ORIGINAL RESEARCH

Comparison of Carotid Plaque Score and Coronary Artery Calcium Score for Predicting Cardiovascular Disease Events: The Multi-Ethnic Study of Atherosclerosis

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***Background*—**Coronary artery calcium (CAC) predicts coronary heart disease (CHD) events better than carotid wall plaque presence; however, differences in the utility of CAC burden and carotid plaque burden across the spectrum of cardiovascular disease (CVD) events is unknown.

***Methods and Results*—**CVD, CHD and stroke/transient ischemic attack (TIA) events were evaluated prospectively in a multiethnic cohort without CVD at baseline. Carotid plaque score was determined by the number of ultrasound-detected plaques in the common, bifurcation, and internal carotid artery segments. CAC was detected by computed tomography. Predictive values were compared using Cox proportional hazards models, C-statistics, and net reclassification, adjusting for traditional CVD risk factors. At baseline, the 4955 participants were mean (SD) 61.6 (10.1) years old and 52.8% female; 48.9% had CAC >0 and 50.8% had at least 1 carotid plaque. After 11.3 (3.0) years of follow-up, 709 CVD, 498 CHD, and 262 stroke/TIA events occurred. CAC score compared to carotid plaque score was a stronger predictor of CVD (hazard ratio [HR], 1.78; 95% CI, 1.16–1.98; $P<0.001$ vs HR, 1.27; 95% CI, 1.16–1.40; $P<0.001$) and CHD events (HR, 2.09; 95% CI, 1.84–2.38; $P<0.001$ vs HR, 1.35; 95% CI, 1.21–1.51; $P<0.001$). CAC score and carotid plaque score were weak predictors of stroke/TIA. CAC score had better reclassification statistics than carotid plaque score, except for stroke/TIA, which had similar predictive values.

***Conclusions*—**CAC score improved prediction, discrimination, and reclassification of CVD and CHD better than carotid ultrasound measures, although prediction and discrimination were similar for stroke/TIA. **(*J Am Heart Assoc*. 2017;6:e005179. DOI: 10.1161/JAHA.116.005179.)**

Key Words: atherosclerosis • cardiovascular disease • carotid artery • imaging • risk factor

Coronary artery calcium (CAC) and carotid artery plaque have been studied extensively as predictors of cardiovascular disease (CVD) events, to further risk stratify individuals to help identify those who will benefit most from aggressive medical and lifestyle risk reduction strategies.[1–8] Traditionally, CAC has been viewed as a marker primarily for coronary heart disease (CHD) risk given that the location of the calcification is in the coronary arterial bed. Proposed drawbacks of CAC scoring is the potential for it to not detect noncalcified plaques and to underestimate stroke and transient ischemic attack (TIA) risk compared with carotid plaque identification, given that the carotid artery provides cerebral blood flow.[4,9] Larger, population-based, prospective studies have shown that despite its anatomical location, CAC presence and burden are strong predictors for CVD events, including stroke and TIA.[4,8,10,11] CAC presence and CAC score are superior to carotid artery intima-media thickness (IMT) for prediction of CHD and CVD events, including stroke and TIA[6,8,12,13]; however, carotid plaque presence is a better predictor of CVD events than carotid IMT.[8,14] Recent studies suggest that a quantitative carotid plaque score may be the best carotid ultrasound predictor of CVD risk.[15] The comparative efficacy of CAC scoring and carotid plaque scoring for CVD risk prediction are unclear and have not been investigated in a single, large, multiethnic cohort with long-term follow-up.[16] The MESA (Multi-Ethnic Study of Atherosclerosis) is a large, ethnically diverse cohort of individuals without

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An accompanying Table S1 is available at http://jaha.ahajournals.org/content/6/2/e005179/DC1/embed/inline-supplementary-material-1.pdf

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clinically evident CVD at baseline and with over 11 years of follow-up. Past analyses in the MESA have focused on carotid IMT or the presence or absence of carotid plaque, but the abilities of CAC and carotid plaque scores predict CVD events have not been compared or described in detail.

Methods

Study Participants and Design

The MESA is a prospective cohort study of the prevalence, causes, and progression of subclinical CVD. The MESA is a population-based sample of 6814 men and women aged 45 to 84 years who were free of known CVD at baseline, recruited from 6 US communities. Study objectives and design have been published previously.[17] All participants gave informed consent. Protocols were approved by the institutional review boards of the field and reading centers.

This analysis was prespecified and included all MESA participants with Exam 1 CAC evaluation and follow-up data (N=4955) who also had Exam 1 carotid plaque assessment (N=4955) measured by the University of Wisconsin Ultrasound Reading Center (Madison, WI).[8] Because plaque assessment only was available for a subset of MESA participants and may introduce bias into the analysis, multiple imputation was used to account for missing data from the entire MESA cohort (N=6783) and findings were analyzed with and without imputation. Demographic, medical history, and laboratory data were obtained from July 2000 to August 2002 and have been described previously in detail.[17]

Carotid Ultrasonography

At Exam 1, B-mode ultrasound was used to image the near and far walls of the right and left distal common carotid artery (CCA), carotid bulb, and proximal internal carotid (ICA) using a Logiq 700 ultrasound system (13 MHz transducer; General Electric Medical Systems, Wauwatosa, WI). The carotid bifurcations and internal carotid arteries were interrogated thoroughly at 9 MHz from both longitudinal and transverse approaches to identify the thickest regions. Images were stored on super-VHS videotape and digitized at a high resolution and frame rates using a Medical Digital Recording (MDR) device (PACSGEAR, Pleasanton, CA) and converted into DICOM digital records. Carotid plaque presence was defined as a focal abnormal wall thickness (IMT, >1.5 mm) or a focal thickening of >50% of the surrounding IMT.[18,19] A total plaque score (range, 0–12) was calculated to describe carotid plaque burden. Of the 12 segments analyzed for each participant, 1 point per plaque was allocated for the near and far walls of each segment (CCA, bulb, and ICA) of each carotid artery that was interrogated. For example, if a participant had a plaque on the near and far wall of the bulb and the far wall of the ICA, their total plaque score would be 3. The excellent reproducibility of the University of Wisconsin Ultrasound Reading Center's carotid ultrasound measurements using MESA images has been previously described in detail.[8] Carotid IMT was not included in this analysis because it has been compared to CAC in the MESA, previously, and the carotid plaque score appears to be superior to it for CVD risk prediction.[8]

CAC Score

Methods for computed tomographic (CT) scanning and interpretation have been reported previously.[20] CAC was assessed at all 6 MESA sites at Exam 1 by using either a cardiac-gated electron-beam CT scanner (Chicago, Los Angeles, and New York Field Centers) or a multidetector CT system (Baltimore, Forsyth County, and St. Paul Field Centers). All scans were over-read by a trained radiologist or cardiologist using an interactive scoring system.[21] CAC was determined by the Agatston score and reported as a continuous variable with excellent reproducibility.[21,22]

CVD Events

Participants were followed from the baseline examination for a median of 11.3 (3.0) years. They were contacted by telephone every 9 to 12 months to inquire about interim hospital admissions, CVD outpatient diagnoses, and deaths. Events were verified with death certificates and medical records. Two physicians, blinded to study data, independently reviewed and classified CVD events. In cases of disagreement, a mortality and morbidity committee determined the final classification. CVD was defined as CHD (definite or probable myocardial infarction, CHD death, resuscitated cardiac arrest, definite angina, and probable angina—if followed by coronary revascularization), stroke (fatal or nonfatal), or other atherosclerotic CVD death.[12] Stroke and TIA were adjudicated by neurologists. Stroke was defined as a focal neurological deficit lasting 24 hours or until death with a clinically relevant lesion on brain imaging, and no nonvascular cause was identified. TIA was defined as a focal neurological deficit lasting 30 seconds to 24 hours, without brain imaging suggesting stroke. In the present analysis, the composite of TIA and stroke are reported because the number of strokes was small. A detailed description of the MESA follow-up methods is available at http://www.mesa-nhlbi.org.

Statistical Analysis

CAC score was analyzed continuously as natural log transformation (ln) of (CAC+1) because over 50% of participants

had zero CAC.[12] Carotid plaque was analyzed as ln (carotid plaque score +1) and as the transformed and untransformed score ranging from 0 to 12 to allow for more-direct comparison in the current analyses and to other studies, respectively. Measures were divided by the SD to present regression coefficients in SD units, allowing for comparison between 2 measures with different units. Survival analysis was performed using a univariate approach with Kaplan–Meier analysis assessing associations between CAC and carotid plaque (predictors) and CHD, CVD, and stroke/TIA events (outcome variables). Cox proportional hazards models were utilized to assess multiple covariates on survival and to account for potential confounders. Each model was adjusted for age, sex, race/ethnicity, education (categories), family income (family income [1 if <$25 000, otherwise 0]), heart rate, body mass index, smoking (never, former, or current), total cholesterol, high-density lipoprotein (HDL) cholesterol, lipid-lowering medication use, presence of diabetes mellitus, systolic blood pressure, and antihypertension medication use. The strength of association for plaque score and CAC score

Table 1. Baseline Characteristics of MESA Participants, 2000–2002

	Complete Cases*	All Participants†
Analytic sample size, n	4955	6783
Age (y), mean (SD)	61.6 (10.1)	62.2 (10.2)
Male sex, % (n)	47.2 (2339)	47.16 (3199)
Race/ethnicity, % (n)		
White	38.8 (1924)	38.5 (2614)
Chinese	12.4 (614)	11.8 (801)
Black	26.0 (1288)	27.7 (1880)
Hispanic	22.8 (1129)	21.9 (1488)
Education, % (n)		
Less than high school	17.3 (855)	18.0 (1220)
High school	46.6 (2308)	46.7 (3165)
More than high school	36.2 (1792)	35.4 (2398)
Family income <$25 000/year, % (n)	31.3 (1549)	31.8 (2157)
Body mass index (kg/m^2), mean (SD)	28.3 (5.5)	28.3 (5.5)
Smoking, % (n)		
Never	50.6 (2507)	50.3 (3412)
Former	36.6 (1812)	36.7 (2486)
Current	12.8 (636)	13.1 (885)
Total cholesterol (mg/dL), mean (SD)	194.3 (35.6)	194.2 (35.7)
LDL cholesterol (mg/dL), mean (SD)	117.3 (31.5)	117.8 (31.5)
HDL cholesterol (mg/dL), mean (SD)	50.8 (14.8)	51.0 (14.8)
Lipid-lowering medication, % (n)	16.1 (796)	16.3 (1102)
Heart rate (beats/min), mean (SD)	63.0 (9.5)	63.1 (5.48)
Systolic blood pressure (mm Hg) mean (SD)	126.2 (21.4)	126.6 (21.5)
Diastolic blood pressure (mm Hg), mean (SD)	71.9 (10.3)	71.9 (10.3)
Antihypertensive medication, % (n)	36.4 (1803)	37.3 (2528)
Diabetes mellitus status, % (n)		
Normal	74.4 (3687)	73.7 (4999)
Impaired fasting glucose	13.6 (675)	13.8 (933)
Untreated diabetes mellitus	2.5 (125)	2.6 (179)
Treated diabetes mellitus	9.5 (468)	9.9 (672)

HDL indicates high-density lipoprotein; LDL, low-density lipoprotein; MESA, Multi-Ethnic Study of Atherosclerosis.
*Complete cases column shows the analytic sample statistics when restricted to participants with carotid plaques measured at exam 1.
†Multiple imputation was used for missing values. SDs reported from observed (not multiply imputed) data.

Table 2. CVD Events and Descriptive Data on Carotid Plaque and CAC

	Complete Cases*	All Participants†
Analytic sample size	4955	6783
CVD event, % (n)	9.8 (487)	9.8 (487)
CVD death	2.1 (102)	2.1 (143)
CHD event, % (n)	7.0 (348)	7.3 (498)
Myocardial infarction	2.6 (128)	3.0 (201)
CHD death	1.3 (63)	1.2 (84)
Resuscitated cardiac arrest	0.4 (22)	0.4 (28)
Definite angina	2.9 (143)	2.9 (196)
Probable angina with PCI	0.2 (12)	0.2 (15)
Stroke, % (n)	2.7 (136)	2.7 (200)
Stroke+TIA, % (n)	3.5 (175)	3.9 (262)
CAC present, % (n)	48.9 (2424)	49.9 (3383)
CAC score (if present), mean (SD)	270.6 (519.9)	290.8 (545.8)
Plaque present, % (n)	50.8 (2516)	54.9 (3722)
Plaque score (if present), mean (SD)	2.6 (1.80)	2.5 (1.8)

CHD outcome includes myocardial infarction, resuscitated cardiac arrest, definite angina, probable angina if followed by coronary revascularization, and CHD death. CVD outcome includes myocardial infarction, resuscitated cardiac arrest, definite angina, probable angina if followed by coronary revascularization, CHD death, stroke, stroke death, other atherosclerotic death, and other CVD death. Stroke/TIA=stroke outcomes include a focal neurological deficit lasting 24 hours or until death with a clinically relevant lesion on brain imaging, and no nonvascular cause was identified. TIA outcome includes a focal neurological deficit lasting 30 seconds to 24 hours, without brain imaging suggesting stroke. CAC indicates coronary artery calcium; CHD, coronary heart disease; CVD, cardiovascular disease; PCI, percutaneous coronary revascularization; TIA, transient ischemic attack.
*Complete cases column shows the analytic sample statistics when restricted to participants with carotid plaques measured at exam 1.
†Multiple imputation was used for missing values. SDs reported from observed (not multiply imputed) data.

was based on the relative size of their hazard ratios (HRs) and the corresponding chi-square test or *Z* test of the HRs will be reported, as in previous MESA publications.[8,12]

Receiver-operating characteristic curves for survival models and net reclassification improvement (NRI) analyses were used to assess the improvement in risk stratification generated by plaque score and CAC score for each outcome.[23] Categorical NRI analyses with bootstrapped SEs were used to assess the improvement for each outcome based on 10-year risk of 10%.

Multiple imputation using sequential chained regression was used to account for all missing values.[8] Estimates were averaged across 10 imputed data sets and Rubin's rules for combining the SEs were used for all models. The multiple imputation model included traditional CVD risk factors, demographic information, CAC scores, and the known outcomes of the entire cohort over the 11-year follow-up period. The percentage of missing data was 0% for the outcome and <1% for all covariates, except low-density lipoprotein (LDL)-cholesterol (2% missing), income (4% missing), and carotid plaque (23% missing).

Results

Participant Characteristics

Baseline characteristics of complete cases (those with carotid plaque measurements, n=4955) and all participants using multiple imputation (n=6783) are described in Table 1. At baseline, 4955 participants underwent baseline carotid ultrasound evaluation with plaque assessment and calculated plaque score by the University of Wisconsin. Participants in the complete case analysis were mean (SD) 61.6 (10.1) years old and 52.8% were female. Participants were ethnically

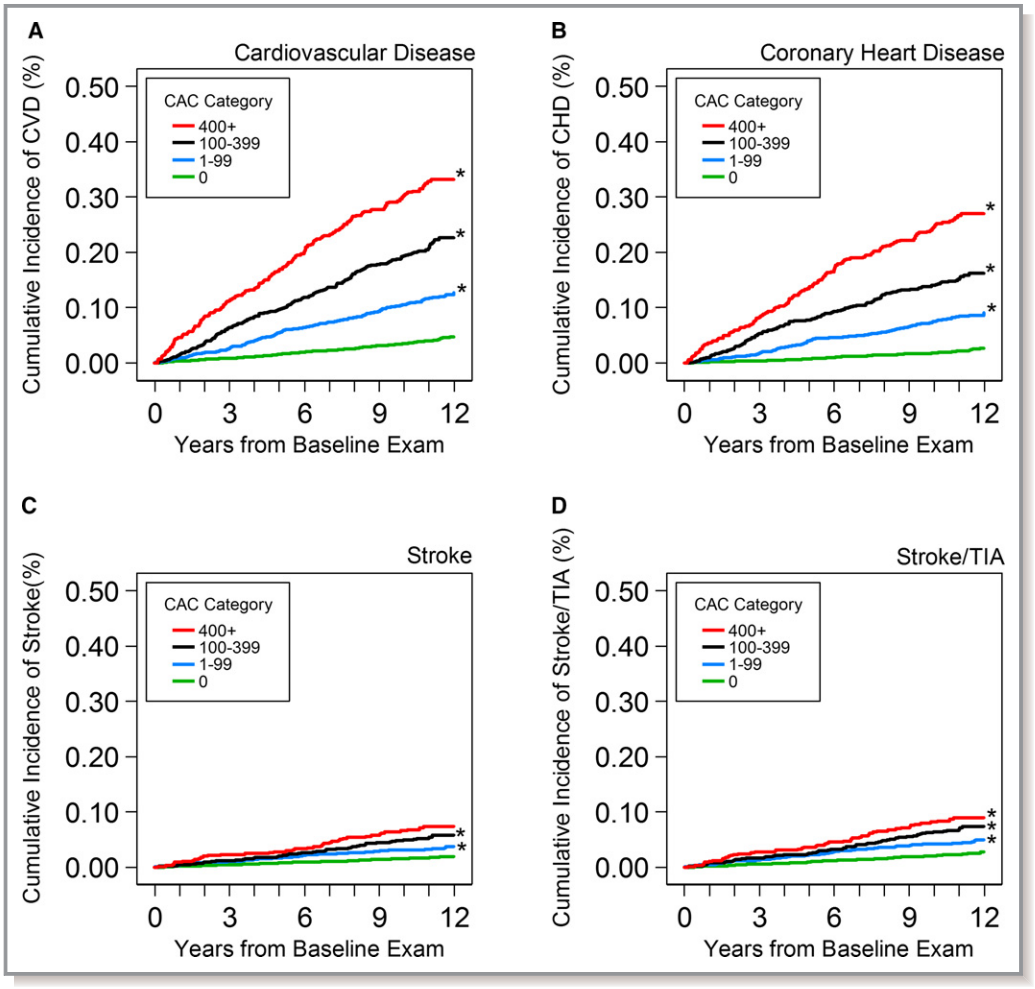

Figure 1. Unadjusted Kaplan–Meier event curves for (A) CVD, (B) CHD, (C) stroke, and (D) stroke/TIA according to coronary artery calcium score. N=4955. **P*<0.05, comparing each category to the next smallest category (eg, for stroke, the difference between 0 and 1 to 99 was significant at the 0.05 level). CAC indicates coronary artery calcium; CHD, coronary heart disease; CVD, cardiovascular disease; TIA, transient ischemic attack.

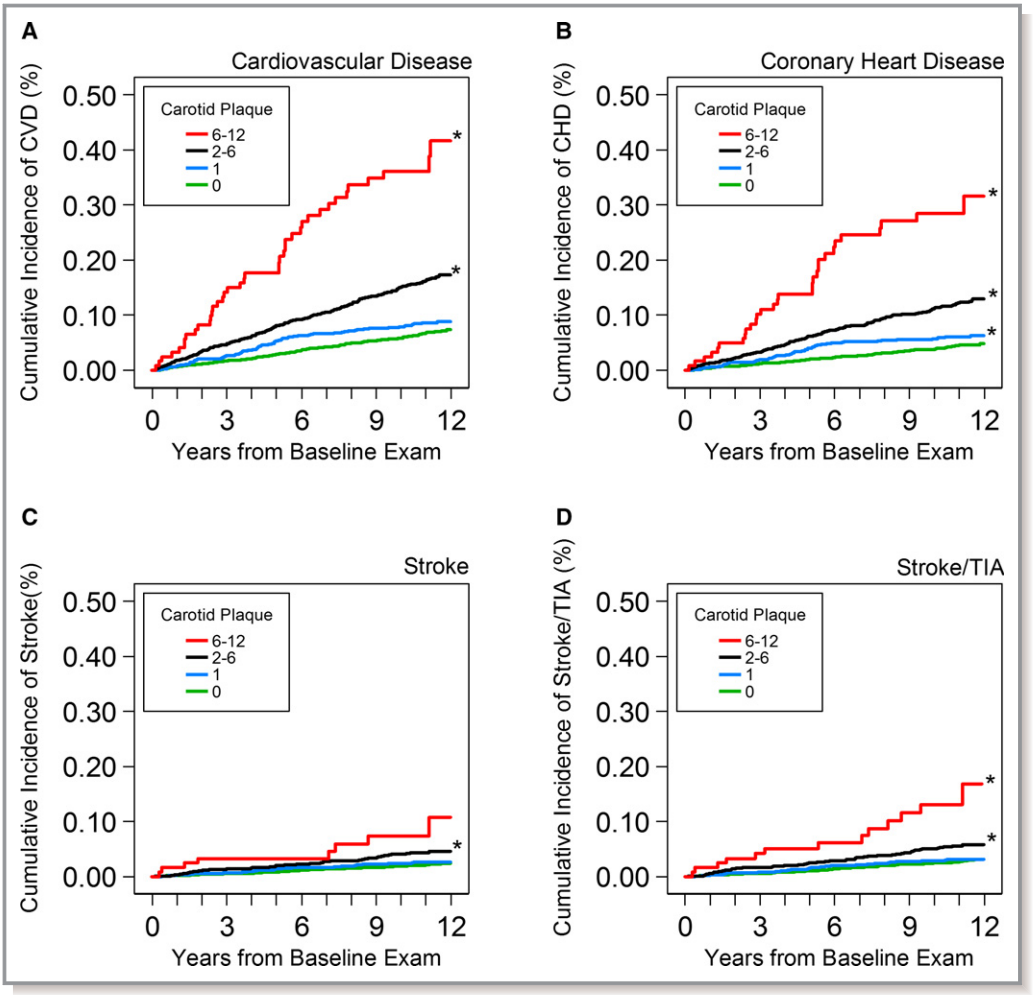

Figure 2. Unadjusted Kaplan–Meier event curves for (A) CVD, (B) CHD, (C) stroke, and (D) stroke/TIA according to carotid plaque score. N=4955. *P<0.05, comparing each category to the next smallest category (eg, for stroke, the difference between 1 and 2 to 6 was significant at the 0.05 level). CHD indicates coronary heart disease; CVD, cardiovascular disease; TIA, transient ischemic attack.

diverse with 1924 (38.8%) white, 614 (12.4%), Chinese, 1288 (26.0%) black, and 1129 (22.8%) Hispanic participants. At least 1 carotid plaque was found in 2516 (50.8%) participants who had a mean plaque score of 2.6 (1.8; Table 2). CAC was present in 2424 (48.9%), with an average CAC score of 270.6 (519.9) units among those with detectable CAC. CVD events are shown in Table 2.

Comparison of CAC Score and Carotid Plaque Score for Predicting Events

The unadjusted Kaplan–Meier survival curves for CVD, CHD, stroke, and stroke/TIA are shown in Figure 1 by CAC score and Figure 2 by carotid plaque score. They show progressive increases in risks of these events, with increasing CAC burden and carotid plaque burden. After adjustment for traditional risk factors, CAC score had a higher HR for predicting CVD events (HR, 1.78; 95% CI, 1.16–1.98; P<0.001) compared to carotid plaque score (HR, 1.27; 95% CI, 1.16–1.40; P<0.001), though both provided incremental improvement over traditional risk factors alone (Table 3). As with CVD, similar findings for CHD events were observed for CAC score (HR, 2.09; 95% CI, 1.84–2.38; P<0.001) and carotid plaque score (HR, 1.35; 95% CI, 1.21–1.51; P<0.001). Both CAC score (HR, 1.24; 95% CI, 1.05–1.47; P=0.012) and carotid plaque score (HR, 1.15; 95% CI, 0.98–1.35; P=0.08) have a mild incremental predictive value for stroke/TIA. Neither CAC nor carotid plaque predicted stroke events alone (without TIA), but the data were limited by the low number of isolated stroke events (results not shown).

Table 3 shows that CAC score significantly improved the Harrell's C-statistic over traditional CVD risk factors for CVD and CHD events (both P≤0.001). The carotid plaque score marginally improved the C-statistic over CVD traditional risk factors alone for CVD (P=0.034) and CHD (P=0.049) events, but the incremental difference in the area under the curve is

Table 3. Risk-Factor–Adjusted Cox Regression Models, C-Statistics, and Net Reclassification Indices for Predicting Incident Events

N=4955	HR (95% CI)	HR *P* Value	C-Statistic	C-Statistic *P* Value	Net Reclassification Index (95% CI)
CVD					
Traditional risk factors alone	…	…	0.74	…	…
+CAC score per 1 SD (2.48 ln+1)	1.78 (1.16–1.98)	<0.001	0.78	<0.001	Event: 3% (−0.8% to 7%) Nonevent: 3% (2–5%)
+Carotid plaque score per 1 SD (0.66 ln+1)	1.27 (1.16–1.40)	<0.001	0.75	0.034	Event: 0.1% (−2% to 4%) Nonevent: 0.3% (−0.2% to 2%)
CHD					
Traditional risk factors alone	…	…	0.75	…	…
+CAC score per 1 SD (2.48 ln+1)	2.09 (1.84–2.38)	<0.001	0.79	<0.001	Event: 13% (5–18%) Nonevent: −1% (−2% to 1%)
+Carotid plaque score per 1 SD (0.66 ln+1)	1.35 (1.21–1.51)	<0.001	0.75	0.049	Event: 1% (−2% to 7%) Nonevent: −0.1% (−1% to 1%)
Stroke/TIA					
Traditional risk factors alone	…	…	0.75	…	…
+CAC score per 1 SD (2.48 ln+1)	1.24 (1.05–1.47)	0.01	0.76	0.13	Event: −0% (−3% to 6%) Nonevent: −0.2% (−1% to 0.2%)
+Carotid plaque score per 1 SD (0.66 ln+1)	1.15 (0.98–1.35)	0.08	0.76	0.40	Event: 1% (−3% to 4%) Nonevent: −0.3% (−3% to 4%)

Multivariable model adjusted for age, sex, race/ethnicity, education (categories), family income <$25 000/year, heart rate, body mass index, smoking (never, former, or current), total cholesterol, high-density lipoprotein cholesterol, lipid-lowering medication use, presence of diabetes mellitus, systolic blood pressure, and antihypertension medication use. CAC indicates coronary artery calcium; CHD, coronary heart disease; CVD, cardiovascular disease; HR, hazard ratio; TIA, transient ischemic attack.

small. Neither CAC score nor carotid plaque score significantly improved the C-statistic over traditional CVD risk factors alone for stroke/TIA (both $P>0.10$).

CAC score significantly reclassified non-CVD events (3% [2–5%]) and CHD events (13% [5–18%]). Carotid plaque score did not consistently reclassify CVD or CHD events or nonevents (Table 3). Neither CAC score nor carotid plaque score consistently reclassified events or nonevents for stroke/TIA (Table 3).

In participants with any carotid plaques (ie, carotid plaque score >0; n=2516), the ability of CAC score to predict CVD, CHD, and stroke/TIA events remained similar to or stronger than carotid plaque score (Table 4). In those with a CAC score >0 (n=2424), carotid plaque score also predicted CVD events and CHD events, similar to or weaker than CAC score (Table 4). In analyses where both CAC score and carotid plaque score were included in the same models, CAC score consistently was a stronger predictor than the carotid plaque score for CVD and CHD events, but not for stroke/TIA events (Table 4). Results with and without multiple imputation were very similar (Table S1).

Discussion

The ability of ultrasound to evaluate carotid IMT and carotid plaque presence have been compared to CAC presence previously, and carotid plaque presence appears to be a better predictor of CVD events than carotid IMT.[8] However, the CAC score is a continuous variable that has not been directly compared to the carotid plaque score, a robust carotid ultrasound marker of atherosclerotic burden, in a large, multiethnic cohort with over a decade of follow-up. Our main finding is that both the CAC score and the carotid plaque score improve prediction of CVD and CHD events compared to traditional CVD risk factors alone; however, the predictive value of the CAC score consistently is superior to the carotid plaque score for all total CVD and CHD. For prediction of stroke and TIA events, CAC and carotid plaque score performed similarly.

Autopsy studies have demonstrated that atherosclerosis is a systemic disease,[24] and subclinical markers of atherosclerosis have significant overlap, supporting the notion that atherosclerosis, even at the early stages, is a systemic process. The relationships between the locations of subclinical vascular disease have been thought to be linked to the types of events they may predict and could impact which type of study providers should use to identify arterial injury. Numerous studies have shown that the degree of CAC has additional incremental value for CVD and CHD events,[2,21,25] but more-recent studies with longer follow-up periods also show an association with CAC and cerebrovascular disease events.[10,11] Similarly, the carotid plaque score is associated

Table 4. Risk Factor Adjusted Cox Regression Models Among All Participants, Those With CAC Score >0, and Those With Carotid Plaque Score >0

	CVD		CHD		Stroke/TIA	
	HR (95% CI)	HR *P* Value	HR (95% CI)	HR *P* Value	HR (95% CI)	HR *P* Value
Complete cases (n=4955)						
Model 1						
Plaque score per 1 SD (0.66 ln+1)	1.09 (0.99–1.20)	0.071	1.11 (0.99–1.25)	0.062	1.10 (0.93–1.29)	0.275
CAC score per 1 SD (2.48 ln+1)	1.73 (1.55–1.93)	<0.001	2.01 (1.76–2.30)	<0.001	1.21 (1.01–1.45)	0.035
Model 2						
Plaque score (untransformed)	1.05 (1.01–1.11)	0.015	1.06 (1.00–1.11)	0.035	1.08 (1.00–1.17)	0.054
CAC score (ln+1)	1.24 (1.12–1.30)	<0.001	1.32 (1.25–1.40)	<0.001	1.07 (1.00–1.15)	0.061
Participants with CAC >0 (n=2424)						
Model 1						
Plaque score per 1 SD (0.66 ln+1)	1.10 (0.99–1.23)	0.075	1.11 (0.99–1.26)	0.085	1.18 (0.96–1.44)	0.11
CAC score per 1 SD (2.48 ln+1)	1.82 (1.53–2.17)	<0.001	1.97 (1.60–2.41)	<0.001	1.33 (0.98–1.80)	0.072
Model 2						
Plaque score (untransformed)	1.06 (1.01–1.11)	0.011	1.06 (1.01–1.12)	0.025	1.10 (1.01–1.20)	0.029
CAC score (ln+1)	1.26 (1.18–1.36)	<0.001	1.31 (1.20–1.42)	<0.001	1.11 (0.98–1.26)	0.098
Participants with plaque >0 (n=2516)						
Model 1						
Plaque score per 1 SD (0.66 ln+1)	1.28 (1.08–1.52)	0.005	1.27 (1.04–1.55)	0.018	1.29 (0.95–1.74)	0.103
CAC score per 1 SD (2.48 ln+1)	1.68 (1.47–1.92)	<0.001	1.91 (1.62–2.25)	<0.001	1.28 (1.02–1.60)	0.03
Model 2						
Plaque score (untransformed)	1.09 (1.03–1.15)	0.003	1.08 (1.02–1.16)	0.015	1.11 (1.00–1.22)	0.041
CAC score (ln+1)	1.23 (1.17–1.30)	<0.001	1.30 (1.22–1.39)	<0.001	1.10 (1.01–1.20)	0.036

Models were adjusted for age, sex, race/ethnicity, education (categories), family income <$25 000/year, heart rate, body mass index, smoking (never, former, or current), total cholesterol, high-density lipoprotein cholesterol, lipid-lowering medication use, presence of diabetes mellitus, systolic blood pressure, and antihypertension medication use. Multivariable models included both CAC score and carotid plaque score. In model 1, both carotid plaque score and CAC scores are log transformed. In model 2, CAC score is log transformed and plaque score is untransformed, ranging from 0 to 12. CAC indicates coronary artery calcium; CHD, coronary heart disease; CVD, cardiovascular disease; HR, hazard ratio; TIA, transient ischemic attack.

with future CHD events despite distance between the carotid and coronary arterial beds.[26–28] It has been proposed that the heterogeneity of mechanisms of cerebrovascular events is a plausible explanation for why more-recent findings contradict the previously emphasized importance of the anatomical location of subclinical disease in regard to the type of events they predict.[11,16,29,30]

This study highlights that although CAC score was, overall, a better predictor of CVD and CHD events, the carotid plaque score had similar predictive value for stroke/TIA events—as predicted by their anatomical location. Though inferior to CAC score for predicting CVD and CHD events, carotid ultrasound remains a relatively inexpensive, noninvasive, radiation-free technique to augment CVD risk prediction, so it may be a more-suitable test in children and young adults. We previously reported the incremental value of increased carotid IMT on risk prediction in the MESA,[8] so it was not included in the present analyses. Also, it recently downgraded to a level III recommendation in the most recent guideline statement on the assessment of CVD risk prediction,[5] though measuring carotid IMT without considering carotid plaque presence or absence already had not been recommended.[18] Whereas detecting carotid plaque is less operator dependent than accurately imaging and measuring carotid IMT, measuring a CAC score is the least operator dependent of these tests.

Limitations

Though the MESA is a large study designed to asses subclinical determinants of CVD, its observational design has well-known limitations. There were a significant number of subjects who were missing carotid ultrasound assessments of plaque at Exam 1. We attempted to mitigate this though the use of multiple imputation to account for missing data and

observed no significant differences between the complete case analyses and the imputed data analysis. The data on stroke and TIA are presented together because of the low number of these event types within the MESA. Finally, the units of CAC score and carotid plaque score are not equal, with CAC ranging from 0 to infinity and carotid plaque being a discrete 0 to 12 score. Regression coefficients were presented in SD units of the measure, allowing for more-generalizable comparisons.

Conclusions

The CAC score improves prediction, discrimination, and reclassification of CVD and CHD risk better than carotid ultrasound measures. CAC and carotid plaque scores had similar prediction and weaker discrimination and reclassification for stroke/TIA events.

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Disclosures

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SUPPLEMENTAL MATERIAL

Table S1. Risk Factor-Adjusted Cox Regression Models for Predicting Incident Events with Multiple Imputation

N= 6,783	Hazard Ratio (95% CI)	Hazard Ratio P value
CVD		
Traditional risk factors alone	-	-
+ CAC score per 1 SD (2.48 ln+1)	1.74 (1.60 - 1.90)	<0.001
+ Carotid plaque score per 1 SD (0.66 ln+1)	1.24 (1.14 - 1.35)	<0.001
CHD		
Traditional risk factors alone	-	-
+ CAC score per 1 SD (2.48 ln+1)	2.02 (1.81-2.25)	<0.001
+ Carotid plaque score per 1 SD (0.66 ln+1)	1.31 (1.18 - 1.46)	<0.001
Stroke/TIA		
Traditional risk factors alone	-	-
+ CAC score per 1 SD (2.48 ln+1)	1.30 (1.14-1.50)	<0.001
+ Carotid plaque score per 1 SD (0.66 ln+1)	1.13 (0.98 - 1.30)	0.08

CVD = cardiovascular disease; CAC = coronary artery calcium; CHD = coronary heart disease; TIA = transient ischemic attack; CI = confidence interval.

Multivariable model adjusted for age, sex, race/ethnicity, education (categories), family income < $25,000/year, heart rate, body-mass index, smoking (never, former, current), total cholesterol, high-density lipoprotein cholesterol, lipid-lowering medication use, presence of diabetes mellitus, systolic blood pressure, and antihypertension medication use.