JACC: CARDIOVASCULAR IMAGING VOL. 2, NO. 3, 2009

ISSN 1936-878X/09/$36.00
PUBLISHED BY ELSEVIER INC. DOI:10.1016/j.jcmg.2008.12.010

Thoracic Aortic Calcium Versus Coronary Artery Calcium for the Prediction of Coronary Heart Disease and Cardiovascular Disease Events

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OBJECTIVES This study compared the ability of coronary artery calcium (CAC) and thoracic aortic calcium (TAC) to predict coronary heart disease (CHD) and cardiovascular disease (CVD) events.

BACKGROUND Coronary artery calcium has been shown to strongly predict CHD and CVD events, but it is unknown whether TAC, also measured within a single cardiac computed tomography (CT) scan, is of further value in predicting events.

METHODS A total of 2,303 asymptomatic adults (mean age 55.7 years, 38% female) with CT scans were followed up for 4.4 years for CHD (myocardial infarction, cardiac death, or late revascularizations) and CVD (CHD plus stroke). Cox regression, adjusted for Framingham risk score (FRS), examined the relation of Agatston CAC and TAC categories, and log-transformed CAC and TAC with the incidence of CHD and CVD events and receiver-operator characteristic (ROC) curves tested whether TAC improved prediction of events over CAC and FRS.

RESULTS A total of 53% of subjects had Agatston CAC scores of 0; 8% 1 to 9; 19% 10 to 99; 12% 100 to 399; and 8% ≥400. For TAC, proportions were 69%, 5%, 12%, 8%, and 7%, respectively; 41 subjects (1.8%) experienced CHD and 47 (2.0%) CVD events. The FRS-adjusted hazard ratios (HR) across increasing CAC groups (relative to <10) ranged from 3.7 ($p = 0.04$) to 19.6 ($p < 0.001$) for CHD and from 2.8 ($p = 0.07$) to 13.1 ($p < 0.001$) for CVD events; only TAC scores of 100 to 399 predicted CHD and CVD (HR: 3.0, $p = 0.008$, and HR: 2.3, $p = 0.04$, respectively); these risks were attenuated after accounting for CAC. Findings were consistent when using log-transformed CAC and TAC Agatston and volume scores. The ROC curve analyses showed CAC predicted CHD and CVD events over FRS alone ($p < 0.01$); however, TAC did not further add to predicting events over FRS or CAC.

CONCLUSIONS This study found that CAC, but not TAC, is strongly related to CHD and CVD events. Moreover, TAC does not further improve event prediction over CAC. (J Am Coll Cardiol Img 2009;2:319–26) © 2009 by the American College of Cardiology Foundation

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Manuscript received June 18, 2008; revised manuscript received November 6, 2008, accepted December 22, 2008.

JACC: CARDIOVASCULAR IMAGING, VOL. 2, NO. 3, 2009
MARCH 2009:319–26

Coronary artery calcium (CAC), a marker of subclinical atherosclerosis assessed by computed tomography (CT), is strongly associated with the risk of future coronary heart disease (CHD) events and mortality (1–7). CAC provides incremental value over global risk assessment (e.g., Framingham risk scores [FRS]) and has been recommended for enhancing cardiovascular risk stratification in intermediate-risk persons (8–10).

Segments of the thoracic aorta can be assessed by the noncontrast CT scan used to assess CAC, without any additional scanning or radiation. Aortic calcium is an established marker of atherosclerosis (11–13). As with CAC, the prevalence of thoracic aortic calcium (TAC) increases with age, is associated with coronary risk factors (14), and correlates closely with CAC (15), but whether TAC predicts CHD and cardiovascular disease (CVD) events has not been previously shown. We aim to examine in a cohort of asymptomatic persons whether TAC predicts CVD events over FRS, and more importantly, over the well-established strength of CAC.

ABBREVIATIONS AND ACRONYMS

CAC = coronary artery calcium
CHD = coronary heart disease
CI = confidence interval
CT = computed tomography
CVD = cardiovascular disease
FRS = Framingham risk score
HR = hazard ratio
ROC = receiver-operator characteristic
TAC = thoracic aortic calcium

METHODS

A total of 2,303 asymptomatic adults (mean age 55.7 ± 9.6 years, 38% female) without a history of CVD who had baseline CT scans assessed both for CAC and TAC were followed up for myocardial infarction, cardiac death, coronary revascularizations, and stroke over a mean follow-up of 4.4 (±0.7) years, ranging from 0.8 to 7.8 years. Subjects were either physician- or self-referred clinical patients who agreed to be part of the cardiac research database (n = 1,304, 57%) or enrollees in the EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) study, which included CAC scanning (n = 999, 43%). Persons with known atrial fibrillation were not included. We could not obtain the follow-up status in 180 subjects, who are not included in the above sample. Except for being younger (mean age 51 years), these subjects were roughly comparable to those subjects included in the study with respect to other risk factors. The current study was approved by the Cedars-Sinai Medical Center Institutional Review Board (Institutional Review Board numbers 3351, 3354, and 3974).

Subjects were scanned using either an electron beam CT (C-150XP Scanner or E-speed, General Electric/Imatron, South San Francisco, California) or multidetector scanner (4-slice Somatom Volume Zoom, Siemens, Berlin and Munich, Germany). Licensed radiologic technicians acquired a single scan on each patient consisting of approximately 30 to 40 slices encompassing the heart from the carina to the apex, with a 30- to 35-cm field of view sufficient to include the entire heart as well as the ascending and descending thoracic arteries. For the electron beam CT scanners, we used 3-mm slices, 100-ms exposure, 130-kV tube voltage, 63 mAs (88 mAs for E-speed), and prospective electrocardiographic triggering at 60% of the RR interval; for the multidetector scanner, we used 250-ms exposures, 2.5-mm slices, 120-kV voltage, 42 mAs, and prospective triggering at 400 ms before the next R wave (16). Breath-holding instructions were also given to minimize misregistration. Foci of CAC were identified and scored by an experienced technician, using semiautomatic software (ScImage, Inc., Los Altos, California), and verified by an imaging cardiologist. Lesion-specific scores were calculated as the product of the area of each calcified focus and peak CT number (scored as 1 if 130 to 199 HU, 2 if 200 to 299 HU, 3 if 300 to 399 HU, and 4 if 400 HU or greater) and summed across all lesions identified within left main, left anterior descending, left circumflex, and right coronary arteries to provide arterial specific calcium scores and across arteries to provide a total Agatston calcium score (17). TAC included calcium scored from segments of the ascending and descending portion of the thoracic aorta visible in the coronary CT scan from the lower edge of the pulmonary artery bifurcation to the apex of the subject's heart. Calcification in the aortic arch was not included in the TAC score we report. Readers differentiated aortic and mitral valvular calcium from aortic wall calcium. Calcification in the aortic root (e.g., above the aortic valve) is included in ascending TAC. An example of ascending and descending TAC as well as CAC in the left anterior descending and right coronary arteries is shown in Figure 1.

A fasting lipid profile plus glucose (Cholestech, Hayward, California), 2 readings of blood pressure (readings averaged), brief medical history, and weight and height for calculation of body mass index were obtained. Diabetes was defined by self-reported history, taking medication, or having a fasting glucose of ≥7.0 mmol/l (126 mg/dl) or casual glucose of ≥11.1 mmol/l (200 mg/dl). The 10-year risk of CHD was estimated by the FRS (18). Those with diabetes were assigned a risk score of 20% (or higher if determined by the FRS calculation).

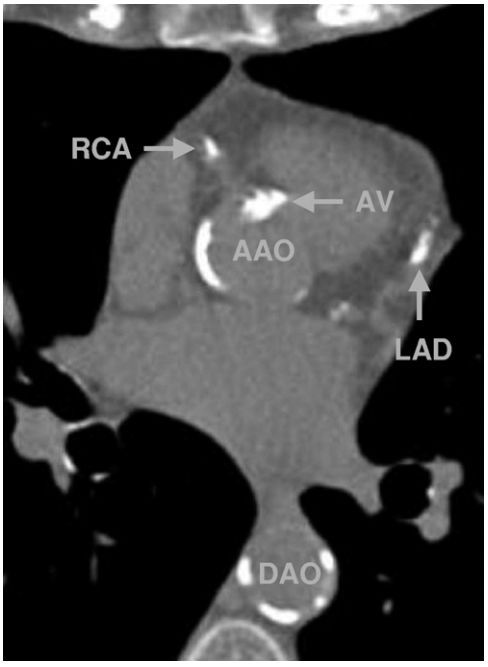

Figure 1. Example of Scan Showing Calcification in the AAO and DAO, and LAD and RCA

Example of scan showing calcifications **(arrows)** in the ascending thoracic aorta (AAO) and descending thoracic aorta (DAO), the aortic valve (AV), left anterior descending artery (LAD), and right coronary artery (RCA). Note that the AV calcification was not included in the aortic scoring.

Follow-up for CHD and CVD events consisted of administering patient questionnaires and interviews and/or using hospital records. Myocardial infarctions, strokes, and deaths were verified by 2 physicians from an independent review of admission reports, discharge summaries, and consultation/laboratory reports. Revascularizations were verified by hospital records. All deaths were verified by National Death Index and/or independent review of death reports by 2 physicians. Hard CHD events included myocardial infarction or cardiac death, total CHD events included hard CHD plus late revascularizations (>90 days), and total CVD included total CHD plus stroke.

STATISTICAL METHODS

We compared age, sex, and risk factor distributions according to CAC and TAC Agatston score category (0, 1 to 9, 10 to 99, 100 to 399, and ≥400 indicating none/minimal, mild, moderate, and significant calcification, respectively, based on guidelines for CAC [19]) and the distribution of CAC with TAC (overall and by age group) using the chi-square test of proportions or analysis of variance. The bivariate relation of CAC and TAC categories with CHD and CVD was examined similarly. Cox proportional hazards regression examined the FRS-adjusted hazard ratios (HRs) for events associated with CAC and TAC calcium categories of 10 to 99, 100 to 399, and ≥400, relative to those with scores 0 to 9 (which formed our reference group, because the CAC = 0 group had an insufficient number of events to serve as a suitable reference group), defining follow-up time as the time between the baseline scan date and the first occurrence of an event. Receiver-operator characteristic (ROC) curves and c-statistics were also obtained from the Cox models, and equality of areas (20) was compared for models examining: 1) FRS alone; 2) FRS plus CAC categories; 3) FRS plus TAC categories; and 4) FRS plus CAC and TAC categories together. To examine comparability of results with continuously measured CAC and TAC, we also conducted similar analyses using log transformations of CAC and TAC. For total CHD and CVD events, only late revascularizations were included, and 5 early revascularizations (<90 days) were censored. Time to the earliest occurrence of the specified event in each analysis was used for the Cox regression analyses. All analyses were performed using Stata version 8 (StataCorp LP, College Station, Texas).

RESULTS

Persons with higher levels of CAC or TAC were significantly older, had higher body mass index, and were more likely to be diabetic, to have higher systolic blood pressure, to have higher FRS, and to have more CHD and CVD events. Although those with higher CAC scores were less likely to be women and had lower high-density lipoprotein cholesterol levels, those with higher TAC scores were more commonly women and current smokers (Table 1).

Overall 53% of subjects had CAC scores of 0, 8% of 1 to 9, 19% of 10 to 99, 12% of 100 to 399, and 8% of ≥400. For TAC, these proportions were 69%, 5%, 12%, 8%, and 7%, respectively. The TAC scores were closely associated ($p < 0.0001$) with CAC scores (Fig. 2). Of 47% (n = 1,088) of subjects with any CAC, slightly over half (51%, n = 554) did not have TAC, and of 31% (n = 724) of subjects with any TAC, 26% (n = 190) did not have CAC. Overall, 45% (n = 1,025) of subjects had both CAC and TAC absent (scores of 0 for

Table 1. Descriptive Statistics and Event Frequencies for Hard CHD, Total CHD, and Total CVD by CAC and TAC Categories

		CAC						TAC					
	Overall (n = 2,303)	**0 (n = 1,215)**	**1 to 9 (n = 182)**	**10 to 99 (n = 438)**	**100 to 399 (n = 278)**	**400+ (n = 190)**	**Trend p Value**	**0 (n = 1,579)**	**1 to 9 (n = 114)**	**10 to 99 (n = 277)**	**100 to 399 (n = 182)**	**400+ (n = 151)**	**Trend p Value**
Age (yrs)	56 ± 10	52 ± 9	56 ± 8	58 ± 9	61 ± 8	64 ± 8	<0.0001	53 ± 8	57 ± 8	60 ± 8	64 ± 7	68 ± 6	<0.0001
Women, n (%)	885 (38)	581 (48)	60 (33)	140 (32)	68 (24)	36 (19)	<0.0001	576 (36)	55 (48)	113 (41)	77 (42)	64 (42)	0.02
Total cholesterol (mg/dl)	213 ± 41	212 ± 39	220 ± 41	214 ± 42	209 ± 43	209 ± 43	0.12	212 ± 40	217 ± 45	213 ± 40	211 ± 39	213 ± 45	0.72
HDL-C (mg/dl)	55 ± 17	56 ± 17	54 ± 16	54 ± 18	52 ± 15	53 ± 16	<0.0001	55 ± 17	55 ± 19	55 ± 15	55 ± 16	57 ± 17	0.09
Body mass index (kg/m^2)	27 ± 5	26 ± 5	26 ± 4	27 ± 5	27 ± 5	27 ± 5	<0.0001	26 ± 5	27 ± 5	27 ± 5	27 ± 4	27 ± 6	0.006
Diabetes, n (%)	157 (7)	55 (5)	9 (5)	46 (11)	17 (6)	30 (16)	<0.0001	92 (6)	8 (7)	19 (7)	24 (13)	14 (9)	0.001
SBP (mm Hg)	129 ± 18	125 ± 17	131 ± 18	131 ± 18	133 ± 18	138 ± 20	<0.0001	126 ± 17	132 ± 17	132 ± 17	135 ± 18	141 ± 21	<0.0001
Current smoking, n (%)	150 (7)	69 (6)	14(8)	30 (7)	22 (8)	15 (8)	0.10	92 (6)	8 (7)	22 (8)	14 (8)	14 (9)	0.04
Family history, n (%)	661 (29)	353 (29)	41 (23)	123 (28)	87 (31)	57 (30)	0.62	460 (29)	35 (31)	79 (29)	51 (28)	36 (24)	0.26
FRS (% 10-yr CHD risk)	7 ± 7	5 ± 6	8 ± 6	9 ± 7	10 ± 7	13 ± 7	<0.0001	6 ± 6	7 ± 7	9 ± 7	11 ± 7	11 ± 8	<0.0001
Hard CHD events, n (%)	16 (0.7)	1 (0.1)	1 (0.6)	2 (0.5)	6 (2.2)	6 (3.2)	<0.0001	5 (0.3)	1 (0.9)	5 (1.8)	3 (1.7)	2 (1.3)	0.003
Total CHD events, n (%)	41 (1.8)	2 (0.2)	2 (1.1)	6 (1.4)	13 (4.7)	18 (9.5)	<0.0001	16 (1.0)	2 (1.8)	8 (2.9)	9 (5.0)	6 (4.0)	<0.0001
Total CVD events, n (%)	47 (2.0)	3 (0.3)	3 (1.7)	7 (1.6)	15 (5.4)	19 (10.0)	<0.0001	20 (1.3)	3 (2.6)	8 (2.9)	9 (5.0)	7 (4.6)	<0.0001

CAC = coronary artery calcium; CHD = coronary heart disease; CVD = cardiovascular disease; FRS = Framingham Risk Score; HDL-C = high-density lipoprotein cholesterol; SBP = systolic blood pressure; TAC = thoracic aortic calcium.

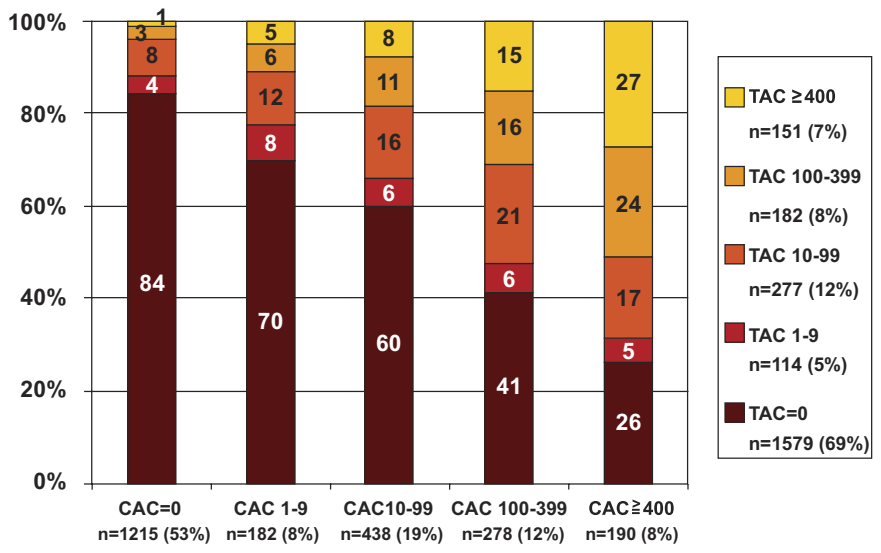

Figure 2. Distribution of TAC According to Category of CAC

Values indicate the percentage of participants in each thoracic aortic calcium (TAC) score category (0, 1 to 9, 10 to 99, 100 to 399, and ≥400) with indicated coronary artery calcium (CAC) scores (0, 1 to 9, 10 to 99, 100 to 399, and ≥400). $p < 0.001$ comparing distribution of TAC groups across CAC groups.

both) and 23% (n = 534) of subjects were positive for both CAC and TAC (scores ≥0 for each) and 18% (n = 424) had at least mild CAC and TAC (scores ≥10 for each). Across increasing age groups, there was a closer relation of presence of CAC and TAC together; in those age <40 years, 15% had either and 2% had both; these figures increased to 28% and 5% for ages 40 to 49 years and 35% and 17% for ages 50 to 59 years, and both CAC and TAC together were more common than one alone by ages 60 to 69 years: 38% and 41%, and especially in those ages ≥70 years: 21% and 72%, respectively.

Sixteen participants (0.7%) had hard CHD events (13 myocardial infarctions and 3 cardiac deaths), 41 (1.8%) with total CHD events (above 16 hard CHD events plus 19 late angioplasties and 6 late bypass surgeries), and 47 (2.0%) with any (total) CVD event (CHD plus 6 strokes). Increasing CAC and TAC categories were significantly associated with the incidence of hard CHD events and total CHD and CVD events (p trend <0.0001 for all, except p = 0.003 for TAC for hard CHD events) (Table 1).

Relative to those with CAC scores <10, those with CAC scores of 100 to 399 and CAC scores of ≥400 had significantly increased risks for future hard CHD events (HR: 10.5 and 12.0, respectively). Total CHD events were significantly more likely for those with

Table 2. Framingham Risk Score–Adjusted Hazard Ratios for Hard CHD, Total CHD, and Total CVD Events From Individual Cox Regression Analyses Including CAC or TAC Categories

	Hard CHD Events	Total CHD Events	Total CVD Events
CAC			
<10 (n = 1,397)	1.0	1.0	1.0
10 to 99 (n = 438)	2.4 (0.3–17.3)	3.7 (1.03–13.3)*	2.8 (0.9–8.3)
100 to 399 (n = 278)	10.5 (2.1–53.9)†	11.9 (3.8–37.0)‡	8.8 (3.4–23.1)‡
≥400 (n = 190)	12.0 (2.2–64.5)†	19.6 (6.3–60.8)‡	13.1 (5.0–34.2)‡
TAC			
<10 (n = 1,693)	1.0	1.0	1.0
10 to 99 (n = 277)	3.8 (1.1–12.6)*	2.0 (0.9–4.6)	1.5 (0.7–3.5)
100 to 399 (n = 182)	2.9 (0.7–12.1)	3.0 (1.3–6.9)†	2.3 (1.04–5.0)*
≥400 (n = 151)	2.1 (0.4–10.8)	2.1 (0.8–5.6)	1.9 (0.8–4.6)

*p < 0.05; †p < 0.01; ‡p < 0.001.
Abbreviations as in Table 1.

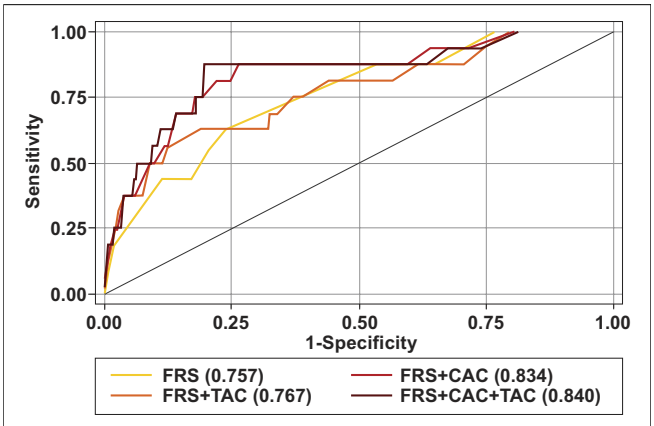

Figure 3. ROC Curve Analysis for CAC and TAC in Predicting Hard CHD Events

Area under the receiver-operator characteristic (ROC) curve is provided in parentheses. The p values for contrasts: addition of CAC over FRS alone, p = 0.10; further addition of TAC, p = 0.67; addition of TAC over FRS alone, p = 0.70. CHD = coronary heart disease; FRS = Framingham Risk Score; other abbreviations as in Figure 2.

CAC 10 to 99, CAC 100 to 399, and CAC ≥400 (HR: 3.7, 11.9, and 19.6, respectively). Total CVD events were significantly more likely for those with CAC 10 to 99, CAC 100 to 399, and CAC ≥400 (HR: 3.4, 8.8, and 13.1, respectively). For TAC, compared with those with TAC <10, increased HRs (FRS-adjusted) were observed for TAC 10 to 99 (HR: 3.8) in predicting hard CHD, and TAC 100 to 399 for total CHD events (HR: 3.0) and total CVD events (HR: 2.3) (Table 2). In separate Cox models containing both CAC and TAC categories together (results not shown), although HRs for CAC remained essentially unchanged, HRs associated with each TAC category were attenuated and no longer significant.

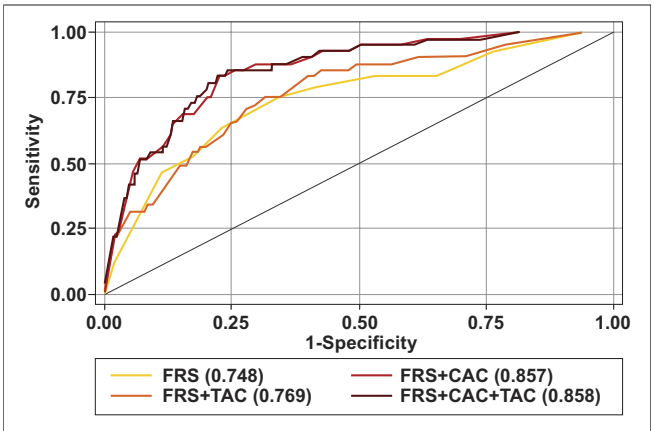

Figure 4. ROC Curve Analysis for CAC and TAC in Predicting Total CHD Events

Area under the ROC curve is provided in parentheses. The p values for contrasts: addition of CAC over FRS alone, p = 0.004; further addition of TAC, p = 0.92; addition of TAC over FRS alone, p = 0.28. Abbreviations as in Figures 2 and 3.

Figures 3 to 5 show results of the ROC analyses for FRS alone, FRS plus CAC or TAC, and FRS plus CAC and TAC. The addition of CAC provided incremental value for predicting events over FRS alone (p = 0.004 for total CHD and p = 0.006 for total CVD events); however, there was no additional value of TAC for predicting events over FRS (p = 0.70, p = 0.28, and p = 0.43 for hard CHD, total CHD, and total CVD events, respectively). Importantly, the addition of TAC to a model consisting of FRS plus CAC also provided no incremental predictive value for hard CHD or total CHD or CVD events (p = 0.67, p = 0.92, and p = 0.99, respectively).

In models in which CAC and TAC were defined continuously, LogCAC significantly predicted both hard CHD (HR: 1.5, 95% CI: 1.2 to 1.9), total CHD (HR: 1.7, 95% CI: 1.4 to 2.0), and total CVD (HR: 1.6, 95% CI: 1.3 to 1.8) events. Although log TAC was not significantly related to the risk of hard CHD (HR: 1.2, 95% CI: 0.99 to 1.4), there was a weak relation with total CHD (HR: 1.2, 95% CI: 1.04 to 1.3) and total CVD (HR: 1.1, 95% CI: 1.02 to 1.3). However, in models with both LogCAC and LogTAC, only LogCAC remained significantly associated with events (hard CHD HR: 1.5, total CHD HR: 1.7, total CVD HR: 1.6, all p < 0.002), whereas LogTAC did not (p > 0.54 for all). From ROC curve analyses, over and above FRS, LogCAC (p = 0.08, 0.002, and 0.004 for hard CHD, total CHD, and total CVD, respectively) but not LogTAC (p ≥ 0.23 for all end points) significantly improved discrimination. Additionally, LogTAC did not add incremental value to FRS + LogCAC (p ≥ 0.82 for all end points).

When we examined our primary results according to CAC and TAC volume (log-transformed) for our end points of hard CHD, total CHD, and total CVD events, these results were entirely consistent with our Agatston score–based analyses and showed that CAC but not TAC remain strong predictors (independent of FRS) of hard CHD, total CHD, and total CVD (p < 0.01 to p < 0.001 for CAC and p > 0.20 for TAC). Moreover, in ROC analyses, CAC provided incremental value over FRS for the prediction of events (p = 0.07 for hard CHD, p = 0.02 for total CHD, and p < 0.01 for CVD events), but TAC did not add further to prediction (p > 0.49).

DISCUSSION

This is the first report examining the role of TAC as a predictor of CHD and CVD events. Although there is a modest relation of TAC to future CHD and CVD events, TAC does not improve prediction of events over global risk assessment. We confirm the established incremental value of CAC in predicting cardiovascular events over and above risk factors or Framingham risk scores as shown previously (3,5,6); others also have shown that CAC independently predicts mortality (4,7). However, no previous investigation has examined the ability of TAC (which can be evaluated in the same scan as CAC without additional scanning or radiation exposure) to predict future cardiovascular events or whether it adds further to prediction over CAC in a large screened cohort.

Aortic calcium in either the ascending or descending thoracic aorta has been shown to be related closely to CAC, suggesting a common underlying systemic vascular atherosclerotic process (21,22). We have previously shown TAC to be associated with several risk factors, including age, low-density lipoprotein cholesterol, body mass index, systolic blood pressure, and cigarette smoking (14). Others have shown age, cigarette smoking, and coronary calcium to best predict calcification of the entire descending aorta down to the iliac arteries (23). Also, aortic calcification is significantly more common in those with (63%) versus without (22%) ($p < 0.05$) multivessel angiographic disease (24) and has a sensitivity of 56% and specificity of 72% for obstructive CAD (25). Finally, abdominal aortic calcium from radiographic images has been shown to predict vascular morbidity and mortality in the Framingham Heart Study (26). Associations of aortic calcium quantitated by CT, including TAC with clinical events, however, have not been previously examined.

Our study has several potential limitations. Importantly, our measure of aortic calcium comprises only that found in the segments of the ascending and descending thoracic aorta visible from the coronary calcium scan; therefore, our results are not applicable to the remainder of the descending aorta, e.g., abdominal aorta, where significant calcium occurs (27). Relationships with overall abdominal aortic calcium and events may be different than what we report for TAC. Also, we had a limited number of end points, particularly hard CHD, which may limit the validity of our findings (e.g., possible model overfitting). However, the consistency of our findings using CAC and TAC as continuous log-transformed predictors, suggests the robustness of our results. We did not have a sufficient number of peripheral arterial disease end points to examine whether TAC was more important than CAC for predicting such events. Moreover, we did not have the power to compare prediction in older and younger groups or by gender separately. Also, because the Agatston score cut points used were developed to classify severity of CAC, one could question whether they can be similarly used to quantitate extent of TAC. However, our analyses using continuous log-transformed scores and volume scores provided consistent results. Finally, as we studied self-referred volunteers mainly of Caucasian ethnicity, our results may not be generalizable to other groups; however, our patient population is thus similar to other screened cohorts (1,3,4), with the exception of population-based studies such as the MESA (Multiethnic Study of Atherosclerosis) (5).

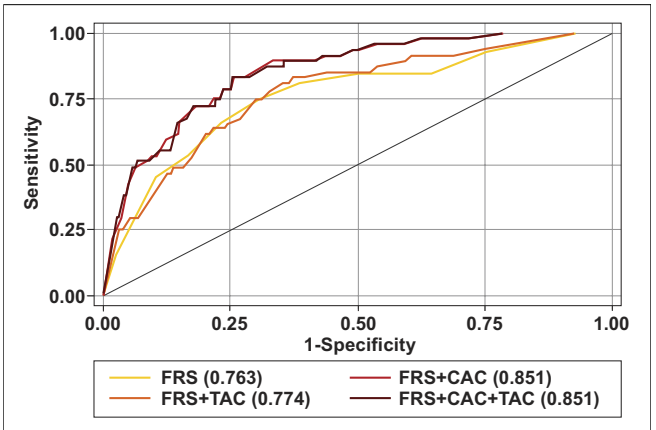

Figure 5. ROC Curve Analysis for CAC and TAC Separately in Predicting Total CVD Events

Area under the ROC curve is provided in parentheses. The p values for contrasts: addition of CAC over FRS alone, $p = 0.006$; further addition of TAC, $p = 0.99$; addition of TAC over FRS alone, $p = 0.43$. CVD = cardiovascular disease; other abbreviations as in Figures 2 and 3.

CONCLUSIONS

CAC screening provides independent and incremental utility in predicting the risk of CVD over global risk assessment, but evaluation of TAC does not further refine clinical event prediction.

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REFERENCES

1. Wong ND, Hsu JC, Detrano RC, Diamond G, Eisenberg H, Gardin JM. Coronary artery calcium evaluation by electron beam computed tomography: relation to new cardiovascular events. Am J Cardiol 2000;86:495–98.
2. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 2004;291:210–5.
3. Kondos GT, Hoff JA, Sevrukov A, et al. Electron-beam tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5,635 initially asymptomatic low to intermediate-risk adults. Circulation 2003;107:2571–6.
4. Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium for all-cause mortality. Radiology 2003;228:826–33.
5. Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of near-term coronary heart disease events in major American ethnic groups: the Multiethnic Study of Atherosclerosis (MESA). N Engl J Med 2008;358:1336–45.
6. Arad Y, Spadaro LA, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. J Am Coll Cardiol 2005;46:158–65
7. Budoff MJ, Shaw LJ, Liu ST, et al. Long-term prognosis associated with coronary calcification. Observations from a registry of 25,253 patients. J Am Coll Cardiol 2007;49:1860–70.
8. Wilson PWF, Smith SC, Blumenthal RS, Burke GL, Wong ND. Task Force #4—How do we select patients for atherosclerosis imaging? J Am Coll Cardiol 2003;41:1898–906.
9. Greenland P, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain. J Am Coll Cardiol 2007;49:378–402.
10. Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography. Circulation 2006;114:1761–91.
11. Witteman JC, Kannel WB, Wolf PA, et al. Aortic calcified plaques and cardiovascular disease (the Framingham Study). Am J Cardiol 1990;66:1060–4.
12. Witteman JC, Kok FJ, van Saase JL, Valkenburg HA. Aortic calcification as a predictor of cardiovascular mortality. Lancet 1986;2:1120–2.
13. Hollander M, Hak AE, Koudstaal PJ, et al. Comparison between measures of atherosclerosis and risk of stroke: the Rotterdam Study. Stroke 2003;34:2367–72.
14. Wong ND, Sciammarella M, Arad Y, et al. Relation of thoracic aortic and aortic valve calcium to coronary artery calcium and risk assessment. Am J Cardiol 2003;92:951–5.
15. Adler Y, Fisman EZ, Shemesh J, et al. Spiral computed tomography evidence of close correlation between coronary and thoracic aorta calcifications. Atherosclerosis 2004;176:133–8.
16. Daniell AL, Wong ND, Friedman JD, et al. Concordance of coronary calcium estimation between multidetector computed tomography and electron beam tomography. Am J Roentgelol 2005;185:1542–5.
17. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827–32.
18. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486–97.
19. Rumberger JA, Brundace BH, Rader DJ, Kondos G. Electron beam computed tomographic coronary calcium scanning: a review and guidelines for use in asymptomatic persons. Mayo Clin Proc 1999;74:243–52.
20. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating curves: a nonparametric approach. Biometrics 1988;44:837–45.
21. Adler Y, Shemesh J, Tenenbaum A, et al. Aortic valve calcium on spiral computed tomography (dual slice mode) is associated with advanced coronary calcium in hypertensive patients. Coron Artery Dis 2002;13:209–13.
22. Cury RC, Ferencik M, Hoffmann U, et al. Epidemiology and association of vascular and valvular calcium in elderly subjects quantified by multi-detector computed tomography. Am J Cardiol 2004;94:348–51.
23. Raggi P, Cooil B, Hadi A, Friede G. Predictors of aortic and coronary artery calcium on a screening electron beam tomographic scan. Am J Cardiol 2003;91:744–6.
24. Yamamoto H, Shavelle D, Takasu J, et al. Valvular and thoracic aortic calcium as a marker of the extent and severity of angiographic coronary artery disease. Am Heart J 2003;146:153–9.
25. Takasu J, Mao S, Budoff MJ. Aortic atherosclerosis detected with electron-beam CT as a predictor of obstructive coronary artery disease. Acad Radiol 2003;10:631–7.
26. Wilson PW, Kauppila LI, O'Donnell CJ, et al. Abdominal aortic calcific deposits are an important predictor of vascular morbidity and mortality. Circulation 2001;103:1529–34.
27. Sutton-Tyrrell K, Kuller LH, Edmundowicz D, et al. Usefulness of electron beam tomography to detect progression of coronary and aortic calcium in middle-aged women. Am J Cardiol 2001;87:560–4.

Key Words: computed tomography ■ risk factors ■ prevention ■ cardiovascular disease.