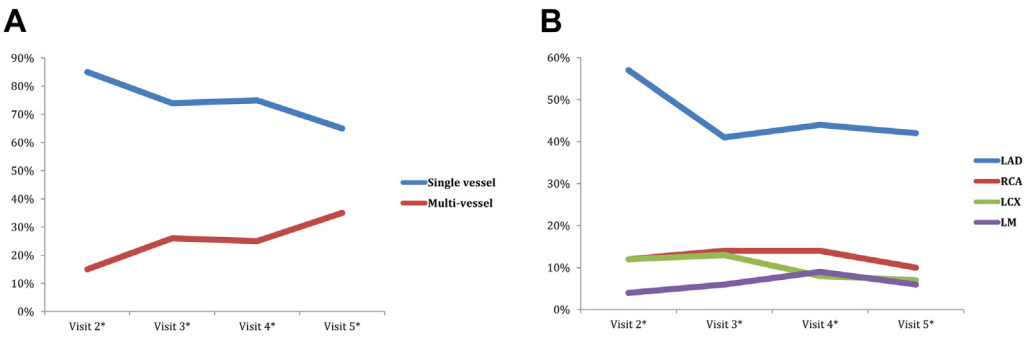

Fig. 1 – (A) Proportion of participants with incident CAC: single vessel vs multivessel. (B) Distribution of incident CAC among participants with single-vessel CAC. *Visits 2, 3, 4, and 5 were at mean 1.7 ± 0.3, 3.2 ± 0.4, 4.9 ± 0.5, and 9.7 ± 0.6 years, respectively, after baseline scan. LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main artery; RCA, right coronary artery.

5. Discussion

Although CAC = 0 is associated with excellent prognosis, presence of even mild CAC is associated with an increased risk of adverse events, and little is known about the transition from CAC = 0 to initially detectable CAC >0. In MESA, we found that new CAC was most commonly found in a single vessel at first detection, with this pattern persisting among subjects of all age, sex, and race groups. Among the individual coronary arteries, the LAD was the most likely location for new CAC. Multivessel involvement of new CAC was more likely among males, Hispanics, Blacks, and in subjects with HTN, DM, and obesity. At the first detection of new CAC, the CAC burden was low, with <5% of subjects having a CAC score of >100. This is the first community-based study to describe the CAC distribution and CAC score burden at the initial detection of new CAC.

5.1. *Prior studies on distribution of coronary atherosclerosis*

The prevalent distribution of atherosclerosis in the coronary arteries has been described in prior cross-sectional studies. Pathological studies have shown that the prevalence and burden of atherosclerosis was higher in LAD, followed by RCA and then LCX.[18,19] However, the differences have not been dramatic and some studies even observed roughly equal frequency of atherosclerosis in the LAD and the RCA and lower frequency in the LCX.[20,21] Tuzcu et al,[22] using intravascular ultrasonography, showed that there was no statistically significant difference in distribution of lesions within different coronary arteries, although there was a trend toward higher prevalence in LAD and lower prevalence within LCX. It has been hypothesized that the preferential development of atherosclerosis in LAD can be due to the difference in the flow patterns in various anatomic locations of coronary arteries.[23] To our knowledge, there are no longitudinal studies describing the geographical incidence of atherosclerosis in the coronary arteries. Using CAC as a marker of atherosclerosis, we showed that incidence of new CAC is higher in LAD compared to RCA and LCX. However, we cannot rule out the possibility that calcium deposition occurs earlier in atherosclerotic lesions in LAD compared with lesions in other coronary arteries (RCA, LCX, and LM).

5.2. *Comparison to prior CAC studies*

In our analysis, we observed that traditional coronary heart disease risk factors including HTN, DM, smoking, high BMI, and high LDL levels are independently associated with development of new CAC. Similar results were seen in

Table 2 – CAC distribution at the first detection of CAC >0.

Distribution of new-onset CAC	All visits (N = 1125)	Visit 2* (N = 170)	Visit 3* (N = 305)	Visit 4* (N = 150)	Visit 5* (N = 500)
Single vessel	72% (807)	85% (144)	74% (226)	75% (113)	65% (324)
LAD	44%	57%	41%	44%	42%
RCA	12%	12%	14%	14%	10%
LCX	10%	12%	13%	8%	7%
LM	6%	4%	6%	9%	6%
Multivessel	28% (318)	15% (26)	26% (79)	25% (37)	35% (176)
2 vessel	20%	12%	20%	18%	24%
3 or 4 vessel	8%	3%	6%	7%	11%

CAC, coronary artery calcium; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main artery; N, number of subjects; RCA, right coronary artery.

* Visits 2, 3, 4, and 5 include subjects who had detectable CAC on a follow-up scan at mean 1.7 ± 0.3, 3.2 ± 0.4, 4.9 ± 0.5, and 9.7 ± 0.6 years, respectively, after baseline scan.

Table 3 – Multivariable-adjusted residual probability (%) of newly detected CAC distribution patterns by age, sex, and race.

Factor	Single vessel				Multivessel	*P* value*
	LAD	RCA	LCX	LM		
Age, y						
45–54	48	14	9	5	24	Reference
55–64	45	14	7	5	29	.11
65–74	39	9	10	8	34	.01
75–84	53	6	13	11	17	.29
Sex						
Female	49	11	9	6	25	Reference
Male	41	13	8	7	31	.049
Race						
White	50	11	8	7	24	Reference
Chinese	54	10	7	5	24	.99
Black	41	13	9	6	31	.05
Hispanic	39	12	11	5	33	.02

CAC, coronary artery calcium; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main artery; RCA, right coronary artery.
Predicted probabilities adjusted for age categories, race categories, sex, time to CAC >0 detection, hypertension, household income, smoking status, use of any lipid-lowering medications, diabetes, LDL-C >160, and obesity (body mass index >30 kg/m^2).
* *P* value is for single vessel vs multivessel involvement of CAC. Refer to Table 1 for sample size of each category.

previous studies.[24–26] The percentage of subjects who developed new CAC (36%) was higher in our study compared to previous studies,[25,26] which is likely due to the older patient population, higher risk factor burden, and longer follow-up of subjects in our study. Although a prior study by Min et al had the advantage of yearly CAC scanning, this study did not investigate the distribution of new CAC on first detection.[24]

Table 4 – Multivariable-adjusted residual probability (%) of newly detected CAC distribution patterns by individual risk factors.

Risk factor	Single vessel				Multivessel	*P* value*
	LAD	RCA	LCX	LM		
No hypertension	46	13	10	6	25	Reference
Hypertension	44	11	7	6	32	.03
Nonsmoker	45	12	9	6	28	Reference
Smoker	44	11	10	6	29	.88
No diabetes	47	11	9	6	27	Reference
Diabetes	35	16	8	5	36	.048
LDL-C <160 mg/dL	45	12	9	6	28	Reference
LDL-C ≥160 mg/dL	46	10	8	8	28	.91
TC/HDL-C ratio ≤3	52	9	7	5	27	Reference
TC/HDL-C ratio >3	44	13	9	6	28	.39
BMI <30 kg/m^2	49	11	8	7	25	Reference
BMI ≥30 kg/m^2	38	13	11	5	33	.02

BMI, body mass index; CAC, coronary artery calcium; HDL-C, high-density lipoprotein cholesterol; LAD, left anterior descending artery; LCX, left circumflex artery; LDL-C, low-density lipoprotein cholesterol; LM, left main artery; RCA, right coronary artery; TC, total cholesterol.
Predicted probabilities adjusted for age categories, race categories, sex, time to CAC >0 detection, hypertension, household income, smoking status, use of any lipid-lowering medications, diabetes, LDL >160, and obesity (BMI >30).
* *P* value is for single-vessel vs multivessel involvement of CAC. Refer to Table 1 for sample size of each category.

Detection of CAC is an excellent method of assessing atherosclerotic plaque presence, and it is important to note that the amount of calcium correlates with the overall magnitude of atherosclerotic plaque burden.[27] Previous cross-sectional studies have suggested that quantity of CAC was significantly higher in LAD than in RCA and LCX.[28–30] However, to our knowledge, there are no longitudinal studies defining the origin and demographic distribution of new CAC in coronary arteries. Therefore, we have extended prior work by demonstrating that new CAC most commonly involves the LAD across all age, sex, and race groups.

The burden of new-onset CAC has been described in some of the studies mentioned previously.[25,26,31] In our study, 52% had a CAC score of 1 to 10, 44% had a CAC score of 11 to 100, and 4% had a CAC score of >100. Our study has a higher burden of new-onset CAC compared to the study by Gopal et al[31] (approximately 69% had CAC score of 1–9, 26% had CAC score of 10–50, and 5% had CAC score >50) and the burden is even less in the study by Koulaouzidis et al[26] (approximately 84% had CAC score of 1–9, 14% had CAC score of 10–50, and 2% had CAC score >50). Our study has an older patient population and higher traditional risk factor burden compared to prior studies, perhaps also explaining our observed burden of new-onset CAC. In addition, lack of annual scanning resulting in increased lag period between the scans can be a contributing factor for the higher CAC burden at first detection in our study.

Cross-sectional burden of CAC among different age, sex, and race groups has been described in previous studies.[32–35] However, no studies have investigated the demographic variation of newly detected CAC. A striking finding from our study is that there is no difference in the burden of new CAC by age, sex, and race group.

5.3. *Clinical implications*

To our knowledge, there are no formal guidelines on repeat CAC testing for routine quantification of CAC progression[36]; however, prior data suggest that a repeat scan in 4 to 5 years appears reasonable in individuals with a baseline score of CAC = 0.[25,26] We have shown that at the first detection of CAC >0, the burden is usually low (<100). This suggests that people rarely convert from CAC = 0 to high CAC scores, which is important because high scores are associated with increased event rates.[37] Therefore, repeat scans to identity subjects with CAC >0 may allow detection while scores are still low and with adequate time to initiate aggressive preventive therapies. Whether this strategy can reduce cardiac events warrants further study. Our data also have implications for readers of cardiac CT scans, allowing readers to be familiar with the most common patterns of new-onset CAC.

6. Limitations

The principal limitation of this study is that annual CAC scanning was not performed. The timing of CAC scans was prespecified per the MESA protocol, which did not call for

Table 5 – CAC burden at the first detection of CAC >0.

Vessel affected	CAC 1–10	CAC 11–100	CAC >100	P value*	Median CAC score (IQR)	P value†
Total population (N = 1125)	52%	44%	4%		9.4 (3.7–22.9)	
Single vessel (N = 807)	65%	34%	1%	.01	5.9 (2.6–14.3)	<.001
LAD (N = 500)	61%	38%	1%		6.8 (2.8–14.9)	
RCA (N = 133)	68%	31%	1%		5.6 (2.3–12.6)	
LCX (N = 107)	80%	20%	0%		3.7 (1.9–8.8)	
LM (N = 67)	66%	34%	0%		7.0 (2.8–16.8)	
Multivessel (N = 318)	20%	68%	12%		26.2 (12.6–54.7)	
Comparison of Single vessel vs multivessel				<.001		<.001

CAC, coronary artery calcium; IQR, interquartile range; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main artery; N, number of subjects; RCA, right coronary artery.

* *P* value is for comparison of CAC burden among individual coronary arteries (LAD vs RCA vs LCX vs LM) as well as between single-vessel vs multivessel involvement.

† *P* value is for comparison of median CAC among individual coronary arteries (LAD vs RCA vs LCX vs LM) as well as between single-vessel vs multivessel involvement.

every participant to have scans at each follow-up visit. Therefore, it is impossible to know when exactly new CAC was developed, and our data should be considered time to first CAC detection rather than strict time to CAC incidence. However, the patterns and implications we have described should still hold, as lack of annual scanning would result in overestimation of the incidence of multivessel CAC and of CAC score burden at the first CAC detection.

In addition, we did not model change in risk factor or change in medication use over the course of the study. It is possible that changing behaviors or therapies may have had an effect on new-onset CAC. As the Agatston method was used to quantify CAC in our study, there is a possibility that certain lesions, especially those with low-density calcium and small areas of calcium (<1 mm^2) can be missed, which could influence our data. In our study, we do not have data regarding CAC distribution in different segments within individual coronary arteries. CAC analysis between coronary artery segments of similar length can provide a better picture of the segments with high chances of developing new CAC. Finally, although we demonstrated the coronary distribution and burden of new CAC, we did not study their prognostic implications. Studies on the prognostic significance of coronary distribution in MESA are forthcoming.[38]

7. Conclusion

Distinguished from referenced work by Min et al[25] and Kronmal et al,[24] this is the first study to describe the distribution of new CAC at its first detection. New-onset CAC most commonly affects 1 vessel and occurs in the LAD. The probability of multivessel involvement of new CAC is higher in certain high-risk groups. Of importance, CAC scores are usually low at onset of new CAC suggesting adequate time to increase aggressiveness of preventive therapies.

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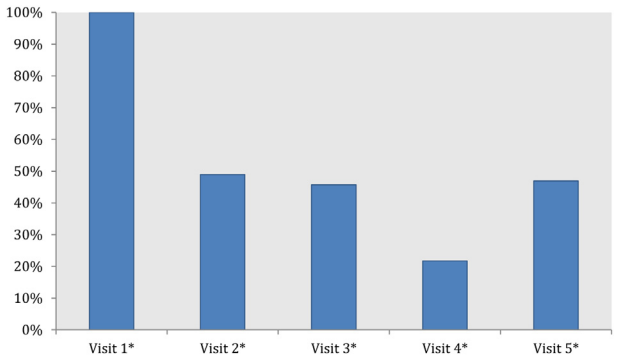

Supplementary Fig. 1 – Percentage of participants with CAC scanning at each visit in MESA. *Visit 1 is the initial baseline scan consisted of entire study population which includes 3112 participants. Visit 2, 3, 4, and 5 were at mean 1.7 ± 0.3, 3.2 ± 0.4, 4.9 ± 0.5, and 9.7 ± 0.6 years, respectively, after baseline scan and consisted of 1522, 1425, 677, and 1461 participants at each visit, respectively.

Supplementary Table 2 – CAC burden at the first detection of CAC >0 stratified by age, sex, and race groups.

Factor	CAC 1–10 (N = 588)	CAC 11–100 (N = 492)	CAC >100 (N = 45)	Median CAC (IQR)
Age group, y				
45–54	52	44	4	9.4 (3.3–22.4)
55–64	50	44	6	10.0 (3.7–25.2)
65–74	54	42	4	8.4 (3.5–21.1)
75–84	56	44	0	6.8 (3.0–20.8)
Sex				
Female	51	45	4	9.8 (3.7–23.8)
Male	54	42	4	8.7 (3.3–21.3)
Race				
White	53	43	4	8.8 (3.7–20.6)
Chinese	47	48	5	11.2 (4.7–22.4)
Black	52	44	4	9.4 (3.1–28.0)
Hispanic	53	43	4	8.9 (3.3–23.1)

CAC, coronary artery calcium; IQR, interquartile range.
CAC burden among subjects from different age, sex, and race groups represented as percentage (%) of patients in different CAC groups (CAC 1–10, CAC 11–100 and CAC >100).

Supplementary Table 1 – CAC burden according to visit.

CAC burden	All visits (N = 1125)	Visit 2* (N = 170)	Visit 3* (N = 305)	Visit 4* (N = 150)	Visit 5* (N = 500)
CAC 1–10	52%	68%	67%	50%	39%
CAC 11–100	44%	31%	31%	47%	55%
CAC >100	4%	1%	2%	3%	6%

CAC, coronary artery calcium.
* Visits 2, 3, 4, and 5 include subjects who had a follow-up scan at mean 1.7 ± 0.3, 3.2 ± 0.4, 4.9 ± 0.5, and 9.7 ± 0.6 years, respectively, after baseline scan.