High Prevalence of Ultrasound Detected Carotid Atherosclerosis in Subjects with Low Framingham Risk Score: Potential Implications for Screening for Subclinical Atherosclerosis

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Background: The cardiovascular (CV) risk assigned by the Framingham risk score (FRS) misses many subjects destined for CV events. Coronary artery calcification (CAC) as measured by computed tomography and carotid intima-media thickness (CIMT) and plaque assessment using B-mode ultrasound can identify subclinical atherosclerosis. The comparative relation of CAC and CIMT and carotid plaque after integration into the FRS is not established. The aim of this study was to develop a CV screening approach incorporating FRS, CAC, and CIMT.

Methods: The prevalence of subclinical atherosclerosis, defined as CAC score > 0, CIMT ≥ 75th percentile, or plaque ≥ 1.5 mm, was determined in the groups with low, intermediate, and high FRS among 136 asymptomatic subjects. The CIMT and CAC values were used to determine "vascular age" and "coronary calcium" age, respectively, with established nomograms.

Results: In the 103 low-risk (FRS < 10%) subjects, 41%, 50%, 59%, and 66% had CAC scores > 0, CIMT ≥ 75th percentile, plaque ≥ 1.5 mm, and CIMT ≥ 75th percentile or plaque ≥ 1.5 mm, respectively. In the 33 subjects with intermediate (n = 14) or high (n = 19) FRS, 70%, 81%, 87%, and 87% had CAC scores > 0, CIMT ≥ 75th percentile, plaque ≥ 1.5 mm, and CIMT ≥ 75th percentile or plaque ≥ 1.5 mm, respectively. Fifty-two percent of subjects with coronary calcium scores of zero had carotid plaque. Adjusted for FRS, body mass index was an independent predictor of abnormal CIMT in the low-FRS group, but not of abnormal CAC. Mean vascular CIMT age was significantly higher than coronary calcium age (61.6 ± 11.4 vs 58.3 ± 11.1 years, P = .001), and both were significantly higher than chronologic age (56.9 ± 10.1 years) (P < .0001 and P < .04, respectively). CIMT upgraded or downgraded FRS by >5% in more cases than CAC (42% vs 17%).

Conclusion: In asymptomatic patients without CV disease, CIMT and plaque assessment are more likely to revise FRS than CAC. Body mass index predicts increased CIMT in low-FRS subjects. These findings may have broad implications for screening in low-FRS subjects. (J Am Soc Echocardiogr 2010;23:809-15.)

Keywords: Plaque, Imaging, Atherosclerosis, Intima media thickness, Coronary calcium score

Atherosclerosis is a common and often lethal disease of the arteries of the heart, brain, and periphery. Many patients with atherosclerosis, even those with severe disease, are asymptomatic and thus unaware of its presence. In 40% to 60% of these individuals, the first indicator of atherosclerosis is an acute myocardial infarction or sudden death.[1] Although potentially modifiable risk factors account for a majority of the population-attributable risk for an initial myocardial infarction,[2,3] many patients with similar risk factors never develop myocardial infarctions. Similarly, cardiovascular (CV) events continue to occur in patients who harbor unrecognized atherosclerosis but are not receiving risk-reducing preventive therapies because they had been misclassified by conventional risk factors and assigned treatment goals not in line with their individual burden of atherosclerosis. Because there are many effective pharmacologic and nonpharmacologic therapies, the early detection of atherosclerosis itself before symptoms occur could provide a major opportunity to prevent many CV events.

Population-based screening tools such as the Framingham risk score (FRS) assign a risk probability, which is effective in assigning risk to populations but is not particularly helpful for individual risk assessment, especially in those at risk for near-term events. Several

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Abbreviations

ARIC = Atherosclerosis Risk in Communities

BMI = Body mass index

CAC = Coronary artery calcification

CI = Confidence interval

CIMT = Carotid intima-media thickness

CV = Cardiovascular

FRS = Framingham risk score

MESA = Multi-Ethnic Study of Atherosclerosis

OR = Odds ratio

imaging modalities are currently available that can identify subclinical atherosclerosis long before CV events occur and have the potential to identify subjects at high risk in need of aggressive intervention and spare those at low risk from the unnecessary use of aggressive therapy. Unlike risk factors, anatomic measures of the intima-media thickness of the carotid artery wall (CIMT) and/or carotid plaque in adulthood and coronary artery calcification (CAC) measured by computed tomography, two of the most commonly used noninvasive techniques to detect subclinical atherosclerosis, represent the cumulative effects of an individual's exposure over years to known and unknown (proatherogenic as well as atheroprotective) risk modifiers.[4-9] The prognostic value of subclinical atherosclerosis detection has been shown to be greater than conventional risk factors such as low-density lipoprotein, high-density lipoprotein cholesterol, total cholesterol, systolic and diastolic blood pressure,[10] diabetes, fasting glucose and insulin, reduced insulin sensitivity,[11] active and passive smoking,[12] and body mass index (BMI), and triglycerides.[13,14] The purpose of this study was to determine comparative prevalence of carotid and coronary atherosclerosis and their respective utility in changing FRS in an asymptomatic adult population.

METHODS

Patient Selection

This study included consecutive asymptomatic individuals aged >18 and <90 years who underwent both CAC and CIMT evaluation at our institution between October 2002 and October 2006. The mean time interval between CAC and CIMT evaluation was 1.1 ± 1.6 years. Those whose image quality for CIMT (n = 4) was suboptimal were excluded from the study. Those with histories of CV events in the coronary, peripheral, or cerebral vascular territory were excluded. The study protocol was approved by the institutional review board of Cedars Sinai Medical Center.

Computed Tomographic Coronary Calcium Score

Scanning was performed using either electron-beam tomography or multislice computed tomography, with acquisitions consisting of approximately 30 to 40 3-mm or 2.5-mm slices for the two tomographic systems, respectively.[15] Foci of CAC were identified and scored by an experienced technician, blinded to patient characteristics, using semiautomatic commercial software on a Netra MD workstation (ScImage, Los Altos, CA) by the detection of ≥3 contiguous pixels (voxel size, 1.03 mm^3) of peak density >130 Hounsfield units within a coronary artery, with scoring verified by an experienced imaging cardiologist. CAC scores were calculated according to the method of Agatston et al,[16] and age-adjusted and sex-adjusted CAC scores were determined according to the database of Raggi et al.[17]

CIMT

Carotid artery imaging was obtained using an ATL 5000 ultrasound system (Philips Medical Systems, Bothell, WA) with an 8-MHz to 15-MHz linear-array transducer. A depth of 4 cm was used and kept constant throughout study. Cine loops were acquired of the common carotid artery, bulb, and internal carotid artery on both the right and left sides at 4 different angles (180°, 150°, 120°, and 90° on the right and 180°, 210°, 240°, and 270° on the left). An additional 60° angle on the right side and 300° angle on the left side were used if CIMT was measurable in only 1 of the 4 angles on each side or if maximum disease was found at these very posterior angles. The near and far walls of the common carotid artery were acquired in the same image, whereas separate images were acquired each to show the near and far walls of the bulb and internal carotid artery at each angle on both sides. CIMT measurements were made offline by freezing frames at the R wave of the electrocardiogram and ensuring clear visualization of the boundaries between the intimal layer and carotid artery lumen and between the medial adventitial layer. Multiple measurements were made by the physician (T.Z.N.) and sonographer (M.G.) of the near and far walls of the distal 1 cm of the common carotid artery, the near and far walls of the carotid bulb, and the near and far walls of the proximal 1 cm of the internal carotid artery in each of the individual angles. A manual tracing was performed between the intimal layer and carotid artery lumen and between the medial adventitial layer, and mean, minimum, and maximum values were derived for each measurement. Any amount of CIMT thickness was included in the measurement. Offline analysis was performed on a Camtronics (Bothell, WA) workstation equipped with vascular analysis software. A mean value of CIMT was calculated on the basis of average of all the measurements (≥18 total measurements on each side) and was used for CIMT analysis. Using data from the Atherosclerosis Risk in Communities (ARIC) study,[5] the composite CIMT from the far wall of all segments of the left and right carotid arteries was used to calculate an age-matched, sex-matched, and race-matched. In 15 randomly selected images used for CIMT measurement, intraobserver variability was 2.3 ± 4%, and interobserver variability was 3.2 ± 2%.

We defined plaque as a focal structure that encroached into the arterial lumen, demonstrating a thickness of ≥ 1.5 mm as measured from the media-adventitia interface to the intima-lumen interface[18] and was 50% greater than the surrounding CIMT value. Bilateral composite mean CIMT only included plaques at the far wall of the common and internal carotid arteries and bulb (as done in the ARIC protocol), but separate evaluation of plaque presence ≥ 1.5 mm also included plaque in the near walls of the common and internal carotid arteries and bulb bilaterally. Thus, plaque assessment incorporated additional near wall segments to those assessed by CIMT. Investigators performing CIMT and plaque assessment were blinded to the CAC results.

Vascular Age

The CIMT and CAC values were used to determine "vascular age"[19,20] and "coronary calcium" age,[21] respectively, with established nomograms.

FRS

FRS and other variables were obtained through clinical and laboratory data review at the time of CAC and CIMT evaluation[22] to evaluate the 10-year risk for coronary heart disease.

Statistical Methods

Mean composite far wall CIMT was converted on the basis of the ARIC study nomogram. Abnormal CIMT was defined as ≥75th percentile for age, race, and gender or by the presence of plaque ≥ 1.5 mm. Two cutoff values for abnormal CAC were defined, an absolute score > 0 as well as coronary calcium score > 75th percentile. Although CAC score > 0 indicates the presence of atherosclerosis, CIMT increases progressively with age, and hence no single cutoff value defines abnormal CIMT. We therefore used the most widely reported method denoting abnormal CIMT, that of ≥75th percentile for age, race, and gender. BMI was categorized as 20 to <25, ≥25 to <30, and ≥30 kg/m^2. Obesity was defined as a BMI ≥ 30 kg/m^2. Spearman's ρ correlation of FRS was performed with CIMT and CAC score = 0 versus CAC score > 0 in the entire group as well as in subsets with low, intermediate, and high FRS defined as FRS 0 to <10, 10 to 20, and >20. One-way analysis of variance and Pearson's χ^2 tests were performed to identify potential predictors of abnormal CAC or CIMT. Univariate predictors were then entered into a logistic regression model. Multiple models were tested adjusting for FRS, the presence or absence of a family history of coronary disease, the use of statins, BMI, and age. Odds ratios (ORs) and 95% confidence intervals (CIs) between predictor variables and outcome variables were derived. Vascular and coronary calcium ages were substituted for chronologic age to obtain CIMT-derived vascular FRS and CAC-derived FRS. Student's *t* test and Spearman's correlation were performed to compare and correlate differences in calculated ages and risk. Data are summarized as mean ± SD or frequencies and percentages.

RESULTS

Baseline Characteristics

Two hundred seventy-seven consecutive patients referred for CIMT evaluation at our institution were initially screened. Of these, 136 had no known CV disease and also underwent CAC assessment before or after the CIMT study. The mean age was 56.7 ± 10.9 years, and 57% were men. Ninety-two percent were Caucasian, 4% were black, 3% were Hispanic, and 1% were Asian. Baseline characteristics of the study population are listed in Table 1. The mean FRS of the study population was 5.9 ± 6 (range, 0.1-29) and the mean CAC score was 152 ± 549 (range, 0-5205). The mean far wall composite CIMT was 0.821 ± 0.206 mm (range, 0.48-1.52 mm), and the mean CIMT percentile was 53 ± 21 (range, 10-95). There were 60 patients with far wall plaques and 30 with near wall plaques. There were 103 subjects with low FRS, 14 with intermediate FRS, and 19 with high FRS.

Chronologic Age Versus Vascular Age

The mean vascular CIMT age (61.6 ± 11.4 years) and coronary calcium age (58.3 ± 11.1 years) were significantly different (P = .001), and both were higher than mean chronologic age (57.4 ± 11 years) (P < .0001 and P < .04, respectively). CIMT upgraded or downgraded FRS by >5% in more cases than CAC (42% of CIMT cases vs 17% of CAC cases). The correlation of FRS with mean far wall CIMT was 0.49 (P < .0001), and the correlation of FRS with CAC was 0.47 (P < .0001). Table 2 shows the effect of CIMT and CAC evaluation on the distribution of FRS category. As shown, CIMT upgraded more subjects to intermediate-risk and high-risk categories among the 103 low-FRS subjects. Both tests readjusted FRS in the intermediate-FRS and high-FRS groups. There was complete agreement between CIMT-adjusted FRS and CAC-adjusted FRS in 91 subjects (76 at low risk, 11 at intermediate risk, and 4 at high risk by CAC and CIMT).

Table 1 Baseline characteristics of the study population (n = 136)

Variable	Value
Age (y)	57.4 ± 11 (34-87)
LDL cholesterol (mg/dL)	109 ± 38 (43-219)
HDL cholesterol (mg/dL)	62 ± 20 (28-120)
Total cholesterol (mg/dL)	194 ± 46 (99-318)
Triglycerides (mg/dL)	109 ± 63 (35-398)
Men	78 (57%)
Hypertension	62 (46%)
Obese	27 (20%)
Smoker	12 (9%)
Prior tobacco use	44 (32%)
Family history	52 (38%)
On statins	59 (44%)

Data are expressed as mean ± SD or as number (percentage).
HDL, High-density lipoprotein; *LDL*, low-density lipoprotein.

Table 2 Effect of IMT and CAC on FRS

	IMT FRS			
	FRS<10%	FRS 10-20	FRS>20%	Total
FRS<10%	78	23	2	103
FRS 10-20%	3	7	4	14
FRS>20%	8	6	5	19
Total	89	36	11	136
	CAC FRS			
	FRS<10%	FRS 10-20	FRS>20%	Total
FRS<10%	88	14	1	103
FRS 10-20%	5	7	2	14
FRS>20%	9	6	4	19
Total	102	27	7	136
	CAC FRS			
IMT FRS	FRS<10%	FRS 10-20	FRS>20%	Total
FRS<10%	76	11	2	89
FRS 10-20%	24	11	1	36
FRS>20%	2	5	4	11
Total	102	27	7	136

FRS, Framingham Risk Score; *IMT FRS*, Vascular age-adjusted FRS; *CAC FRS*, CAC age-adjusted FRS.

FRS, Coronary Calcium Score, and Carotid Plaque in the Overall Population

Table 3 shows the prevalence of atherosclerosis in the study population. The mean FRS for those with carotid plaque versus those without plaque was 7.0 ± 7.0 versus 4.0±3.0 (P < .01). The OR for FRS to predict carotid plaque was 1.13 (95% CI, 1.03-1.23; P = .01). Carotid plaque was present in 52%, 81%, and 89% in those with CAC scores of 0, 1 to 99, and >100, respectively (P for trend

Table 3 Distribution of subclinical atherosclerosis in the study population

Variable	n (%)
Plaque ≥ 1.5 mm	90 (66)
Plaque ≥ 1.5 mm (CAC score = 0)	26 (52)
CIMT ≥ 75th percentile	43 (32)
CIMT ≥ 75th percentile or plaque ≥ 1.5 mm	97 (71)
CAC and IMT< 75th percentile	78
CAC ≥ 75th percentile only	15
Both CAC&CIMT>75th percentile	11
CAC score = 0	71 (52)
CAC score = 1-99	33 (24)
CAC score > 100	32 (24)

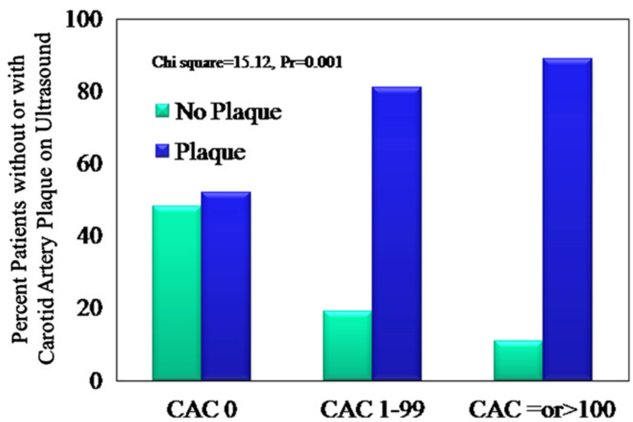

Figure 1 Bar graph showing the relationship between carotid plaque and CAC. Plaques was defined as a focal protrusion of intima-media ≥ 1.5 mm and >50% of the neighboring segment. There is increasing prevalence of carotid plaques with increasing CAC scores.

= .002; Figure 1), but the prevalence of CIMT ≥ 75th percentile did not increase with progressively increasing CAC (Figure 2). In multiple logistic regression analysis, adjusted for FRS, the odds of carotid plaque were greater for a CAC score of 1 to 99 (OR, 3.22; 95% CI, 1.14-9.11; $P < .03$) and CAC score > 100 (OR, 5.35; 95% CI, 1.37-20.8; $P < .02$) compared with a CAC score of 0. The areas under the receiver operating characteristic curve for predicting the presence of carotid plaque were 62% for FRS and 72% when CAC was added to FRS ($P < .02$). BMIs were significantly higher in subjects who had atherosclerosis by both CAC score > 0 and CIMT ≥ 75th percentile (29.2 ± 5.1 kg/m^2) compared with those without atherosclerosis by both tests (25.6 ± 3.8 kg/m^2). Those with CAC scores > 0 only (26.1 ± 4.2 kg/m^2) or CIMT ≥75th percentile only (26.5 ± 5.6 kg/m^2) had intermediate BMIs ($P < .01$ within groups). In the subgroup with BMIs < 25 kg/m^2, there was a progressive decrease, and in subgroups with BMIs ≥ 30 kg/m^2 (obese subjects), there was a progressive increase in subclinical atherosclerosis detected by both CAC and CIMT (Figure 3).

Discrepancies in Atherosclerosis Detection by CAC, CIMT, and Plaque

Fifty-two percent of patients with CAC scores of 0 had documented carotid plaque, whereas 13% of subjects (n = 17) with CIMT ≥ 75% percentile had CAC scores of 0 ($P = .03$, $\chi^2 = 4.8$). Only 11% of subjects had CAC ≥ 75th percentile without abnormal CIMT or presence of plaque. When CAC score > 0 was considered abnormal, 32% of subjects (n = 42) had CIMT ≥ 75th percentile or plaque but normal CAC, and only 8% (n = 11) had abnormal CAC but normal CIMT and no plaque. Forty percent (n = 54) were positive and 21% (n = 28) were negative by both tests. When CAC ≥ 75th percentile was considered abnormal, 57% subjects (n = 77) had CIMT ≥ 75th percentile or plaque but normal CAC, and only 5% (n = 8) had abnormal CAC but normal CIMT and no plaque. Fifteen percent (n = 20) were positive and 23% (n = 31) were negative by both tests. When the plaque cutoff was increased to 2 mm rather than 1.5 mm and a CAC score > 0 was considered abnormal, the tests performed more comparably. Thus, 30% of patients (n = 41) were positive by both tests, 34% (n = 46) were negative by both tests, 18% (n = 25) were positive by ultrasound, and 18% (n = 24) were positive by CAC. There was variability in the distribution of atherosclerosis for CIMT as well. Thus, focal atherosclerosis with plaque was found in 66% of subjects, whereas CIMT ≥ 75th percentile was present in only 32%.

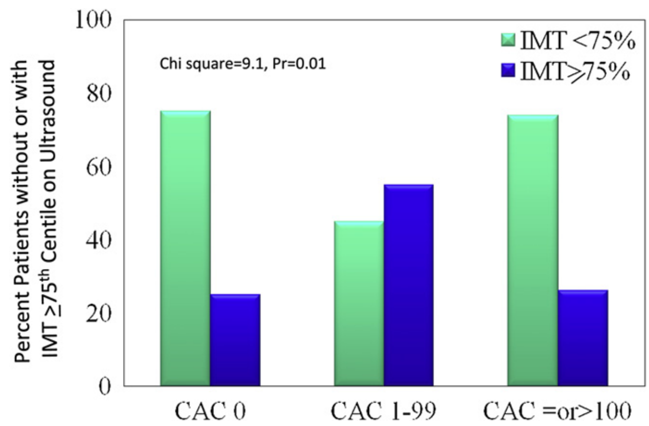

Figure 2 Bar graph showing the relationship between CIMT and CAC. Abnormal CIMT was defined as ≥75th percentile of age-adjusted, race-adjusted, and gender-adjusted norm. Unlike the relationship of CAC with carotid plaque, the relationship with CIMT was weaker and nonlinear.

Carotid Atherosclerosis and CAC in Low-Risk Group

In the 103 subjects constituting the low-risk group, 41%, 50%, 59%, and 66% had CAC scores > 0, CIMT ≥ 75th percentile, plaque ≥ 1.5 mm, and CIMT ≥ 75th percentile or plaque ≥ 1.5 mm, respectively. In the 33 intermediate-risk or high-risk subjects, CAC scores > 0 were present in 70%, CIMT ≥ 75th percentile in 81%, plaque ≥ 1.5 mm in 87%, and CIMT ≥ 75th percentile or plaque ≥ 1.5 mm in 87%. Among the low-risk group, patients with plaques (n = 61) were significantly older (57.6 ± 9.5 years) compared with those without plaques (n = 42) (51.2 ± 8.6 years) ($P < .001$), without differences in gender, BMI, family history of CV disease, CAC score, systolic or diastolic blood pressure, total cholesterol, high-density lipoprotein, low-density lipoprotein, or triglycerides. On logistic regression analysis using FRS, BMI, and gender, BMI was the only predictor of CIMT ≥ 75th percentile in the low-risk group (OR, 1.19; 95% CI, 1.04-1.36; $P < .01$). None of the variables were predictors of CAC score > 0 in the low-risk group. There was higher statin use among those with plaques (OR, 2.5; 95% CI, 0.97-6.6; $P = .060$) and CAC scores > 0 (OR, 4.2; 95% CI, 1.7-9.6; $P < .01$).

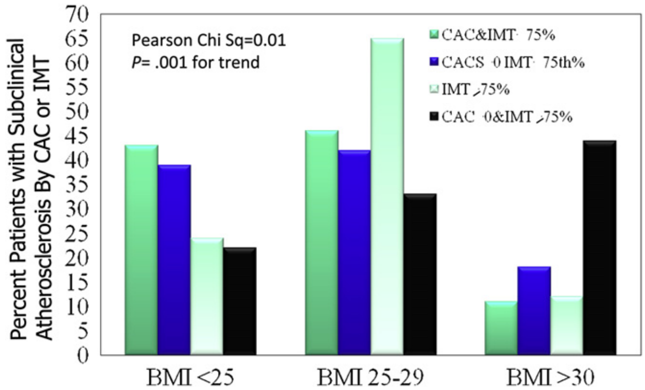

Figure 3 Bar graph showing the prevalence of subclinical atherosclerosis across 3 groups of increasing BMI. Note a decreased severity of atherosclerosis by both CAC and IMT for BMI < 25 kg/m^2 and an increase in atherosclerosis severity by both CAC and IMT for BMI > 30 kg/m^2.

DISCUSSION

The principal finding of this study is that a significant percentage of individuals irrespective of FRS have subclinical atherosclerosis on imaging evaluation by ultrasound and CAC. CIMT upgraded more patients to intermediate and high risk than CAC. BMI was an independent predictor of abnormal CIMT, but not abnormal CAC in the low-risk group. Both CAC or CIMT with or without plaque assessment found high prevalence of atherosclerosis in the intermediate-risk and high-risk groups.

CIMT assessment along with evaluation of all segments of the carotid arteries, including the near and far walls, for the presence of a focal plaque is most likely to detect subclinical atherosclerosis in the low-risk group.[23]

Both tests have been recommended as screening tools among asymptomatic subjects.[24] Ultrasound is more readily available, is portable, involves no radiation (unlike the CAC scan),[25] and picks up earlier abnormalities. In addition, nonsonographers can be trained to perform it effectively,[26] and it can be repeated without risk. However, CIMT evaluation is more operator dependent than CAC, and its measurement is labor intensive. Carotid plaque assessment is not as standardized as CIMT or CAC. CAC assessment, on the other hand, is a more objective and reproducible measurement but is associated with radiation. The combination of CIMT and CAC could be considered in some patients, depending on the results of the first test. If either test's results are abnormal, subjects would be aggressively treated (by lifestyle adjustment and medications), but if the results are negative, subjects would be considered at very low risk and unlikely to benefit from pharmacotherapy for dyslipidemia. Our findings suggest that CIMT may find atherosclerosis in those with BMIs $\geq$ 30 kg/m^2 and those who are deemed at low risk.

Our findings suggest that as many as 66% of subjects with low FRS have subclinical atherosclerosis by CIMT and plaque assessment. The significance of a higher rate of detection of atherosclerosis in the low-risk group remains unclear from our study. Many population-based studies that have examined the relations of CIMT and the presence of focal plaque to CV disease morbidity and mortality[3-5,27,28] have shown that increased CIMT is a powerful predictor of coronary and cerebrovascular complications (unadjusted risk ratio, 2-6), although adjustment of risk factors makes this association less powerful.[3] A recent study found that adding CIMT and plaque to FRS improved the prediction of coronary heart disease in the ARIC study.[29] Although a high CAC score predicts increased risk for adverse CV events, a CAC score of 0 may be associated with increased events with increasing FRS.[30] The findings of a prevalence of CAC score > 0 in 32% of women with low FRS in the Multi-Ethnic Study of Atherosclerosis (MESA) and a >5-fold incidence of CV events in this group support the evaluation of atherosclerosis in those with low FRS.[31] Although we did not evaluate effects on outcome, aggressive lipid lowering in the presence of low FRS and increased CIMT has been shown to affect CIMT-a surrogate marker for atherosclerosis.[32]

CIMT, CAC, and Age

Although both CIMT and CAC are able to characterize subclinical atherosclerosis, the results of the two tests are only weakly correlated, possibly because coronary calcification represents a more advanced stage of vascular disease.[33] A prior study among older adults showed that a significant minority did have increased CAC that was associated with <80th percentile of age-predicted CIMT.[33]

Carotid Plaque as a Predictor of Subclinical Atherosclerosis

Plaque area and volume are generally considered better predictors of atherosclerotic disease rather than CIMT, the primary contributors to which are age and hypertension.[34] More reliable quantitative indicators such as plaque area, volume, percentage stenosis, degree of calcification, and plaque echolucency may better characterize the distinct lesion phenotypes of atherosclerosis.[34,35] One study in >2000 patients found that approximately 44% of the low-risk individuals by FRS had a 10-year vascular risk of 18.3% in the presence of carotid plaque thickness > 1.9 mm, and subjects with carotid plaques had a 2.8-fold increased risk for combined vascular events in comparison with subjects without carotid plaque.[36] In light of the high prevalence of plaque and because of the higher predictive value of plaque for incident CV disease, it may be appropriate to screen for the presence of plaque by ultrasound in low-risk subjects. If plaque is identified, no further evaluation may be necessary; otherwise, complete bilateral CIMT assessment should be performed. It is to be noted, however, that we performed a very comprehensive evaluation by ultrasound that made image acquisition and analysis labor intensive, which may be difficult to implement in clinical practice.

Limitations

The findings of this study represent an observation, and the definitive impact of an intervention was not tested. However, large outcome, primary prevention treatment trials of middle-aged individuals with defined atherosclerosis on the basis of a measure of CIMT or CAC will likely not be performed given the expense involved as well as the dilemma of withholding treatment from those with subclinical atherosclerosis. Clinicians may therefore use some approach other than clinical risk assessment alone for individual patient care. CAC and CIMT evaluations were on average 12 months apart, but this should not significantly detract from study findings given the slow progression of subclinical atherosclerosis. Forty-four percent of the subjects were receiving lipid-lowering treatment, which may have influenced study results. Although the duration of statin use was not recorded in patients' histories, most patients started statins after CIMT or CAC results, so lipid-lowering treatment is not expected to have influenced findings on imaging evaluation. Subjects in the study may represent a biased and health-conscious group who sought

CV risk evaluation despite being asymptomatic and having intermediate to low FRS. The group also likely represents subjects of higher socioeconomic status, considering that both screening tests required out-of-pocket expense of approximately $800 ($400 each). The Agatston method to measure coronary calcium uses attenuation cofactors determined at a 3-mm slice thickness, although it now possible to obtain subcentimeter resolution. Using subcentimeter resolution may detect very low levels of coronary calcium in some individuals with CAC scores of 0 on the basis of the Agatston method. However, given the large volume of published literature based on the Agatston method, this method continues to be used in clinical practice. Finally, our study findings are confined largely to Caucasians, who formed the bulk of study population.

CONCLUSIONS

In our study, comprising predominantly Caucasians adults, subclinical atherosclerosis as defined by CAC and CIMT was more prevalent that that suggested by the FRS, and vascular age was higher compared with chronologic age. CAC correlated better with the presence of carotid artery plaque than CIMT > 75th percentile. A significant number of subjects had carotid artery plaque despite the presence of CAC scores of 0. In low-risk subjects, initial screening by CIMT and plaque assessment is likely to provide the highest yield to detect subclinical atherosclerosis.

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