

## Coronary calcification is more predictive of carotid intimal medial thickness in black compared to white middle aged men

Aiman El-Saed<sup>a,\*</sup>, Akira Sekikawa<sup>a,b</sup>, Daniel Edmundowicz<sup>c</sup>,  
Rhobert W. Evans<sup>a</sup>, Kim Sutton-Tyrrell<sup>a</sup>, Takashi Kadowaki<sup>b</sup>,  
Jina Choo<sup>a</sup>, Tomoko Takamiya<sup>b</sup>, Lewis H. Kuller<sup>a</sup>

<sup>a</sup> Department of Epidemiology, Graduate School of Public Health, Pittsburgh, USA

<sup>b</sup> Department of Health Science, Shiga University of Medical Science, Japan

<sup>c</sup> Preventive Cardiology, Cardiovascular Institute, UMPC Health Plan, Pittsburgh, USA

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### Abstract

**Background:** Race-specific data for the association between coronary artery calcification (CAC) and carotid intimal medial thickness (IMT) are limited. We sought to compare black-white specific associations of these two measures.

**Methods:** We conducted a population-based study of 379 randomly selected men aged 40–49 years (84 black and 295 white) from Allegheny County, US (2004–2006). Agatston CAC score was evaluated by electron-beam tomography and carotid IMT was evaluated by ultrasonography.

**Results:** Compared to white men, black men had similar prevalence of CAC ( $p=0.56$ ) and higher total carotid IMT ( $p<0.001$ ). In black and white men, CAC score had significant positive correlations with total carotid IMT ( $r=0.47$  and  $r=0.24$ , respectively,  $p<0.001$  for both) as well as the IMT for the common carotid artery (CCA), internal carotid artery and carotid bulb. The associations of CAC with total and CCA IMT were significantly stronger in black ( $\beta=0.07$  and  $\beta=0.05$ , respectively) than white men ( $\beta=0.03$  and  $\beta=0.01$ , respectively) after adjustment for traditional coronary risk factors ( $p=0.046$  and  $p=0.036$ , respectively).

**Conclusions:** In black and white middle aged men, CAC score had significant positive correlations with total and segmental carotid IMT. CAC was more predictive of total and CCA IMT in black than white men independent of coronary risk factors.

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**Keywords:** Epidemiology; Atherosclerosis; Coronary calcification; Carotid intimal medial thickness; Caucasian; Black

### 1. Introduction

Carotid intimal medial thickness (IMT) measured using B-mode carotid ultrasonography is a well-recognized surrogate marker of generalized atherosclerosis [1]. Carotid IMT measures the extent of cellular accumulation and matrix deposition in the intima as well as smooth muscle hypertrophy in the media [2]. At a relatively later stage in the natural history of atherosclerotic lesion progression, calcium is deposited

in the complex atherosclerotic lesions in an actively regulated process [3,4]. Calcified coronary plaque, as measured by electron-beam tomography scanning (EBCT), is increasingly used as a marker of subclinical coronary atherosclerosis. Both carotid and coronary arteries may have lesions at different stages of the atherosclerotic process. Although carotid IMT and coronary artery calcification (CAC) measure different stages or aspects of atherosclerotic lesions, both are predictive of future coronary heart disease irrespective of race [5–7].

Race-specific data for black versus white men was lacking in the previous studies that examined the relation between CAC and carotid IMT [8–12]. It is unclear if race affects the relation between CAC and carotid IMT. Moreover, most of these studies presented data for the IMT of only the common

\* Corresponding author at: University of Pittsburgh, Health Studies Office, 130 N. Bellefield Avenue, Rm 405, Pittsburgh, PA 15213, USA.  
Tel.: +1 412 383 3132; fax: +1 412 624 7805.

E-mail address: amest30@pitt.edu (A. El-Saed).

carotid artery (CCA) limiting the ability to compare data from different carotid segments [9,11,12]. In this study, we examined the relation between CAC and carotid IMT for the CCA as well as the internal carotid artery (ICA), carotid bulb and a total measure including all carotid sites in white and black men aged 40–49 years.

## 2. Methods

### 2.1. Study population

The current report used data from the ERA-JUMP study that compared atherosclerosis between white, black, and Japanese American men (a high CHD population) and Japanese men (a low CHD population) born after World War II [13]. Only black and white men who had data for both CAC and carotid IMT were included in the current analysis. Participants were population-based bi-racial samples of 379 randomly selected men aged 40–49 recruited between 2004 and 2006 from Allegheny County, Pennsylvania, US (84 black and 295 white men). Exclusion criteria were (1) clinical cardiovascular disease, (2) type 1 diabetes, (3) cancer except skin cancer in the past 2 years, (4) renal failure, and (5) genetic familial hyperlipidemias. Informed consent was obtained from all participants. The study was approved by the Institutional Review Board of University of Pittsburgh, Pittsburgh, PA, US.

### 2.2. Exposure assessment

The study protocol was described in detail elsewhere [13]. In brief, a self-administered questionnaire was used to obtain information on demography, smoking habits, alcohol drinking, medication use, and other factors. Fasting serum and plasma samples were collected and used for measuring serum lipids, fasting glucose, CRP, fibrinogen, and other factors. Current smoking was defined as smoking cigarettes over the last month. Pack-years were calculated as years of (current or past) smoking multiplied by the number of cigarettes per day divided by 20. Alcohol drinkers were defined as drinking alcohol 2 days per week or more. Ethanol consumption per day was estimated assuming that concentrations of alcohol were 5% for beer, 12% for wine, and 40% for liquor. Hypertension was defined as systolic BP  $\geq$  140 mmHg, diastolic BP  $\geq$  90 mmHg, or use of anti-hypertensive medications. Diabetes mellitus was defined as fasting serum glucose level  $\geq$  126 mg/dL or use of anti-diabetic medications.

### 2.3. Outcome assessment

As previously described [13], EBCT was done using a GE-Imatron C150 EBCT scanner (GE Medical Systems, South San Francisco, US). Readings of the scanning were done at the Cardiovascular Institute, Pittsburgh, US using

the widely accepted Agatston CAC scoring method [14]. Carotid scanning was done at the ultrasound laboratory in Pittsburgh, US using a Toshiba 140A scanner equipped with a 7.5 MHz-linear-array imaging probe and applying a continuous quality-assessment programs to assure scanning quality [15]. Total carotid IMT was the average of available IMT measurements at eight segments (the right and left near and far walls of right and left CCA and far walls of ICA and carotid bulb).

## 3. Statistical analyses

*t*-Test, the *Mann–Whitney U* test, or  $\chi^2$ -test were used to compare demographic characteristics and risk factors between black and white men (Table 1). Unadjusted mean carotid IMT was compared between black and white men using *t*-test. Adjusted mean carotid IMT was compared between both populations using general linear model after

Table 1  
Comparison of the major characteristics of black and white men<sup>a</sup>

	Black (n = 84) <sup>b</sup>	White (n = 295) <sup>b</sup>	<i>p</i> -Value
Age (years)	45.0 $\pm$ 2.8	45.0 $\pm$ 2.9	0.881
Body mass index (kg/m <sup>2</sup> )	29.8 $\pm$ 6.1	27.8 $\pm$ 4.2	0.006
Waist girth (cm)	99.4 $\pm$ 13.8	98.6 $\pm$ 11.5	0.615
Systolic blood pressure (mmHg)	126.7 $\pm$ 16.8	122.6 $\pm$ 11.1	0.039
Diastolic blood pressure (mmHg)	74.9 $\pm$ 12.9	73.3 $\pm$ 8.6	0.274
Total cholesterol (mg/dL)	206.3 $\pm$ 46.7	211.8 $\pm$ 38.0	0.323
LDL cholesterol (mg/dL)	128.5 $\pm$ 41.1	134.5 $\pm$ 33.8	0.177
HDL cholesterol (mg/dL)	50.6 $\pm$ 15.6	47.6 $\pm$ 12.5	0.068
Triglycerides (mg/dL) <sup>c</sup>	108 (79, 171)	129 (93, 186)	0.084
Fasting glucose (mg/dL)	102.6 $\pm$ 16.3	101.1 $\pm$ 13.9	0.436
Fasting insulin ( $\mu$ IU/mL)	14.9 $\pm$ 8.4	15.2 $\pm$ 8.3	0.809
Fibrinogen ( $\mu$ mol/L)	307.9 $\pm$ 66.4	290.6 $\pm$ 70.8	0.055
C-reactive protein (mg/L) <sup>c</sup>	1.48 (0.82, 2.93)	0.92 (0.49, 1.82)	<0.001
Current smoker (%)	31.0	7.5	<0.001
Pack-years among smokers <sup>c</sup>	9.8 (5.0, 14.8)	11.0 (5.0, 22.0)	0.142
Alcohol drinker (%)	34.5	44.4	0.106
Ethanol (g/day) <sup>c</sup>	3.6 (0, 24.7)	4.9 (1.0, 15.4)	0.436
Exercise (%)	71.4	73.9	0.651
Education beyond 16 years	17.9	50.5	<0.001
Hypertension (%)	34.5	15.3	<0.001
Diabetes (%)	10.7	3.4	0.007
Lipid medications (%)	9.5	12.9	0.406

<sup>a</sup> Mean and standard deviation unless mentioned otherwise.

<sup>b</sup> CRP and fibrinogen were missing in 8 and 14 participants, respectively.

<sup>c</sup> Median and inter-quartile range.

Table 2  
Carotid intimal medial thickness (IMT) and coronary artery calcification (CAC) in black and white men

	Black (n = 84)	White (n = 295) <sup>a</sup>	p-Value
Unadjusted IMT (mean ± S.E.)			
Total IMT	0.74 ± 0.01	0.68 ± 0.01	<0.001
CCA IMT	0.75 ± 0.01	0.67 ± 0.01	<0.001
ICA IMT	0.64 ± 0.02	0.59 ± 0.01	0.024
Bulb IMT	0.83 ± 0.02	0.77 ± 0.01	0.012
Adjusted IMT <sup>b</sup> (mean ± S.E.)			
Total IMT	0.73 ± 0.01	0.68 ± 0.01	<0.001
CCA IMT	0.73 ± 0.01	0.67 ± 0.01	<0.001
ICA IMT	0.62 ± 0.02	0.59 ± 0.01	0.077
Bulb IMT	0.83 ± 0.03	0.77 ± 0.02	0.018
Unadjusted CAC (% and 95% CI)	54.8 (44.0–65.5)	51.2 (45.5–56.9)	0.564
Adjusted CAC <sup>b</sup> (% and 95% CI)	56.5 (44.7–68.3)	58.8 (51.2–66.3)	0.697

Total: average of right and left CCA, ICA, and carotid bulb. CCA: common carotid artery, ICA: internal carotid artery, and bulb: carotid bulb.

<sup>a</sup> ICA IMT data were missing for one white participant.

<sup>b</sup> Adjusted for age, BMI, systolic and diastolic blood pressure, fasting glucose, pack-years smoked, ethanol intake, HDL-C, LDL-C, triglycerides and lipid lowering medications.

Table 3  
Correlation of total and segmental carotid IMT with CAC score in black and white men

	Black (n = 84)		White (n = 295) <sup>a</sup>	
	r <sup>b</sup>	p-Value	r <sup>b</sup>	p-Value
Total IMT	0.47	<0.001	0.24	<0.001
CCA IMT	0.38	<0.001	0.22	<0.001
ICA IMT	0.27	0.014	0.22	<0.001
Bulb IMT	0.38	<0.001	0.14	0.018

Abbreviations as in Table 2.

<sup>a</sup> ICA IMT data were missing for one white participant.

<sup>b</sup> Spearman's coefficient r.

adjustment for traditional coronary risk factors and lipid lowering medications (Table 2). Spearman coefficient r was used to examine the correlation between CAC score and IMT (Table 3). Since IMT is a well-recognized surrogate marker of generalized atherosclerosis [1], we choose to

predict IMT using CAC. The presence of CAC was defined as CAC score >0. Age-adjusted general linear models were run to predict carotid IMT (total and segmental) using CAC among black and white men before and after adjustment for traditional coronary risk factors and lipid lowering medications (Table 4). The significance of race–CAC interaction term in predicting carotid IMT were tested in general linear models including both races to detect black-white differences in CAC–IMT associations. All p-values were two-tailed. p-Value <0.05 was considered as significant. SPSS software (release 14.0, SPSS Inc., Chicago, US) was used for all statistical analyses.

#### 4. Results

Table 1 shows the general characteristics of black and white men. Mean age was similar (45 years). Compared to

Table 4  
General linear models (GLM) prediction of carotid IMT (dependent variable) in the presence of CAC (predictor) in black and white men

Dependent variable	Black (n = 84)				White (n = 295) <sup>a</sup>				Inter-action p-value <sup>b</sup>
	β	95% CI	p-Value	Model R <sup>2</sup>	β	95% CI	p-Value	Model R <sup>2</sup>	
Age-adjusted mean IMT									
Total IMT	0.09	0.04–0.15	0.001	0.20	0.04	0.02–0.06	<0.001	0.07	0.023
CCA IMT	0.10	0.05–0.15	<0.001	0.15	0.03	0.01–0.05	0.004	0.07	0.009
ICA IMT	0.08	–0.01 to 0.16	0.065	0.08	0.06	0.03–0.09	0.001	0.04	0.376
Bulb IMT	0.11	0.03–0.19	0.011	0.20	0.05	0.01–0.10	0.033	0.03	0.086
Multi-adjusted mean IMT <sup>c</sup>									
Total IMT	0.07	0.01–0.13	0.024	0.28	0.03	0.01–0.05	0.039	0.12	0.046
CCA IMT	0.05	–0.01 to 0.11	0.084	0.28	0.01	–0.01 to 0.03	0.324	0.16	0.036
ICA IMT	0.07	–0.03 to 0.17	0.161	0.09	0.04	0.01–0.08	0.016	0.08	0.584
Bulb IMT	0.12	0.02–0.22	0.020	0.24	0.04	–0.01 to 0.09	0.117	0.01	0.055

Abbreviations as in Table 2.

<sup>a</sup> ICA IMT data were missing for one white participant.

<sup>b</sup> Significance of race–CAC interaction term in a model including both races.

<sup>c</sup> Adjusted for age, BMI, systolic and diastolic blood pressure, fasting glucose, pack-years smoked, ethanol intake, HDL-C, LDL-C, triglycerides and lipid lowering medications.

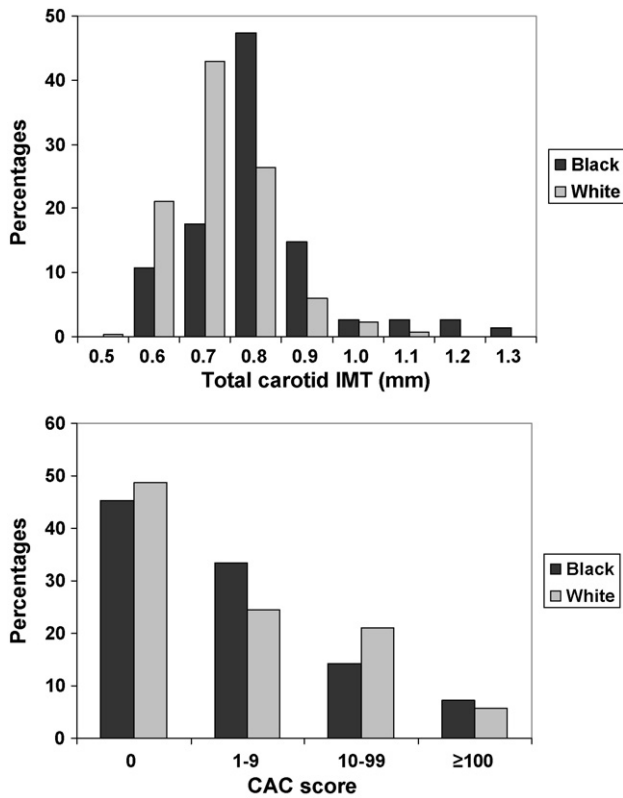


Fig. 1. Distribution of total carotid IMT (above) and CAC score (below) in black and white men.

white, black men had higher prevalence of hypertension, diabetes and current smoking but lower prevalence of higher education. Black men had higher BMI, systolic blood pressure, and C-reactive protein compared to white men. There was a trend of higher HDL-C and lower triglycerides in black compared to white men. Total cholesterol, LDL-C, lipid lowering medications and alcohol drinking were not significantly different between both populations.

Fig. 1 showed the distributions of total carotid IMT and CAC score in black and white men. The peak of IMT distribution was slightly shifted to the right in black compared to white men while the distribution of CAC score was similar in both populations. Black men had significantly higher total carotid IMT (mean ± S.E. = 0.74 ± 0.01 for black men and 0.68 ± 0.01 for white men,  $p < 0.001$ ) as well as IMT for CCA, ICA, and carotid bulb compared to white men. The differences remained significant after adjustment for traditional coronary risk factors including age, BMI, systolic and diastolic blood pressure, fasting glucose, pack-years smoked, ethanol intake, HDL-C, LDL-C, triglycerides (Table 2). The prevalence of any CAC was not significantly different between black and white men (54.8% versus 51.2%, respectively,  $p = 0.564$ ). Among those who had CAC, the median CAC score was 7 in black men (range: 1–811) and 12 in white men (range: 1–735).

CAC score in both black and white men, had significant positive correlations with total carotid IMT as well as IMT

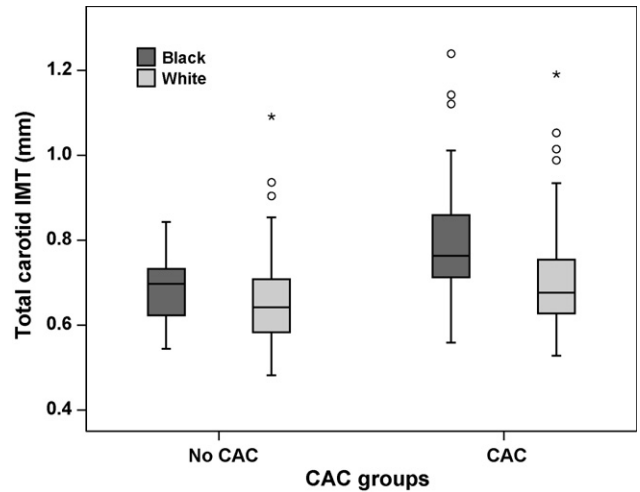


Fig. 2. Total carotid IMT (median and inter-quartile range in mm) in black and white men by CAC groups.

for CCA, ICA, and carotid bulb (Table 3). Correlations tend to be stronger in black than white men, for example, Spearman’s  $r$  for CAC score with total carotid IMT were 0.47 in black men and 0.24 in white men ( $p < 0.001$  in both). In black men, the correlation was strongest with the total carotid IMT ( $r = 0.47$ ,  $p < 0.001$ ) and least strong with IMT of ICA ( $r = 0.27$ ,  $p = 0.014$ ). In white men, the correlation was strongest with the total carotid IMT ( $r = 0.24$ ,  $p < 0.001$ ) and least strong with IMT of carotid bulb ( $r = 0.14$ ,  $p = 0.018$ ) (Table 3).

In those who had or had no CAC, total IMT was higher among black than white (Fig. 2). After adjustment for traditional coronary risk factors and lipid lowering medications, those with positive CAC in both populations had higher total and segmental carotid IMT (0.05–0.12 mm in black men and 0.01–0.04 mm in white men) (Table 4). In total and segmental carotid IMT measures tested in general linear models, the variability in carotid IMT that could be explained by coronary calcification as measured by adjusted  $R^2$  tends to be higher in black compared to white men after adjustment for traditional coronary risk factors (Table 4). The association of CAC with total and CCA IMT were significantly stronger in black than white men before ( $p = 0.023$  and  $p = 0.009$ , respectively) and after adjustment for traditional coronary risk factors ( $p = 0.046$  and  $p = 0.036$ , respectively). The association of CAC with ICA and carotid bulb IMT were stronger but not significant in black than white men (Table 4).

### 5. Discussion

To our knowledge, this is the first study that presents data for black-white specific relations of CAC with total and segmental carotid IMT measures. In both populations in the current study, CAC score had significant positive correlations with total and segmental carotid IMT. This was expected since both CAC and carotid IMT are atherosclerotic measures

that are predictive of future coronary heart disease irrespective of race [5–7]. For white men, similar to our finding, Wagenknecht et al. [11] found a significant positive correlation of IMT of CCA and coronary calcium of 0.36 among white men and women (aged 32–83 years) which was attenuated but still significant after adjusting for age, sex and diabetes. We found no study examining the association of CAC and carotid IMT among black populations.

In black and white men in this study, CAC was better correlated with the total carotid IMT than its segmental components. Most previous studies examining the association between CAC and carotid IMT [9,11,12] examined only the IMT of the CCA limiting the ability to compare CAC with total versus segmental carotid IMT. Supporting our finding, Crouse et al. reported that the mean aggregate IMT was superior to the IMT of individual carotid segments in predicting coronary artery disease as measured by coronary angiography [16].

CAC in this study was more predictive of total and CCA IMT in black than white men. We examined the associations of traditional coronary risk factors and lipid lowering medication with CAC and carotid IMT in both black and white men (data not shown). More CAC was explained in black than in white men by these risk factors ( $R^2 = 0.53$  and  $0.25$ , respectively) and similarly more total carotid IMT was explained in black than in white men by these risk factors ( $R^2 = 0.24$  and  $0.11$ , respectively). Black men who had similar CAC and higher carotid IMT would have more IMT variability to be explained by CAC. Whether race impacts the prediction of coronary events using multiple measures of subclinical atherosclerosis needs further research.

Although correlations between CAC score and carotid IMT tend to be stronger in black than white men, in both populations the correlations were not overwhelmingly high. The findings were not surprising since atherosclerosis is a diffuse disease that could affect coronary and carotid arteries to a different extent and may be at different onset. Moreover, CAC and carotid IMT measure different stages or aspects of atherosclerotic lesions in two vascular beds. Supporting our findings, a study comparing calcium deposits and IMT in the same carotid arteries also did not find a perfect correlation ( $r = 0.45$ ) [11].

Among middle age men in this study, black men had higher levels of total and segmental carotid IMT but similar prevalence of coronary calcification. Similarly, a number of studies have shown that black men had higher IMT of CCA than young [17], middle age [18] and old white populations [19]. Two population-based studies of middle aged men and women [20,21] and one prospective study in post-menopausal women [22] reported similar coronary calcification between black and white men. However, black men had lower coronary calcification in other epidemiological studies [23,24]. In one study [23], black men and women aged 45–84 with less prevalent smoking and more prevalent statins use were examined. No sex or age stratified data were presented to allow fair comparison. In the other study [24], after

stratifying data by sex in a similar age group, the lower CAC in black was significant in women but marginally significant in men. Pathologically, it has been reported that adolescent and young black men compared to their white counterparts have more extensive fatty streaks in their aorta and coronary arteries but similar raised lesions (fibrous plaques) [25] suggesting that black men have a slower progression rate of atherosclerotic lesions compared to white men. Doherty et al. [26] reported that black men suffer more CHD at a lower coronary calcium burden than white men.

One important limitation of our study is the cross-sectional design, however, both CAC and carotid IMT were reported to predict not only incident but also prevalent coronary artery disease [27]. Also, our findings can only be generalized to white and black men in their forties.

In conclusion, among men age 40–49 years in this study, black men had higher levels of total and segmental carotid IMT but a similar prevalence of coronary calcification despite a worse coronary risk. In both populations, CAC score had significant positive correlations with total and segmental carotid IMT. CAC had a stronger correlation with total carotid IMT than segmental carotid IMT. CAC was more predictive of total and CCA IMT in black than in white men independent of traditional coronary risk factors. The current data may indicate that black men could have more CHD at a lower coronary calcium burden than white men.

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