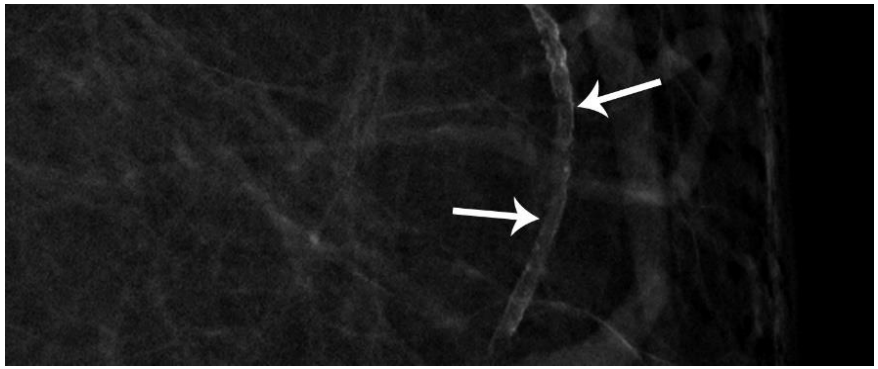
Breast Arterial Calcification and Coronary Artery Disease

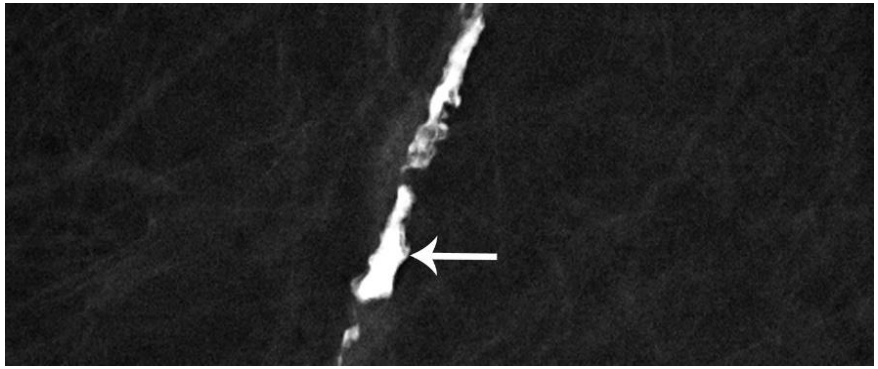
Jung-Won Suh, MD

Seoul National University Bundang Hospital

Breast Arterial Calcification (BAC)

- BAC, frequently observed on screening mammography, have been considered an incidental finding without increased risk for breast cancer.
- BAC is recognized by its typical tram-track appearance, distinct from ductal calcification

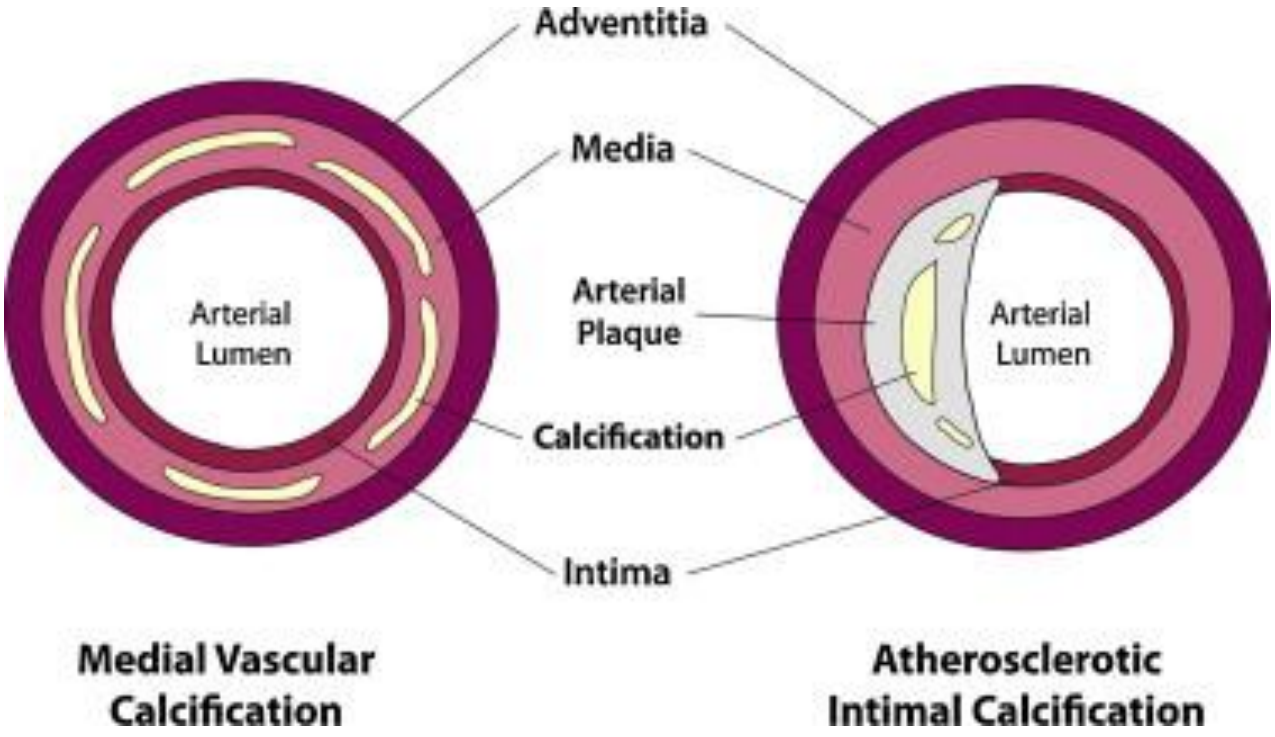




Suh JW, Yun BL, J Cardiovascular Imaging 2018

Breast Arterial Calcification

- Medial calcification, indicative of arteriosclerosis



Binder M, Roberts CA, Int J Paleopathology

Breast Arterial Calcification

- Risk factors of BAC partly overlap with those of CVD.
  - Age, diabetes, parity : positive
  - Smoking : negative
  - Hypertension, obesity or dyslipidemia : neutral

- Presence of BAC is associated with prevalent and incident CVD.

- This suggests that medial arterial calcification might contribute to CVD through a pathway distinct from the intimal atherosclerotic process.

The association between BAC and CVD : longitudinal studies

Author, year	Nation	Population	n	Mean age, years	BAC prevalence	Follow-up, years	Outcome	HR	95% CI
Kemmeren ,1998[34]	Netherlands	General	12,239	57.5	9.1%	16.8	All-cause mortality	1.29	1.06-1.58
							Cardiovascular mortality	1.29	1.01-1.66
							CHD mortality	1.44	1.02-2.05
							Cerebrovascular mortality	0.88	0.49-1.61
							Other cardiovascular mortality	1.38	0.89-2.16
Iribarren, 2004[35]	United States	General	12,761	56	3.0%	24.8	CHD	1.32	1.08-1.60
							Ischemic stroke	1.41	1.11-1.78
							Heart failure	1.52	1.18-1.98
Schnatz, 2011[36]	United States	General	1,454	56.3	16.3%	5	CHD	3.54 (OR)	2.28-5.50
Abou-Hassan, 2015[37]	United States	End stage renal disease	202	58.3	58.4%	4.1	Coronary artery disease	1.06 (OR)	0.48-2.38
							PAD	4.56 (OR)	1.20-17.3
Hendriks, 2015[38]	Netherlands	General	1,540	57	8.6%	13.2	CHD	1.44	1.02-2.01
							Stroke	1.39	0.92-2.08
							PAD	1.37	0.74-2.52
							Composite of CHD, stroke, PAD	1.39	1.00-1.93

Suh JW, Yun BL, J Cardiovascular Imaging 2018

Can BAC improve the prediction of subclinical CAD in asymptomatic women?

Background

- Although ASCVD risk prediction algorithms currently play an important role in identifying high-risk patients who may benefit from preventive intervention, they are not adequate by themselves, especially in women.

- Therefore, additional strategies beyond the measurement of traditional risk factors are needed to identify women who may benefit from medical therapy.

Objectives

- We sought to investigate whether evaluations of BAC on mammography can predict subclinical CAD on CCTA in asymptomatic women.

- We also tried to evaluate the potential utility of BAC for refining risk assessment in asymptomatic women based on the 10-year ASCVD risk.

Yoon YE, Kim KM….Suh JW. JACC Cardiovasc Img. 2019

BBC cohort : the women health registry study for bone, breast and CAD

- This cross-sectional study comprised consecutive self-referred women ≥40 years of age who underwent digital mammography, DXA, and CCTA, as part of a general health evaluation at the Health Promotion Center, SNUBH (Mar 2011~Feb 2013).

- **2,100 women** were included in the final analysis

Yoon YE, Kim KM….Suh JW. JACC Cardiovasc Img. 2019

Mammography

- The number, length, and density of BACs were evaluated.

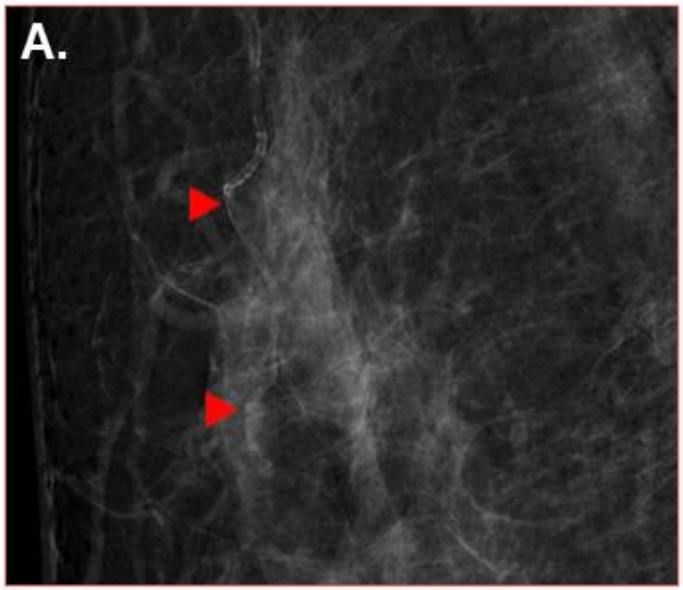
- These three scores were summed for each woman, and the total BAC score was divided into three grades: none (0), mild (1-6), and severe (7-12).

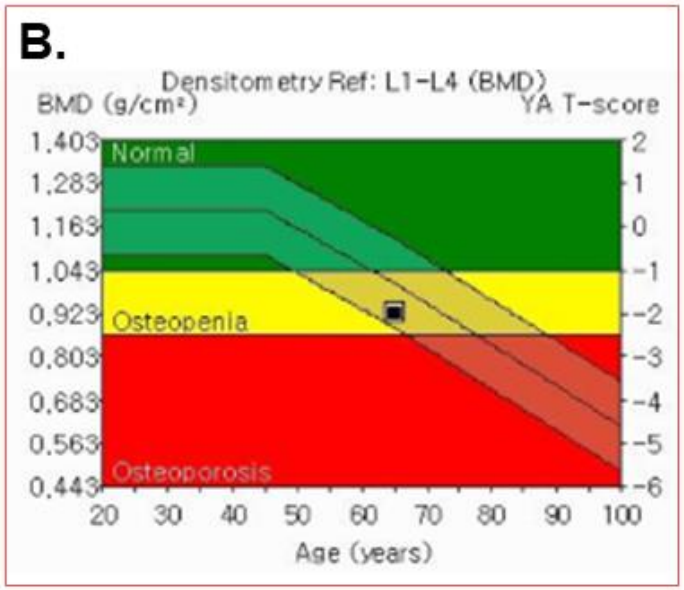
CCTA

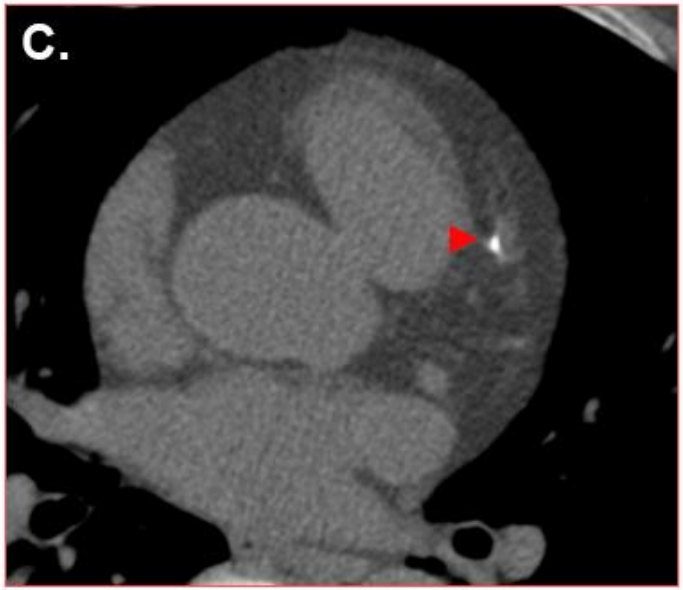
- The coronary arterial calcification (CAC) score was measured using the Agatston scoring system, and the presence of CAC was defined as a CAC score >0.

- Coronary atherosclerotic plaque (CAP) was defined as the presence of any clearly discernible atherosclerotic plaque lesion >1 mm^2 that could be discriminated from the coronary artery in at least 2 independent image planes

Representative case (F/65)







SNUH SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

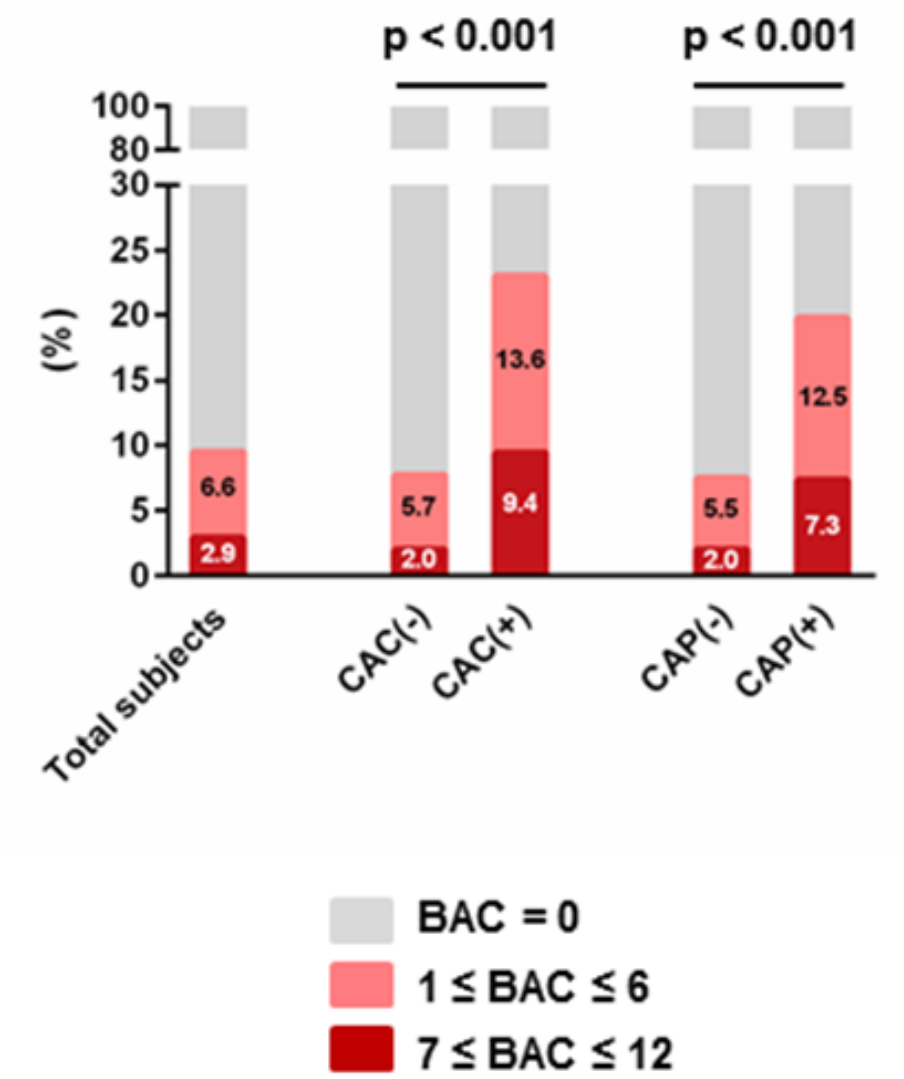
Yoon YE, Kim KM….Suh JW. JACC Cardiovasc Img. 2019

Baseline characteristics

	Entire study population (n = 21,00)
Age, years	52 ± 7
Postmenopausal women, n (%)	1,321 (62.9%)
Number of parity	1.9 ± 1.0
Hypertension, n (%)	319 (15.2%)
Hyperlipidemia, n (%)	1,156 (55.0%)
Diabetes mellitus, n (%)	87 (4.1%)
Current smoking, n (%)	70 (3.9%)
Family history of CAD, n (%)	247 (20.6%)
Antihypertensive medication, n (%)	260 (12.4%)
Antihyperlipidemic medication, n (%)	152 (7.2%)
Antidiabetic medication, n (%)	69 (3.3%)
Body mass index, kg/m^2	22.7 ± 3.0
Systolic blood pressure, mmHg	110 ± 16
Diastolic blood pressure, mmHg	64 ± 10
Hemoglobin, g/dL	13.3 ± 1.2
Serum creatinine, mg/dL	0.7 ± 0.1
Fasting blood glucose, mg/dL	89 ± 16
HbA1c, %	5.6 ± 0.6
Total cholesterol, mg/dL	202 ± 35
Triglyceride, mg/dL	92 ± 58
High-density lipoprotein, mg/dL	60 ± 14
Low-density lipoprotein, mg/dL	124 ± 32
PCE-based 10-year ASCVD risk, %	2.1 ± 2.7
10-year ASCVD risk < 5%	1,915 (91.2%)
5% ≤ 10-year ASCVD risk < 7.5%	110 (5.2%)
7.5% ≤ 10-year ASCVD risk	75 (3.6%)
KRPM-based 10-year ASCVD risk, %	3.3 ± 2.9
10-year ASCVD risk < 5%	1701 (81.0%)
5% ≤ 10-year ASCVD risk < 7.5%	231 (11.0%)
7.5% ≤ 10-year ASCVD risk	168 (8.0%)
Presence of BAC, n (%)	199 (9.5%)
BAC score	0.5 ± 1.8
Lumbar spine BMD	1.120 ± 0.167
Lumbar spine T-score	-0.34 ± 1.35
Low bone mass (T-score ≤ -1.0), n (%)	716 (34.1%)
Presence of CAC	235 (11.2%)
CAC score	10.1 ± 95.3
Presence of CAP	328 (15.6%)
CAP ≥50% diameter stenosis	37 (1.8%)
CAP involving >4 segments	18 (0.9%)

Yoon YE, Kim KM….Suh JW. JACC Cardiovasc Img. 2019

Proportion of BAC grade according to the presence of CAC or CAP



Women with CAC or CAP showed increasing proportions of both mild and severe BAC than women without CAC or CAP.

SNUH SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Yoon YE, Kim KM….Suh JW. JACC Cardiovasc Img. 2018

Multivariable analyses of the factors associated with CAC and CAP

	Adjusted for PCE-based 10-year ASCVD risk			Adjusted for KRPM-based 10-year ASCVD risk			Adjusted for all covariates*		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Presence of CAC									
BAC presence (BAC score >0)	2.53	1.72-3.71	<0.001	2.18	1.48-3.21	<0.001	2.87	1.67-4.93	<0.001
BAC score	1.15	1.08-1.22	<0.001	1.12	1.06-1.19	<0.001	1.20	1.10-1.31	<0.001
Presence of CAP									
BAC presence (BAC score >0)	2.26	1.60-3.21	<0.001	2.00	1.41-2.85	<0.001	2.52	1.53-4.18	<0.001
BAC score	1.13	1.07-1.20	<0.001	1.11	1.05-1.17	<0.001	1.18	1.08-1.29	<0.001

*Adjusted for age, parity number, hypertension, diabetes mellitus, family history of premature CAD, current smoking, body mass index, systolic blood pressure, fasting blood glucose, cholesterol, triglyceride, and high-density lipoprotein-cholesterol.

The presence and severity of BAC maintained significant associations with CAC and CAP, after adjustment for the 10-year ASCVD risk as assessed by either the PCE or KRPM and for conventional risk factors.

Improvement of conventional risk algorithm by BAC

- For the prediction of CAC and CAP, the addition of BAC presence to the 10-year ASCVD risk significantly increased the AUC (0.71 to 0.72, p = 0.016; and 0.66 to 0.68, p = 0.010, respectively) and resulted in net reclassification index improvements (0.304, p <0.001; and 0.245, p <0.001, respectively).

Conclusion

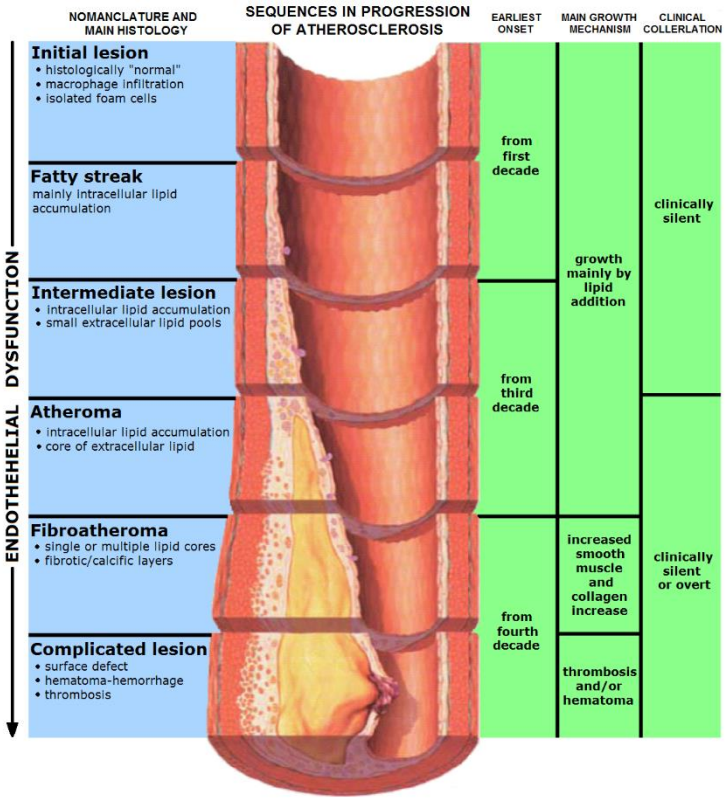
- The presence and severity of BAC were significantly associated with the risk of subclinical CAD in asymptomatic women.
- The evaluation of BAC provides an independent and incremental value over conventional risk algorithms.

Can BAC Predict Progression of Coronary Atherosclerosis in Asymptomatic Women?

Yeonyee E. Yoon, Kyoung Min Kim, Wonjae Lee, Jong Soo Han, Eun Ju Chun, Soyeon Ahn, Sun Mi Kim, Sang Il Choi, Bo La Yun, Jung-Won Suh

SNUH 분당서울대학교병원
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Atherosclerosis is a dynamic process !



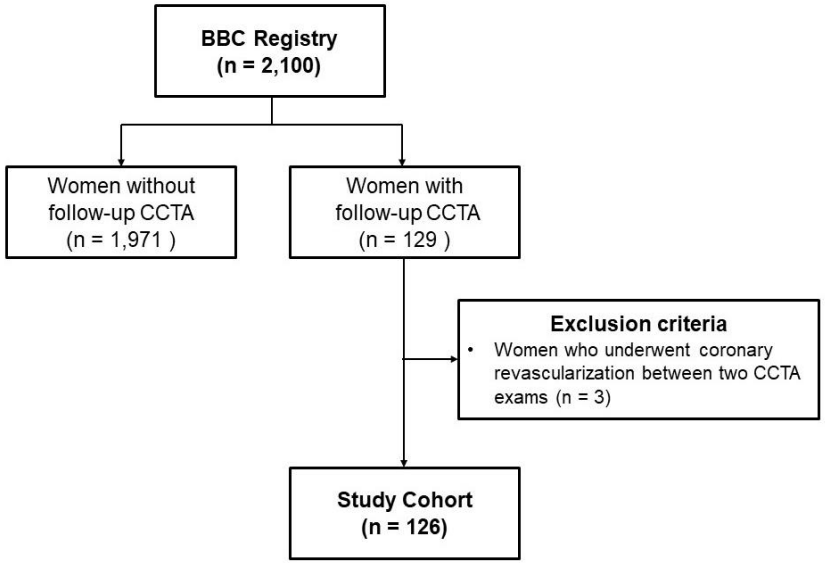
- CAC or CAP progression might provide insight into ongoing disease activity.
- CAC or CAP progression detected by serial CCTA were independently associated with the occurrence of cardiovascular events.
- However, no current guideline advocate for more than one CAC scoring or CCTA scan.

Study Aim

- We aimed to evaluate whether the evaluation of BAC using mammography could predict coronary atherosclerosis progression on CCTA in asymptomatic women.

Method

Study Population



CCTA Analysis

- CAC score by Agatston scoring system
- Segment stenosis score (SSS)
  - Modified American Heat Association 15-segment criteria
  - No CAP (0), CAP with max DS <50% (1), max DS ≥50% (2)

  → The score of all 15 segments summed : 0~30

- CAC progression rate

$(\sqrt{\text{CAC score}}_{\text{follow-up}} - \sqrt{\text{CAC score}}_{\text{baseline}}) /$ interscan duration

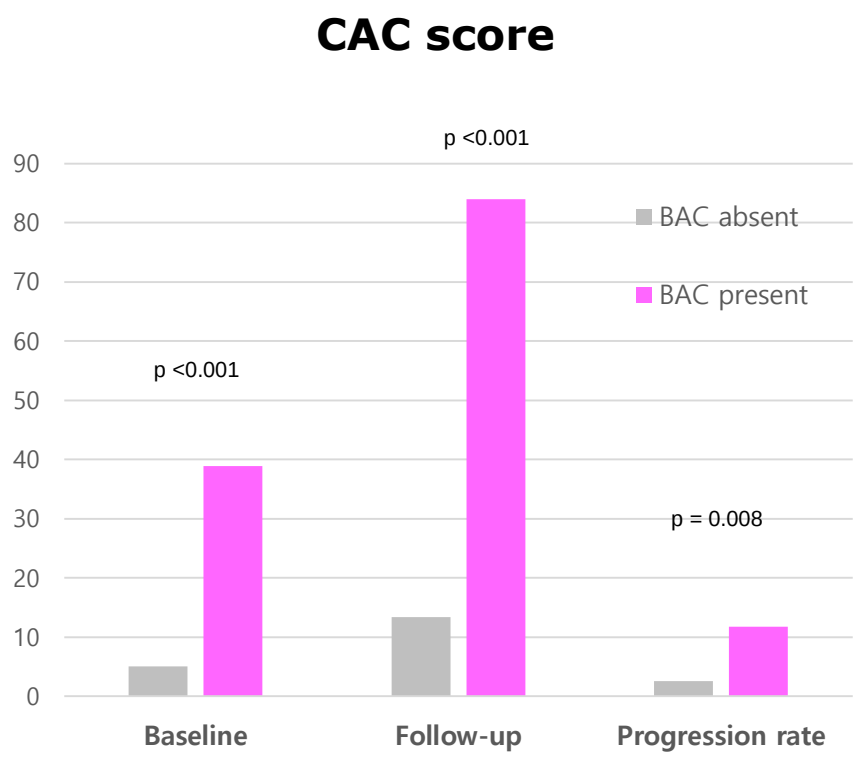
- CAP progression rate

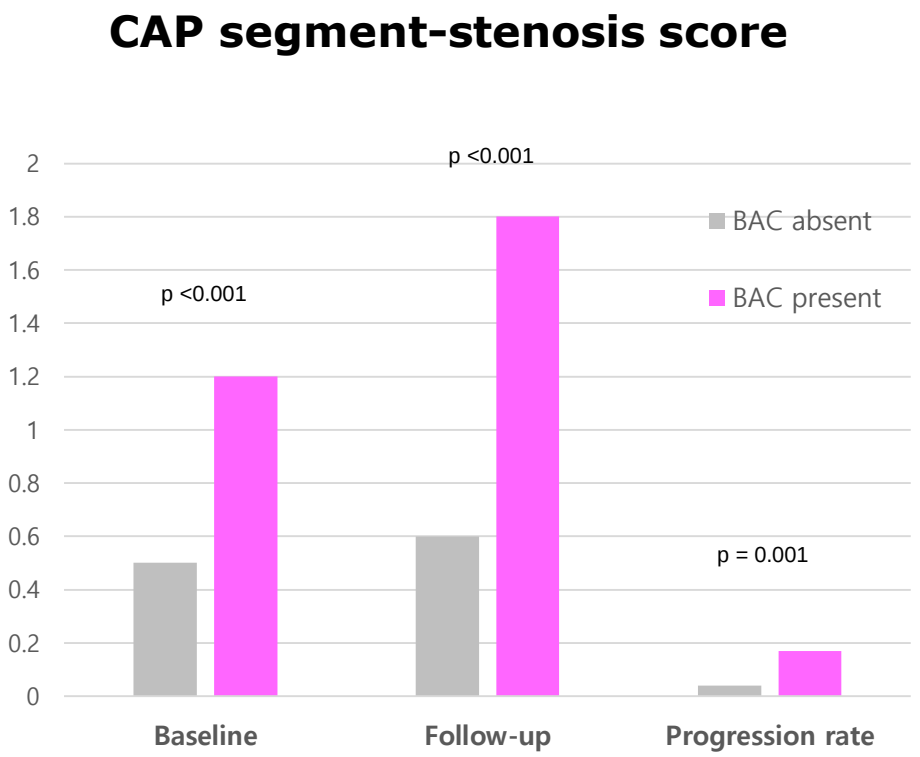
$(\text{SSS}_{\text{follow-up}} - \text{SSS}_{\text{baseline}}) /$ interscan duration

Yoon YE, Kim KM.. Suh JW, Sci Rep. *in revision*

BAC and CAC, CAP Progression

- 126 women, 54.5±7.0 years
- Median interscan duration : 4.3 years (IQR, 3.2-5.0 years)
- CAC progression in 42 (33.3%) women, and CAP progression in 26 (20.6%) women



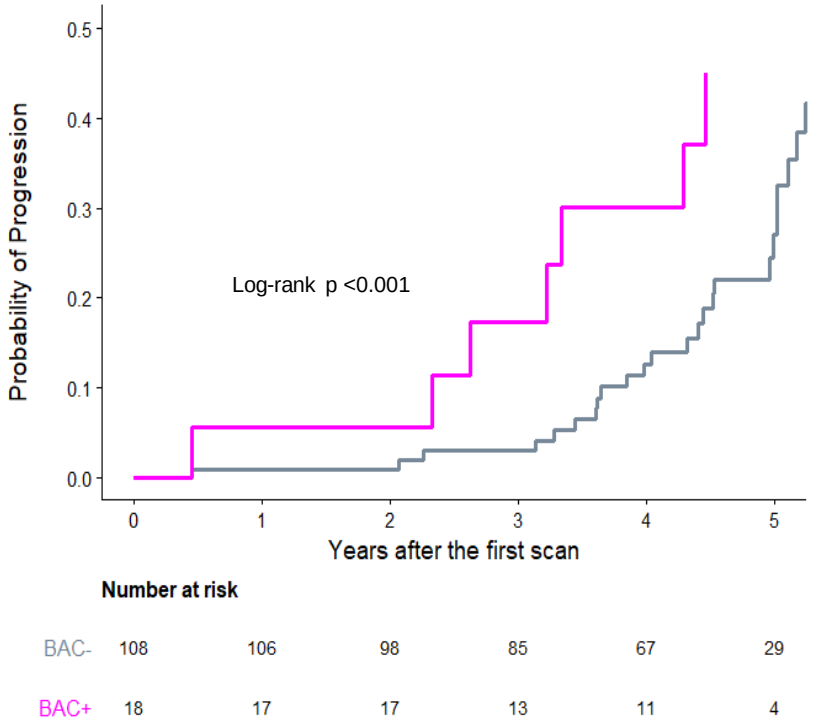


CACS and SSS were significantly higher in women with BAC than in women without BAC at both baseline and follow-up. The progression rates of CAC and CAP were also higher in women with BAC than in women without BAC.

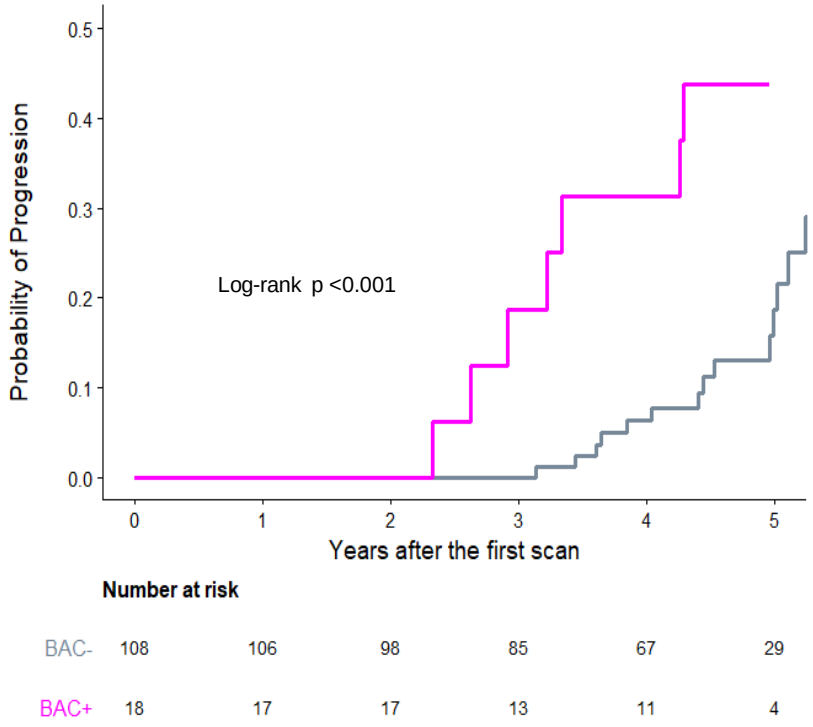
Yoon YE, Kim KM.. Suh JW, Sci Rep. *in revision*

The cumulative proportion of CAC and CAP progression according to the presence and absence of BAC

CAC progression



CAP progression



Women with BAC at baseline had a significantly higher chance of CAC and CAP progression compared to that in women without BAC.

Yoon YE, Kim KM.. Suh JW, Sci Rep. *in revision*

Multivariable Linear Regression Analysis for CAC Progression Rate

	Model 1 (Clinical RFs + BACS)				Model 2 (Clinical RFs + CACS + BACS)				Model 3 (Clinical RFs + Segment stenosis score + BACS)			
	β	95% CI	t	p	β	95% CI	t	p	β	95% CI	t	p
Age, years	-0.015	-0.040 - 0.011	-1.158	0.250	-0.019	-0.045 - 0.006	-1.497	0.137	-0.023	-0.047 - 0.002	-1.858	0.066
Number of parity	0.060	-0.077 - 0.198	0.871	0.386	0.044	-0.093 - 0.181	0.641	0.523	0.052	-0.077 - 0.181	0.806	0.422
Hypertension, n (%)	0.120	-0.237 - 0.478	0.669	0.505	0.107	-0.246 - 0.460	0.602	0.549	0.155	-0.181 - 0.490	0.914	0.363
Current smoking, n (%)	0.196	-0.846 - 1.237	0.373	0.710	0.174	-0.855 - 1.203	0.336	0.738	0.259	-0.718 - 1.236	0.527	0.600
Systolic blood pressure, mmHg	0.006	-0.002 - 0.014	1.421	0.158	0.006	-0.002 - 0.014	1.530	0.129	0.003	-0.005 - 0.011	0.783	0.435
Serum creatinine, mg/dL	0.398	-1.235 - 2.032	0.484	0.630	0.575	-1.050 - 2.199	0.702	0.485	-0.049	-1.597 - 1.500	-0.062	0.950
HbA1c, %	0.493	0.323 - 0.663	5.736	<0.001	0.497	0.329 - 0.666	5.855	<0.001	0.431	0.268 - 0.594	5.241	<0.001
High-density lipoprotein, mg/dL	-0.007	-0.018 - 0.003	-1.365	0.175	-0.006	-0.017 - 0.004	-1.192	0.236	-0.006	-0.016 - 0.004	-1.222	0.224
Low-density lipoprotein, mg/dL	0.002	-0.003 - 0.006	0.738	0.462	0.001	-0.003 – 0.005	0.581	0.563	0.001	-0.003 – 0.005	0.559	0.577
Statin therapy after CCTA	-0.021	-0.445 - 0.402	-0.100	0.921	-0.051	-0.471 – 0.368	-0.243	0.809	-0.170	-0.574 – 0.234	-0.834	0.406
CACS					0.003	0.000 - 0.007	1.875	0.064				
SSS									0.238	0.116 - 0.361	3.864	<0.001
BACS	0.087	0.009 - 0.164	2.221	0.029	0.080	0.004 - 0.157	2.076	0.040	0.079	0.006 - 0.151	2.146	0.034

RFs, risk factors; CACS, coronary artery calcification score; BACS, breast arterial calcification score

Yoon YE, Kim KM.. Suh JW, Sci Rep. *in revision*

Multivariable Linear Regression Analysis for CAP Progression Rate

	Model 1 (Clinical RFs + BACS)				Model 2 (Clinical RFs + CACS + BACS)				Model 3 (Clinical RFs + Segment stenosis score + BACS)			
	β	95% CI	t	p	β	95% CI	t	p	β	95% CI	t	p
Age, years	0.002	-0.003 – 0.007	0.916	0.362	0.002	-0.003 – 0.007	0.779	0.438	0.002	-0.003 – 0.007	0.775	0.440
Number of parity	0.004	-0.023 – 0.030	0.291	0.772	0.003	-0.024 - 0.030	0.207	0.836	0.004	-0.023 – 0.030	0.266	0.791
Hypertension, n (%)	-0.026	-0.095 – 0.043	-0.746	0.457	-0.027	-0.096 – 0.042	-0.769	0.444	-0.025	-0.094 – 0.045	-0.704	0.483
Current smoking, n (%)	0.073	-0.128 – 0.274	0.721	0.472	0.072	-0.130 – 0.273	0.705	0.483	0.076	-0.126 – 0.277	0.745	0.458
Systolic blood pressure, mmHg	0.001	0.000 – 0.003	1.793	0.076	0.001	0.000 – 0.003	1.818	0.072	0.001	0.000 – 0.003	1.620	0.108
Serum creatinine, mg/dL	0.122	-0.193 – 0.437	0.767	0.445	0.134	-0.185 – 0.452	0.834	0.406	0.104	-0.216 – 0.423	0.644	0.521
HbA1c, %	0.031	-0.002 – 0.063	1.840	0.069	0.031	-0.002 – 0.064	1.851	0.067	0.028	-0.006 – 0.062	1.651	0.102
High-density lipoprotein, mg/dL	0.000	-0.002 – 0.002	0.126	0.900	0.000	-0.002 – 0.002	0.189	0.851	0.000	-0.002 – 0.002	0.172	0.864
Low-density lipoprotein, mg/dL	0.000	-0.001 – 0.001	0.378	0.706	0.000	-0.001 – 0.001	0.319	0.750	0.000	-0.001 – 0.001	0.332	0.741
Statin therapy after CCTA	-0.023	-0.105 – 0.059	-0.560	0.577	-0.025	-0.107 – 0.057	-0.606	0.546	-0.029	-0.113 – 0.054	-0.693	0.490
CACS					0.000	0.000 – 0.001	0.645	0.520				
SSS									0.010	-0.016 – 0.035	0.762	0.448
BACS	0.020	0.005 – 0.035	2.629	0.010	0.019	0.004 – 0.034	2.556	0.012	0.019	0.004 – 0.035	2.577	0.011

RFs, risk factors; CACS, coronary artery calcification score; BACS, breast arterial calcification score

Yoon YE, Kim KM.. Suh JW, Sci Rep. *in revision*

Conclusions

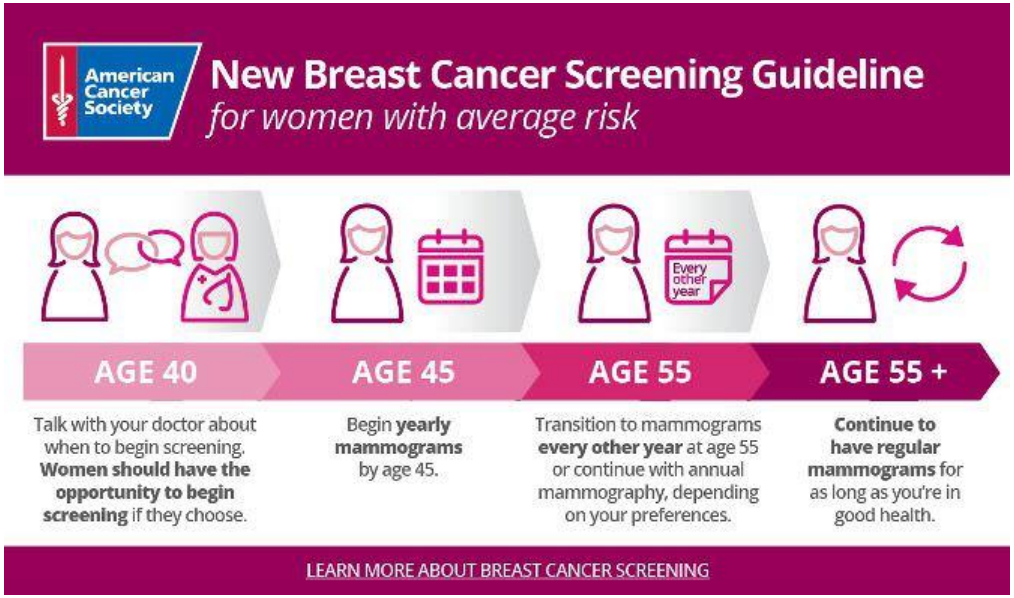
- BAC, which is currently suggested as a potential women-specific risk marker for coronary artery disease, is also related to the progression of coronary atherosclerosis as evidenced by increase in CAC score and CAP segment-stenosis score.

- Especially, the BAC score is independently associated with the annualized progression of CAC and CAP.

- Although these findings support the value of BAC in identifying asymptomatic women at increased risk of future cardiovascular disease, further studies are warranted to evaluate whether the evaluation of BAC in asymptomatic women will translates into long-term clinical benefit.

Yoon YE, Kim KM.. Suh JW, Sci Rep. *in revision*

Mammographic Screening



- Current clinical practice guidelines recommend annual mammographic screening in asymptomatic women, although the recommended age may vary depending on the medical resources and demographic characteristics.

2014 WHO Position Paper on Mammography Screening
JKMA 2015;58:408-19

Take Home Message

Given that millions of women undergo mammography, a significant relationship between CAD and BAC would provide the opportunity to improve risk stratification and to predict progression of CAD without additional cost and radiation exposure.

Thank you for your kind attention !!

suhjw1@gmail.com

So far, researches about 'breast arterial calcificaton (BAC)' were done with the semi-quantitative methods (presence/ absence or BAC score). Expert radiologists calculate the 'BAC score' according to the number, length, and density of BAC (Figure 1 in the attached file).

The MINERVA cohort study group attempts quantification of BAC mass using digital mammography and they may be able to suggest specific cut-off levels to predict future cardiovascular events after the completion of the MINERVA cohort study.

TABLE 2 Accuracy of 10-yr ASCVD risk, BAC, and BMD Data for Predicting the Presence of CAC and CAP

	% of Presence of CAC (95% CI)	% of Presence of CAP (95% CI)
PCE-based 10-yr ASCVD risk ≥7.5%		
Sensitivity	17.2 (12.6-22.6)	13.4 (10.0-17.7)
Specificity	98.1 (97.4-98.7)	98.3 (97.5-98.8)
PPV	53.3 (41.5-64.8)	58.7 (46.7-69.7)
NPV	90.4 (89.0-91.6)	86.0 (84.4-87.4)
KRPM-based 10-yr ASCVD risk ≥7.5%		
Sensitivity	28.9 (23.2-35.2)	24.4 (19.8-29.4)
Specificity	94.6 (93.5-95.6)	95.0 (93.9-96.0)
PPV	40.5 (33.0-48.3)	47.6 (39.9-55.5)
NPV	91.4 (90.0-92.6)	87.2 (85.6-88.6)
Presence of BAC (BAC score >0)		
Sensitivity	23.0 (17.8-29.0)	19.8 (15.7-24.6)
Specificity	92.2 (91.0-93.4)	92.4 (91.1-93.6)
PPV	27.1 (21.2-34.0)	32.7 (26.3-39.7)
NPV	90.5 (89.2-91.7)	86.1 (84.5-87.7)
Severe BAC (BAC score >6)		
Sensitivity	9.36 (5.9-13.8)	7.3 (4.8-10.8)
Specificity	98.0 (97.2-98.6)	98.0 (97.2-98.6)
PPV	36.7 (24.9-50.2)	40.0 (27.8-53.5)
NPV	63.3 (49.8-75.1)	85.1 (83.5-86.6)

BAC appear to be associated with an increased risk of CVD events, while only being associated with some of the known cardiovascular risk factors, illustrating that medial arterial calcification might contribute to CVD through a pathway distinct from the intimal atherosclerotic process.39) Medial calcification may lead to CVD through increased arterial stiffness because BAC could be a marker of a more generalized tendency to develop medial calcification in other vascular beds.37)38) The lack of distensibility may lead to higher peak pressures in distal vessels, resulting in damage and remodeling and exacerbation of ischemia produced by co-existing atherosclerosis. Stiffening of the large arteries may also promote atherosclerosis by altering flow characteristics.40)

Demographics and Comparison of women with and without follow-up CCTA

	Women without follow-up CCTA (n = 1971)	Study Cohort (n = 126)	p
Age, years	52.3 ± 7.2	54.5 ± 7.0	0.001
Post-menopausal women, n (%)	1220 (61.9%)	98 (77.8%)	<0.001
Parous woman	1695 (86.0%)	112 (88.9%)	0.436
Number of parity	1.9 ± 1.0	2.1 ± 1.2	0.191
Hypertension, n (%)	288 (14.6%)	30 (23.8%)	0.008
Diabetes mellitus, n (%)	81 (4.1%)	5 (4.0%)	1.000
Hyperlipidemia, n (%)	1082 (54.9%)	71 (56.3%)	0.822
Current smoking, n (%)	68 (4.0%)	2 (1.8%)	0.345
Family history of CAD, n (%)	224 (20.0%)	23 (29.9%)	0.055
Body mass index, kg/m^2	22.7 ± 3.0	23.3 ± 2.9	0.003
Systolic blood pressure, mmHg	110.5 ± 15.7	112.7 ± 18.1	0.299
Diastolic blood pressure, mmHg	63.6 ± 10.2	65.1 ± 11.8	0.232

Demographics and Comparison of women with and without follow-up CCTA

	Women without follow-up CCTA (n = 1971)	Study Cohort (n = 126)	p
Hemoglobin, g/dL	13.3 ± 1.2	13.3 ± 1.2	0.432
Serum creatinine, mg/dL	0.7 ± 0.1	0.7 ± 0.1	0.570
Fasting blood glucose, mg/dL	88.8 ± 15.0	91.6 ± 23.8	0.137
HbA1c, %	5.6 ± 0.6	5.7 ± 0.8	0.064
Total cholesterol, mg/dL	202.0 ± 35.1	207.3 ± 38.6	0.179
Triglyceride, mg/dL	91.3 ± 56.9	99.5 ± 68.1	0.183
High-density lipoprotein, mg/dL	59.6 ± 13.9	58.4 ± 13.3	0.373
Low-density lipoprotein, mg/dL	123.6 ± 32.2	128.7 ± 33.7	0.105
CAC presence, n (%)	206 (10.5%)	27 (21.4%)	<0.001
CAC score	10.0 ± 97.6	9.9 ± 40.4	<0.001
CAP presence, n (%)	286 (14.5%)	39 (31.0%)	<0.001
Segment stenosis score	0.3 ± 1.0	0.6 ± 1.1	<0.001
BAC presence, n (%)	181 (9.2%)	18 (14.3%)	0.082
BAC score	0.5 ± 1.7	0.8 ± 2.2	0.061

Univariable Linear Regression Analysis for CAC and CAP Progression Rate

	CAC progression rate			CAP progression rate		
	β	95% CI	p	β	95% CI	p
Age, years	0.022	0.002-0.041	0.034	0.007	0.003-0.010	<0.001
Post-menopausal women	0.169	-0.169-0.507	0.323	0.029	-0.034-0.092	0.364
Parous woman	0.254	-0.193-0.700	0.263	-0.034	-0.117-0.050	0.429
Number of parity	0.129	0.015-0.243	0.027	0.018	-0.003-0.040	0.095
Hypertension	0.296	-0.031-0.622	0.076	0.014	-0.048-0.075	0.666
Diabetes mellitus	1.448	0.773-2.122	<0.001	0.064	-0.071-0.198	0.350
Hyperlipidemia	0.237	-0.044-0.518	0.097	0.051	-0.002-0.103	0.058
Current smoking	0.244	-0.939-1.427	0.684	0.039	-0.170-0.249	0.709
Family history of CAD	-0.194	-0.600-0.213	0.346	-0.035	-0.111-0.040	0.350
Body mass index, kg/m^2	0.044	-0.004-0.091	0.072	0.005	-0.004-0.014	0.269
Systolic blood pressure, mmHg	0.010	0.003-0.018	0.009	0.002	0.000-0.003	0.023
Diastolic blood pressure, mmHg	0.011	-0.001-0.023	0.063	0.003	0.001-0.006	0.002
Hemoglobin, g/dL	0.109	-0.010-0.229	0.072	0.004	-0.018-0.027	0.719

Univariable Linear Regression Analysis for CAC and CAP Progression Rate

	CAC progression rate			CAP progression rate		
	β	95% CI	p	β	95% CI	p
Serum creatinine, mg/dL	0.085	-1.607-1.777	0.921	0.128	-0.188-0.443	0.425
Fasting blood glucose, mg/dL	0.014	0.008-0.019	<0.001	0.001	-0.001-0.002	0.319
HbA1c, %	0.497	0.343-0.651	<0.001	0.040	0.008-0.072	0.016
Total cholesterol, mg/dL	0.002	-0.002-0.005	0.415	0.000	-0.000-0.001	0.365
Triglyceride, mg/dL	0.002	0.000-0.004	0.020	0.000	-0.000-0.000	0.316
High-density lipoprotein, mg/dL	-0.009	-0.019-0.002	0.111	0.000	-0.002-0.002	0.929
Low-density lipoprotein, mg/dL	0.002	-0.002-0.006	0.282	0.000	-0.000-0.001	0.333
Statin therapy after CCTA	0.177	-0.285-0.640	0.449	0.002	-0.085-0.089	0.963
CAC presence	0.607	0.281-0.933	0.000	0.128	0.068-0.188	<0.001
CAC score	0.005	0.001-0.008	0.008	0.001	0.000-0.001	0.075
CAP presence	0.642	0.359-0.925	<0.001	0.068	0.012-0.124	0.017
Segment stenosis score	0.335	0.224-0.446	<0.001	0.032	0.009-0.055	0.006
BAC presence	0.482	0.089-0.876	0.017	0.129	0.057-0.200	0.001
BAC score	0.074	0.010-0.138	0.024	0.023	0.116-0.035	<0.001

Study Limitation

- Only 126 women remained for the current analysis even though BBC registry consisted of 2,100 consecutive women who underwent digital mammography, dual-energy X-ray absorptiometry, and CCTA as part of a general health evaluation.
  - ✓It is not surprising that only small number of women from BBC registry underwent repeated CCTA examination considering that most Korean health check-up centers are currently trying to curb the use of CCTA in asymptomatic individuals.
  - ✓Therefore, the current study provides valuable information regarding the association between BAC and progression of CAC and CAP and set the stage for outcome trial, which is required to evaluate whether the identification of BAC in asymptomatic women will translate into long-term clinical benefit.

Study Limitation

- Since follow-up CCTA was not guided by a specific study protocol, the interscan duration varied among study participants.
  - ✓ In the observational study, such effects are inevitable.
  - ✓ To minimize the effect of variations in the interscan duration, we calculated annualized CAC and CAP progression (CAC and CAP progression rate).

Study Limitation

- The CAP burden was estimated by using segment-stenosis score instead of volumetric measure of plaque. It is because of that not all the CCTA imaging data had been stored in a sufficient level for the plaque volumetry.
  - ✓ Prospective studies are needed to determine whether BAC is predictive for the increase in CAP volume, and if so, whether it is also associated with changes in plaque composition.