A Comparison of Assessment of Coronary Calcium vs Carotid Intima Media Thickness for Determination of Vascular Age and Adjustment of the Framingham Risk Score

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CLINICAL STUDY

A Comparison of Assessment of Coronary Calcium vs Carotid Intima Media Thickness for Determination of Vascular Age and Adjustment of the Framingham Risk Score

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The Framingham Risk Score (FRS) has become the standard tool to determine coronary heart disease (CHD) risk. Recent studies have demonstrated that FRS underestimates CHD risk in a number of patient populations. One strategy that has been proposed to improve the diagnostic accuracy of FRS is to use imaging of subclinical atherosclerosis to define a "vascular age" and use this age to calculate FRS. Both computed tomography assessment of coronary artery calcium (CAC) and ultrasonographic assessment of carotid intima-media thickness (CIMT) have been proposed as modalities that can be employed to assess vascular age. In the present study, the authors compared CAC vs CIMT for the assessment of vascular age and adjustment of FRS. In the cohort as a whole, CAC- and CIMT-derived vascular age correlated well. Further study is needed to verify the accuracy of vascular age–adjusted FRS using both CAC and CIMT and to determine whether there are specific patient demographics that favor either imaging modality. **Prev Cardiol.** *2010;13:117–121.*

The Framingham Risk Score (FRS) has become the standard tool to determine coronary heart disease (CHD) risk. The FRS uses an assessment of a patient's traditional risk factors to arrive at an estimated 10-year risk of CHD. Recent studies have suggested that FRS may underestimate CHD risk in a variety of patient demographics.[1–3] As a result, a variety of diagnostic tools have been developed that are aimed at defining CHD risk with greater sensitivity than FRS.[4–6] In recent years, the development of methods for direct visualization of subclinical atherosclerosis has shown promise as a means of better defining CHD risk by detecting early asymptomatic disease. Two of the most promising techniques for the determination of subclinical atherosclerosis include computed tomography coronary calcium scoring (CAC)[7] and B-mode ultrasonographic assessment of carotid intima-media thickness (CIMT).[8] Both of these techniques have demonstrated an increased sensitivity for the detection of CHD risk vs traditional risk factor analyses.[9]

While CIMT or CAC assessment improves upon our ability to detect early disease, an unresolved issue in the field of atherosclerosis imaging is how to integrate the findings of these imaging studies into a patient's overall risk profile. A novel approach that has recently been proposed is the use of CIMT or CAC to define a patient's vascular age, or the age at which the individual's measurement would represent the 50th percentile of a reference database.[10] By redefining a person's age according to the results of CIMT or CAC and using this vascular age to calculate FRS, one may be able to better define the likelihood of CHD developing beyond traditional risk factors. While CIMT and CAC have both been utilized to develop a vascular age, few data are available comparing these 2 modalities.[11] The goal of the present study was to compare the results of vascular age assessments and resultant adjustments in FRS in individual patients using both CAC and CIMT.

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Table. Clinical Characteristics of the Study Cohort

	Mean	Range
Age, y	55	38–79
Male, %	60	N/A
History of hypertension, %	60	N/A
Smoker, %	15	N/A
Total cholesterol, mg/dL	206	130–490
LDL-C, mg/dL	117	70–178
HDL-C, mg/dL	44	28–59
Framingham Risk Score	12	1–18
Framingham 10-y event (%)	9	1–30
Calcium score, Agatston units	127	0–1411
CAC-adjusted age, y	65	38–152
CIMT, mm	0.78	0.57–1.10
CIMT-adjusted age, y	68	42–104

Abbreviations: CAC, coronary artery calcium; CIMT, carotid intima-media thickness; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

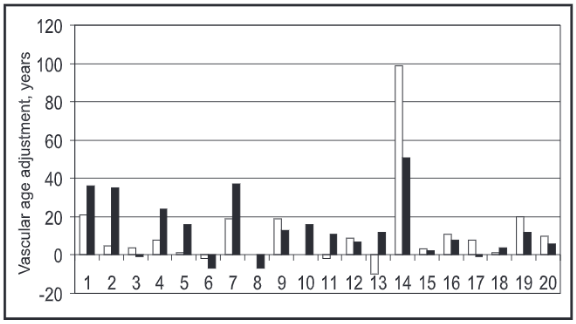

Figure 1. Comparison of age adjustments for individual subjects using coronary artery calcium (CAC; white bars) and carotid intima-media thickness (CIMT; black bars). Numbers on the x-axis represent individual patients (P=.989 for age adjustment in years for entire cohort, CAC vs CIMT).

METHODS

Patients (n=20) underwent both CAC and CIMT assessments within a 30-day period. Patients were recruited from those who had been referred for CAC assessment by their primary physician. Patients were excluded if they had a history of carotid artery disease by prior carotid imaging or had undergone carotid surgery in the past.

Gated non-contrast CAC examination was performed using a 64-slice GE LightSpeed VCT Scanner (General Electric Medical Systems, Milwaukee, WI). Images were obtained at 2.5 mm and reconstructed at 2.5 mm. A coronary calcium score was obtained from scan data using a GE Advantage Windows 4.2 post-processing workstation. CIMT data were obtained using standard ultrasound equipment with a 12-mHz linear array vascular ultrasound probe and offline CIMT software with automated edge-detection (Phillips Imaging Systems, Bothell, WA). Mean integrated CIMT was calculated for 1 cm of the far wall of the distal common carotid artery from each of 6 imaging planes (3 each for the left and right carotid). The maximum of the 6 mean integrated CIMT measurements was reported.

CAC and CIMT were then converted to a corresponding vascular age using linear regression equations derived by the authors using data from the Multiethnic Study of Atherosclerosis (MESA)[12] for CAC and Atherosclerosis Risk in Communities Study (ARIC)[13] for CIMT, respectively.

Statistical Analysis

Correlations between CAC and CIMT were performed using Pearson correlation. Direct comparisons were performed using a Student *t*-test (for data with normal distribution). When comparisons were made between CAC scores and other data sets, a Mann-Whitney rank sum test was utilized due to the non-normal distribution of CAC across the patient population. For all statistical analyses, a P value $<.05$ was considered statistically significant. Statistical analyses were performed on SigmaStat 3.1 Software (Systat, San Jose, CA).

RESULTS

Twenty patients were enrolled in the study and completed both CAC and CIMT assessments. Clinical characteristics of the study population are summarized in the Table. The mean age was 55.8 years (range, 41–79) and the median FRS was 12 (range, 1–18), yielding a median FRS 10-year predicted CHD event rate of 5% (range, <1%–30%). Based on clinical data, 10 patients (50%) had a "low" FRS 10-year event rate (0%–5%), 6 (30%) had an "intermediate" FRS 10-year event rate (6%–20%), and 4 (20%) had a "high" FRS 10-year event rate (≥21%).

The median CAC score was 24 (range, 0–1411) and median CIMT was 0.675 mm (range, 0.570–1.100 mm). When CAC was used to calculate a vascular age, a mean vascular age of 67 was obtained, or an average addition of 11.3 years to the mean chronological age of 55.7 (P=.011). When CIMT was used to calculate vascular age, a mean vascular age of 68.5 was obtained, or an average addition of 12.8 years to the mean chronological age (P=.016). Thus, both CAC and CIMT yielded vascular ages that added significantly to the chronologic ages of the cohort as a whole.

The magnitude of the age correction was similar for both CAC and CIMT. Within individual patients, there were varying degrees of discordance with regard to the vascular age adjustments obtained with CAC vs CIMT, although the 2 techniques did not yield significantly different age adjustments for the cohort as a whole (Figure 1). Furthermore, when directly compared, the vascular

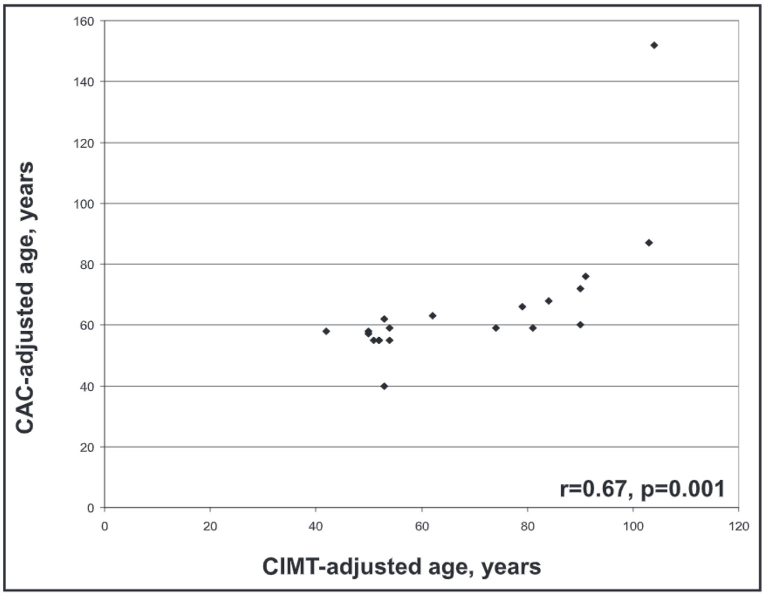

Figure 2. Correlation of adjusted age using coronary artery calcium (CAC) vs carotid intima-media thickness (CIMT) in years (Pearson correlation, r=.67, P=.001*).*

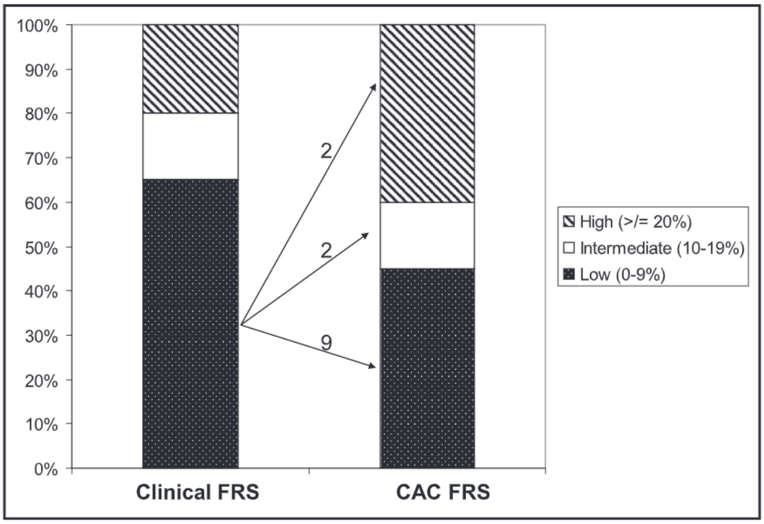

Figure 3. Breakdown of unadjusted vs coronary artery calcium (CAC)–adjusted Framingham Risk Score (FRS).

age data obtained from CAC and CIMT showed highly significant correlation (Figure 2).

In order to have an impact on clinical decision making, the use of CAC or CIMT to adjust the FRS would need to have an impact on the overall assessment of cardiovascular risk. Examination of individual FRS adjustments demonstrated that the use of CAC resulted in the reclassification of 4 of 13 (31%) patients classified as low-risk by the standard FRS (Figure 3; 2 reclassified as moderate-risk, 2 reclassified as high-risk). Similarly, the use of CIMT resulted in the reclassification of 5 of 13 (38%) patients classified as low-risk by the standard FRS (Figure 4; 4 reclassified as moderate-risk, 1 reclassified as high-risk). When results of FRS readjustment by CAC vs CIMT on individual patients were compared, adjusted risk was concordant in 15 and discordant in 5, including 2 patients assessed as low-risk by CAC and intermediate-risk by CIMT, 2 patients assessed as high-risk by CAC and intermediate-risk by CIMT, and 1 patient assessed as intermediate-risk by CAC and low-risk by CIMT (data not shown).

DISCUSSION

Our study is to the best of our knowledge the first comparative study of the effect of utilization of vascular age algorithms using CAC and CIMT on the

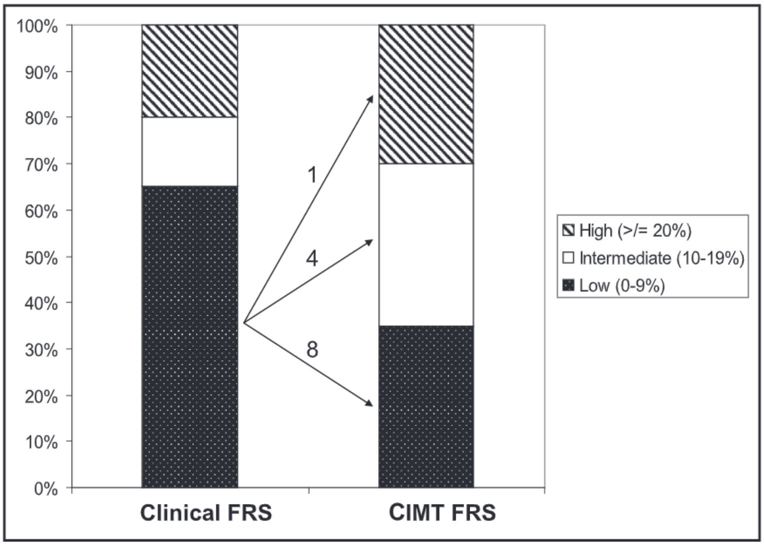

Figure 4. Breakdown of unadjusted vs carotid intima-media thickness (CIMT)–adjusted Framingham Risk Score (FRS).

FRS. The concept of using vascular age in place of chronologic age is based on the theory that the assessment of subclinical atherosclerosis by direct vascular imaging and conversion of a patient's chronologic age to the age at which the amount of that patient's subclinical atherosclerosis represented an "average value" would lead to a more accurate assessment of a patient's true cardiovascular risk.[14] In our patient cohort, vascular age adjustments using both CAC and CIMT increased overall cardiovascular risk in the majority of patients as assessed by the FRS. In addition, CAC and CIMT appeared to yield similar information with regard to assessment of vascular age and adjustment of FRS for the presence of subclinical atherosclerosis. Notably, however, our small sample assessment of CAC and CIMT yielded discordant data in several individuals. The specific characteristics of these patients and, more important, the explanation behind these discordant results cannot be elucidated in our small sample size. In addition, because the present study did not follow patients to the occurrence of events, comparative accuracy of the 2 techniques cannot be assessed. Further studies are required to better define the patient characteristics that lead to discordant assessments when subclinical atherosclerosis is assessed by CAC vs CIMT and to define guidelines for the selection of imaging modality based on individual patient characteristics.

While the obvious major limitation to this study is its small sample size, the fact that CAC and CIMT were strongly correlative suggests that a strategy of adjusting FRS using vascular imaging is possible using either technique. As a cohort study comparing CAC and CIMT, longitudinal outcome data are of course not available. A recent analysis of the MESA data suggested that CAC assessment has superior sensitivity to CIMT for detection of subclinical atherosclerosis and cardiac risk[15]; however, prior studies have produced conflicting results on this issue.[16] Furthermore, no study to date has examined the validity of vascular age adjustment of FRS in the prediction of CHD events. Clearly, prospective studies to further evaluate the contribution of vascular age determinations based on CIMT and CAC to coronary risk assessment are warranted.

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