

# Coronary artery calcification distribution and progression in over 70 000 asymptomatic individuals: implications for assessment intervals and optimal testing age

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### **Aims**

To assess the prevalence and progression of CAC in asymptomatic individuals and evaluate the duration for which a CAC score of 0 persists over time.

# Methods and results

This retrospective cohort study included 70 389 asymptomatic individuals aged over 30 years from Korea, with at least two CAC score assessments (2010–22). Subgroups were defined based on follow-up intervals: the entire cohort, those with at least four assessments within 10 years, and those with follow-up after five years. Analyses focused on age- and sex-specific CAC distributions, incidence and timing of new CAC, and changes in CAC scores among those with an initial score of 0 over 6–12 years. Among participants (mean age  $40.5 \pm 6.6$  years; 87% men), 84% had a baseline CAC score of 0, and 3% had scores > 100. Notably, 93% of women had a CAC score of 0, with the highest percentages observed in younger women. Incident CAC developed in 16% of participants with an initial score of 0 within five to six years, with just 1% exceeding score of 100. Extended follow-up data showed a consistently low prevalence of significant CAC scores, with only 4% exceeding scores > 100 after 10 years.

### Conclusion

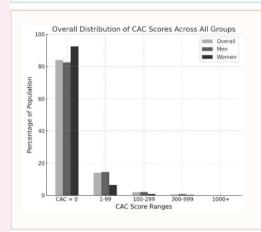
In a large Korean cohort of over 70 000 asymptomatic adults, most had baseline CAC = 0, indicating low subclinical atherosclerosis. Significant calcification (CAC > 100) was rare within 5–6 years, with only 4% exceeding 100 by 10 years, even among older subgroups.

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# **Graphical Abstract**

# Title: Long-Term Stability of Zero Coronary Artery Calcification in 70,000 Asymptomatic Korean Adults



### **Key Points**

- High Prevalence of Zero CAC: Among 70,000 asymptomatic adults (30–84 years; mean 40.5 years), 84% had CAC=0 at baseline.
- Younger Women: Up to 98% of those aged 30–39 had no detectable CAC, reflecting a very low prevalence of subclinical atherosclerosis.
- Minimal Progression: Among participants with baseline CAC=0, at 5–6 years, significant calcification (CAC>100) was rare; only 4% exceeded CAC=100 by 10 years.
- Older Subgroups: Men ≥40 years and women ≥50 years with baseline CAC=0 also showed slow progression, with only ~1–7% exceeding 100 over 6–12 years.

Conclusion: In this large Korean cohort, a baseline CAC=0 remained stable for most individuals over 5–10 years, with only 4% exceeding CAC=100 at 10 years.

**Keywords** 

coronary artery calcification • optimal testing intervals • age-specific prevalence • sex-specific prevalence • cardiovascular risk

# Introduction

Coronary artery calcification (CAC) is a well-established marker of atherosclerosis and a reliable predictor of future cardiovascular events. CAC measurement provides cost-effective, independent prognostic value for coronary artery disease (CAD),<sup>1–4</sup> particularly by enhancing risk stratification for individuals at intermediate cardiovascular risk.<sup>5</sup> The absence of CAC is associated with a significantly reduced likelihood of future cardiovascular events.<sup>6–8</sup> However, as atherosclerosis progresses, an initial CAC score of zero does not guarantee long-term stability, as CAC can develop in certain individuals over time.<sup>9–11</sup> Studies indicate that CAC progression is associated with adverse cardiovascular outcomes, independent of the initial CAC scores or clinical risk factors, highlighting the potential value of periodic reassessment in certain cases.<sup>12</sup>

Coronary computed tomography (CCT) is a widely utilized modality for CAC detection, though the potential radiation risks associated with repeated scans warrant careful consideration. A single CAC scan delivers an estimated radiation dose of  $\sim\!1$  millisievert (mSv). While the cancer risk from this level of radiation exposure is relatively low, it is essential to minimize cumulative exposure, particularly since repeated scans could elevate long-term cancer risk. Hus, determining optimal testing intervals and identifying individuals who would benefit most from the reassessment is crucial to reduce unnecessary radiation exposure.

Large-scale cohort studies investigating CAC progression among individuals with an initial score of zero remain scarce, <sup>15,16</sup> leaving the optimal interval for repeat CAC assessment undefined.<sup>17–21</sup> Establishing a standardized interval for repeat CAC scanning could improve clinical care, by reducing healthcare costs, and minimizing radiation exposure.

Moreover, large-scale studies examining CAC prevalence and distribution across age and sex in asymptomatic populations remain limited. Previous studies are constrained by smaller sample sizes or are predominantly focused on non-Asian populations, which may limit the generalizability of their findings. <sup>22–25</sup> A detailed understanding of age- and sex-specific CAC distribution in healthy populations is crucial for refining CAC testing strategies and CAC application in clinical practice.

This study analysed age- and sex-specific CAC prevalence, incidence, and progression rates in a large cohort, with the goal of providing evidence-based guidelines on optimal testing intervals and the appropriate age for initiating CAC evaluations.

# **Methods**

# Study design and population

This retrospective cohort study was conducted at the Kangbuk Samsung Health Promotion Center in Seoul, South Korea, and included participants aged >30 years who underwent routine health examinations, including CAC scoring, between March 2010 and December 2022. Most participants (>80%) were employees (or spouses thereof) of companies or local governmental organizations, undergoing examinations provided under the Industrial Safety and Health Law, which mandates annual or biennial health screenings at no cost. The remaining participants underwent these examinations at their own expense.

We identified 213 023 individuals who underwent CAC assessment as part of routine health examinations. Of these, 137 640 individuals were excluded because they had only a single CAC measurement, leaving 75 383 participants with at least one follow-up assessment. Among these, 4549

individuals were excluded due to missing data on key variables, including alcohol consumption (n=4431), body mass index (BMI) (n=82), systolic blood pressure (n=79), and glucose level (n=41). Additionally, 494 individuals with a history of CAD were excluded. Since 49 individuals had both missing data and a history of CAD, their exclusion was accounted for only once. After these exclusions, the final analytic cohort comprised 70 389 participants.

This study was approved by the Institutional Review Board at Kangbuk Samsung Hospital (IRB No. 2024-07-005), with informed consent waived due to the retrospective design and use of de-identified data.

# Data collection and assessment

Baseline demographic and clinical characteristics—including age, sex, lipid profiles (LDL-C, HDL-C, triglycerides, and total cholesterol), glucose level, BMI, smoking status, high alcohol intake, education level, and the presence of HTN or DM—were collected using standardized questionnaires and clinical examinations. These variables were reassessed at each follow-up. Participants' characteristics were stratified by both baseline and follow-up CAC scores.

# **CAC** assessment

CAC measurements were performed using a multidetector computed tomography (MDCT) scanner (Lightspeed VCT XTe 64-slice, GE Healthcare) according to a standardized scanning protocol ( $40 \times 2.5$  mm section collimation, 400 ms rotation time, 120 kV tube voltage, 124 mAs with ECG-gated dose modulation). In 2018, a Siemens MDCT system was introduced, followed by replacement of the GE scanner in 2022. Throughout these transitions, a uniform 5 mm slice thickness and standardized protocol were maintained. The Agatston method was used to calculate CAC scores in all scans.

# Study outcomes

The primary outcome was defined as incident CAC, identified by a CAC score > 0 at follow-up among individuals with a baseline CAC score of 0. The secondary outcome was annual CAC progression in participants with a baseline CAC score > 0.

# Statistical analysis

Baseline characteristics were summarized using means and standard deviations for continuous variables and frequencies or percentages for categorical variables. Differences between groups were assessed using one-way analysis of variance for continuous variables and  $\chi^2$  tests for categorical variables. For comparisons between those with a CAC score of 0 and those with a CAC score > 0 at follow-up within the groups with baseline CAC score of 0 or >0, t-tests were used for continuous variables and  $\chi^2$  tests were used for categorical variables. A significance level adjusted for multiple comparisons was applied (Bonferroni's correction).

Since patients did not undergo annual testing, they were categorized into three groups: the entire cohort (Dataset 1), those who underwent CAC testing at least four times within 10 years (Dataset 2), and those who had a follow-up CAC measurement five years after the initial scan (Dataset 3). Statistical significance was set at a two-tailed *P*-value of <0.05. All analyses were conducted using STATA version 18.0 (StataCorp LLC, College Station, TX, USA).

# **Results**

# Baseline characteristics and follow-up CAC

Participants were categorized according to their baseline and follow-up CAC scores into four groups: (i) baseline CAC score of 0, remaining 0 at follow-up (n = 49~967); (ii) baseline CAC score of 0, developing CAC at follow-up (n = 9065); (iii) baseline CAC score > 0, reverting to 0 at follow-up (n = 395); and (iv) baseline CAC score > 0, remaining elevated

at follow-up ( $n=10\,962$ ) (Table 1). The mean follow-up period was  $5.77\pm2.77$  years, with a median of 5.71 years. Overall,  $70\,389$  participants (mean age,  $40.5\pm6.6$  years) were included, of whom 87% ( $n=61\,261$ ) were men. Among individuals with a baseline CAC score of 0, 85% remained CAC-free (group 1), whereas 15% developed new CAC (group 2). Participants in group 2 were slightly older (mean age,  $41.0\pm5.9$  years) and predominantly male (96%), with higher rates of hypertension (24% vs. 12%) and diabetes (8% vs. 4%) compared with group 1.

Of the 194 091 participants initially identified, 123 702 underwent only one CAC examination, while 70 389 had two or more (see Supplementary data online, *Table S1*). Differences in risk factors between single-test and multiple-test participants were modest and not clinically substantial.

# Age- and sex-specific distribution of CAC

Among the 70 389 participants, 84% had a baseline CAC score of 0, while only 3% had a score exceeding 100 (*Table 2*). For men, 83% had a CAC score of 0, and 3% had a score over 100. Specifically, 92% of men aged 30–39 had a CAC score of 0, with <1% having scores over 100. Among women, 93% had a CAC score of 0, and 1% had scores exceeding 100. Notably, 98% of women aged 30–39 had a CAC score of 0, and <1% had scores over 100. In the 40–49 age group, 95% of women had a CAC score of 0, and <1% had scores over 100.

After excluding 4074 individuals with DM and 12 122 with HTN, of whom 1651 had both DM and HTN, the proportion of participants with a baseline CAC score of 0 who developed CAC during follow-up decreased from 15% to 13% (see Supplementary data online, *Tables* S2 and S3). Additional details are provided in the supplementary tables.

Among men aged 40–84, 74% had a baseline CAC = 0 and 5% had scores  $\geq$  100. In women aged 50–84, 67% had CAC = 0, whereas 7% had scores  $\geq$  100 (see Supplementary data online, *Table* S4).

# Incidence and progression across follow-up intervals

The incidence of new CAC from an initial score of 0 and the progression of existing CAC were analysed, stratified by follow-up intervals (*Table 3*). The study included three groups: the overall population ( $N=70\,389$ ), individuals with at least four CAC exams within 10 years (N=8511), and individuals with a 5-year follow-up ( $N=13\,423$ ). In the overall population, 15% of participants with an initial CAC score of 0 developed new CAC over an average follow-up period of 5.7 years. The mean time to incident CAC was 6.1 years. For participants with baseline CAC > 0, the mean annual progression was 20.0. For individuals who underwent at least four CAC exams within 10 years, 43% developed new CAC, with a mean time to incident CAC of 5.6 years. The mean annual progression for those with baseline CAC > 0 was 23.1.

Among men aged  $\geq$ 40 (N = 61 261), 21% of those with a baseline CAC score of 0 developed new CAC over a mean follow-up of 5.8 years, while progression in those with baseline CAC > 0 averaged 21.6 units annually (see Supplementary data online, Table S5). In women aged  $\geq$ 50 (N = 9128), 12% of those with a baseline CAC = 0 developed new CAC after a mean of 5.3 years, and those with a baseline CAC > 0 progressed at 18.9 units annually. Comparable findings were observed in participants who underwent multiple CAC evaluations within 10 years and in those who followed for 5 years.

# Five-year incidence and progression of CAC

For participants with a 5-year follow-up, 16% developed new CAC. The mean time to incident CAC was 5.5 years, and the mean annual progression for those with baseline CAC > 0 was 22.4.

Table 1 Baseline characteristics of participants stratified by CAC score at baseline and follow-up

	Total	CA	CAC = 0 at baseline		75	CAC > 0 at baseline		P-value**
		CAC = 0 at $f/up$	CAC > 0 at f/up	P-value*	CAC = 0 at f/up	CAC > 0 at f/up	P-value*	
Number	70 389	49 967	9065		395	10 962		
Age (years)	$40.5 \pm 6.6$	$39.3 \pm 5.7$	$41.0 \pm 5.9$	<0.001	$42.7 \pm 8.4$	$45.8 \pm 8.1$	<0.001	<0.001
Men (%)	61 261 (87.0)	41 932 (83.9)	8657 (95.5)		368 (93.2)	10304 (94)	0.989	<0.001
Vigorous exercise frequency (%)				0.036			0.049	<0.001
<3 time/week	60 556 (86.0)	43 348 (86.8)	7767 (85.7)		348 (88.1)	9093 (83.0)		
≥3 time/week	9212 (13.1)	6241 (12.5)	1218 (13.4)		42 (10.6)	1711 (15.6)		
Unknown	621 (0.9)	378 (0.8)	80 (0.9)		5 (1.3)	158 (1.4)		
LDL-C, mg/dL	$131.0 \pm 32.3$	$128.5 \pm 31.2$	$137.1 \pm 32.4$	<0.001	$139.1 \pm 32.5$	$136.6 \pm 35.2$	0.271	<0.001
HDL-C, mg/dL	$53.5 \pm 13.6$	$54.4 \pm 13.9$	$50.7 \pm 12.2$	<0.001	$51.8 \pm 13.2$	$51.5 \pm 13.1$	>0.999	<0.001
TG, mg/dL	$142.5 \pm 95.6$	$135.0 \pm 88.8$	$162.0 \pm 105.7$	<0.001	$152.7 \pm 104.2$	$160.5 \pm 110.2$	0.292	<0.001
TC, mg/dL	$201.5 \pm 35.0$	$199.0 \pm 33.7$	$209.5 \pm 35.3$	<0.001	$205.2 \pm 34.6$	$206.4 \pm 38.8$	0.989	<0.001
Glucose, mg/dL	$98.3 \pm 16.4$	$96.7 \pm 13.4$	$100.6 \pm 19.3$	<0.001	$101.4 \pm 26.1$	$104.0 \pm 23.0$	0.099	<0.001
Smoking (%)	18 508 (26.3)	11 950 (23.9)	2987 (33.0)	<0.001	91 (23.0)	3480 (31.8)	0.002	<0.001
High alcohol intake (%)	8799 (12.5)	5501 (11.0)	1437 (15.9)	<0.001	44 (11.1)	1817 (16.6)	0.008	<0.001
Higher education (%)	59 028 (83.9)	42 198 (84.5)	7594 (83.8)	600.0	341 (86.3)	8895 (81.1)	0.044	<0.001
ВМІ	$24.7 \pm 3.2$	$24.4 \pm 3.2$	$25.4 \pm 3.1$	<0.001	$26.0 \pm 3.4$	$25.4 \pm 3.1$	0.001	<0.001
(%) NLH	12 122 (17.2)	6086 (12.2)	2198 (24.3)	<0.001	100 (25.3)	3738 (34.1)	0.001	<0.001
DM (%)	4074 (5.8)	1755 (3.5)	747 (8.2)	<0.001	30 (7.6)	1542 (14.1)	0.001	<0.001
HTN medication (%)	5154 (7.3)	2033 (4.1)	919 (10.1)	<0.001	53 (13.4)	2149 (19.6)	0.004	<0.001
DM medication (%)	1819 (2.6)	645 (1.3)	312 (3.4)	<0.001	11 (2.8)	851 (7.8)	<0.001	<0.001
LIPID medication (%)	3040 (4.3)	1279 (2.6)	466 (5.1)	<0.001	28 (7.1)	1267 (11.6)	0.012	<0.001

Follow-up period: mean of 5.77 ± 2.77 years, median of 5.71 years. Values are expressed as means ± standard deviation, medians (interquartile range), or percentages. High alcohol intake was defined as > 20 g/day for women, > 30 g/day for men. Higher education was defined as education higher than college or university graduate.

CAC, coronary artery caldfication; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglycerides; TC, total cholesterol; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus.
\*\*Indicates statistical significance for comparisons between participants with a baseline CAC score of 0 who had CAC = 0 at follow-up and those who developed CAC (CAC > 0) at follow-up. This P-value also reflects comparisons between participants with a baseline CAC score > 0 who reverted to 0 at follow-up and those who remained > 0 at follow-up.

\*\*\*Indicates statistical significance for comparisons between participants with a baseline CAC score of 0 and those with a baseline CAC score > 0.

Table 2 Dis	Table 2         Distribution of CAC scores by age and sex at baseline	CAC scores	s by age an	d sex at ba	seline									
Group	CAC = 0	4	9-9	10–19	20–29	30–39	40-49	20-99	100–199	200–299	300-399	400-499	200-999	1000+
Overall	59 032 (83.9%) 2608 (3.7%) 1274 (1.8%) 1837 (2	2608 (3.7%)	1274 (1.8%)	1837 (2.6%)	1110 (1.6%)	1075 (1.5%)	530 (0.8%)	1374 (2.0%)	959 (1.4%)	391 (0.6%)	184 (0.3%)	102 (0.1%)	162 (0.2%)	69 (0.1%)
Men	50 589 (82.6%) 2463 (4.0%) 1212 (2.0%) 1716 (2	2463 (4.0%)	1212 (2.0%)	1716 (2.8%)	1026 (1.7%)	704 (1.1%)	498 (0.8%)	1285 (2.1%)	908 (1.5%)	367 (0.6%)	176 (0.3%)	99 (0.2%)	151 (0.2%)	67 (0.1%)
Women	8443 (92.5%) 145 (1.6%)	145 (1.6%)	62 (0.7%)	121 (1.3%)	84 (0.9%)	53 (0.6%)	32 (0.4%)	89 (1.0%)	51 (0.6%)	24 (0.3%)	8 (0.1%)	3 (0.0%)	11 (0.1%)	2 (0.0%)
Men 30–39	25 961 (92.3%) 668 (2.4%) 310 (1.1%)	668 (2.4%)	310 (1.1%)	382 (1.4%)	219 (0.8%)	140 (0.5%)	90 (0.3%)	200 (0.7%)	99 (0.4%)	25 (0.1%)	15 (0.1%)	7 (0.0%)	9 (0.0%)	2 (0.0%)
Men 40-49	22 517 (79.2%) 1439 (5.1%)	1439 (5.1%)	733 (2.6%) 1009 (3.5%)	1009 (3.5%)	580 (2.0%)	394 (1.4%)	268 (0.9%)	696 (2.4%)	467 (1.6%)	173 (0.6%)	62 (0.2%)	36 (0.1%)	47 (0.2%)	16 (0.1%)
Men 50–59	1934 (49.1%)	307 (7.8%)	144 (3.7%)	278 (7.1%)	185 (4.7%)	125 (3.2%)	112 (2.8%)	311 (7.9%)	261 (6.6%)	114 (02.9%)	56 (1.4%)	30 (0.8%)	55 (1.4%)	24 (0.6%)
Men 60–69	168 (25.3%)	44 (6.6%)	25 (3.8%)	41 (6.2%)	36 (5.4%)	41 (6.2%)	26 (3.9%)	(%6.6) 99	(%6.6) 99	45 (6.8%)	36 (5.4%)	15 (2.3%)	35 (5.3%)	20 (3.0%)
Men 70+	9 (9.3%)	5 (5.2%)	0 (0.0%)	6 (6.2%)	6 (6.2%)	4 (4.1%)	2 (2.1%)	12 (12.4%)	15 (15.5%)	10 (10.3%)	7 (7.2%)	11 (11.3%)	5 (5.2%)	5 (5.2%)
Women 30-39	3178 (97.6%)	24 (0.7%)	12 (0.4%)	16 (0.5%)	9 (0.3%)	6 (0.2%)	3 (0.1%)	4 (0.1%)	3 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Women 40-49	4514 (94.9%)	70 (1.5%)	33 (0.7%)	43 (0.9%)	35(0.7%)	11 (0.2%)	10 (0.2%)	25 (0.5%)	12 (0.3%)	2 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)	0 (0.0%)
Women 50-59	616 (79.2%)	31 (4.0%)	10 (1.3%)	31 (4.0%)	15 (1.9%)	14 (1.8%)	10 (1.3%)	23 (3.0%)	13 (1.7%)	10 (1.3%)	3 (0.4%)	1 (0.1%)	1 (0.1%)	0 (0.0%)
Women 60–69 122 (43.9%)	122 (43.9%)	15 (5.4%)	6 (2.2%)	26 (9.4%)	21 (7.6%)	16 (5.8%)	8 (2.9%)	25 (9.0%)	19 (6.8%)	9 (3.2%)	3(1.1%)	2 (0.7%)	5 (1.8%)	1 (0.4%)
Women 70+	13 (21.3%)	5 (8.2%)	1 (1.6%)	5 (8.2%)	4 (6.6%)	(%8.6) 9	1 (1.6%)	12 (19.7%)	4 (6.6%)	3 (4.9%)	2 (3.3%)	0(0.0%)	4 (6.6%)	1 (1.6%)

The percentages are calculated based on the total count within each age group and gender.

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Table 3 Incidence of new CAC from an initial score of zero and progression of existing CAC stratified by follow-up intervals

Dataset	Total <i>N</i>	Initial CAC = 0 N	Initial CAC = 0 and developing incident CAC. N (%)	Mean (SD) and median (IQR) time for incident CAC (years)	Annual progression of CAC for baseline CAC > 0 N	Mean (SD) and median (IQR) annual progression of CAC for baseline CAC > 0
Dataset 1	70 389	59 032	9065 (15.4%)	6.1 (2.6)	10 962	20.0 (48.9)
				6.0 (4.1, 8.0)		9.0 (3.0, 9)
Dataset 2	8511	5161	2191 (42.5%)	5.6 (2.5)	3341	23.1 (31.5)
				5.3 (3.8, 7.6)		13.0 (5.2, 13.0)
Dataset 3	13 423	10 801	1688 (15.6%)	5.5 (2.2)	2561	22.4 (52.9)
				5.0 (4.6, 5.5)		10.8 (4.3, 10.8)

Dataset 1: overall population (N = 70389). Dataset 2: individuals with at least four CAC exams within 10 years (N = 8511). Dataset 3: individuals with a 5-year follow-up (N = 13423). CAC, coronary artery calcification; SD, standard deviation; IQR, interquartile range.

Of the 1688 individuals who had a baseline CAC = 0 and later developed incident CAC by 5 years, the mean CAC score was 17.5, and the median (IQR) was 8.0 (3.0–21.0) (see Supplementary data online, Table S6). Only 2% (26 participants) exceeded a CAC score of 100, indicating minimal progression in most cases.

In men aged  $\geq$ 40 with baseline CAC = 0, 18% advanced to CAC > 0 over 5 years (mean CAC = 17.6) (see Supplementary data online, Table S7), and women  $\geq$  50 had an 8% rate of new CAC (mean CAC = 17.7) (see Supplementary data online, Table S8). These findings imply that older adults who begin with CAC = 0 still exhibit minimal progression in most cases.

Among men 40 years of age or older, 46.2% had no baseline risk factors (hypertension, diabetes, current smoking, or LDL  $\geq$  160 mg/dL), 38.8% had one, 12.9% had two, 2.0% had three, and 0.1% had four (see Supplementary data online, *Table S9*). Among those with a baseline CAC score of 0, the proportion who maintained a CAC score of 0 at five years was 81.1% in those with one risk factor, 73.6% in those with two, 65.1% in those with three, and 25.0% in those with four. Mean and median follow-up CAC scores were higher among participants who had more baseline risk factors.

# Long-term stability of zero CAC

Longitudinal changes in CAC scores were tracked in participants with a baseline CAC score of 0 over follow-up intervals ranging from 6 to 12 years (*Table 4*). Most participants consistently maintained a CAC score of 0 throughout the study period. Clinically significant progression, defined as a CAC score exceeding 100, was rare. At the 6-year follow-up, 83% of participants retained a CAC score of 0, with <1% progressing to a score above 100. This low rate of clinically significant progression remained stable across follow-up intervals: by the 10-year mark, 67% of participants still had a CAC score of 0, while 4% had scores over 100. At 12 years, 56% retained a CAC score of 0, and 7% had progressed to scores above 100.

For men aged  $\geq$ 40 with CAC = 0, 79% remained at 0 after 6 years, 65% after 10 years, and 54% after 12 years, with 0.6%, 4%, and 7% exceeding CAC = 100, respectively (see Supplementary data online, *Table S10*). In women  $\geq$  50 with CAC = 0, 89% maintained a score of 0 at 6 years, 84% at 10 years, and 81% at 12 years, with ~1% exceeding 100. Although some calcification occurred over time, these data suggest that a baseline CAC = 0 is associated with low rates of significant progression in older adults, over intervals up to 12 years.

# **Discussion**

This study provides a comprehensive analysis of the distribution and progression of CAC in a substantial cohort of over 70 000

asymptomatic individuals. By analysing data in 10-year age intervals and stratifying results by sex, it offers valuable insights for targeting specific populations and optimizing CAC testing intervals.

In this Korean cohort of relatively young, asymptomatic adults, the majority exhibited a CAC score of 0. For instance, 92% of men and 98% of women aged 30–39, as well as 95% of women aged 40–49, had no detectable CAC. The low prevalence of significant CAC in this population suggests a minimal likelihood of detecting clinically relevant calcification, especially among younger women.<sup>26</sup>

Follow-up data indicated that incident CAC typically develops in about five to six years for individuals with an initial CAC score of 0, irrespective of the follow-up intervals. Even in cases where CAC was detected during this period, the degree of calcification was minimal; only 1% (26 out of 1700) had scores > 100, indicating a negligible overall calcification burden. This finding suggests that even a five-year interval for reassessment might be more frequent than necessary. The stable and predictable nature of CAC progression in this population supports extending testing intervals without compromising the ability to detect clinically meaningful changes.

Extended follow-up data revealed that among participants with a baseline CAC score of 0, the prevalence of clinically significant CAC scores remained consistently low over time. At the 6-year follow-up, only 1% had a CAC score > 100. This proportion remained low at 4% after 10 years. This low incidence indicated that significant CAC progressed minimally for these individuals over extended periods. Therefore, for individuals with an initial CAC score of 0, extended testing intervals might be appropriate.

Separately, among the 11 357 participants with a baseline CAC > 0, 395 (3.5%) were observed to have CAC = 0 at follow-up. Their initial calcification burden was minimal (median [IQR], 1 [1–3]), suggesting that this 'reversion' likely reflects minor technical variations (e.g. slice misalignment and motion artefacts) rather than true plaque regression.

Our findings hold several important clinical implications. First, this study provides comprehensive data on CAC distribution in a large Korean population, specifically stratified by age and sex. This is particularly valuable because prior studies have reported that East Asians generally exhibit lower average CAC scores compared with White populations, as observed in the Multi-Ethnic Study of Atherosclerosis (MESA). Thus, our findings may not be directly applicable to populations with a higher burden of atherosclerotic cardiovascular disease, such as those in Northern and Eastern Europe, the United States, or South Asia. The Vertheless, by presenting CAC proportions across age and sex groups, our study offers a useful reference for cardiovascular risk assessment and developing culturally specific health interventions.

Secondly, CAC assessment should be applied more selectively within asymptomatic populations, especially among younger and female

Freq.  0 1-4 5-9 10-19 20-29 30-39 100-199 38 200-299 53 300-399 65	12 years later	11 ye	11 years later	10 yea	10 years later	9 yea	9 years later	8 yea	8 years later	7 yea	7 years later	6 year	6 years later
	Percent	Freq.	Percent	Freq.	Percent	Freq.	Percent	Freq.	Percent	Freq.	Percent	Freq.	Percent
	56.4	1465	61.9	2613	67.3	3749	9.69	5484	74.1	6229	77.8	9730	82.8
	2.8	171	7.2	279	7.2	396	7.4	466	6.7	490	6.1	662	9.5
	4.6	101	4.3	149	3.8	202	3.8	246	3.3	272	3.4	312	2.7
	7.4	142	9	231	0.9	314	2.8	378	5.1	343	4.3	408	3.5
	5.2	110	4.7	140	3.6	181	3.4	206	2.8	203	2.5	220	1.9
	4.6	83	3.5	83	2.1	119	2.2	136	1.8	128	1.6	122	1.0
	2.8	52	2.2	79	2.0	68	1.7	110	1.5	110	4:	68	8.0
	6.4	125	5.3	173	4.5	202	3.8	198	2.7	160	2	149	1.3
	3.8	89	2.9	101	2.6	92	1.7	121	1.6	23	0.7	40	0.3
	1.5	27	1.1	21	0.5	24	0.5	13	0.2	12	0.2	13	0.1
	6.0	7	0.3	7	0.2	9	0.1	7	0.1	m	0.0		
400-499		2	0.2	2	0.1	2	0.1	4	0.1				
500–999 5	0.5	∞	0.3	4	0.1	2	0.1			2	0:0	c	0:0
1000~	0.1	2	0.1	2	0.1								
Total 1012	100	2366	100	3884	100	5384	100	7402	100	8005	100	11 748	100
CAC 0 maintained 571	26.4%	1465	61.9%	2613	67.3%	3749	%9.69	5484	74.1%	6229	77.8%	9730	82.8%
CAC > 0 441	43.6%	901	38.1%	1271	32.7%	1635	30.4%	1918	25.9%	1776	22.2%	2018	17.2%

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individuals, who typically have a very low prevalence of CAC. Thirdly, the finding that clinically significant CAC did not emerge until five to six years later, with only  $\sim\!4\%$  reaching scores above 100 after 10 years, indicates that extending screening intervals beyond five to six years may be beneficial. This approach may help reduce healthcare costs, minimize cumulative radiation exposure, and further supports the safety and efficacy of lengthening assessment intervals for low-risk individuals.  $^{28-30}$ 

These findings are consistent with previous studies. Gopal et  $al.^{17}$  proposed a five-year interval for repeat CAC testing in individuals with an initial score of 0. Similarly, Lee et  $al.^{20}$  have found that the progression of CAC in asymptomatic individuals with an initial score of 0 is generally slow, supporting extension of assessment intervals. Shen et  $al.^{21}$  also observed that a baseline zero CAC score in low-risk Asian populations is associated with a low incidence of CAC progression over a five-year period, supporting the use of extended screening intervals.

Notably, this study is distinguished by its large cohort size of over 70 000 participants, detailed stratification by age, sex, and follow-up frequency, and robust methodology, which enhance the reliability and generalizability of the findings.

# Limitations

This study has several limitations. First, participant subjects were not randomized and did not uniformly undergo follow-up CAC testing, which introduced the potential for selection bias. However, as shown in Supplementary data online, Table S1, individuals who underwent multiple examinations exhibited statistically significant yet modest risk-factor differences compared with those who had a single test, indicating no major baseline imbalances overall. Secondly, missing data on key variables required exclusions that may limit generalizability if excluded individuals had systematically different risk profiles. Thirdly, our single-centre setting and relatively young, Asian cohort may not represent older or more diverse populations; however, subgroup analyses in men  $\geq$  40 years and women  $\geq$  50 years indicated that baseline CAC = 0 remained largely stable even in older adults. Fourthly, participants underwent follow-up at varying intervals, which we addressed by stratifying them according to follow-up frequency to capture differences in CAC progression timelines. Finally, because we did not collect long-term clinical outcomes, our findings should be viewed as observational, rather than definitive evidence for specific screening intervals. 31,32 Nonetheless, the large sample size, standardized imaging protocols, and comprehensive data collection collectively support the robustness of our main findings.

Future research should focus on validating these findings in more diverse populations to enhance the generalizability of results. Longitudinal studies tracking the same cohort over time are needed to provide more detailed insights into individual CAC progression. Additionally, investigating optimal interval to test different risk groups will help refine CAC testing guidelines and improve clinical outcomes.

# **Conclusions**

In this large Korean cohort of more than 70 000 asymptomatic adults, the majority—particularly younger women—had baseline CAC = 0, indicating a low burden of subclinical atherosclerosis. Among those with an initial CAC = 0, clinically significant calcification (CAC > 100) did not emerge until 5–6 years, and only 4% surpassed 100 by 10 years. Even among older subgroups (men  $\geq$  40, women  $\geq$  50), just 4% and  $\sim$ 1%, respectively, exceeded CAC = 100 at 10 years.

# Supplementary data

Supplementary data are available at European Heart Journal - Cardiovascular Imaging online.

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# Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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